SCIENTIFIC ABSTRACT BOOK

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and

APTI

Disso Research Presentation India 2021 - Online

A Scientific competition for young pharmaceutical researchers across Academia and Industry

All-India Finals : 17th July 2021

Organised by: Society for Pharmaceutical Dissolution Science (SPDS)

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SPDS
Society for Pharmaceutical Dissolution Science

Society for Pharmaceutical Dissolution Science (SPDS) was registered on 16th July 2012 in Mumbai with the objective of promoting science and technological development in the field of Dissolution Science among pharmaceutical professionals, academia, students, regulatory bodies, etc.

SPDS is the only professional body in the world dedicated to Dissolution Science and its application.

:: Vision ::

To be one of the most prominent professional body focusing on Dissolution Science among the Pharmaceutical Industry and Academia.

:: Mission ::

To dissipate science & advancement taking place in the field of Dissolution related to clinical application and methods.

SPDS is incorporated as a Charitable Trust (not-for-profit) under Regn. No. Maharashtra State, Mumbai 1487/2012 GBBSD Dated 16th July 2012.

:: Purpose::

To Promote & Update the development of Science & Technology in Dissolution among the Indian Pharmaceutical Professionals/Academia.

Objectives:

- Conduct high quality & value-adding workshops/seminars/training which helps Pharma Industry Professionals /Academia to enhance their skills & knowledge and thereby perform their job more effectively and efficiently.
- Work closely with Universities/colleges/other Professionals Bodies and Regulatory Bodies and thereby equip the Ph.D./postgraduates/Pharmacy students through training and workshops to understand the modern & advanced dissolution systems/equipment and software.
- Create a value-adding website through which members and industry professionals can place their issues related to dissolution/method developments etc and an expert panel will offer solutions to the issues.
- Create an e-magazine with invited articles from the members, industry & across the globe and circulate to all members.
- Identify & Work closely with the young upcoming scientists/Chemists/Pharmacists from our Industry and academia and train them with high quality presentation skills and help them to publish papers and make effective presentations in the national and international forum

In collaboration with

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and

Disso Research Presentations India 20201 - Online

A Scientific Research Presentation Competition for Young Pharmaceutical Researchers across Academia and Industry.

Website: http://drpi.spds.in

DRPI
(Disso Research Presentations India)

Since the inception of **SPDS** in 2012, **DISSO India** - a truly international scientific conference spreading the science and advancement of Dissolution Sciences has become a way of life and an annual event for **SPDS**. The spread of COVID-19 pandemic in 2020 lead to severe effects worldwide including travel restrictions and conduct of in person conferences. **SPDS** found an opportunity in this major adversity, and in 2020, **DISSO India** was held online with plenary lectures from worldwide experts. The overwhelming success of **DISSO India Online 2020** was followed by **DISSO America 2020 Online**, an event by **SPDS American chapter** and co-sponsored by the American Association of Pharmaceutical Scientists (AAPS).

As the research presentations could not be included in the main event, a special event for students, 'Dissolution Research Presentations India 2020 – Online (**DRPI 2020 - Online**)' was held as a premier and PAN India competition for young researchers across academia as well as industry. Another key highlight of this event was the collaboration with Association of Pharmaceutical Teachers of India (**APTI**), as co-hosts for the competition.

The focus of **DRPI 2020 - Online** was to showcase at one forum, novel dissolution related research carried out by faculty and students, and by industry researchers across India. It was a huge opportunity and encouragement in terms of recognition for the achievers. The competition last year was held among various regions of India (North, South, East-Central and West), with each Zone pushing forward best talent and innovation, coupled with an unbiased and totally anonymized evaluation process.

Further, in 2021, the second DRPI event in online mode was conducted, **DRPI 2021-Online**. This event generated a great deal of interest and saw a much larger participation in terms of number of institutions (110 from across India) and the number of abstracts (>200) received. Some improvements/ highlights added in the 2021 event- one more zone, viz. Central zone was added; partnership with one more global association of high acclaim in the Pharma World, **AAPS** (Association of American Pharmaceutical Scientists) and more number of awards - separate for M.Pharm, Ph.D. and Industry participants; the awards were sponsored by **SOTAX, ACG, BASF.**

Vinod P. Shah
Ex-USFDA, Pharmaceutical Consultant, USA
SPDS - International Chairman and SPDS - US Founder President

Biosketch

Dr Shah is a Pharmaceutical Consultant; Steering Committee member of Non-Biological Complex Drugs (NBCD) hosted at Lygature in The Netherlands (2011-Present); International Chairman of Society of Pharmaceutical Dissolution Science (SPDS) (2012 – Present); President of SPDS-US chapter (2019 - present) and expert consultant with NDA Partners (2016 – Present). He received his Pharmacy degree with Gold Medal distinction from Madras University, India in 1959 and Ph. D. in Pharmaceutical Chemistry from the University of California, San Francisco in 1964.

Dr Shah worked at US FDA (Food and Drug Administration) from 1975-2005. At FDA, he developed several Regulatory Guidances for Industry in the area of dissolution, SUPAC, bioanalytical method validation, topicals, bioequivalence and biopharmaceutics.

Dr Shah was Scientific Secretary (2003 – 2011) of International Pharmaceutical Federation (FIP); Chair of Regulatory Sciences Special Interest Group of FIP (2011-2016) and Biopharmaceutics Consultant at USP (2005-2014). Dr Shah is author/co-author of over 330 scientific papers and is a co-editor of four books.

Dr Shah was the President of American Association of Pharmaceutical Scientists (AAPS) in 2003. He is a Fellow of AAPS and FIP. Dr Shah is a recipient of many FDA, National and International Awards.

Vinod P. Shah, Ph.D.

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VPS Consulting, LLC

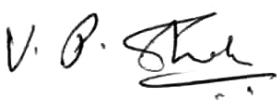
July 3, 2021

It is my great pleasure to welcome Dissolution Research Scholars from all over India to DRPI 2021 event. This is a flagship competition event for young pharmaceutical research students and scholars in the area of dissolution science.

The genesis of the event dates back to the Disso India 2020, where Dr. Saranjit Singh of NIPER, Mohali, India suggested Dr. L. Ramaswamy, General Secretary, SPDS to have poster presentation session which will encourage student/guide involvement, participation and presentation. Dr. Ramaswamy with this inspiration, motivated his able and dedicated team of faculty to organize a student's competitive research presentation program termed *Dissolution Research Presentation India* (DRPI). The faculty team under the Chairmanship of Dr. Saranjit Singh and guidance of Dr. Ramaswamy together with Dr. Mala Menon, Dr. Krishnapriya, Dr. Hema Nair and Dr. Varsha Pradhan, and with the excellent IT help from Mr. Tarun Soni organized and implemented DRPI 2020 event, first of its kind in India and probably in the world. The DRPI 2020 was organized by SPDS jointly with Association of Pharmaceutical Teachers of India (APTI). The abstracts from the research scholars were evaluated for their abstract writing skills and delivery style by team of experts. It is a fine way of training students for their future role and an excellent way to promote and recognize young researchers in the area of dissolution science.

This year, DRPI 2021 event has been well organized with the greater number of enthusiastic faculty from all over India. It is a pleasure to see that the DRPI 2021 is cosponsored with American Association of Pharmaceutical Scientists (AAPS) and APTI. The dream of Dr. Ramaswamy of SPDS and DRPI scientific committee is to expand the event globally in near future, and to transform "I" of DRPI to read from India → International. I wish this to be a great success.

I am happy to be part of this worthy event, and I welcome and congratulate all the research participants and winners.



Vinod P. Shah, Ph.D., FAAPS, FFIP,

SPDS-International Chairman and SPDS-US Founder President

Andrew M. Vick, Ph.D.

President, AAPS, USA

Biosketch

Dr. Andrew Vick has 23 years of experience working within the pharmaceutical industry in the fields of toxicology, nonclinical and clinical pharmacology, and drug disposition. Currently, Dr. Vick is responsible for financial, operational, and scientific oversight of all Midwest sites within Charles River's North American Safety Assessment business. In this role, Dr. Vick oversees a biomedical staff of >3,000 who are involved in diverse aspects of nonclinical and clinical development. He also serves as the Executive Sponsor to several global pharmaceutical companies, where he provides strategic advice, customized program and study designs, regulatory advice, and risk mitigation tactics.

Previous roles have included: VP of Analytical Services for WIL Research, EVP of Pharmacokinetics, Dynamics, and Metabolism at Seventh Wave Laboratories, Scientific Director of the BioPharma Services Division of Millipore, Principal Scientist within the Drug Disposition and Toxicology department of Eli Lilly and Company, and preclinical scientist at Biogen. In these roles, Dr. Vick contributed to the design, conduct, and interpretation of preclinical and clinical testing strategies for both small organic and biotherapeutic molecules across a variety of therapeutic indications and stages of development.

Dr. Vick earned his B.S. in Zoology and Ph.D. in Pharmaceutical Chemistry from The Ohio State University. He continues his support of the University as an Adjunct Professor in the College of Pharmacy. Dr. Vick also serves in the role of President for the American Association of Pharmaceutical Scientists.

aaps® American Association of Pharmaceutical Scientists

Advancing Pharmaceutical Sciences, Careers, and Community

Dear DRPI 2021 participants –

The American Association of Pharmaceutical Scientists (AAPS) is honored to collaborate with SPDS on this important competition, which showcases the strength of Indian science and innovation in a field that is of such great importance to the advancement of solid oral dosage form development. AAPS is proud to collaborate with SPDS, as we understand the critical contributions that the society is making to the sharing, growth, and deepening of knowledge and expertise in dissolution science.

The DRPI competition demonstrates the strength of India's engagement in this field and its commitment to a future of excellence in pharmaceutical science. You, the scientists who are competing in this event, are the future. We can only succeed in advancing public health by sharing our scientific knowledge and collaborating to the best of our abilities, as you are demonstrating.

Patient self-administered solid oral dosage forms rarely draw the headlines they deserve for their role in the global fight against diseases. India's scientists are leading the world in this arena, earning India the title "Pharmacy to the World." When AAPS' leadership committed to bringing scientists from across the drug development spectrum together in its new strategic plan, India's vibrant, active scientific community was immediately discussed. We could not be more impressed by your accomplishments.

It has been our honor to accept the SPDS invitation to participate in Disso India 2021, and our pleasure to experience the quality of the conference and see the expertise, passion, and commitment of this community of scientists.

We look forward to collaborating with you in the future and further strengthening the bonds of scientific knowledge exchange, collaboration, and fellowship that exist between SPDS and AAPS. From our leadership we send you the most heartfelt congratulations on your contributions to this great competition. We wish you all the best for your future scientific endeavors!
On behalf of AAPS

Andrew M. Vick, Ph.D.
2021 AAPS President

Tina S. Morris, Ph.D.
AAPS Executive Director

Vijay Kshirsagar
Director and CEO, TRAC Consulting, India
SPDS Founder President

Biosketch

Vijay is an accomplished Quality, Regulatory & Analytical professional with more than 40 years of rich experience of working for reputed pharma companies. Last, he worked for Unichem as Executive Vice President responsible for CQA, Regulatory & Analytical Research. Since 2013 he works as consultant for number of Pharma companies in India & outside.

Prior to Unichem he worked for Ranbaxy, Sun , Lupin, IPCA, German Remedies in various senior positions like Director-Quality , GM-Quality etc . He has successfully represented his company in US and UK courts regarding IP related matters (Para IV). Vijay has led from front for successful completion of several regulatory inspections by US FDA, MHRA, EDQM, ANVISA, WHO, TGA etc. both for Drug Products & API's. He is the Founder President of SPDS. .

He has been a frequent trainer in India & abroad having spoken on wide range of cGMP related topics.He is also working on the board of Directors of ISPE-India. IDMA has conferred upon him an 'Outstanding Analyst Award 2011' for his contribution towards pharmaceutical analysis. In 2015, he has been awarded by USP, India office, for his contribution to USP's Stakeholders Forum. Vijay is a Master of Science in Organoanalytical Chemistry by Research from Mumbai University.

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Dear Friends,

I am immensely pleased to write this message on the eve of this very prestigious online event, DRPI (Disso Research Presentations India 2021), which is going to encourage pharmaceutical research especially the one related to dissolution. We at SPDS feel proud about our association with APTI (Association of Pharmaceutical teachers of India) & AAPS (American Association of Pharmaceutical Scientists) for successful organization of this event. This is the 2nd event in succession, and I can see that the magnitude of event has almost doubled in just 1 year.

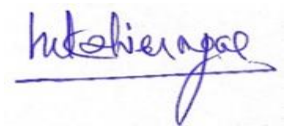
Thank you very much Dr Saranjit Singh, who conceptualized this idea and was well supported by most dynamic people like Dr. Ramaswamy, Dr. Mala Menon, Dr. Arvind Basal, Dr. Padma Devarajan ,Dr. Bhupindersingh Bhoop, Dr. Krishnapriya, Dr Hema Nair, all our Zonal Chairs, Committees & Sub-committees . The total efforts and commitment shown by our Pharmaceutical teachers across India is phenomenal.

Right from the beginning of SPDS, we have been fortunate to have tremendous support from renowned Professors from various reputed colleges of India . Little did we understand that it would us so much to conduct an event like this.

It is our wish and dream at SPDS that nearly 500 colleges should participate in this event during the coming years and Industry also should join in this platform to encourage research in the minds of young researchers.

Wish this event an enormous success that it well deserves. Like what Dr. Ramaswamy (General Secretary-SPDS) said once, let such efforts lead to further innovation finally leading to emergence of Chemistry-Nobel Laureate from India.

Stay Safe, Stay Healthy!



Vijay Kshirsagar
President – SPDS

Padma Devarajan

Dean-Research & Innovation and Professor in Pharmacy, Institute of Chemical Technology, India
SPDS President

Biosketch

Dr (Ms) Padma V. Devarajan is Professor in Pharmacy and former Head and Coordinator M.Tech Pharmaceutical Biotechnology, Department of Pharmaceutical Sciences and Technology at the Institute of Chemical Technology, Mumbai, India. She is a Member of the Board of Governors, President of the Innovation Council and Incharge of the World bank Technical Education Quality Improvement Programme(TEQIP) at the Institute of Chemical Technology, the only ELITE University and Centre of Excellence in the state of Maharashtra in India, among the top institutes in the country and also globally acclaimed. Her research interests include colloidal carriers for targeted delivery in cancer and infectious diseases, Veterinary Drug delivery, Bioenhancement strategies, and Mucosal DDS as alternative to parenteral administration and QbD in drug development. She has over 100 publications and presentations in cited journals and national/international conferences, and five book chapters in the area of drug delivery. Her book on "Targetted Drug Delivery- Concepts and Strategies " published by Springer won her the Prof. N. R.Kamath Book Award at ICT. Her book on Intracellular Targetted Delivery by Receptor Mediated Endocytosis as Editor and Author is recently published by Springer.

She has filed many patents international/ national, has seven patents granted and five patents licensed. Her research is funded through a number of Grants from the Government and the industry including companies from Japan, Germany and USA. She is also a consultant to the Pharma Industry.

She was Board Member, Member on the Board of Scientific Advisors and Chair of the Young Scientist Mentor Protégé Committee of the Controlled Release Society Inc.,USA, Chair of the Outstanding Paper Award Committee of the journal Drug Development and Translational Research, of the of the Controlled Release Society Inc., USA. She is Patron Member of the Controlled Release Society Indian Chapter and Member on the Editorial board of the Asian journal of Pharmaceutical sciences an Elsevier publication and European Journal of Drug Metabolism and Pharmacokinetics a Springer Publication.

Prof. Devarajan is a gold medallist of Mumbai university at B.Pharm, and former President of the Alumni Association of UDCT/ICT. She is a nominated Fellow of the Maharashtra Academy of Sciences, a recipient of the American Association of Indian Pharmaceutical Scientists Distinguished Educator and Researcher Award 2011, the VASVIK award for Industrial Research to Women in 2011 and the Association of Pharmaceutical Teachers of India (APTI) Prof. C J Shishoo Award for Research in Pharmaceutical Sciences. Her publication in the International Journal of Pharmaceutics on Gastroretentive drug Delivery, won the prestigious Eudragit Award 2015. She won the Bengaluru Nano Innovation Award for a Nanosystem developed for Veterinary Infection, the IPA-ACG Scitech award for innovation in Solid Dosage form and the OPPI Scientist Award 2018.

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Elite Status and Centre of Excellence–Govt. of Maharashtra
National Rank 1 in Atal Innovation Ranking (ARIIA), by MHRD, Category : Govt Aided Universities (2020)

Prof. Dr. Padma V. Devarajan
FMAS, FICS
Dean Research & Innovation,
Institute TEQIP Coordinator,
Past President ICT Innovation Council,
Member Board of Governors,
Coordinator - M.Tech Pharmaceutical Biotechnology,
Professor in Pharmacy and former Head,
Department of Pharmaceutical Sciences and Technology

MESSAGE

Dear Delegates,

It feels so wonderful to watch the enthusiasm, the motivation, and the spirited activity around DRPI 2021. Initiated during the pandemic in 2020, this event which focused entirely on creating a platform for students and young researchers is among the visionary decisions of SPDS. DRPI is a focused conference wherein presentations revolve around the theme of dissolution, in keeping with the objectives of SPDS of disseminating the science and technology of dissolution. Importantly it has created huge difference in the mindset of formulators particularly in the academia who have learnt to appreciate the immense possibilities of this aspect of formulation development, which earlier was probably one among many tests.

The response received confirms that DRPI is among awaited the pharma events and is here to stay. The COVID pandemic had created a lull in academia and research activities. DRPI 2020 brought in hope and light to trigger young minds back into action. The huge success of DRPI 2020 and the humming activity across the nation across academic institutions stands testimony to the importance of DRPI 2021. This time participation is not only from academia, but industry has also put its best foot forward to participate.

DRPI is a great platform for students and faculty alike, for learning, expanding one's knowledge base, understand research perspectives, catch up with latest trends in dissolution related research and strengthen one's research capability. Mentoring students on honing their presentation skills, is an important feature that differentiates DRPI from other student events.

The high-quality presentations with a focus on Dissolution and related aspects, is testimony that DRPI serves as a forum for spreading knowledge in a niche and focus area, that SPDS wishes to promote. Heartfelt thanks to all my colleagues from across various academic institutes in India, industry participants and of course to all our students from across the nation for their active participation with great fervour.

DRPI is a winning platform not only for the winners but all participants, as each one would go back with some new learning, which is in itself an award or reward!!

Best wishes to all. Stay safe, stay happy!!

Prof. Padma V. Devarajan
President - SPDS

Arvind Kumar Bansal

Professor & Head, Department of Pharmaceutics, NIPER, SAS Nagar, India
SPDS All India Scientific Chair

Biosketch

Dr Arvind Kumar Bansal is currently Professor and Head, department of Pharmaceutics at National Institute of Pharmaceutical Education and Research (NIPER) - SAS Nagar, Punjab, India. He earned his M Pharm (Pharmaceutics) (1988) and Ph.D. (1993) from University of Delhi, India. Prof Bansal worked as Senior Scientist and Group Leader in JK Pharmaceuticals and Ranbaxy Research Laboratories, for 8 years. Therein he conceptualised, evolved formulation strategies, developed and transferred the technology to production shop floor, for NCEs and generic drug products. Prof Bansal joined NIPER in 2000 and developed expertise in areas of pre-formulation and formulation development encompassing characterization and stabilization of the amorphous form, polymorphism, pseudo-polymorphism, particle engineering, screening salt forms, improvement of oral bioavailability and lyophilization. His research group works with the mission statement - 'developing science based industrially viable pharmaceutical technologies' and works closely with pharmaceutical industry to create opportunities for commercial exploitation of the products. Dr Bansal was conferred prestigious Fellow of American Association of Pharmaceutical Sciences in 2016. He is the only Indian, working in India, to be awarded this Fellow status. He has won prestigious awards like AAiPS Distinguished Educator and Researcher Award, Innocentive Award, OPPI Award and IPA-ACG Scitech Innovation Award 2018 for Best Innovative Development of Solid Dosage Form. Prof Bansal's research group has completed more than 550 industry-sponsored projects, granted 11 patents, filed 27 patents, and published 170 research articles and 27 review articles. He has total citations of 8011, with h-index of 47, in Google Scholar. He is an editorial board member of 'Journal of Excipients and Food Chemicals', 'Drug Development Research' and 'Pharmaceutics'. He is also an Advisor to the editorial board of 'Journal of Pharmaceutical Science' and 'Molecular Pharmaceutics'. He is the Scientific Chair of Society for Pharmaceutical Dissolution Science (SPDS), since 2018. Recently his lab has out-licensed a platform technology on "Nano crystalline solid dispersions – NanoCrySP".

MESSAGE

S.A.S. NAGAR

Prof. Arvind K. Bansal
Professor and Head
DEPTT. OF PHARMACEUTICS

राष्ट्रीय औषधीय शिक्षा एवं अनुसंधान संस्थान
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July 5. 2021

Society for Pharmaceutical Science (SPDS) is the only scientific society globally, that focuses on the science of dissolution. Latter is fast expanding into allied areas like biorelevant dissolution medium, dynamic dissolution, PBPK, automation and hydrodynamics of dissolution. Disso India, the flagship event of SPDS has become a globally recognized event and is now co-sponsored by American Association of Pharmaceutical Scientists (AAPS). DRPI (Disso Research Presentations India) was conceived in 2020 and has fast become a sought-after event in academia and industry. Now AAPS has also come forward to collaborate with the event. It is important to spread awareness about science of dissolution and its applications to the young pharmacists. This would ensure robust growth in this critical area of pharmaceutical development and regulatory affairs.

Dr Lakshmanan Ramaswamy's vision, Dr Vinod Shah's mentorship and able Chairman ship of Professor Saranjit Singh's, is propelling this event to the next level of excellence. They are ably supported by a dedicated team of academicians from various pharmacy colleges of India. The event not only strengthens the scientific aspects but also provides opportunity to students to learn nuances of soft skills that are critical for professional success.

I feel very good to be part of SPDS events like Disso India, DRPI which are purely science and research based events. As a scientific Chair of SPDS, I wish to thank all the Committee members and the Zonal Chairs, co-chairs for getting deeply involved in all the process of evaluation stages of the abstracts received. My thanks to all the judges who accepted the invite and participated in the All-India semi-finals and finals of the evaluation. My sincere congratulations for all those participated in DRPI and especially those who have won in semi-finals and finals.

I wish DRPI 2021 a grand success and a memorable learning experience for students and young industry professionals.

Arvind K Bansal, PhD, FAAPS
Scientific Chair - SPDS

L. Ramaswamy
Managing Director, SOTAX India Pvt Ltd, Mumbai
SPDS General Secretary

Biosketch

Dr. L. Ramaswamy, a postgraduate in management and doctorate in pharmaceutical Business Administration, a Professional more than 4 decades of successful experience in various capacities in Indian Pharmaceutical Industry. He is currently the Managing Director – SOTAX India Pvt Ltd, a company from Switzerland pioneer Dissolution Science. Prior to SOTAX India he worked for Sarabhai Chemicals as a full time Director and CEO, Managing Director of Stiefel India Pvt Ltd (Which is merged with GSK later), Unichem Laboratories. He represented the Biotechnology Delegation organized by Govt of India to Canada in 2007. Also, he was nominated as the member of the advisory committee of DDRS, Budapest, Hungary.

Dr L Ramaswamy has been a visiting faculty in reputed management Institutes in Mumbai and given many guest lectures including at IIM (Bang), Madurai Kamaraj University, NMIMS, etc. He has published many articles on Management and Human Resources Development.

He was instrumental in conceiving the idea and need for a Society like SPDS and initiated the movement by bringing the Pharma Industry Scientists and Pharmaceutics Faculties from various pharmacy colleges under one roof and registered this initiate as Society for Pharmaceutical Dissolution Science (SPDS) at Mumbai.

Society for Pharmaceutical Dissolution Science

7, Prabhat Nagar, Jogeshwari West, Jogeshwari West, Mumbai, Maharashtra 400102
TEL : 91 22 26851903

Regn. No. Maharashtra State, Mumbai 1487/2012 GBBSD Dated 16/07/2012

Dear Colleagues,

It is indeed a pleasure and privilege for me to be the General Secretary of SPDS and an integral part of DRPI 2021. This is the second time we are conducting DRPI online Collaborating with APTI (Association of Pharmaceutical Teachers of India) and AAPS (American Association of Pharmaceutical Scientists) one of the largest and most prestigious Professional Pharma Body globally.

The key role performed by DRPI, All India Scientific Chair Dr. Saranjit Singh, (Prof & HoD Pharm. Analysis, NIPER, Mohali), All India Vice Chair, Dr. (Prof) Mala Menon (Adjunct Prof of Pharmaceutics, BCP, Mumbai), Central Core committee members, All the Zonal Chairs and Vice Chairs of the five Zones, with other SC team members have contributed towards the success of the event. We received excellent response from the Pharma Industry, academia, Partners, which shall make the event a memorable one.

The contribution by the Judging panel who evaluated all the online presentations very patiently and the role they played made the whole process of finding the young SPDS Researcher for the year 2021 a unique, unbiased and accurate.

I am sure that all the DRPI 2021 Online Research Presenters shall find their time spent at the petition enriching and enlightening. My sincere thanks to all the Teachers & Guides who have motivated a good number of young Research Students and their managers who have given their approval for their participation in this conference. Most importantly, an event of this scale would not have been possible without the support of all our partners. My sincere thanks to all the companies who have joined as a sponsor, for helping manifest this vision of ours. I must mention the support from our all India Chair , Dr Saranjit Singh, Vice Chair , Prof Mala Menon, SPDS President, Vijay Kshirsagar, The Conference co Ordinator Ms. Bhakti Poonia , our Multi Media expert, Tarun Soni, Ms Neetu Singh & Rajesh & Team from Design Accent who are our online event Organisers, Dr Prakash Bhosle & Mr. Yash Choksi for giving good press releases timely with social media marketing and all other trustees, Members, together made my functioning very easy and enjoyable at DRPI.

I wish you all a great Disso Research Presentations DRPI 2021.

Dr. L. Ramaswamy
General Secretary

Saranjit Singh

Prof. & HOD Dept of Pharm Analysis, and Acting Director, NIPER SAS Nagar
DRPI All India Scientific Chair

Biosketch

Dr Saranjit Singh is Ex-Dean and Professor and Head of the Department of Pharmaceutical Analysis at the National Institute of Pharmaceutical Education and Research (NIPER) at S.A.S. Nagar, Panjab, India. He is a renowned academician, having ~42 years of teaching and research experience. He is known for excellence in research, and is well recognized International expert in the areas of drug stability testing, degradation chemistry, impurity and metabolite profiling. He has published ~220 research papers, general articles and book chapters. Till date, his team has executed ~100 industry sponsored projects involving most sophisticated instruments.

He is a member of Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations and also has been a temporary advisor to the World Health Organization in the Expert Committee on Specifications for Pharmaceutical Preparations. He has delivered more than 500 invited lectures, and has spoken at the forums of AAPS, USP, DIA, IPA, IDMA, etc. He has guided a large number of Master's and Ph.D. students. He is an editorial board member of several leading journals, and reviewer to almost all leading journals in the area of Pharmaceutical Analysis. He is recipient of Professor M.L. Khorana Memorial Lecture Award from Indian Pharmaceutical Association; and Outstanding Analyst and Eminent Analyst awards from Indian Drug Manufacturers Association.

MESSAGE

राष्ट्रीय औषधीय शिक्षा एवं अनुसन्धान संस्थान
NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH (NIPER)
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Prof. Saranjit Singh, Ph.D
Professor and Head, Department of Pharmaceutical Analysis

The coronavirus pandemic has deterred the holding of physical conferences and events in a big way. Disso India, the conference held annually by SPDS also faced the same difficulty. The last physical Disso India event was held at Chandigarh in 2019, where apart from panel lectures, poster award sessions were held for students. Owing to pandemic, the Disso India event in 2020 was conducted online from 13-16 May, but it focused only on invited lectures by experts. I was Chairman for a session, and finding that no event had been planned for students, I suggested holding one as an award competition. I was surprised, when then and there, Dr Ramaswamy accepted the idea, and he requested me to play the role of Scientific Committee Chairman, promising that the event will be organized soon. Quickly everything was streamlined and a successful event was held under the title 'Disso Research Presentations India (DRPI) Online 2020' in the first week of June in collaboration with APTI. This competition event acted as a big boost to faculty and their research students, and young scientists from Industry, who otherwise were restricted to their places, as the institutions/industry were closed country-wide or working with minimum strength.

In the first quarter of 2021, the pandemic was towards a rise, so both DISSO India 2021 and DRPI 2021 were again planned to be conducted in an online mode. This time the DRPI event was better organized, keeping in view the feedback from the hurriedly held DRPI 2020. This time, we had the honour of mentorship from AAPS in addition to the collaboration with APTI. The faculty, students and young scientists across the country showed big enthusiasm and 200 plus abstracts were received from all over the country, which was distributed into five zones. With the active support of members of SPDS Executive, Disso India Organizing Committee DRPI Central and Zonal Scientific Committees, and the very efficient and skilful IT team, DRPI 2021 online mega event was conducted in a much more structured manner, with event deadlines spanning from May to July 2021. It set a benchmark in holding online events, not only nationally, but also internationally.

I am happy that the abstracts received for DRPI 2021 have been compiled in this Abstract Book. Great efforts by the Scientific Committee members went into reading and suggesting corrections on each abstract to the authors, so as to help improve the quality of writing by the young researchers. It is highly satisfying to see that the very basic objectives of the DRPI competition, to raise the level of writing and presentation skills, and create scientific temperament of high order among young scientists, have been well achieved.

My personal gratitude to each and every individual who has been a part of this event, which was conducted in most fair manner, and is planned to be conducted at an International level in 2022.

सिंह

Prof. Saranjit Singh

Mala Menon
Adjunct Professor-Pharmaceutics at Bombay College of Pharmacy, Mumbai
DRPI All India Scientific Vice-chair

Biosketch

Dr Mala Menon, currently Adjunct Professor-Pharmaceutics at Bombay College of Pharmacy, Mumbai India has 37 years of experience in academia and two years of industrial experience. She has completed her education – B.Pharm, M.Pharm & Ph.D. (Tech) from Mumbai University.

Her key research areas include Drug Delivery Systems-Conventional & Novel type, Pulmonary & Nasal Delivery Systems, Novel Vaccine Delivery Approaches, Probiotic formulations, Novel Veterinary Drug Delivery systems, Ocular Drug Delivery Systems. She has guided over 35 M.Pharm and 10 Ph. D. students. She has received several research grants from government agencies like AICTE, UGC, BRNS, Mumbai University. Her research team has handled many projects from renowned industries including Abbott, Mother Dairy, Glenmark, M/S Infovet, Saif-Vet Med, Getz Pharma, Famy Care, Valois Pharma (France), Yash Pharma, Pfizer, Gattafosse, Lubrizol, ACG, USV, Lupin (USA).

She is an Expert member of Research & Recognition Committee for the Ad-hoc Board of Studies, in subject of Pharmacy, SNDT University, since May 2016.

She has contributed 43 research papers in peer reviewed National and International journals, 4 book chapters and more than 85 presentations at various conferences and workshops. Her research group has received 18 Best Poster/ Oral presentation awards. She has 1 patent granted; filed patent applications, with two of them on Veterinary Drug Delivery systems, in the process of tech transfer.

She has delivered 25 Talks at National Conferences, Seminars, Workshops, and at Pharmacy Colleges on Inhalation & Nasal Drug delivery, Probiotics, Targeted Drug delivery and Microcapsules, Nanoparticulate systems, Veterinary drug delivery systems.

She is a reviewer for several National & International Journals and part of Editorial team of Indian J. Pharm Sci (published by IPA) and e-Disso newsletter (published by SPDS).

She has received several awards including the Dr. P. D. Patil Best Pharmaceutical Scientist Award for 2015-16, awarded by the Association of Pharmacy Teachers of India (APTI)-Maharashtra State Branch; "Best Professor of Pharmaceutics" from National Education Awards (8th edition) by ABP News Channel in July 2017; "Promising Innovation in Solid Dosage Form" award sponsored by IPA-ACG Scitech in Dec. 2018 at IPC 2018, Delhi; "Best Professor in Pharmaceutics Award" under 26 th Business School Affaire and Dewang Mehta National Education Award in Nov. 2018; "Distinguished Professor Award" at the Stakeholder Workshop (SPAICS)- sponsored by National Science & Technology Management Information System (NSTMIS), a Divn of DST, held at Smriti College of Pharmacy at Indore in Sept, 2019.

She is a member of many professional societies: IPA (Indian Pharmaceutical Association-Life member); Controlled Release Society (Indian Local Chapter);Association of Pharmacy Teachers of India (Life Member); SPDS (Society for Pharmaceutical Dissolution Sciences)- Executive Committee member.

The Indian Pharmaceutical Association - Maharashtra State Branch`s

BOMBAY COLLEGE OF PHARMACY

(Autonomous-Maharashtra State Government Aided Institute)
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Vision : To be a leader in Pharmacy Education, Pharmacy Training and Research in Pharmaceutical Sciences
Mission: To educate and train students in the knowledge and practice of pharmaceutical sciences
To contribute to improvement of health of the society through education programs
To contribute to improvement of health of the society through research programs

I have been associated with SPDS (Society for Pharmaceutical Dissolution Science) right from its start as One of the Trustees; SPDS is a unique Scientific Society, the only of its kind in the world. It has been a great privilege to be a part of SPDS learning and interacting with great scientific minds like Dr Vinod Shah, Dr Banakar, as well as researchers from industry and academia, and of course with Dr Ramaswamy, the lifeline and mover of this unique scientific society!

Right from 2013, when we had the first DISSO INDIA conference, I have been in charge of the Poster Session and competition, with the responsibility of inviting abstracts from researchers in academia and industry from all over India, which continued till 2019. However, in 2020, with Covid 19 outbreak, it became necessary to switch over to online competition, and the Research Presentation Competition evolved into a separate event- Dissolution Research Presentation India (DRPI), for which APTI (Association of Pharmacy Teachers of India) partnered with SPDS. I thank SPDS and DRPI committee members, who entrusted on me the responsibility as the Vice Chair of the All-India Scientific Committee, to take this event forward across the different zones of India.

Being part of the DRPI scientific committee, was an exciting experience working with the many professors, students and industry professionals across India and abroad. I acknowledge with thanks the guidance received from our All-India Chair, Dr. Saranjit Singh, and support from all the Central and Zonal committee members, judges; this has helped the DRPI Online event take shape and culminate into a successful platform for students, especially. This year, in addition to APTI, the AAPS (American Association of Pharmaceutical Scientists), came forward to partner with SPDS for the DRPI 2021 Online event; this speaks volumes about the quality of this unique scientific event. My sincere thanks to both the organizations for joining hands with SPDS.

In this short span of two years, DRPI 2021 Online hasgenerated a lot of enthusiasm in both research students and faculty of Pharmacy colleges all over India. Despite the pandemic and problems, more than 200 abstracts have been received. This event is an excellent example of Industry-Academia collaboration.

I look forward to DRPI expanding and reaching out to all regions of India and in the years to come, and eventually extend outside India to become an international event!

Wishing the DRPI 2021 event a great success!

All the Best Wishes to the Young Researcher Participants!

Dr Mala Menon

- Approved by AICTE, PCI, UGC, DTE, Permanent affiliation to University of Mumbai and Recognized by DSIR as SIRO (Govt. of India)
- Accreditated by National Board of Accreditation for UG Program for the Academic Years 2017-18 to 2021-22 i.e. up to 30.06.2022
- National Institutional Ranking Framework India Ranking 6th in 2016, 15th in 2017, 8th in 2018, 24th in 2019
- Best Industry Linked Pharmacy Institution (Established Degree) 1st in 2013 & 2014, Mentor in 2015 & 2nd in 2019
- Member of
- We are available on:

5K0819

Krishnapriya Mohanraj
Professor of Pharmaceutical Analysis, Bombay College of Pharmacy, Mumbai
DRPI Scientific Core Committee member

Biosketch

Prof Krishnapriya Mohanraj is Professor of Pharmaceutical Analysis, Chairperson-Industrial Collaborations and Resource Mobilization, Coordinator- AICTE Quality Improvement Program and President, Institute Innovation Council at Bombay College of Pharmacy- BCP, a premier Pharmacy institute. She is former Principal in charge, BCP. She is a passionate educator, motivating and training students, analysts, chemists and faculty in the nuances of pharmaceutical analysis and medicinal chemistry; and a researcher developing novel and cost-effective techniques useful for the industry. She has more than 30 years of academic and research experience.

Her research expertise includes Chiral Chromatography, enzymatic resolution, impurity profiling, structural elucidation using spectral techniques, synthesis and characterization of impurities/metabolites, bioanalytical method development, pharmacokinetics and therapeutic drug monitoring, herbal analysis and bioactivity guided fractionation, computer aided drug design, anti-infective studies, analytical method development and validation, and hyphenated techniques (LC-MS/MS, HPTLC-MS and ICP-MS). She has received funding of more than INR 7 crores from various government agencies and Industry, both from India and abroad. She co-established National Facility of Research and Training in Integrated Analytical Strategies for Discovery, Development and Testing of Drugs, Pharmaceuticals and Nutraceuticals at Bombay College of Pharmacy under the Drugs and Pharmaceuticals Research Promotion Scheme of the Department of Science and Technology and the facility is now fully functional

She has coauthored a book – Synthesis of Drugs- A Synthon Approach. She has a Technology Transfer, a patent, and several award -winning publications and presentations to her credit. She is a consultant for Pharma Companies, both in India and in the USA.

Prof Krishnapriya is Member of Research Recognition Committee of Pharmacy, IQAC committee, Ad hoc Faculty of Pharmacy, Ad hoc Board of Post Graduate Education in Pharmacy, Board of Studies for Bioanalytical Sciences and Board of Studies of Pharma Analytical Sciences, Syllabus framing committees at various State Universities, deemed to be Universities and autonomous colleges. She has been resource person at many seminars, faculty development programs and technical conferences for the pharmaceutical industry, including the 4th IPA-EDQM Technical conference, Mumbai organized by the Indian Pharmaceutical Association and European Directorate for Quality Medicines and Healthcare and the Technical Conference Chiral India 2012, 2015 and 2019 organized by Chemical Weekly. She has conducted many "Train the Trainer" programs and workshops and several technical development programs, tailormade for the industry

She is recipient of the UKIERI Indo UK Staff Exchange Program 2011-12 Award by the British Council and was awarded Fabulous Global Healthcare Leader Award at World Health and Wellness Congress and Awards, 2020. She completed her M Pharm and PhD (Tech) from the reputed Institute of Chemical Technology, Mumbai, India.

MESSAGE

Bombay College of Pharmacy Estd 1957 Autonomous

The Indian Pharmaceutical Association - Maharashtra State Branch`s
BOMBAY COLLEGE OF PHARMACY
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Vision : To be a leader in Pharmacy Education, Pharmacy Training and Research in Pharmaceutical Sciences
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To contribute to improvement of health of the society through research programs

Greetings!

Wishing Online Disso Research Presentations India 2021- DRPI 2021 all the best.

It is really an honor and privilege to be associated as a member of DRPI Scientific core committee for selecting the awardees for the Young Researcher Award across three categories, viz. Industry Research, PhD Research and M Pharm Research.

Society of Pharmaceutical Dissolution Science (SPDS) has been regularly conducting the annual Disso-India conference, with emphasis on Dissolution related themes, where poster presentations by students were always part of the program. Last year, when Disso India was conducted online for the first time, it was Dr Saranjit Singh who requested that there be some forum for the students to showcase their research work. Dr Ramaswamy then envisaged online DRPI 2020 to highlight research in dissolution and allied areas and SPDS took up the baton, to conduct the same. After the successful DRPI 2020, the competition has bloomed into DRPI 2021- surpassing all expectations.

The collaboration with APTI and AAPS has widened the reach and prestige of the competition. Being an online program, the participation of a vast number of talented students from across India, without the hassles of travel, is possible- truly a boon in this pandemic.

The hallmark of this competition is the high-end digital support which facilitates anonymous abstract submission and unbiased evaluation with names of candidates and organizations not disclosed till the very end. Many academicians and industry personnel from India and abroad are putting in many man-hours to evaluate and select the best from the best.

I take this opportunity to thank the leaders at the helm – for inspiration, my fellow team members – for unstinting support, the participants, and their mentors- for the great insights in research, the sponsors-for their generosity and the audience- for their encouragement.

Each participant is a winner – even though only some are blessed to receive an award.

Saluting the spirit of DRPI-2021 to bring to the fore research on dissolution related sciences and providing an opportunity for industry-academia interactions.

Prof. Krishnapriya Mohanraj
Professor of Pharmaceutical Analysis

- Approved by AICTE, PCI, UGC, DTE, Permanent affiliation to University of Mumbai and Recognized by DSIR as SIRO (Govt. of India)
- Accreditated by National Board of Accreditation for UG Program for the Academic Years 2017-18 to 2021-22 i.e. up to 30.06.2022
- National Institutional Ranking Framework India Ranking 6th in 2016, 15th in 2017, 8th in 2018, 24th in 2019
- Best Industry Linked Pharmacy Institution (Established Degree) 1st in 2013 & 2014, Mentor in 2015 & 2nd in 2019
- Member of
- We are available on:

Farhan Ahmad
Professor and Dean, Jamia Hamdard, New Delhi
DRPI North Zone Chair

Biosketch

Dr. Farhan Jalees Ahmad, PhD, is currently a Professor, School of Pharmaceutical Education & Research, Jamia Hamdard, New Delhi, India is an internationally known researcher in the area of Pharmaceutical Sciences. The focus of his group has been in the area of Nanomedicine and many of his nano products have been approved by the DCGI and successfully transferred to the Defense Services for use in the armed forces. Nano DPI with a lung deposition of >60% was clinically proved in patients of COPD. He has published more than 550 publications, 12 Book chapters, 11 books and has a US patent, three PCTs and 24 Indian patents. With a total citation of 14400, H Index of 53 and i-10 index of 308, Professor Ahmad's work has been clearly well received by the scientific community. He has supervised -35 M. Pharma students and -43 PhD scholars. Besides this, he continues to offer consultancy to small pharmaceutical setups. He has been granted projects to a tune of rupees 5.5 crores from National agencies like DBT, CCRUM, AYUSH, UGC, DST and International agencies like FIP and OPCW etc. He has earned many accolades including Young Scientist Fast Track from DST, Scientist of the Year-2005 from NESA, UGC Research Award 2011, Bharat Jyoti Award 2011, Pharma Ratan 2017, ABAP Senior Scientist Award 2017 and also prizes in scientific poster session in National Pharmacy Symposium. He has served IPA, Delhi Branch in the capacity of Member Executive Committee, Honorary Secretary and as President for two terms.

MESSAGE

Society for Pharmaceutical Dissolution Science was formed on 16th July 2012 in Mumbai with a Vision to be one of the most prominent professional bodies focusing on Dissolution Science among the Pharmaceutical Industry, Academia and Regulators and till date SPDS is the only professional body dedicated to Dissolution Science and its Applications.

The Society has successfully achieved its vision and mission by organizing this International event of DRPI in the year 2020 and 2021.

As chairmen of the North Zone committee I observed a major change in the interest of the research scholars in dissolution science. Despite being a commonly employed test in the pharmaceutical and biopharmaceutical industry, the fundamentals of dissolution testing are very often not correctly understood. The focus of scholars is more towards formulation part then its evaluation but in last one year this event has created awareness and interest in this science of drug delivery evaluation.

In the depressing environment of Covid 19 this event has brought cheers to the whole pharmacy community, linked us to the experts of national and international repute.

Today there is need to develop clinically relevant in vitro dissolution Methods and Specifications

There is a need to develop discriminating In Vitro Release Testing methods for Special Dosage Forms. A large number interesting and smart dosage form have been introduced in the last 10 years. The quality of all of these dosage forms would be easily measured if a discriminating in vitro release tests were available. The quest for new in vitro release tests and in vitro in vivo correlation is a ongoing process where students should invest.

I am thankful to the entire team of North Zone committee for their untiring support and contribution to this event.

(Prof. Farhan Jalees Ahmad)

Professor, Department of Pharmaceutics,
School of Pharmaceutical Education & Research,
Dean, School of Interdisciplinary Sciences & Technology,
Jamia Hamdard, New Delhi-110062

Biswajit Mukherjee
Professor, Jadavpur University, Kolkata
DRPI East Zone Chair

Biosketch

Prof. (Dr.) Biswajit Mukherjee, M.Pharm., Ph.D., W.B.C.S., F.I.C., F.I.C.S., Professor in Pharmaceutics and former Head of the department, the Department of Pharmaceutical Technology, Jadavpur University, Kolkata is a former DAAD (German Academic Exchange Services) Fellow, Germany and Ex-Guest Scientist, German Cancer Research Center (DKFZ), Heidelberg, Germany. He is the former coordinator, AICTE-sponsored Quality Improvement Programme (QIP) Nodal cell (Pharmacy), Department of Pharmaceutical Technology Jadavpur University, Kolkata and Joint Coordinator, Centre for Advance Research in Pharmaceutical Technology, Jadavpur University. He is a former visiting fellow of the School of Pharmacy, University of London, London, UK and a former Indo-Hungarian Education Exchange Fellow, National Research Institute for Radiobiology & Radio hygiene, Budapest, Hungary. He is also a recipient of Finland government scholarship. He has worked as a guest Scientist in German Cancer Research Centre, Heidelberg after receiving the Overseas Research Associateship Award, Department of Bio-Technology (Govt. of India). He is also a former faculty of University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh. He works on Antisense Technology and chemoprevention in cancer model. He has been working on novel drug deliveries particularly transdermal patches and nano-size liposomal and niosomal formulations as well as nanoparticles and drug targeting. He is the recipient of UGC research award 2009. He has received some other awards too. He became the co-chairman, Scientific Services Committee, LOC, 56th Indian Pharmaceutical Congress in Kolkata, India in the first week of December 2004. He delivered an invited lecture in the Presidential symposium of 62nd Indian Pharmaceutical Congress at Manipal, Karnataka. He is also the recipients of APTI Dr. C. J. Shishoo award.

Dr. Biswajit Mukherjee

M.Pharm., Ph.D., F.I.C., F.I.C.S.
Professor in Pharmaceutics
Coordinator, QIP Nodal Cell (Pharmacy)
Joint Coordinator,
Centre for Advance Research in Pharmaceutical Sciences,
Jadavpur University, Kolkata
Former DAAD Fellow (Germany) and Ex-guest Scientist,
German Cancer Research Center (DKFZ)
Heidelberg, Germany
Indo-Hungarian Education Exchange Fellow,
Budapest, Hungary
Former Fellow Scientist, School of Pharmacy,
University of London, London, U.K.
Ex. Biotechnology Overseas Associate,
Department of Biotechnology
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Message July 05, 2021

Congratulations to SPDS for coming out with a good program like DRPI (Disso Research presentations India) !!
I am pleased to be the Eastern Zone Scientific Committee Chair with a team of expert teachers and Professors. The whole process of inviting the abstracts, categorizing, and doing the evaluation online is very professional and without any bias. I am optimistic that DRPI will emerge as a massive event in the coming years where still a large number of research projects shall be received from all over India over the years.

DRPI has a brilliant and outstanding effort to transmit the radiations of a vibrating program through the involvement of several pharma-students and budding researchers in our country. A major goal is to provide an unbiased platform for pharma-students and young researchers to become successful and leading scientific/ industrial professionals of dissolution sciences with unlimited scope in drug development and drug delivery. DRPI 2021 is one step ahead of DRPI 2020 regarding the increased number of participants and dedication of the organizers.

It is my wish and appeal to all teachers of Pharmacy in our country to encourage the students to participate we in this program every year and inject quality in the research projects. I have come to understand that this year, more than 100 Pharmacy colleges have participated in DRPI 2021. It is possible with the efforts of all next year we can aim to bring 200 colleges under this platform so that we can motivate both research students and their guides with good encouragement.

I also wish to thank all the Scientific Committee members of DRPI-2021, East Zone, including the Vice-Chairs and Coordinators. They exhibited exemplary teamwork and dedication in the evaluation process for shortlisting the abstracts up to the semi-final round.
I wish every success of the DRPI 2021.

Professor (Dr.) Biswajit Mukherjee
Department of Pharmaceutical Technology
Jadavpur University
Kolkata - 700032, India

Vandana Patravale
Professor of Pharmaceutics, ICT, Mumbai
DRPI West Zone Chair

Biosketch

Dr. Vandana B. Patravale is currently a Professor of Pharmaceutics at the Institute of Chemical Technology, Mumbai, India. She has around 30 years of teaching and research experience. She has over 200 refereed publications with over 9000 citations (H index 48, i10 118), 22 granted patents , 20 patents in pipeline and 2 trademark registries. She has published 2 books and 25 book chapters with international publishers. Dr. Patravale has been active in teaching, research and service throughout her career. She has recently been inducted as an independent director of a device manufacturing company and listed as top 2% of World scientist's in pharmacy. Her areas of research include development of nanocarriers with major emphasis on infectious diseases, cancer and neurodegenerative disorders; medical device development, nanodiagnostics and nanovaccines. She was awarded Abdul Kalam Technology Innovation National Fellowship 2021,Fellowship of Indian Chemical Society 2020, Kukreja Oration award 2020, APTI s Dr. Manjushree Pal Best Pharmaceutical Scientist Award 2019, Shri Amrut Mody distinguished researcher award 2018, OPPI women scientist award 2015, Bill Melinda Gates grant award 2015,Best Pharmaceutical Scientist award 2014, VASVIK award 2013, Veneto nanotech award 2013, APTI best teacher award 2012, Fellowship of Maharashtra Academy of Sciences, 2011 and K.H. Garda Distinguished researcher award 2009. She is Vice president-CRS Indian chapter, editorial board member DDTR, editor CRS IC and APTI women forum newsletters. She is actively collaborating with researchers as well as industries within country and abroad and has completed Indo-Swiss, Indo-Japan, Indo-UK projects. She is executing all major grants from Indian Government focusing on product development. She has transferred about 20 technologies to industry including drug eluting stents being marketed in more than 65 countries.

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National Rank 1 in Atal Innovation Ranking (ARIIA), by MHRD, Category : Govt Aided Universities (2020)
NAAC A++ CGPA 3.77

Message

It is with immense pleasure that I welcome the opportunity to Chair the Online Scientific Committee from the West Zone in the DRPI 2021 held Online. The Society for Pharmaceutical Dissolution Science (SPDS) has almost completed a decade in their glorious run with an objective of promoting the science of dissolution in all technological developments. Being the only scientific body focused on the dissolution technology, it is a great opportunity for audiences from both academic and scientific backgrounds to learn and share their research. As the Chair of West Zone and the Convener of Association of Pharmaceutical Teachers of India, Women's Forum (APTI), I am delighted to see the encouraging response received for this online conference co-hosted by SPDS and APTI.

Pharmaceutical research has shown incredible potential over the last decade and dissolution research has been an integral part in this process. Be it conventional or nanotechnology based pharmaceuticals, dissolution has always been at the core and impacted not only their ability to enter the market but have also influenced the global R&D functioning. It has been a vital decision making research step for pharmaceutical, biotechnology, as well as nutraceutical industries.

The world of science has always been an equal mix of infinite opportunities and a unique set of challenges. The science of dissolution is no different and has been posing researchers with numerous barriers especially while dealing with regulatory bodies. The continuous evolution in the field of dissolution is apparent from the numerous advanced systems that have been introduced to cater to the complex dosage forms. I am sure that many more innovative techniques are in pipeline for the future generation of researchers.

I am confident that this DRPI 2021 Online would enlighten the minds of our young researchers and help them become inquisitive in the pursuit of further research. I am sure they will benefit from the thought provoking discussions and QnA sessions. I look forward to seeing these young minds present their research amongst a great line-up of judges. I wish SPDS and APTI all the very best for DRPI 2021 Competition, I am sure it is going to be a great experience for all.

Prof. Vandana B. Patravale
Chair, West Zone
DRPI 2021 – Online

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Nayanabhiram Udupa
Research Director, Shri Dharmasthala Manjunatheshwara University (SDMU), Dharwad, Karnataka
DRPI South Zone Chair

Biosketch

Dr. N. Udupa obtained BPharm, MPharm and PhD from Banaras Hindu University, Varanasi. He worked in pharmaceutical industries (IDPL and Citadel) for 8 years. He has been working in academics for more than 3 decades. He is presently working as Research Director at Manipal University, Manipal. Dr N Udupa has more than 450 publications, 500 conference presentations, about 100 review articles, 15 books (as editor) and 15 patents to his credit. He has delivered 250 guest lectures. Dr N Udupa has received 57 grants of worth of about 7 Cr. He has guided 70 PhDs and more than 100 M Pharm dissertations.

Dr Udupa has received several awards and few of them are: "Pharmacy Teacher of the year award" by 54th IPC Trust, Pune in 2010, "IPA Fellowship Award 2009" by IPA in New Delhi 2009, "Pharmaceutical Scientist of the year 2008" award from IAPST in 2008, Association of Biotechnology and Pharmacy Conferred "Honorary Fellowship Award 2007" in Guntoor, "Principal of the Year 2001 award" by APTI in 2001, "Dr. P.C. Dandiya Endowment Trust Research Award, at Jaipur in Feb. 1997, "STARS Award 2011" at Bangalore in 2011, "Talented Scientist Award" in 3rd ICMPHP at University of Colombo, Sri Lanka in 2011, Prof. C. J. Shishoo Award at 17th APTI National Convention, Manipal, 12-14th in 2012, Acharya P. C. Ray Gold Medal Award IPA in 2012, ""Schroff Memorial National Award"" in 64th IPC at Chennai in 2012. He has several honorary positions such as Ph.D. registration committee member (Bangalore University, RGUHS and MAHE), Chairman, monitoring committee of TIFAC CORE in NDDS, Baroda, Advisory Board member of TIFAC CORE in Pharmacogenomics, Manipal. He has received several Fellowship such as Controlled Release Society, Japanese Drug Delivery Society, FIP, AICTE, Dr. T.M.A. Pai Foundation, etc.

Dr Udupa is an Editorial board member/ Editor in several journals including IJPS, Indian Drugs, Pharma Today, Pharma Link, Indian Journal of Hospital Pharmacy, International Journal of Community Pharmacy, etc. Born in Kinnigoli, Mangalore District Karnataka on 15th July 1953, Dr N Udupa has professional experience of 36 years. Dr N Udupa has served as President, Rotary Club Manipal Town 2017-18 and won Second place in Medium Clubs in District 3082. He executed about 100 community service projects under Rotary Club Manipal Town.

Dr Udupa's research interests are: Development and evaluation of various novel drug delivery systems, polyherbal drug formulations, cosmeceuticals, nutraceuticals, etc. Dr N.Udupa was Scientific Convener of Indian Pharmaceutical Congress hosted by IPCA from 2010 to 201"

SHRI DHARMASTHALA MANJUNATHESHWARA UNIVERSITY

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Congratulations to SPDS for successfully bringing out the second edition of the student research competition as 'DRPI 2021 Online' and providing a platform for rewarding original research in the area of dissolution and related sciences and encouraging them. This effort will surely serve to foster the scientific temperament in our young and upcoming researchers.

As the Scientific Chair of the South Zone Committee, I have been closely involved with the competition at every step. The total dedication and contribution of teachers from every corner of India in screening the abstracts and evaluation of the presentations is praise worthy. I would like to use this opportunity to thank each one of them and urge them to spread the word and ensure more participation from every nook and corner of this country at all our future events.

It is praise worthy that the Society for Pharmaceutical Dissolution Sciences has found able partners in APTI and now also AAPS which will enable DRPI to scale new heights.

Also, what is commendable is the absolute unbiased evaluation of each abstract received from the very preliminary round till the final one. The whole sequence of events is tuned to be totally digitalized right from submission till the final felicitation.

I wish SPDS and DRPI all the very best and hope the event grows to be the highly coveted and prestigious forum for research presentations as envisioned by all of us working in the team.

I greatly appreciate the theme of DRPI 2021 event under the leadership of Dr. Saranjit Singh and Dr. Ramaswamy.

Dr. N. Udupa

Dr. N. Udupa
RESEARCH DIRECTOR
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University, Dharwad-580 009.

Swarnalata Saraf
Professor & Director, University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur, CG
DRPI Central Zone Chair

Biosketch

Dr. Swarnlata Saraf graduated from Indian Institute of Technology, BHU, Varanasi, and received her Ph.D. from Dr. H. S. Gour University Sagar, India. She guided 35 Master's Degrees and 18 Ph.D. students. She wrote 6 books & numerous chapters in edited books, filed patents, and contributed more than 200 scientific publications. She served as an editorial board member, reviewer of research journals & books. She served as an expert of national and international research projects & their screening committee. According to Google Scholar, she bears 8000 citations, H-index 44 and i-10 index 140, and has received national awards from various professional bodies. She handled research projects funded by national public agencies (India). As per the recently released database by Stanford University, She is among the top 2% of World Scientists. Her area of interest is pharmaceutics, nanotechnology, herbal drug delivery, and cosmetic technology. She has widely traveled abroad like the USA, UK, Switzerland, UAE, and many more for professional and academic activities.

Dr. Swarnlata Saraf
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University Institute of Pharmacy,
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Message

I would like to congratulate the Society for Pharmaceutical Dissolution Science, India for organizing the **Disso. Research Presentation India 2021-online**. As Chair of the newly formed Central zone team of SPDS and Vice president of associating body-APTI of the event, it is my pleasure to welcome one and all to participate in this significant and prestigious event.

As we know, In vitro dissolution testing continues to play a major role in drug product development, quality control, and support post-product approval formulation and manufacturing changes. The scientists have increasing access to in vitro tools that can be used to build a link to in vivo performance and to guide formulation candidate selection, formulation process development, and to assess and respond to biopharmaceutics risks including informing the success of essential formulation bridging studies for the routine release of the product. Therefore, Pharmaceutical industries implement dissolution specifications in routine quality control laboratories under conditions described in relevant compendia.
I am extremely proud to have such an opportunity to exchange education and research online. I am sure that the knowledge and experience of Disso. researchers will contribute to developing Disso. Science in the future.

Varsha Pradhan
Independent Consultant- Regulatory, Gurgaon Haryana, India
DRPI Nort zone Program Co-ordinator

Biosketch

Dr. Varsha Pradhan has a professional career spanning 27 years which includes the entire life cycle management of a drug & medical device coupled with an understanding of Indian & global Pharma education. She is a MPharm from ICT Mumbai (1992) & a PhD from School of Pharmacy & Technology Management, NMIMS Mumbai (2010). She was the recipient of UNIDO fellowship for Post graduate training in Pharmaceutical Technology in Belgium in 1992. To further upgrade her education in regulatory she is currently pursuing her MS in Regulatory Sciences at the University of Maryland Baltimore USA.

Her industrial experience includes production areas of GSK in Sterile Process department, formulation development in Cipla for generics oral solids, topical, injectables, Project Leader in Sandoz leading a team for successful transfer of technology for several dosage forms, market research Consultant in Sidvim Life Sciences, and Pharmacovigilance QA Consultant at APCER Life Sciences. In academia she contributed to bridge the gap between industry and academia & bagged the "Best Faculty Award 'in 2010 at NMIMS School of Pharmacy & Technology Management Mumbai. She holds an Indian Patent for her work on Nasal drug delivery systems. She has been an invited speaker on various PCI sponsored Faculty Development programs & has also conducted technical refresher programs for industry employees.

She is also the Secretary of the recently registered Society For Paediatric Medicines & Healthcare Initiative (PMHI) at Institute of Chemical Technology, (ICT) Mumbai. She is working on several collaborative projects with European Paediatric Formulation Initiative (EuPFI) related to paediatric medicine.

Currently she is a Consultant in Regulatory Affairs & Post Market Vigilance for medical device market at Asia Actual India Pvt. Ltd. and a Visiting Professor for MPharm (Regulatory Affairs) at Delhi Pharmaceutical Sciences & Research University, New Delhi.

Dr. Varsha is also an active member in SPDS (Society for Pharmaceutical Dissolution Science) since its inception and a Central Scientific committee coordinator from North Zone of India.

Dr. Varsha Pradhan

M. Pharm. Ph.D. (Pharmaceutical Sciences)
Consultant- Regulatory Affairs
Asia Actual India (OPC) Private Limited

ASIA ACTUAL
GROWING MEDICAL DEVICE SALES

MESSAGE

7th July 2021

Greetings! A warm welcome to all participants of DRPI 2021. With a humble beginning last year amidst the pandemic, the DRPI 2021 is enjoying an enthusiastic and energetic student participation from across the country making it an important event in the national pharmaceutical calendar. Pharmaceutical professionals are experiencing a steep learning curve in scientific content coupled with information technology advances. On this platform, I see my personal vision of bridging the gap between industry and academia also taking shape.

It is indeed a privilege and pleasure for me to get associated with DRPI from last year and was able to contribute being a part of the Central core committee from North Zone. I see the young minds in the arena of pharmaceutical research coming up with new ideas and innovations. A platform like DRPI shall be helpful to show case their research to the world through virtual medium.

It is my appeal to all Professors of Pharmaceutics and Pharma Analysis in our country to motivate and induce their students to prepare their research abstract for next year 2022 competition right from today so that we have at least one abstract presentation from each college in the coming years.

The competition has the best of scientific minds as evaluators both from academia and industry. The vibrant leadership of this event is open to ideas from all the stakeholders setting the stage for an engaging and absorbing contest. I also take this opportunity to thank AAPS & APTI for their support with which I visualise DPRI to become a global event.

My best wishes to all the participants in this event!

Dr. Varsha Pradhan

Hema Nair
Associate Professor, Sri Venkateshwara College of Pharmacy, Hyderabad
DRPI South Zone Program Co-ordinator

Biosketch

Dr. Hema A. Nair is presently Associate Professor of Pharmaceutics at Sri Venkateshwara College of Pharmacy, Hyderabad. She has a B. Pharm and M. Pharm from University of Mumbai, a Ph.D. from the S.N.D.T. Women's University and a Diploma in Patent Law from Nalsar Law University. Professional path prior to this comprises of a brief stint in the formulation development department at FDC, Mumbai, followed by teaching for 15 years at Bombay College of Pharmacy at UG and P.G. levels. She has successfully explored academic pursuits including securing research funding from several granting agencies (UGC, AICTE ICMR, etc.), guiding students towards masters (29) and Ph.D (2), handling industrial projects, delivering invited lectures and so on. Her research contributions include 20 plus articles including original research papers, book chapters and reviews and nearly 50 presentations at various national and international conferences. Several of her research contributions, both published in peer reviewed journals and presented at various conferences have won awards. She is passionate about motivating youngsters to engage in self-development, to understand their science and to move beyond cutting and pasting.

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(Website : www.surabhieducationalsociety.com)

In early 2000, while the world was paralyzed by the pandemic and the 'New Normal' as we now call this tech driven life style, had not even set in, SPDS was quick to rise to the challenge. Disso India was quickly planned and efficiently executed in the online mode in May 2020. Moreover, DRPI, a student competition too rapidly took shape in the digital space in partnership with APTI. These adaptations speak volumes about the commitment of SPDS to the science of dissolution and its measurement. With its noble intent of encouraging and rewarding scientific talent in the student community, I am certain DRPI will go a long way and its reach will soon extend deeper into our country and spread abroad.

The alignment of its objectives with that of AAPS has already earned DRPI an endorsement by AAPS. What better partner could one ask for? All my good wishes to DRPI for scaling greater heights with each passing year.

I am indeed very happy to the part of DRPI 2021 core committee and wish to thank SPDS for providing this opportunity. The unbiased nature of the total evaluation process and the complete digitalization are unique to this event. At a personal level it has been a tremendous learning experience as well as a privilege to work shoulder to shoulder with the stalwarts among the Indian pharmaceutical academic community & Industry professionals for the organization of this event.

Also, my best wishes to all the participants who had submitted their research projects for this only of its kind All India competition.

Dr. Hema Nair

Aoociate Professor of Pharmaceutics

Program Co-ordinators : DRPI 2021

Pintu De

Associate Professor, Dept. of Pharmaceutical Technology, JIS University, Kolkata

DRPI Program Co-ordinator East Zone

BIOSKETCH

Dr. Pintu Kumar De has joined JIS UNIVERSITY in the Department of Pharmaceutical Technology as an Associate Professor in the year 2017. He is an alumni of Jadavpur University from where he obtained his Graduation (B. Pharm), Post-Graduation (M. Pharm in Pharmaceutics) and Doctoral (PhD in Pharmacy) degree. He has Qualified in GATE-98 with 87.60 Percentile and hold All India Rank of 302. He is having more than 21 years of teaching experience in the AICTE and PCI affiliated teaching institutions of West Bengal, Odisha and Sikkim. He is also having one year administrative experience as Principal in a college and more than one year experience as Head of the Department (HOD) in a University. He has supervised more than 20 PG students in their dissertation work and acted as a co-supervisor of one PhD scholar from JU. He authored and co-authored more than 35 research and review articles in national and international journal of repute. Presently he is supervising three PG and six research scholars of JIS University for their PhD thesis. His area of research interest is TDDS, Nanoparticulate, Microparticulate and Topical drug delivery system. With his keen ability to conduct academic program, research activities and administrative responsibilities Dr. De will definitely be an integral part in the growth of the Department of Pharmaceutical Technology, JIS University. Wish him every success in his life.

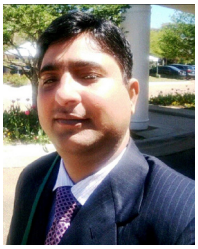
Sujata Sawarkar

Professor, Department of Pharmaceutics, SVKM's DBNCP, Mumbai

DRPI Program Co-ordinator West Zone

BIOSKETCH

Dr. Sujata Sawarkar is Professor and Head of Department, Pharmaceutics, SVKM's Dr. Bhanuben Nanavati College of Pharmacy, India. Before joining academics Dr. Sujata Sawarkar was associated with major pharmaceutical companies in India at managerial position, in the field of Research and Development, formulation development of conventional and novel dosage forms for regulated and domestic market. Several oral solid dosage forms and sterile products developed by her team have received approval in US and EU and have been commercialized. She has about total 22 years of research and teaching experience. Her research interests include Formulation Development of novel drug delivery and targeted systems based on nanotechnology for oral, ophthalmic, colonic and vaginal delivery, development of evaluation techniques for novel drug delivery systems, Translational research. Dr. Sujata Sawarkar has been Executive Member of Controlled Release Society (India Chapter) since 2014 and Secretary of Controlled Release Society (India Chapter) CRS IC for 2017-2019. She has been invited reviewer for Indian Drugs, AAPS PharmSciTech, International Journal of Nanomedicine Dove Press, Drug Design, Development and Therapy, Journal of Bioequivalence & Bioavailability, European Journal of Pharmaceutics and Biopharmaceutics and Journal of Cosmetic Dermatology. Dr. Sujata Sawarkar has received research project grants worth about 1crore rupees (10 million INR i.e. about 1.34 million USD) from Industry and Government funding agency. She has presented about 50 research papers in national and international conferences like CRS Inc. and AAPS. She has several papers published in peer reviewed journals like AAPS PharmSciTech, International Journal of Pharmaceutics, Critical Reviews in Therapeutic Drug Carrier systems, Drug Development and Translational Research, Frontiers in Pharmacology, Expert Opinion on Drug Delivery, Journal of Drug Delivery Science and Technology. She has coauthored 7 book chapters and two books. She has one granted and 6 published patents. Dr. Sujata Sawarkar has been awarded Research and Industry Outcome by SVKM's Dr. Bhanuben Nanavati College of Pharmacy in 2018 and 2020, Received Travel Grant from Controlled Release Society and All India Council of Technical Education for attending and presenting paper at 42nd & 46th Annual Meeting & Exposition of the Controlled Release Society in July 2015 and July 2019 respectively.



Amber Vyas

Professor, Department of Pharmaceutics, SVKM's DBNCP, Mumbai

DRPI Program Co-ordinator West Zone

BIOSKETCH

Dr. Amber Vyas was a visiting Scientist, Department Pharmaceutics, University of Minnesota, USA as UGC Raman International Fellow in year 2016-17. He has been shortlisted thrice for UGC research award. Dr. Vyas is currently working at University Institute of Pharmacy, Pt. Ravi Shankar Shukla University, Raipur (C.G.). He did his M. Pharm in Pharmaceutics from K.L.E.S's College of Pharmacy, Belgaum, (K.A) and Ph.D. from University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur (C.G.).

He has qualified National level test GATE 2003 with 80.34 percentile and all India rank 1257. He is recipient of 8th Young Scientist Award (medical sciences) of Chhattisgarh Council of Science and Technology, Chhattisgarh in 2010 and was also awarded with young scientist award for best oral presentation of research paper in National conference organized by Pharmanext and Medixfora in 2011 at Shimla (H.P.).

He has nearly 15 years of research and teaching experience. He has to his credit 05 books, 10 book chapters and more than 70 research/review papers published in national and international journals witch cumulative impact factor of around 50. He has delivered invited talks at several conferences/workshops as subject expert and resource person. He has also visited foreign countries like Italy, Malaysia and USA for research paper presentation.

He is member board of studies, University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur, (C.G) India and approved paper setter, examiner and evaluator of various universities like Chhattisgarh Swami Vivekananda Technical University, Bhilai, C.G., Pt. Ravishankar Shukla University Raipur, Jiwaji University, Gwalior (M.P.), Vikram University, Ujjain (M.P.) and Rajiv Gandhi Proudyogiki Vishwavidyalaya, Bhopal (M.P.).

He is approved Ph.D. Guide in pharmacy under faculty of technology at University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur, (C.G) India.

His has availed research grant of around Rs. 1.25 Cr. till date. The research project includes Major Research Project funded by CG-COST , UGC-MRP, and DST- Nanomission. He has life membership of APTI and IPA. His areas of thrust include development of novel drug delivery systems, formulation of poorly soluble drugs and cyclodextrin based delivery system.

Co-chairs : DRPI 2021 - North Zone

Arun Nanda

Professor in Pharmaceutics, MD University, Rohtak

Biosketch

Dr. Arun Nanda is a graduate and post graduate in Pharmacy from Delhi University, Delhi. Doctorate from Jamia Hamdard, Delhi, and has also graduated in Law (LLB), from M.D. University, Rohtak.

Dr. Nanda has been into teaching right after his M. Pharm. and has served a number of Universities and private colleges in various capacities, with more than 30 years of teaching experience. He has written two books, six book chapters, authored more than 140 papers in national and Inteenational journals and has widely delivered lectures on venous topics in Pharmacy. He has successfully supervised 13 Ph.D. scholars and is also presently guiding several PG research scholars in the area of Novel Drug Delivery Systems and Regulatory Affairs. He was Principal Investigator in UGC SAP Programme at M.D. University, Rohtak. He is a Registered Scientific Advisor under Patents Rules, 2003, in Pharmaceuticals, with Govt. of India.

Prof. Nanda had been Chairman, IAEC; member Executive Council, and various academic / administrative bodies, at M.D. University, Rohtak. He has been associated with several Universities, as member of Board of Studies / Selection Committee / Research Committee, and also at UGC, New Delhi, AICTE New Delhi, PCI, New Delhi, CSIR, National Board of Accreditation (NBA), New Delhi, National Assessment and Accreditation Council (NAAC), Delhi, etc.

Prof. Nanda is a life member of various professional bodies, such as IPA, IPGA, APTI and IHPA, in India. He has been on the panel (as Referee) of various national and International journals of repute, in Pharmacy and allied disciplines.

Presently, he in working as Professor in Pharmaceutics at Department of Pharmaceutical Sciences, M. D. University, Rohtak. He is also Director, Aryabhata Central Instrumentation Laboratory, M.D. University, Rohtak.

Roop Krishen Khar

Director, B.S.Anangpuria Educational Institutions, Faridabad, Delhi NCR

Biosketch

Prof. Roop Krishen Khar is a renowned academician and a research scientist . He served in various Administrative and Academic positions for more than 35 years at Jamia Hamdard in the capacities of DEAN and HOD of Faculty of Pharmacy, Dean Students Welfare, Placement officer and Proctor of Jamia Hamdard. He has supervised 86 Ph.D,. 200 M.Pharm. theses and published more than 300 research papers in International & National journals with cumulative impact points of more than 450; H index of 60, i-10 index of 175 and citations of 17249.. Dr. Khar is inventor of two US & 15 Indian Patents. He has published Thirteen text books, including the , 4th revised edition (2013) of Leon Lachmans Text Book of Industrial Pharmacy.and Introduction to Novel Drug Delivery Systems (2020 CBS) Presently Prof. Khar is professor and DIRECTOR of, B. S. Anangpuria Group of Institutions, Faridabad (NCR). He serves in Advisory capacity in many Institutions and Universities. He is Director of a leading Pharma Manufacturing company UNICURE (INDIA) LTD and Executive Director of a consultancy company FORMULATORS KONCEPT LTD. He is the chairman of Good Society of Clinical Research approved by Drugs Controller Genral of India and Accredited by NABH. He is fellow of Indian Pharmaceutical association. He has been the member of "Unani Pharmacopoeia Committee" (2008-2011) and a member of Parliamentary committee on Fixed Dose combinations of Min of Health and family Welfare since 2017. He is recipient of life time achievement award of Indian Pharmaceutical Association in Dec 2018 and is the Trustee of DELHI PHARMACEUTICAL TRUST.

Co-chairs : DRPI 2021 - East Zone

Bhakti Barik

Professor & Academic Director, College of Pharmaceutical Sciences, Puri

Biosketch

Dr. Bhakti Bhusan Barik is presently working as Professor & HOD Department of Pharmaceutical Technology, Brainware University, Kolkata. Earlier he worked in different institutions like College of Pharmaceutical Sciences, Puri, Odisha as Academic Director and Head of PG Dept; Bharat Technology, Uluberia, West Bengal, as Professor & Principal; College of Pharmacy, Jazan University, Kingdom of Saudi Arabia as professor & Coordinator; Utkal University, Bhubaneswar, as professor &Head of Pharmacy Dept. He is awarded with Best Teacher Award and few other awards. He receives few research project grants from UGC& AICTE. 35 yrs of teaching experience, 32 yrs of research experience, 12 Ph.D, 100 M.Pharm guidance, 66 research publications, more than hundred presentations in national and international conferences. Visited several countries like USA, Germany, Spain, China, Saudi Arabia, UAE etc.

USN Murty

Director, NIPER, GuwahatiDelhi NCR

Biosketch

Dr USN Murty is currently working as a Director of NIPER-Guwahati, Assam & Officiating Director at NIPER-Raebareli, Lucknow, U.P. He did M.Sc from Andhra University in 1980 and Ph.D from Osmania University in 1990. He started his research career in WHO Centre Pondicherry in 1981 followed by Central Sericultural Research and Training Institute (CSR&TI) Mysore in 1983. He joined in CSIR-IICT in 1984 as a Scientist B rose to the level of Chief Scientist and Head Biology Division. His research interests are Biotechnology, Toxicology, Bioinformatics, Integrated Vector control and Disease Modeling and Public Health. He published more than 198 papers in peer reviewed journals, contributed 12 chapters and edited three books. He is the recipient of many National and International awards/recognitions to name few Zandu Award, WHO/TDR, German Research Foundation, US Defense, NASI Member, ICMR Biomedical Research award, etc. Dr Murty is a Visiting Professor in York University Canada, University of Hyderabad. He was holding the positions of In-charge Director of CSIR-IICT, Hyderabad, Project Director and Dean of National Institute of Pharmaceutical Education and Research, Hyderabad and Director (Officiating), NIPER Mohali. Presently he is the Founder Director of NIPER Guwahati, where he established 08 National Centres,08 departments and secured 19th Rank in NIRF-2021 within a short span of time. Science popularization is his passion and ambition.

Co-chairs : DRPI 2021 - West Zone

Munira Momin

Principal & Professor, SVKM's BNCP, Mumbai

Biosketch

Dr. Munira Momin is a recipient of highly prestigious Nehru-Fulbright International Higher Education administrator's excellence award-2019. Dr. Momin is the first pharmacy professional to receive this award since the inception of the award by the Govt. of India and Govt. of USA, under USIEF. She is Currently serving as a Principal and Professor at SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, India. Under her leadership, the institute has received many accolades to count a few, accreditation by NBA with Full accreditation status for five years, NIRF rank 30th, Two times national winner of Best Industry Linked Pharmacy degree college Award of AICTE-CII, DST-FIST grant of 100 lakh. The college has received around 1 crore industry collaborative research funding in last three years. She has institutionalized number of innovative practices in teaching and research. The college has seen a complete transformation on research and student's professional and societal activities. Under her guidance and mentorship, the college faculty have received government grants from CCRUM BRNS, DBT, Rajiv Gandhi Science and Technology Commission (RGSTC), AICTE, SERB to count a few total amounting to 2.2 crores. To mention about her academic background, she obtained her B. Pharm and M. Pharm (Pharmaceutics) from L.M. college of Pharmacy, Gujarat University, Ahmedabad, India. She has received F H Jani gold medal for securing highest marks in Pharmaceutical technology subjects in B. Pharm. She is a recipient of Prof M. L. Khurana Memorial Award for Best Research Paper published during the Year 2008-09 in Pharmaceutics and Bio-Pharmaceutics. She is the recipient of IDMA-ACG Best Research paper 2019-20 Award. Dr. Munira has published several research papers in national and international journals. The cumulative impact factor of Thompson Reuters of Dr. Momin's research and review papers is more than 110. She, as a PI and Co-PI has received research grants (Industry collaborative research and Govt. funding), with total amount of more than 1.8 crore. She has one patent granted, eight patents in pipeline and one trademark to her credit. Dr. Momin has four books and 4 book chapters on pharmaceutics, and related subjects.

Shrinivas Savale

CEO, AIC-LMCP Foundation, Ahmedabad

Biosketch

Shrinivas S. Savale, Ph.D., is the CEO of AIC-LMCP Foundation, an Atal Incubation Centre focusing on Pharmaceutical and Healthcare Sector, hosted by L. M. College of Pharmacy, Ahmedabad, and supported by AIM, NITI Aayog, GoI. He is an acknowledged leader with over twenty-two years of professional experience in drug research, development and compliance, in pharmaceutical organization, CRO set-up and academia. He has expertise in the areas of regulated bioanalysis, biopharmaceutics and early clinical development including bioequivalence for small molecules and biosimilars/ biologicals, GxP (GLP, GCP, GMP) compliance including data integrity, gap analysis and resolution for electronic data workflow and IT systems in GxP environment, CRO/Vendor qualification, electronic solutions deployment for automation of bioanalytical/clinical laboratory workflows (LIMS, SDMS)/ clinical workflow (Phase I/BA-BE) and has been supporting pharmaceutical organizations and CROs in these areas. He has been part of various startup and innovation related initiatives at L. M. College of Pharmacy such as Member of Committee and Mentor for SSIP and Incubation Centre Representative of IIC. He was also an Adjunct Professor - Quality Assurance (MPharm and PharmD Courses). He was associated with Torrent Pharmaceuticals Ltd. as General Manager–Bio-Evaluation; Clinigene International Ltd. (presently Syngene International Ltd.) as Head-Bioanalytical Research; and Torrent Research Center as Scientist-II at Medicinal Chemistry Division. He received Ph.D. in Pharmaceutical Sciences from Gujarat University, Ahmedabad. He served as the Track Screening CHAIR, Bioanalytics - Chemical Entity, Abstract Screening Committee, AAPS PharmSci 360, AAPS, 2018; Member, Steering Committee and Member, Clinical PK-PD subcommittee, Biosimilars Focus Group (BSFG), AAPS; Abstract Screener – AAPS National Biotechnology Conference (2021) and AAPS Annual Meetings (2010 onwards); the Founding Chairperson, Regulated Bioanalysis–APA India; Member of Steering Committee for Global Bioanalysis Consortium (GBC) on harmonization of bioanalytical guidance (via APA-India) representing Asia-Pacific region and is an active member of the organizing committee for Regulated Bioanalysis. He is the Chair-Gujarat Chapter at Society for Pharmaceutical Dissolution Science (SPDS), India. He has been a Reviewer for various national and international scientific journals; invited speaker at various national and international conferences and has 22 publications, a book chapter and many scientific presentations to his credit.

Kusum Devi

Principal & Professor, Nitte College of Pharmaceutical Sciences, Bangalore

Biosketch

Dr.V Kusum Devi, Principal & Professor, Nitte College of Pharmaceutical Sciences, Bangalore. BOS Chairman for UG Studies, Rajiv Gandhi University of Health Sciences, Bangalore.
33 Years of Research & Teaching Experience –In Pharma, & Herbals, Foods and Cosmetics.
Worked as Professor & HOD at Al-ameen college of Pharmacy, Bangalore. Worked as the Principal of Milind Institute of Pharmacy, Bangalore,
Championed the following Patents and Research grants :
Complete specifications have been filed for "A vesicular drug delivery system for Antiretroviral (AIDS) therapy"
'Nanosponges and process of preparation thereof' Indian Patent, 201741029843 filed 23rd August 2017.
Received different Research grants as PI, CO-PI and mentor, received research grants with a total amount of >1.2 crore rupees, from Pharmaceutical Industries and various Government funding agencies like CSIR, DST, AICTE, ICMR, VGST, IPA, and RGUHS.
Dr V Kusum Devi has authored 4 textbooks on Pharmaceutical Engineering to her professional credit. More than 30 guest lectures were delivered on plethora of eminent research topics at various institutes namely- Shri Rawatpura Sarkar institute of Pharmacy, Laureate Institute of Pharmacy-Kothog, Gujarat Technological University, National Institute of Unani Medicine, Dayanand sagar college of Pharmacy, Government Ayurvedic College, BLDE's College of Pharmacy, Manipal College of Pharmaceutical Sciences, T.John college of Pharmacy, Institute of Health Management and Research, Krupanidhi College of pharmacy, K.L.E. college of Dental Sciences, Government college of Pharmacy, Visveshwarapuram Institute of Pharmaceutical Sciences, KMCH college of Pharmacy etc. Recieved Best paper, best poster awards from various associations like IHPA, IPC, Bangalore India Bio, IACDE and IES PG Convention, ICMBPS, APTICON, Krupa Pharmacon, DRPI etc.

Professional Credits:

Consultant – Subject Expert, Canadian Pharma multinational Abbott Laboratories
Invited for lectures in pharmaceutics, Teach Global Pvt Ltd., Hyderabad
Resource person, Medical Education Research Centre – Pharmacy Division.

• BOS member for PG studies, • Member- Ph.D. registration committee • Approved PG & Ph.D. guide • Technical expert. RGUHS
Guest faculty Stride Acro Labs Treasurer & Coordinator (Academic Staff College) APTI Co-chairperson for Scientific Committee of south zone DRPI

Presannakumaran P N

Prof & HoD Pharm Chem, Pushpagiri College of Pharmacy, Tiruvalla

Biosketch

Dr. Presannakumaran is presently Prof. & Head of Pharmaceutical Chemistry, Pushpagiri College of Pharmacy, Tiruvalla, Kerala. After completion of a Bachelor's degree in Chemistry from Christian College, Chengannur, Kerala, he has earned his B.Pharm, M.Pharm and Ph.D from Govt. Medical College, Trivandrum.

In a professional career spanning 36 years, 30 years have been devoted to teaching. Prior to his appointment as Lecturer in Pharmacy in 1991, he has served as an Approved Analytical Chemist in a drug manufacturing unit for 5 years. He has served as Asst. Professor, Associate Professor and Professor of Pharmacy at various Govt. Medical Colleges in the State. During his tenure in the Government sector, he undertook additional duties like Officer-in-charge of Toxicology Laboratory, Central Instrumentation Laboratory, Oral Morphine Manufacturing Unit, QC Manager of Kerala Medical Services Corporation etc. He acted as a member of the Expert Committee for licensing patent and proprietary Ayurvedic drugs, Govt. of Kerala. He has also served as Nodal Officer for implementing the scheme "Starting of Drug testing Laboratories for Quality Assessment of Drugs at Four Govt. Medical Colleges in the State". He has been an inspector to National Board of Accreditation, AICTE, PCI, University of Kerala and Kerala University of Health Sciences. He has served as a member of the Academic Council, University of Kerala and a member of the Board of Studies in Pharmaceutical Sciences, University of Kerala and Kerala University of Health Sciences.

He has attended several National and International conferences and has presented 5 papers in National conferences and 4 papers in International conferences and has 8 publications in International journals to his credit.

Gautam Singhvi

Asst Prof, BITS Pilani, Pilani

Biosketch

Dr. Gautam Singhvi is working as an Assistant Professor in the Department of Pharmacy, BITS, Pilani. He has industrial research experience on solid oral, pellets, and complex pharmaceutical product development. Currently, he is involved in industrially feasible nanocarriers-based formulation development and optimization for various therapeutic agents. His team is extensively working on topical drug delivery systems for rheumatoid arthritis, psoriasis, and fungal infections. He is also involved in solubility-dissolution enhancement of poorly water soluble drugs and IVIVC of designed formulations. He has more than 100 publications in reputed international peer-reviewed journals and 15 book chapters in international publishers such as Elsevier, Springer, and Willy. He is actively involved in sponsored research projects in collaboration with the pharmaceutical industries. As an inventor, he has filed 8 formulation patents and has completed industry projects. He is also a peer reviewer of several international journals. He is very passionate about practicing the newer teaching pedagogy in his classroom teaching and motivating students to face the challenges of the new era.

Kamlesh Dashora

HoD & Assoc Prof, Institute of Pharmacy, Vikram University, Ujjain

Biosketch

Dr. Kamlesh Dashora has more than 20 years of teaching experience and 3 years of industrial experience. At present, working as Head of the Department at institute of pharmacy, Vikram university Ujjain. I have published more than 70 research and review articles in international and national repute journals and also published 5 books. And have also guided 12 Ph.D students.

DRPI 2021 Zonal Committee Members

North Zone

Anurag Verma	Prof, TMCP, TMU, Moradabad
Arti Thakkar	Assoc Prof, Amity Inst. of Pharmacy, Noida
D C Bhatt	Prof, Dept of Pharmaceutical Sciences, GJUST, Hisar
Gaurav K Jain	Assoc Prof, DPSRU, New Delhi
Harish Dureja	Prof, MDU, Rohtak
Meenakshi Chauhan	Assoc Prof, DIPSAR, New Delh
Musarrat Warsi	Asst Prof, College of Pharmacy, Taif University, Taif, Saudi Arabia
Nayyar Parvez	Prof, Sharda University, Greater Noida
Prashant Kesharwani	Asst Prof, Jamia Hamdard, New Delhi
Rajesh Agrawal	Head, R&D, Modi-Mundipharma, Modipuram, Meerut
Rupa Mazumder	Prof & Dean, NIET (Pharmacy Institute), Greater Noida
Saima Amin	Assoc Prof, Jamia Hamdard, New Delhi
Sanju Nanda	Prof, MDU, Rohtak
Shiv Kumar Yadav	Prof, B. S. Anangpuria Institute of Pharmacy, Faridabad
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East Zone

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Advanced dissolution test to address crosslinking in different types of hard-shell capsules and method for improving the same.

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Background and Rationale: Alteration of dissolution characteristics of capsule formulations owing to crosslinking and pelliculization is a well-known phenomenon. Crosslinking in capsule shells forms a three-dimensional molecular network of higher molecular weight and in addition it also reduces hydrophilicity of the molecules by loss of ionizable amino groups. Thus, exposure of capsule formulations to environmental factors and/or chemical catalysts results in formation of a swollen, very thin, tough, rubbery, water-insoluble membrane, known as "pellicle" which alters the dissolution characteristics of capsule formulations, and the dissolution values often drop to the point of rejection. Therefore, crosslinking and dissolution behavior of crosslinking promoting model drugs such as etodolac and hydrochlorothiazide from conventional gelatin, hydroxypropyl methylcellulose (HPMC) and starch capsule shells has been evaluated and effect of addition of anti-crosslinking agent on minimizing pellicle effect.

Methods: Etodolac and hydrochlorothiazide capsules were prepared by aqueous wet granulation process. Formulations were prepared with and without stabilizer and encapsulated in hard gelatin, HPMC and starch capsules. The capsules were then subjected to accelerated storage conditions (40°C/75%RH). The dissolution studies for prepared capsules were carried out in accordance with USP 28 using USP apparatus I. Further, shell dissolution studies were carried at 0, 4, 8 and 12 weeks, emptied and dissolution time of hard capsule shells per se were determined using USP apparatus II (paddle) at 50 rpm and 37 ± 0.5º C.

Results and Discussion: The release profile of etodolac and hydrochlorothiazide from HPMC capsules remained the same throughout the 12 week accelerated stability studies. Gelatin and starch capsules showed extensive crosslinking and a significant drop in dissolution profile of the model drugs throughout the test period. The above results were further corroborated by evaluating dissolution time of various capsule shells containing etodolac and hydrochlorothiazide formulations. Dissolution time for HPMC capsules remained constant while dissolution time for gelatin and starch capsules increased dramatically with observed pellicle formation. The study confirmed that HPMC capsules owing to its non-susceptibility to crosslinking are effective delivery systems, for products possessing dissolution problems due to crosslinking of capsule shells. The study also demonstrated that capsule shells other than gelatin shells could be protected from crosslinking by incorporating cross linking reducing-combination of glycine and citric acid in the formulation.

Conclusion: Comparative evaluation of the crosslinking tendency of HGC, starch and HPMC capsule shells was the purpose of the present work. Novel HPMC capsules were found to be effective delivery systems for products possessing dissolution problems due to crosslinking of capsule shells. In addition, the novel capsule shells could be protected from crosslinking by incorporating glycine and citric acid to the capsule preparations.

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Bioscintigraphy: A tool to envisage *in vivo* performance of modified release solid orals

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Background and Rationale: For solid orals, including modified release dosage forms, *in-vitro* dissolution is considered as surrogate for *in-vivo* bioavailability. However, more than 50% of modified release solid orals that qualify dissolution fail to show bioequivalence[1]. This poor *in vitro - in vivo* correlation is attributed to use of specialized polymers to control rate and site of drug release and inability of dissolution tests to simulate real time GIT environment. Bioscintigraphy® is an emerging technique known to generate real time visualisation of the *in-vivo* performance of drug products and therefore bioscintigraphy assisted with dissolution could act as a surrogate for bioavailability of modified release formulations[2].

The objective of the present study is to envisage the reason for bioinequivalence of dissolution qualified solid oral delayed release formulations of mesalamine using bioscintigraphy involving surface labeling with technetium.

Method: An open label, four-arm, single center, randomized, single dose scintigraphy study was conducted in healthy volunteers to evaluate the *in vivo* performance of delayed release mesalamine products. Three in-house developed formulations X, Y and Z were compared with the innovator product (Asacol HD, Allergan Pharmaceuticals).

Results and Discussion: The three formulations passed the dissolution criteria proposed by FDA for the Innovator product during the pretreatment stage (no individual value exceeds 1% dissolved in 0.1N HCl) and the evaluation stages (no individual value exceeds 1% dissolved at pH 6.0 and Q= 80% at 1.5 hrs in pH 7.2). Nevertheless, product X, Y and Z failed to pass the bioequivalence test. Bioscintigraphy depicted that the products X, Y and Z demonstrated different *in vivo* performance compared to Asacol.

As depicted by imaging, Asacol HD successfully initiated and completed disintegration in colon, the desired target site for mesalamine. Bioscintigraphy showed that product X initiated dispersion in the small intestine and product Y showed incomplete disintegration in the colon, responsible for failure to achieve bioequivalence. Interestingly, product Z did not disintegrate in GIT in all the 6 subjects and intact tablet excreted with faeces. The reason for bioinequivalence was well understood by Bioscintigraphy and formulations were modified accordingly to achieve bioequivalence.

Conclusion: *In-vitro* dissolution combined with Bioscintigraphy could be the gold standard for determining bioequivalence of modified solid orals. This approach will lead to development of cost-effective and quality products.

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A NOVEL CHRONOTHERAPEUTIC SYSTEM FOR TIME AND SITE SPECIFIC DELIVERY: MICROSPHERE AND TABLET IN CAPSULE SYSTEM

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Background and Rationale: Chronotherapeutic drug delivery system is the application of biological rhythm to pharmacotherapy and the special drug delivery system to synchronize drug concentration to rhythms in the disease condition. Present study is to develop and evaluate microspheres and tablets in a capsule system for the treatment of rheumatoid arthritis and it is the dual pulse release system [1]. The rationale of current study is to minimize dosing frequency and for the treatment of morning stiffness and night pain allied with rheumatoid arthritis.

Methods: **A) Development of formulations**: The capsule system contains an enteric coated cap filled with Drug X microspheres (sustained release) that lock the impermeable capsule body (coated with ethyl cellulose). The Capsule body consists of Drug X loaded core tablet in the bottom (immediate release) which is sealed with swellable hydrogel plug tablet.

B) *In vitro* study of the capsule was performed at pH 1.2 for 2 h; then replaced with phosphate buffer 6.8 pH for 6 h; then replaced again with phosphate buffer pH 7.4 for 2 h.

Results and Discussion: Formulation selected for capsule system were MP1 due to least particle size and maximum cumulative release, T3 for their least disintegration time (4±0.040 min) and maximum cumulative release and HP2 for their maintenance of lag phase that was 6 h which is similar to intestinal transit time.

Conclusion: This formulation included two pulses in one system for reduction of dose frequency and better treatment of night pain and morning stiffness of rheumatoid arthritis patients.

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Crohn's disease and its impact on drug dissolution

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Background and Rationale: Crohn's disease (CD) is one of the major inflammatory bowel diseases. It causes alteration in the physiology of GIT, including changes in the pH of luminal fluids, overexpression of CYP metabolizing enzymes in the intestine and colonic region, increase in the expression of P-gp in the intestine, changes in the human serum albumin level, etc. All these changes have a tendency to alter the pharmacokinetics (PK) of the drugs[1]. Verapamil is one such drug that has a stereoselective increase in plasma levels in CD patients as compared to the control group, as evidenced from 9-fold and 2-fold increments in AUC of S- and R-form, respectively,[2]. The mechanisms underlying the higher PK include the altered expression of CYP enzymes and P-gp transporter in the gut and/or change in the *in vivo* dissolution rate of the drug in CD patients. In the present study, we carried out dissolution studies in biorelevant media to explore the role of the latter parameter in altered PK of verapamil in CD patients.

Methods: The biorelevant media mimicking the composition of the intestinal and colonic fluids in CD patients and healthy subjects in fasted and fed conditions were prepared. The fasted and fed state intestinal media of healthy and diseased conditions had variable bile salts: lecithin concentration, representing minimum (low CD medium) and maximum (high CD medium) limits. In colonic media, osmolality was also varied along with bile salt: lecithin concentration. Dissolution studies were carried out in USP type II apparatus.

Results and Discussion: *A. Dissolution studies in intestinal media:* Similar release profiles were obtained for verapamil in healthy and CD high medium in the fasted state probably due to the similar composition of media. Conversely, there was a high release rate of verapamil in CD low medium (91%), compared to the healthy state and CD high medium (84%). In the fed state, the release profiles of the drug in healthy and CD high media were identical, while a higher extent of drug release was observed in CD low medium.

B. Dissolution studies in colonic media: Contrary to the intestinal media, higher drug release was observed in the case of CD low and healthy state media, as compared to CD high media in the fasted state. In the fed state, the drug showed a higher rate and extent of dissolution in CD low and CD high media, as compared to the healthy state. The reason attributed to changes may be the variable media compositions in these cases.

Conclusion: The biorelevant dissolution studies revealed that the drug showed differential dissolution behavior in CD conditions as compared to the healthy state. But the observed changes in dissolution were not significant to explain the observed altered PK of verapamil in the CD state. Therefore, other mechanisms are needed to be explored to investigate the exact mechanism of PK variability of verapamil in CD.

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Design and *In vitro* Release Studies of Orodispersible Film of Promethazine

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Background and Rationale: Promethazine is a drug of choice used in the management of motion sickness currently available as a tablet in the market. Orodispersible films (ODF) are more beneficial in comparison to the tablets and capsules, because oral films tend to dissolve or disperse within a few minutes after placing in the mouth[1]. Thus, it was envisaged that the development of ODF will provide faster drug availability and rapid relief.

Methods: ODF of promethazine were prepared by the solvent casting method [2]. The 3^2 factorial design was employed for optimization using the Design of Experiment (DoE) approach. The developed and optimized oral films were evaluated for various *in vitro* attributes, viz., tensile strength, thickness, swelling index, disintegration, and dissolution studies. The *in vitro* dissolution of the drug-loaded films was performed using USP type I apparatus (i.e. Basket type) in 900 ml of dissolution medium (distilled water). The conditions of the release studies maintained were 37±0.5 °C and 50 rpm. The sample volumes of 5 ml were withdrawn at an interval of 1 minute up to 70 % release, followed by an interval of 2 minutes until the end of the study.

Results and Discussion: The developed film has shown 1703.3 (±5.77) kg/cm^2, 13.33 (±0.44) % and 28.85 (±0.93) % and 129.33 (±2.51) sec of tensile strength, percentage elongation, swelling index, and disintegration times, respectively. The optimized formulation has shown higher drug dissolution i.e., > 95 % in 15 min with >70 % in 5 min.

Conclusion: ODF is a novel concept in solid dosage forms, which is more patient compliant. Thus, from the above studies, it can be concluded that the developed ODF can provide immediate relief from motion sickness during traveling. Also, these can be easily taken by geriatric and pediatric patients.

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Development and Investigation of Fluconazole Mucoadhesive Buccal Patches

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Background and Rationale: Oral candidiasis (OC), which is a fungal disease in the oral cavity, is caused by a species called *Candida albicans.* OC is the foremost reason for mortality and morbidity for cancer patients. Oral cancer has been considered as the most communal and invasive type of cancer. The main objective of this study is to formulate buccal mucoadhesive patch of fluconazole to provide sustained drug release in the mouth, and also to improve patient compliance, specially for the immune-compromised patients, as it bypasses hepatic first pass metabolism. The patches were evaluated for their physio-chemical as well as pharmaceutical characteristics and proved to be a conventional dosage form.

Methods: A) Preparation of Plain and drug-loaded patches: Solvent casting technique was used for the preparation of patches. Mucoadhesive polymers were used for the preparation of plain patches (without drug) and evaluated for pre-formulation studies. The optimum patch preparation was selected for the incorporation of fluconazole drug. Mucoadhesive polymer (HPMC E15), Plasticizer (propylene glycol), ethanol were combined together and stirred on a magnetic stirrer at 50 rpm to obtain a homogenous mixture. And, finally 10 gm of drug was added to the solution for final formulation, followed by hot air oven drying at 40°C for 24 hr.

B) *In vitro* release profile of Fluconazole patch: USP-Type (II) Dissolution apparatus (Paddle Type) operated at 50 rpm with phosphate buffer solution (pH 6.8) was used for determining the drug release profile from the patch and showed sustained release of drug.

Results and Discussion: The prepared patches showed no harm to oral mucosa and the percentage of drug release was found to be above 80%. The result of the optimized patch was analyzed by Higuchi's plot and Korsmeyer-peppas model. The release exponent (n) described the drug release mechanism from the matrices and was considered by regression analysis by using the equation [$Mt/ M\infty = Kt^n$] Where, Mt/M is the fraction of amount of released drug (within the range 0.10–0.60) at time t and K is the constant providing the geometrical and structural properties of the released model. *In vitro* drug release was found to be more sustained for that formulation which contained a higher proportion of HPMC E15 and hence F3 formulation exhibited the highest release of drug with 98.05%.

Conclusion: In the present work, formulation and evaluation of fluconazole buccal films was done by using different polymers like HPMC E15, E5, K100, propylene glycol and ethanol in different concentrations. The formulation incorporated with highest concentration of HPMC E15 was shown to possess optimum range with better outcomes of release profile and proved to be used as an alternative dosage form for treatment of oral candidiasis.

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Dissolution studies on bilayered tablets for treatment of menstrual cramps

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Background and Rationale: NSAIDs and analgesics can be effectively used for reducing menstrual muscle cramps and several painful conditions caused due to prostaglandins if administered in modified release bilayered dosage form. Conventional existing combination requires frequent usage or increased dosage of NSAIDs which can lead to serious cardiovascular and GI conditions [1]. Therefore, modified release bilayered dosage form can be given with reduced drug dose and enhanced drug release than the conventional existing combination. It can also increase patient compliance by giving desired pharmacological action for a prolonged period of time. In the present study, bilayered tablets of Mefenamic Acid (MFA) and Acetaminophen were prepared. The main objective was to increase the solubility of MFA by forming complexation and using it to develop a modified release bilayered tablet having natural polymers for delivering immediate relief from the immediate release (IR) layer of MFA followed by sustaining the action for 12 hours by Acetaminophen.

Methods: MFA was complexed with β Cyclodextrin (βCD) in different ratios for enhancing the solubility using kneading method [2]. The solubility of the complexed drug was evaluated against pure drug at pH 1.2, 4.7, 6.8, 7.4 and in distilled water. The most efficient ratio was examined for compatibility using FTIR and crystallographic structures using x-ray diffraction. IR layer of MFA- βCD complex was developed using different superdisintegrants like sodium starch glycolate (SSG), crospovidone and croscarmellose sodium in varying concentrations, whereas sustained release (SR) layer of Acetaminophen was developed having natural polymers like xanthan gum and guar gum in different concentrations along with other pharmaceutically acceptable excipients. Most optimized formulations from both layers were taken for bilayer tablet formulation development.

The *in vitro* drug release was determined using USP apparatus II having 900 mL of 0.1N HCl (pH=1.2) for initial two hours followed by 0.05M phosphate buffer (pH=6.8) for the next 10 hours maintained at 37± 0.5°C with 75 rpm. The samples withdrawn were filtered and analysed spectrophotometrically at 243nm and 286nm respectively. Drug release kinetics of the SR layer was determined and the release was fitted into zero and first order equation. Further, the drug release mechanism was evaluated by plotting the dissolution data according to Korsmeyer-Peppas equation.

Results and Discussion: The most effective Drug-βCD complex selected was 1:1. It very well showed multifold increase in solubility as compared to the pure drug. The developed IR and SR layer tablets had good hardness, weight uniformity, drug content (nearly 100%), friability (<1%) and disintegration time as desired within limits. The most optimized batches [from IR layer was MF3 (10% of SSG) and from SR layer was AF4 (5% of xanthan gum)] were taken for bilayer tablet formulation, and it showed twice the drug release in half of the dosage than existing marketed formulation. The SR layer followed zero order release kinetics and the release mechanism shows case II transport with swelling. The best fit model was Higuchi having a regression coefficient of 0.9942.

Conclusion: The physicochemical properties and *in vitro* release of drugs showed that the bilayer tablet formulation follows zero order release with case II transport and can be used for controlled release of MFA and Acetaminophen with enhanced drug release, which might enhance patient compliance. It can reduce/eliminate the conditions caused due to high/often dose administration of NSAIDs.

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Establishing *in vitro-in vivo* Correlation and Lung Performance of Inhaled Drug Products using Gamma Scintigraphy

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Background and Rationale: The inhaled products are used for both locally and systemically acting drugs. Unlike solid orals, no standardised dissolution or *in vivo* methodology exists for estimating pulmonary delivery/ bioavailability of inhaled products, and aerodynamic particle size distribution (APSD) is recognized as the pivotal performance parameter [1]. Nonetheless, APSD poorly correlates with lung deposition, dosing interval, lung kinetics and overall pulmonary performance. The present study utilizes gamma-scintigraphy based *in vivo* mucociliary clearance (MCC) and lung deposition (LD) as a tool to predict pulmonary performance of inhaled products [2]. The correlation with *in vitro* dissolution was also established.

Methods: For the purpose, open label, two arm, single period, single dose study was designed for both cases to assess each objective in healthy individuals (IEC approval No:GSER/2018/NR-AP/016; dated 05-09-2018). **Case study 1** evaluated the difference in MCC and LD of a Tc-radiolabelled hydrophilic drug (Salbutamol) and hydrophobic drug (Budesonide). **Case study 2** evaluated the difference in MCC and LD of a Tc-radiolabelled micronized and nano-sized budesonide.

Results and Discussion: Case study 1: Both the drugs used in this study were micronized. Dissolution data in phosphate buffer (pH 7.4) showed that the release of salbutamol was faster (79.5% in 2h) compared to that of budesonide (21.5% in 2h). Scintigraphy analysis was done over a period of 4 h and lung concentrations were determined to calculate MCC and LD. As expected, budesonide showed lower MCC (23.8%) compared to salbutamol (72.6%). The data correlates well with findings of dissolution data and hydrophobic budesonide with lower dissolution rate demonstrated slower MCC and prolonged lung retention. The LD was found to be higher for salbutamol at each time point.

Case study 2: Comparative dissolution of micronized and nano-sized budesonide showed faster drug release for nano-sized budesonide (44.0% in 2h) compared to micronized (21.5% in 2h). The MCC using scintigraphy correlates well and nano-sized budesonide with higher solubility demonstrated nearly 2-fold higher MCC (45.1%) compared to micronized (23.8%). The LD also correlated and was found to be higher for nanosized budesonide being more water soluble.

Conclusion: The well designed, modified dissolution estimations alongside scintigraphy based MCC and LD evaluations could act as a surrogate for determining lung performance of conventional and advanced inhaled products. Further they may be useful for determining dose and dosage schedule for inhaled products.

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Formulation and Evaluation of Bioadhesive Composite Dental Film for Management of Toothache

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Background and Rationale: Toothache is the pain in and around the teeth and jaws. It is one of the most common symptoms of dental caries or tooth decay. The innermost part of the tooth contains the tooth pulp which becomes inflamed, infected or injured when toothache begins. Tooth pain may be sharp, throbbing or constant. Etoricoxib is a synthetic, nonsteroidal anti-inflammatory drug (NSAID) with antipyretic, analgesic, and potential antineoplastic properties. It is a a BCS class II drug. Etoricoxib specifically binds to and inhibits the enzyme cyclooxygenase-2 (COX-2), resulting in inhibition of the conversion of arachidonic acid into prostaglandins.

Method: A) A film was prepared by using solvent evaporation technique. In Petri-dish accurately weighed polymers such as hydroxypropyl methyl cellulose (HPMC E-15) and Eudragit RL100 were dissolved in methanol with continuous stirring then kept aside to form a clear solution. Drug (Etoricoxib) was dissolved in the above solution and mixed until a clear solution was obtained. Polyethylene glycol 400 used as plasticiser was added to the above solution. The resultant solution was propelled on the Petri dish and dried at room temperature for 24 h. An inverted funnel was placed over the Petri-dish to avert the fast evaporation of the solvent. Dried films were taken out after 24 h and stored in desiccators.

B) *In vitro* Release Study: The *in vitro* drug release studies were carried out in dissolution USP-I apparatus. The dental film was dipped into 900 ml simulated salivary fluid. The solution was stirred at 50 rpm and temperature was maintained at 37^{o}C. The sample was withdrawn at different intervals and replaced with the same volume of salivary solution. Samples were analyzed by UV spectrometric method at 235 nm.

Results and Discussion: The final selected dental film was found to have following properties- thickness (0.018± 0.003 mm), average weight (125.3 ±0.15 mg), percent moisture loss (4.66) and percent moisture absorption (45.33), folding endurance (> 250) and drug content (98.45%). *In vitro* release of etoricoxib from film in simulated salivary fluid was found to be > 95% in 6 hr.

Conclusion: It can be concluded that the designed dental film of etoricoxib was found to possess good physical characteristics indicating suitability. *In vitro* release study was found to be better and may have the potential to overcome the disadvantage of poor and erratic bioavailability associated with presently marketed oral tablet/ gel preparations.

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Increased bioavailability of levobunolol from nanoparticle-laden contact lenses for glaucoma therapy

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Background and Rationale: Glaucoma is a major cause for the permanent loss of vision around the globe. The common treatment methodologies currently available such as eye drops suffer from various drawbacks like patient noncompliance due to repeated administration and poor (1–5%) bioavailability leading to poor efficacy and wastage of drug. The objective of this research was to formulate Eudragit-based nanoparticles laden contact lens of levobunolol to obtain a higher bioavailability at the therapeutic level.

Methods: Different ratios of Eudragit 100 and polyvinyl alcohol were used to formulate nanoparticles by nanoprecipitation methodology. Resultant nanoparticles were evaluated and optimised using entrapment efficiency, morphology of surface, particle size and zeta potential. Further, soaking method was employed to incorporate the optimised nanoparticles into the contact lens which were then evaluated and compared for optical clarity, shelf life, equilibrium swelling, and *in vitro* drug release in simulated tear fluid followed by *ex vivo* transcorneal permeation.

Simulated tear fluid (STF pH 7.4) was used as a medium for *in vitro* drug release study. The study was carried out at the room temperature in a shaking incubator at 100 rpm. In order to maintain sink conditions, equal volume of fresh STF was substituted at each interval (every 24 h). The UV-visible spectrophotometric measurement at 257 nm was used to estimate the dynamic concentration of the drug in the STF and the release profile was assessed by plotting graphs of cumulative drug release (µg) versus time.

Results and Discussion: The optimised nanoparticle formulation had the particle size 102.61 nm ± 3.92, zeta potential − 22.2 mV ± 2.76 and entrapment efficiency 86.99% ± 1.90. Better results were shown by nanoparticles incorporated into contact lenses when compared to drug solution-loaded lenses with respect to the equilibrium swelling index and transmittance. The *in vitro* release indicated more bioavailability and sustained drug profiles (84.33% ± 0.34 of drug release over a period of 12 days) as compared to drug solution-loaded lenses (89.282% ± 0.900 of drug release over a period of 3 days). *Ex vivo* transcorneal permeation studies showed more permeation (6.75% ± 0.170) through contact lenses as compared to marketed eye drops (3.03% ± 0.088).

Conclusion: This research demonstrates the beneficial results of drug-laden contact lenses to serve as a better medium for the continued delivery of ocular drugs without affecting the physical and optical characteristics of the lens content.

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Preliminary establishment of *Musa acuminata* Linn mucilage as pharmaceutical excipient in tablet formulation

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Background and Rationale: The present research work has been enforced by the utilization of banana mucilages. These are biocompatible, biodegradable, economical, great structural versatility and preferred polymers due to their low toxicity, easy availability, minimum regulatory approval issues. The objective of this research study was to isolate, purify and investigate the tablet binding property of the mucilages from *M. acuminata* and examine the various physicochemical and pharmaceutical properties, and the comparison of *in vitro* drug release profiles with semi synthetic or synthetic polymers. The isolated mucilage may provide an alternative to other natural polysaccharide or their synthetic counterparts to design and formulate appropriate advanced drug delivery systems for conventional or modified drug release.

Methods: (A) Isolation of Mucilage from Bananas: The polysaccharide mucilage was isolated from *Musa acuminata* by heat assisted aqueous extraction technique. **(B) Preparation and Compression of granules into 250 mg Aceclofenac Tablets:** Nine optimized batches of aceclofenac tablets were formulated by a technique of wet granulation. The die cavity having diameter of 11 mm and punches having flat faces was implemented in a rotary tablet compression machine having 10 stations. **(C) *In vitro* release profile of Aceclofenac tablets comprising banana mucilage as binder:** Dissolution investigation of nine formulated batches of aceclofenac tablets was enforced by utilizing USP- Type II dissolution apparatus (Paddle Type), which is functionalized at 50 rpm speed in phosphate buffer solution (pH 6.8), and regulated at temperature of 37±0.5°C.

Results and Discussion: This investigation results demonstrated that the release of aceclofenac from all nine batches of tablets to be above 80% within the duration of 30 min. The results of dissolution data of optimized batches (F1 and F2) were analyzed using Kitazawa plots. The time T_{80} , T_D of F1 emerged to be 25 min and 15 min respectively and time T_{80} , T_D of F2 batch emerged to be 25 min and 10 min respectively.

Conclusion: The investigational results generated in this research study establish physicochemical, pharmaceutical and structural features for the first time of the mucilage polysaccharides isolated from the fruit of *M. acuminata* for successful application as a natural excipient in food and pharmaceutical industries. The mucilage isolated from bananas can be safely used as a binder in the conventional tablet formulations at 35-40 mg concentration.

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Understanding the *in vivo* behaviour of celecoxib-sodium polymeric amorphous salt solid dispersions using biorelevant dissolution

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Background and Rationale: Recent studies show that amorphous salts and their polymeric solid dispersions enhance *in vitro* solubility and dissolution rate in buffers, improve the *in vivo* pharmacokinetics, and increase physical stability.[1,2] However, mechanisms on how these amorphous salt solid dispersions (ASSDs) behave inside the body remain elusive. Biorelevant dissolution, which has quite recently been increasingly used to understand the intraluminal behavior of supersaturating drug delivery systems, offers a good way to explore the *in vivo* performance of our formulations. Accordingly, we investigated the *in vivo* behavior of celecoxib-sodium ASSDs (with PVPVA and Soluplus as the polymers) using this approach.

Methods: A) Generation of amorphous formulations: The ASSDs and ASDs were prepared by spray drying with optimized parameters. The drug-to-polymer ratio was 6:4 (% weight by weight basis) and the drug-to-counterion ratio was 1:1 (stoichiometric basis).

B) *In vitro* dissolution studies: The dissolution studies were conducted using USP Type II apparatus containing 500 mL biorelevant media (FaSSGF and FaSSIF V1) set at 37±0.5 ℃ and 75 rpm. 5 mL aliquots were withdrawn at predefined time points, and an equal volume was replenished to maintain sink conditions. The samples were quantified using a validated analytical method.

C) Solubility studies: The solubility studies were carried out for both the crystalline and amorphous forms of the drug in both biorelevant media. The concentration obtained after 24h was reported as the crystalline solubility, whereas the onset of liquid-liquid phase separation from the supersaturated solution of celecoxib was reported as the amorphous solubility.

Results and Discussion: The ASDs with PVPVA showed the highest release in both FaSSGF and FaSSIF V1. Also, a large difference was obtained between the crystalline and amorphous solubility of celecoxib in both media. Moreover, the ASSDs with Soluplus released lower amounts of the drug than those with PVPVA, possibly due to Soluplus' interaction with lecithin in FaSSIF V1. Several other insights could then be obtained. First, the polymer type affects the maximum concentration obtained in both media. Second, in the gastric environment, the ASSDs do not show any significant performance improvement ($p>0.05$) over the crystalline drug. Third, the ASDs show a higher release ($p<0.001$) than the corresponding ASSDs. Moreover, none of the amorphous formulations release drugs to an extent that liquid-liquid phase separation occurs. Lastly, future studies on salt disproportionation and recrystallization could confirm the mechanism for the peculiar profile of celecoxib-sodium-PVPVA ASSD in FaSSIF V1.

Conclusion: Biorelevant dissolution provides significant insights into the *in vivo* behaviour of celecoxib-sodium polymeric ASSDs. The ASDs show a better dissolution performance than the corresponding ASSDs, and none of the amorphous formulations undergo liquid-liquid phase separation in the biorelevant media.

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A Modified Alternate *In Vitro* Dissolution Study for The Polysaccharide Based Colon Targeted Drug Delivery Systems Using Probiotic Cultures

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Background and Rationale: In the case of polysaccharide-based colon targeted dosage forms, an alternate simulated colonic fluid (SCF) has already been reported using probiotic cultures as an alternative to animal sacrifice. However, instead of using the earlier reported complex continuous increment of dissolution media volume and pH adjustment starting with 200 ml at pH 1.2 for initial 2 hrs, then adjusted to 900 ml at pH 6.8 for next 3 hours and finally adjusted to 900 ml pH 7.4 and added with 100 ml of bacterial culture or faecal/caecal content to make final 1000 ml of SCF up to 18 hours at 100 rpm and 37 ± 0.5°C in a USP Type-I *in-vitro* dissolution testing apparatus[1], a simplified alternate method with 900 ml of pH 1.2 for the initial 2 hrs, then replaced with 900 ml of pH 6.8 for the next 3 hrs, followed by replacing it with 900 ml of pH 7.4 SCF along with 100 ml of FTM containing probiotic cultures i.e., total 1000 ml of pH 7.4 SCF containing colonic bacterial enzymes for up to 18 hrs at 100 rpm and 37 ± 0.5°C in a IP type-II *in-vitro* dissolution testing apparatus was evaluated. A pectin and ethyl cellulose coated otilonium bromide loaded multiparticulates were used as the colon targeted dosage form.

Methods: A) Preparation of coated drug loaded pellets: The drug otilonium bromide was fast loaded on the nonpareil sugar seeds (#30) using a binder solution of PVP-K30 in (70:30) isopropyl alcohol and water. The drug loaded pellets were coated with a mixed polymeric coating solution of ethyl cellulose and high methoxylated pectin in (40:60) water-acetone. Any possible drug-polymer interactions were checked in-prior using FT-IR and DSC[2].

B) *In vitro* release studies: *In-vitro* release study of the capsules containing coated multiparticulates was conducted using IP *in vitro* dissolution apparatus (type –II basket) at 100 rpm at 37± 0.5°C. Dissolution studies were performed sequentially in 900 ml of 0.1 N HCl at pH 1.2 for 2 hrs (simulated gastric fluid), 900 ml of Phosphate buffer pH 6.8 (simulated intestinal fluid) for next 3 hrs. Then in 900 ml of Phosphate buffer pH 7.4, 100 ml of biomix-1 culture in FTM was added, purged with CO_2 for 10 minutes as the 1000 ml of simulated colonic fluid and *in vitro* dissolution was conducted up to 18 hrs in this SCF.

Results and Discussion: No major drug-polymer incompatibilities were observed both in the FT-IR and in DSC studies. The release of less than 5% drug in the SGF after 2 hours and less than 20% drug in SIF after 5 hours and the release of most of the drug, once the formulations came in contact with the SCF as well as release patterns and kinetics were found to be as per with the previous studies using earlier methods.

Conclusions: To mitigate the time-consuming in-between pH and resulting volume adjustments during the earlier reported processes, this method was found to be at par with the earlier studies as well as far more simple, easy and suitable.

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Biocompatible Phospholipid-based Nano Vesicular Drug Delivery System of Ketoprofen: Development, *In vitro* Release and *Ex vivo* Permeation Studies

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Background & Rationale: Oral route is considered as one of the most convenient modes of drug administration. However, it involves multiple challenges. Thus, we need to adopt alternative drug delivery routes. The present work describes systematic development of biocompatible phospholipid based Permeation Enhancing Nano Vesicles (PENVs) for improving delivery of ketoprofen through topical route.

Methods: Screening of different components and process parameters were carried out for their suitability to prepare the nano-vesicles (NVs). Systematic optimization using central composite design with two factors, i.e., amount (% w/w) of phospholipid and ethanol and at three levels. The optimized NVs were further loaded with different terpenes to prepare the PENVs. Finally, PENVs were incorporated in a gel base. Developed PENVs and gel formulation were characterized and evaluated. The *in-vitro* release and *ex-vivo* permeation studies were carried out on Franz diffusion cell assembly using semi permeable membrane and rat skin, respectively.

Results & Discussion: The preliminary studies indicated suitability of hydrogenated phospholipid for the development of ketoprofen NVs. Optimized NVs were found to exhibit 69% entrapment efficiency, 51% transmittance, 328 nm mean vesicle size and polydispersity index of 0.25. Rheological analysis indicated pseudoplastic flow and smooth texture of the vesicle gel formulation. *Ex vivo* permeation studies indicated higher penetration (0.43 times) and skin retention (4.26 times) of drug from the optimized PENVs gel *vis-à-vis* conventional gel. Stability studies confirmed that cold storage is the best suitable condition for the vesicle-gel.

Conclusion: The study pertaining to the development of a stable PENV gel formulation indicated its robust and biocompatible nature, along with improved drug permeation. Systematic optimization methodology using experimental designs helped in identifying the best possible formulation with desirable properties.

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Discriminatory Dissolution study of nanocrystal loaded microparticles for fixed dose combination of simvastatin and ezetimibe

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Background and Rationale: Nanocrystals loaded nano embedded microparticles (DNEM) of the fixed dose combination of simvastatin (SIM) and ezetimibe (EZE) were generated using a proprietary technique, NanoCrySP ® . It is a bottom-up process wherein the drug, crystallization-inducing excipient and stabilizer are spray dried from a solution. The resulting solid powder of DNEM (0.5 to 20 µm) consisted of drug nanocrystals (<1000 nm) dispersed in a matrix of the excipient. Size determination of embedded crystals is challenging using techniques such as Zetasizer and microscopic techniques, as the excipient needs to be dissolved to form a suspension of drug nanocrystals for analysis. A single discriminatory dissolution method was developed to differentiate % SIM and EZE release from DNEM, nano- and microsuspensions. It was aimed to provide performance-based evidence and corroborate similarities or differences in crystal size of SIM and EZE in DNEM determined using techniques like Zetasizer, SEM and TEM.

Methods: (A) Preparation and characterization of DNEM: DNEM were generated by spray drying SIM and EZE in presence of mannitol (MAN) as crystallization inducing excipient and Tocopheryl polyethylene glycol succinate (TPGS) as stabilizer, in ratio 24:6:69.9:0.1% respectively, at parameters as follows- feed flow rate-1.5ml/min, inlet temperature-140˚C, atomization pressure-1.2kg/cm^2 , vacuum-95 to 100 mmWC using nozzle with internal diameter of 0.7mm in co-current spray mode. DNEM were characterized for optimal product characteristics such as crystallinity, crystallite size of embedded nanocrystals and assay.

(B): Discriminatory dissolution study: Media screened were- water containing 0.05% SLS, sodium phosphate buffer pH 7, sodium phosphate buffer pH 7 containing 0.01, 0.025 and 0.25% SLS. A USP Type II dissolution apparatus was used with 900 ml media maintained at a temperature of 37±0.5˚C and 50rpm. Nanosuspension of DNEM (167mg) and microsuspension of physical mixture of SIM (D 90 - 15.3µm) and EZE (D 90 - 4.3µm) in ratio 40 and 10 mg were prepared in 2 ml of 0.5%w/v sodium carboxymethyl cellulose for dissolution study. Similarly, a nanosuspension of SIM (D 90 - 668nm) and EZE (D 90 - 299nm) was prepared using media milling. Samples withdrawn at various time points were filtered through a 0.1µm filter and analyzed in HPLC. Dissolution profiles were compared, wherein, similarity factor (f2) greater than 50 (50–100) signified 'sameness' of the two profiles and less than 50 signified 'difference'.

Results and Discussion: The crystal size of SIM and EZE in DNEM was found out to be 600nm each using scanning electron microscopy and Zetasizer. Buffer pH 7 containing 0.025% SLS provided size based discrimination of SIM and EZE release from DNEM, nanosuspension and microsuspension. The f2 values for release of SIM and EZE from DNEM vs. nanosuspension and DNEM vs. microsuspension were 79.02, 72.14, 42.70 and 43.99, respectively. This indicated that the crystal size of SIM and EZE in DNEM were in the nano range and close to nanosuspension.

Conclusions: Discriminatory dissolution method can serve as an invaluable tool for establishing functional equivalency of particle size in DNEM formulations as they pose challenges in direct determination of particle size distribution.

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Dissolution studies on HSA nanoparticles encapsulating Ropinirole for targeted delivery in brain to treat ischemic stroke

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Background & Rationale: Stroke is the second leading cause of mortality and morbidity. Ischemic stroke (87%) is the commonest form of stroke. The reperfusion event is essential for protecting brain tissue in the penumbra, accomplished through rt-PA therapy. Reperfusion, however, exacerbates ischemic damage owing to excess ROS accumulation and Ca^{2+} overload in mitochondria, thus, favouring the opening of mitochondrial permeability transition pore (mtPTP). This pore releases various apoptotic factors eventually leading to cell death. Hence, in this work, Ropinirole hydrochloride (Rop) was repurposed on the basis of its anti-apoptotic potential aiming to inhibit the opening of mtPTP for the possible treatment of ischemic stroke and reperfusion injury (I/R injury). Also, we propose to achieve the targeted drug delivery of Rop due to its low bioavailability (~50%) by developing gamma-L-glutamyl-cysteine decorated HSA nanoconstructs entrapping Rop *via* receptor-mediated endocytosis.

Methodology: The Rop was encapsulated in HSA nanocarriers (Rop-NPs) *via* desolvation method[1]. Thereafter, gamma-L-glutamyl-cysteine was adsorbed on Rop-NPs (C-Rop-NPs). The *in vitro* release study of Rop from Rop-S (free drug solution) and C-Rop-NPs was investigated employing dialysis bag method in phosphate buffer at pH-4.0 and 7.4 in order to simulate the physiological conditions of brain and plasma, respectively[2].

Results and Discussion: The *in vitro* release study showed that in comparison to Rop-S, where 91.36±2.74% and 104.15±3.42% of Rop was released within an hour, C-Rop-NPs exhibited initial rapid release (47.95±1.43% and 40.34±0.48% in 0.25 h) followed by sustained release of the remaining drug over 5 hour at pH-4.0 and 7.4, respectively. These results suggested that there was no significant difference in cumulative percent drug release at the physiological pH-7.4 and acidic pH-4.0 identifying with the stroke progression, respectively. Additionally, the biphasic release profile of Rop offers a unique benefit as the initial drug release shall provide desired therapeutic concentration immediately hence, salvaging the penumbra region as quickly as possible whereas sustained delivery could sustain the therapeutic action for longer duration.

Conclusions: Tailor-made surface engineered C-Rop-NPs could be conferred as a promising tool for offering high clinical potential in ischemic brain *via* targeted drug delivery even at lower doses. Furthermore, the prolonged release of drugs might contribute to low dosing frequency thereby, reducing systemic toxicity. This might help in generating cost-effective novel nanoformulation against I/R injury and consequently, adhering to patient compliance.

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Evaluation of release mechanism of pH-responsive Fluocinolone Acetonide nanogels for psoriasis

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Background & Rationale: Psoriasis, a chronic inflammatory multi-organ disease is known to be the most prevalent autoimmune disease in humans. Due to the variations in the pH on the surface of skin (5-6) and psoriatic lesions (pH 4-5), pH-responsive nanogels will play an effective role. Here, we have formulated nanogels containing Fluocinolone Acetonide (FA) [1] and a pH-sensitive polymer N, N, N- Trimethyl Chitosan (TMC) [2]. The aim of this study is to evaluate the pH-responsive behaviour of our nanogels (FA-NG) and its drug release mechanism.

Methods: *In vitro* drug release studies of FA-NG: *In vitro* drug release studies of FA-NG were conducted at pH 4.0 (psoriatic skin) and pH 6.0 (healthy normal skin) by cellophane membrane barrier method at 37°C and 50 rpm. The nanogel was dispersed in 10 mL of pH 4.0 buffer and pH 6.0 separately, which formed the donor fluid. The receptor fluid was a mixture of pH 4.0 buffer and PEG in the ratio 7:3. Sink condition was maintained in all the experiments. Samples were withdrawn at predetermined intervals from receptor fluid and replaced with fresh buffers. The released drug in each time point was quantified spectrophotometrically at 239 nm. Model fitting into Higuchi, Hixon Crowell and Korsmeyer Peppas was done.

Results and Discussion: FA-NG released higher FA at pH 4 than pH 6. About 58% of FA was released at 12th h from the nanogels and was found to increase up to 78% at 24th h in pH 6. In pH 4, FA release was higher with 69% of FA being released at 12th h from the nanogels, and was found to increase up to 85% at 24th h. This clearly highlights the pH-responsive behaviour of FA-NG and their increased drug release at psoriatic skin. Hixon crowell was found out to be the best fitting model with R^2 0.9383.

Conclusions: The higher release of FA-NG at pH 4 (psoriatic skin) is attributed to increased swelling of the FA-NG due to the protonation of free amine groups in TMC. These studies demonstrate the potential of FA-NG for effective treatment of psoriasis.

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Exploring SMVT Assisted Biotinized Pluronic/Bilesalt Mixed Micelles for Improving Oral Bioavailability of Insulin

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Background and Rationale: Every year the world witnesses an upsurge in the number of patients suffering from diabetes and it is predicted that the rate of mortality due to diabetic complications would double by the end of 2034[1] . Such statistics keep a burden on underdeveloped and developing countries to increase expenditure in the healthcare system and they are unable to provide affordable treatment access to patients. Insulin is the most widely used biomolecule for controlling blood sugar levels and available as an injectable for subcutaneous administration. However, the subcutaneous route has its own limitations like patient non-compliance, lipid dystrophy and peripheral hyperinsulinemia. Oral delivery strategies are becoming popular compelling needs to circumvent above mentioned constraints. However, physicochemical properties of Insulin like poor permeability and instability in GI fluids keep onerous challenges to delivering it orally[2]. In this work, we developed targeted Pluronic/bile salt mixed micelles to improve permeability, gastrointestinal stability and oral therapeutic efficacy of Insulin.

Methods: A) Biotinized Pluronic/modified bile salt mixed micelles: Biotinized Pluronic has been prepared for achieving marketability to Small Multi Vitamin Transporters (SMTV). Bile salts (sodium deoxycholicacid) are conjugated with amino acids (glycine and lysine) to emphasize the formulation aspect of micelles. Specific synergy effects of pluronic are obtained when pluronics are mixed with bile salts. The developed formulations exhibited particle size < 300 nm along with % EE >70%.

B) *In-vitro* release studies: *In-vitro* release studies were performed by using dialysis bag method (Cellulose acetate membrane, molecular cut off: 12-14 kD). *In vitro* studies of prepared formulations were carried out in three different media SGF (pH 1.2), SIF (pH 6.8) and PBS (pH 7.4) to mimic the physiological conditions upon oral administration. Formulations equivalent to 1 mg of Insulin were diluted with a small amount of media and filled in a dialysis bag. The dialysis assembly was then suspended for incubation at 37±2°C with continuous shaking at 80 rpm in the shaker bath for 2 h in SGF. Further the assembly transferred into SIF and incubated for 6 h and finally to PBS for 24 h. Aliquots are collected at predetermined time points (equal volume of fresh buffer was replaced to maintain sink conditions). Withdrawn samples were filtered through 0.45 µm filters and analysed for Insulin content by validated RP-HPLC method.

Results and Discussion: *In-vitro* release profiles of prepared formulations ($P>0.05$) showed ~12% release in SGF after 2 h and ~20% after 6 h in SIF and ~22% in PBS which led to cumulative release ~54%. Whereas, free insulin is completely released (~ 100%, $P\leq 0.01$)) within 6 h. Different mathematical models were applied for establishing drug release mechanisms. It revealed that insulin released from formulations followed Higuchi kinetics.

Conclusion: In nutshell, the biotinized targeted Pluronic/bile salt mixed micelles approach could be impelled as a promising strategy in improving the oral deliverability of "Injection Only" Peptide, Insulin.

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Phospholipid Complex of Ferulic Acid with Enhanced Dissolution Profile: Exploring Drug Release Kinetics using Mathematical Modeling

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Background & Rationale: Dissolution is considered a pivotal tool in the development of oral drug products or novel drug delivery systems, be it innovators or generics. Drug release kinetic modeling tends to unravel scientific miniature underlying the mechanisms of drug release from the corresponding devices. Therefore, the current studies were undertaken to demonstrate the application of drug release kinetic modelling in the development of phospholipid complex of ferulic acid (FA), a BCS Class IV bioactive reported to exhibit poor and variable oral drug absorption.

Methods: Phospholipid (PL) complex was prepared by solvent evaporation method. The stoichiometric ratio for the synthesis of complexes was determined using Job's method. *In vitro* drug release studies were carried out employing a dialysis membrane method in phosphate-buffered saline pH 7.4 at 37ºC at 100 rpm. The dissolution profiles of pure FA and the complex were analysed for drug release mechanics using first-order, zero-order, Hixon-Crowell cube-root, Weibull, Baker-Lonsdale and Korsmeyer-Peppas models.

Results and Discussion: The apt composition for the most stable PL complex was found to be 2:7 as per Job's method. Hydrogen bonding was found to exist between the hydroxyl of drug and amide group of phospholipid as inferred from FTIR and NMR studies. Further XRD studies corroborated the synthesis owing to a substantial decrease in crystallinity. NMR studies highlighted interaction due to shift of OH and COOH groups. The dissolution profiles of PLC exhibited distinct superiority with enhanced and extended drug release characteristics (85.4±1.2%) vis-à-vis pure drug (19.3±2.4%) and physical mixture (57±1.4%) at 24 h. An improved dissolution rate (3.99%/min) was observed vis-a-vis pure FA (0.88%/min) and its physical mixture (2.78%/min) respectively. Varying degrees of fitness were obtained with the different mathematical models to the *in vitro* drug dissolution data, indicating the corresponding outcomes. Data fitting using Korsmeyer-Peppas model indicated non-Fickian drug release with value of n as 0.773.

Conclusion: Overall, the formulated PLCs successfully demonstrated the enhanced as well as extended-release profile *vis-a-vis* that of the pure ferulic acid.

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Predicting Pharmacokinetic Variability of Voriconazole in Adults and Pediatrics as a Function of Bile Salt Using *In Vitro* Dissolution Studies and PBPK Modelling

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Background & Rationale: Voriconazole is a potent triazole antifungal agent and displays wide variability in the pharmacokinetics between adults and children [1,2]. In the present study, PK-Sim software has been employed to assess the pharmacokinetic variability of voriconazole between adult and pediatrics with particular focus on the integration of the biorelevant *in vitro* dissolution data.

Methods: A) Development of adult and pediatric PBPK model: Initial adult and pediatric PBPK models were developed employing PK-Sim (version 9.1; Bayer Technology Services GmbH, Leverkusen, Germany), a commercial PBPK software tool. A perfusion-limited model incorporating adult clearance values and physiological characteristics was created first. Similarly, a pediatric model was created by extrapolating the adult model, incorporating the pediatric clearance values and physiological characteristics. Simulations yielded pharmacokinetic parameters were compared against published values and the models were validated using the percentage error.

B) Incorporating *in vitro* biorelevant dissolution data in developed adult and pediatric PBPK models: Experimentally obtained *in vitro* dissolution profiles of voriconazole in both QC buffer and biorelevant media were directly incorporated as input into the developed adult and pediatric model. Parameters such as pH (1.1-6.8), fluid volume (500 ml & 900 ml) and bile salt concentrations (1.5mM & 3mM) were incorporated in the model to closely relate with the *in-vitro* dissolution experimental conditions. Simulated plasma concentration time profiles obtained by incorporating the biorelevant dissolution data (performed in lab) were compared to the baseline models to assess the effect of bile salt variability of pharmacokinetics between adult and pediatrics.

Results and Discussion: All adult and pediatric oral models predicted the pharmacokinetic parameters that corresponded with the observed values within a range of 4-30 % prediction error. The errors for predictions of all pharmacokinetic parameters were within the accepted limit of <50 %, indicating the validity of the model. It was found that the simulated profile for the adult model based on the biorelevant dissolution data was showing 3-fold decrease in plasma concentrations, AUC (Pred-525.55 µmol*min/L vs. Obs-1519.24 µmol*min/L) and Cmax (Pred-1.89 µmol/L vs. Obs-4.28 µmol/L). Still, the model needs refinement to get the predicted values close to the observed values. In the pediatric model, the hepatic intrinsic clearance was more profound. The predicted plasma concentrations for the pediatric model are anticipated to be low as compared to the adult model.

Conclusions: Variation in GI composition particularly in context with the bile salt variability affects the plasma concentrations of Voriconazole. Thus, we can conclude that by performing *in-vitro* dissolution studies in biorelevant media for adult and pediatrics and incorporating *in vitro* dissolution data in PBPK model can predict the pharmacokinetics parameters related to specific population. Such an approach can help in predicting pharmacokinetics studies for specific populations and may reduce the cost of *in vivo* pharmacokinetic studies.

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Supersaturated Self-Emulsifying Drug Delivery System for Improving Oral Bioavailability of Quercetin

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Background and Rationale: Conventional SEDDS exhibits limited drug solubility in the pre-concentrate phase making them less desirable for oral delivery[1] . Hence, we aim to develop supersaturated SEDDS (sSEDDS) with high drug loading in pre-concentrate along with rationally screened precipitation inhibitor (PI). Here, Quercetin (QT) is selected as a model drug. The QT-sSEDDS enables QT to extend and maintain the supersaturated (metastable) state by inhibiting nucleation rate and crystal growth formation when exposed to the aqueous environment. This allows a higher amount of QT to be in solubilized form and exhibit improved oral bioavailability[2].

Methods: Drug loading and screening of PI was performed based on pre-concentrate solubility and apparent solubility profile to formulate QT-sSEDDS. Physicochemical characterization for QT-sSEDDS was performed to evaluate droplet size, drug release and functional stability. Optimised QT-sSEDDS was assessed for its GI fluids, physicochemical and storage stability. Lipid digestion rate and solubilisation potential of QT-sSEDDS was evaluated using pH-stat lipolysis method. *In vitro* biological characterization (uptake, cytotoxicity and apoptosis) in HeLa, A549 and Caco-2 cells was performed. Finally, *in vivo* pharmacokinetic profile was examined in Sprague Dawley rats.

Results and Discussion: Based on pre-concentrate solubility and apparent solubility profile, drug loading of 60 mg/g and HPMC E5 (2.5% w/w) as PI was optimised to form QT-sSEDDS. The formulation revealed spherical droplets of size 127±25 nm with PDI of 0.45±0.11. The QT-sSEDDS was able to maintain the DPPH scavenging ability of QT indicating its functional stability. The QT-sSEDDS was found to be stable in SGF and SIF in terms of their size and PDI. Further, 3 month stability data (as per ICH guidelines) also confirmed that the QT-sSEDDS were stable. The formulation revealed ~75, 85 and 80 % drug release in SGF, SIF and phosphate buffer respectively. The pH-stat lipolysis correlated the volume of NaOH required to neutralize the liberated fatty acid with the extent of lipid digestion. QT- sSEDDS and other counterparts revealed almost similar lipid digestion rate as lipid components were kept unchanged. The solubilisation potential using pH-stat was evaluated for 1 h and demonstrated a higher aqueous drug fraction for QT-sSEDDS than QT-sSEDDS without PI. This indicates that PI in QT-sSEDDS was able to maintain the supersaturated state in lipolysis media which may drive the absorption flux. In cell culture studies the QT-sSEDDS revealed significantly higher uptake (qualitative and quantitative) in all the cell lines in comparison to naïve groups. Moreover, QT-sSEDDS exhibited an improved cytotoxic effect by exhibiting ~1.9 fold reduction in IC 50 values in HeLa and A549 cells. Similarly, QT-sSEDDS exhibited higher apoptotic potential in both the mentioned cancer cell lines in comparison to free QT. This is due to the higher internalization ability of sSEDDS which allows higher cytosolic QT level. However, Caco-2 cells revealed >80% viability at all tested concentrations indicating the biocompatibility of the developed system. The *in vivo* pharmacokinetic study showed ~2.2 increase in C max for QT-sSEDDS in comparison to conventional QT-SEDDS. Further, QT-sSEDDS exhibited ~ 2 and 1.7 fold increase in AUC compared to conventional QT-SEDDS and QT-sSEDDS (without PI).

Conclusions: Overall this work demonstrated that high drug loading and incorporation of PI improved the biopharmaceutical performance of poorly water-soluble drug i.e. QT. Thus, sSEDDS can be explored further for oral delivery of other poorly soluble drugs.

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Topical Quercetin SMEDDS loaded hydrogel for improved efficacy in Diabetic foot ulcer

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Background & Rationale: Diabetic foot ulcer (DFU) occurs in nearly 35% population of diabetic population. The top priority in treating DFU is to avoid amputation. Up to 85 percent of diabetic foot-related amputations can be prevented with a holistic approach. Owing to the long cycle and high cost with respect to wound treatment, developing efficacious and economical treatment is urgent and imperative in clinical practice. Quercetin (QCT) is a polyhydroxy flavonoids found in various plants. It possesses wide pharmacological activities therefore shows high medicinal value. Importantly, QCT can improve common wound healing by increasing fibroblast proliferation, while decreasing fibrosis and scar formation. With both anti-oxidation and anti-inflammatory properties, QCT is a beneficial therapeutic candidate to benefit wound healing process. Although the log P (1.82 ± 0) of QCT is theoretically adequate to permeate the skin, it's rather limited solubility in water (0.5l g/ml) is believed to hinder its topical application. With an attempt to improve healing rate and provide a formulation for effective local wound care and control infection so as to reduce the amputations. Aim of this study is to develop and optimize QCT SMEDDS loaded hydrogel for effective treatment of DFU.

Methods: Solubility of QCT in different oils, surfactants and co-surfactants was assessed in order to prepare SMEDDs of QCT using saturation solubility method and constructing pseudo ternary phase diagrams. Optimised QCT SMEDDS was converted into hydrogel using Carbopol 934P. Optimized formulation was characterized by self-emulsification efficiency study, droplet size, and polydispersity index, zeta potential, *in vitro* drug release, texture analysis and spreadability, *ex vivo* permeation study using egg membrane, Strat-M, pig ear skin and excised rat skin**.** *In vitro* antimicrobial activity against *S. aureus* and *E.coli* was also assessed on seeded agar plates. *In vivo* wound healing activity of prepared formulation was performed on Streptozotocin (STZ) diabetic induced Swiss albino mice and compared with standard marketed gel used for wound healing. Confocal Laser Micro Spectroscopy was done to check the permeation and dispersion through the skin.

Results and Discussion: The optimized formulation exhibited mean particle size of 101±*3.5* nm with PDI 0.172 and zeta potential –29.2 mV.The solubility studies showed an improvement in solubility of the *ex vivo* permeation studies 6 fold increase as compared to QCT. The antimicrobial studies concluded that QCT showed better antimicrobial efficacy when compared with plain QCT and marketed gel against broad-spectrum bacteria including *E. coli* and *S. aureus*. The *in vivo* studies including wound contraction and histopathological examinations presented that topical application of QCT emulgel enhanced diabetic wounds healing faster than marketed gel and control.

Conclusion: The dissolution profiles of QCT SMEDDS exhibited distinct superiority with enhanced drug release characteristics (89.3±2.6%) vis-à-vis pure drug (20.3±2.4%) at 24 h. Overall, the study describes QCT SMEDDS loaded hydrogel with significantly improved dissolution profile and *in vivo* activity as compared to the plain drug.

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3D Printed Hollow Microneedles Array using Stereolithography for Efficient Transdermal Delivery of Rifampicin

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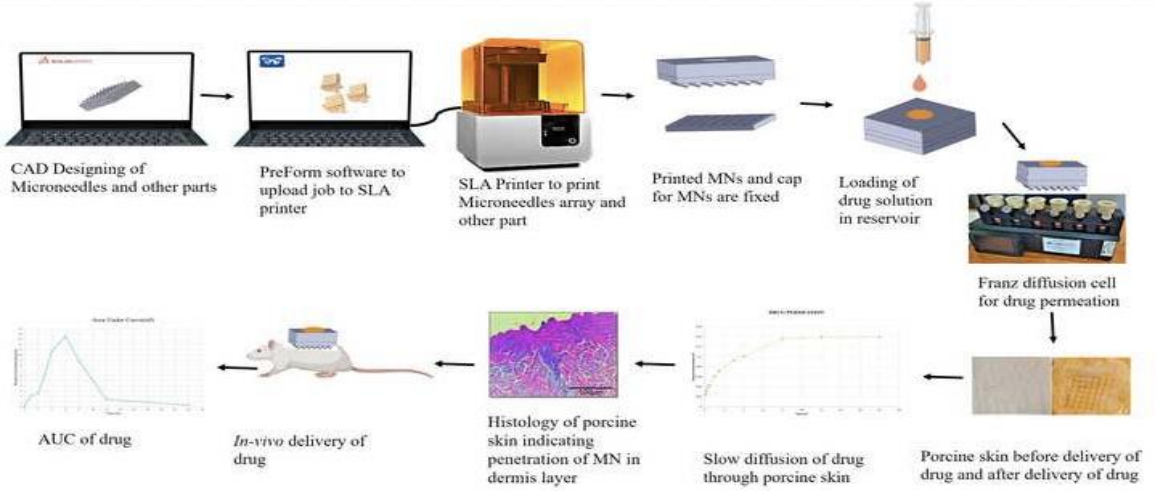
Background & Rationale: A side-open hollow microneedles (HMNs) array design is investigated for the transdermal delivery of high molecular weight antibiotics i.e., rifampicin (RIF, Mw 822.94 g/mol) which suffers from gastric chemical instability, low bioavailability, and severe hepatotoxicity[1].

Methodology: A 3D printed assembly of HMNs array, conjoined with a reservoir void, was designed and additively manufactured utilizing stereolithography (SLA) mediated 3D printing technology[2,3] utilizing a proprietary class-I resin. The HMNs array was utilized for transdermal delivery of high molecular weight RIF. HMNs morphology was designed with sub-apical holes present in a quarter of the needle tip to improve its mechanical strength and integrity of the HMNs array.



Results & Discussion: The HMNs array was fabricated & validated through optical microscopy and electron microscopy to ascertain the print quality and uniformity across the array. The system also exhibited sufficient mechanical strength for failure and penetration analysis. The *ex-vivo* permeation and consequent transport of RIF across porcine skin were observed & found slow-diffusion mediated RIF permeation across skin membrane.

Conclusions: Finally, *in vivo* examinations of RIF administration through the MNs reservoir system in SD rats revealed efficient penetration and desired bioavailability. Overall, enhancements in the HMNs array design showed marked improvement in the printability and RIF delivery aspects from the HMNs as well.

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A Systematic Approach for Development of Sustained Release Bilayer Matrix Tablet of Aceclofenac

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Background & Rationale: The design of modified release drug product is usually intended to optimize a therapeutic regimen by providing slow and continuous delivery of drug over the entire dosing interval whilst providing greater patient compliance and convenience [1] . Bi-layer tablets consist of one immediate release (IR) layer for loading dose with the aim of reaching a high serum concentration in a short period of time; while the sustained release (SR) layer is designed to maintain an effective plasma level of the drug for a prolonged period of time [2]. Aceclofenac is classified as a BCS Class II drug (low solubility and high permeability). Its absorption is dissolution rate limited leading to variable bioavailability. Its biological half-life (3-4 h) makes it suitable for SR products. The aim of this study was to develop a bilayer matrix tablet of aceclofenac, using HPMC and MC as matrix material for controlling the dissolution of the drug. The effect of different formulation parameters on the dissolution of drugs was studied using statistical designing of experiments.

Methods: Compressed bi-layer matrix tablets were manufactured with granules prepared by wet granulation method. The drug content for IR and SR layer was 50 mg and 150 mg respectively. Lactose was used as filler for IR layer, whereas Hydroxy Propyl Methyl Cellulose (HPMC) with Ethyl Cellulose were used as low-cost biocompatible polymer for SR layer. Sodium Starch Glycolate (SSG) was used as superdisintegrant in the Immediate Release Layer (IR). Starch and PVP K30 were used as binder for the IR layer and SR layer respectively. Composition of both IR and SR layers were optimized with mixer design using Design Expert software. HPMC and EC were independent variables for SR layer whereas starch and SSG were independent variables for IR layer. HPLC method was developed for analysis of drug. Dissolution studies were performed at 37^0C using USP type II apparatus with phosphate buffer (pH 6.8) as dissolution medium. DDSolver program was used for study of drug release kinetics, comparison of dissolution profiles with commercially available product like ZERODOL-CR- 200 MG.

Results & Discussion: The granules had excellent flowability. The optimized 650 mg compressed tablets had hardness of 5 kg/cm2. The drug in the IR layer was released to contribute ~42% drug release within 1 h. ~93% drug was released within 8 h. As per the correlation coefficient, Krosmeyer Peppas was the best fitted model describing the drug release kinetics. The release rate constant was 4.7 and the value of diffusional exponent (n) was 0.5. It clearly indicated that the release mechanism was governed by diffusion only. Upon comparison of dissolution profile with ZERODOL-CR-200 MG the mean Difference factor (f1), and Similarity factor (f2) were 3.46, and 82.73 respectively. Thus, this product was equivalent to the commercially available product.

Conclusions: A Bi-layer matrix tablet of aceclofenac was developed with a systematic approach. Mixture design was successfully applied to find the best composition for IR layer and SR layer individually. The optimized product was equivalent to ZERODOL-CR-200 MG.

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An Experimental Investigation for the Possibility of a Novel Gastro-Retentive Raft Liquid Dosage Form for the Treatment of *Helicobacter pylori* Infection

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Background & Rationale: Peptic ulcers are open sores that develop on the inner lining of the stomach and duodenum and are induced by various non-pathogenic as well as pathogenic factors. *Helicobacter pylori* (*H. pylori*) is a primary pathogen for peptic ulcers[1]. It is reported that absorption of an antibiotic through the mucus layer is more effective for *H. pylori* eradication than absorption through the basolateral membrane [2,3]. The present study aimed to design and develop a novel gastro-retentive raft liquid dosage formulation to prolong gastric retention time and achieve controlled release of the medicament at the site of action.

Methods: The metronidazole-loaded raft formulations were prepared according to Abouelatta et al., 2018 by using ion-sensitive *in situ* gel-forming polymers [4]. The raft formulation was evaluated for various parameters, for instance, rheological property, raft weight, volume, density and buoyancy, *in vitro* floating time and gelling capacity and *in vitro* drug release from raft formulation using standard methodology [5].

Results and Discussion: The metronidazole loaded formulation floated within 1 minute on the liquid surface of the *in vitro* model. The *in situ* gel of all the raft formulations maintained floatation for more than 24 hours. Among the prepared formulations, formulation F5 exhibited results within acceptable limits compared to the other batches of formulations. The *in vitro* drug release was 81.83 %, with a maximum deviation ± 0.54 after 8 hours in 0.1 M HCl. The formulation followed first-order release kinetics, and metronidazole was released by combination of diffusion and erosion mechanisms.

Conclusion: The drug, metronidazole, was released from the dosage form slowly in the stomach. It significantly prolonged the gastric residence time of metronidazole.

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Coated Microneedle For Transcutaneous Delivery Of Cyclosporine: Characterization, *In Vitro* Evaluation And *In Vivo* Anti-psoriatic Efficacy Against Imq Induced Psoriasis

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Background & Rationale: Cyclosporine (CsA) and methotraxate tablets are the first line of prescription products in various autoimmune disorders like rheumatoid arthritis, psoriasis, etc (1). However, CsA metabolite causes irreversible renal damage on long term use. Although, it is the best candidate for subcutaneous administration (2), it is very inconvenient and painful to take CsA injections every week: further acute reactions like chills, fever, body ache, and dyspnoea often occur because of the solvents used for the preparation of the injections. Few attempts have been made for transdermal delivery of CsA. However its high molecular weight (>1000 Da) and skin barrier functions limit its efficient transdermal utility (3). Microneedle array (MN) has been proved to be the most effective technique that combines the beneficial effects of both transdermal patches and a hypodermic needle. Therefore, we aimed to develop microneedle arrays for poke and release of cyclosporine transcutaneously for systemic effect against psoriasis like inflammation.

Methods: A) Preparation of the micromold and CsA-coated microneedle arrays

We used resin and hydrate blend and micron-sized needles for the preparation of the micromold. CsA-coated microneedle arrays were prepared by coating CsA on the PVA needles by micro-molding-cum-solvent casting method.

B) Characterisation: Fabricated MNs were characterised for patch dimensions, strength and hygroscopicity, drug loading, *in vitro* insertion testing, *in vitro* drug release, *ex vivo* skin permeation, MN skin dissolution and cyclosporine skin deposition studies. For *in vivo* anti-psoriatic activity, PASI scoring, spleen morphological assessment and biochemical assessment were performed.

Results and Discussion: Needles were found to be with desired strength and dimensions with 85.14 ± 4.5% drug loading per cm^2 of the patch. MN showed slow moisture gain in the humid condition with good strength for skin penetration (up to 630 µm). More than 60% reduction in the needle length was observed in 30 min of skin insertion. MN showed fast (87% in 60 min) drug release and efficient permeation through the skin layer in 60 min after insertion into porcine skin. The developed MN showed significant reduction in PASI scoring and pro-inflammatory cytokine levels and remarkable reduction in the spleen size. It was found to be stable for 6 months in accelerated stability conditions.

Conclusions: In conclusion, the developed MN array was proved to be a good alternative to the conventional dosage forms and is able to deliver therapeutic amounts of cyclosporine transdermally to the systemic circulation for the treatment of psoriasis-like inflammation for long term use.

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Design of aquasomal drug delivery system of curcumin: *in vitro* dissolution studies

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Background & Rationale: With the search for new approaches in the past few decades, aquasomes have turned out to be one of the most promising novel drug delivery systems. Aquasome is a three-layered self-assembled spherical nanoparticulate carrier system comprising of an inner nanocrystalline solid core, coated with polyhydroxy oligomers, over which adsorption of the drug molecules or the biochemically active molecules takes place.

Methods: Aquasomes were prepared of calcium phosphate inorganic core coated with a cellobiose film and further curcumin was adsorbed over it. After characterization of morphology, particle size distribution, entrapment efficiency and drug loading, in vitro release studies were performed. *In vitro* dissolution studies of curcumin from loaded aquasome into phosphate buffer 6.8 was determined using membrane filter of pore size 0.22µ and compared with that of pure curcumin.

Results and Discussion: Incomplete release was seen in case of pure drug. Enhanced dissolution was observed and the release kinetics of curcumin loaded aquasomes exhibited first order kinetics and the release was gradual. Release studies from aquasomes showed greater dissolution than that of pure drug.

Conclusion: Thus, aquasomal drug delivery system can be used for the enhancement of the solubility of poorly soluble drugs.

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------ ☺ ------

Development of sustained release tablet of diclofenac sodium using water soluble derivative of chitosan

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Background & Rationale:

Sustained release (SR) products are intended for an optimized therapeutic regimen that provides continuous delivery of drug at a predetermined rate over the entire dosing interval. Diclofenac sodium is a BCS class II Non-Steroidal Anti-Inflammatory drug having a biological half-life of 2-3 h. It has a very high affinity for plasma protein (bound fraction ~99%). SR tablets of 50mg diclofenac sodium are commercially available. Chitosan is a popular biopolymer that is soluble at acidic pH (1% acetic acid solution, pH 3.5) [1]. This limits it's use as an excipient in tablets. Chitosan and it's water-soluble derivative have good mucoadhesive properties. The aim of this study was to synthesize carboxy-methylated water-soluble derivative of chitosan and use it in the preparation of matrix tablet as a multipurpose excipient viz binder and drug release modifier..

Methods:

Preparation of carboxymethylated water-soluble chitosan:

0.5 gm chitosan was added in solution of 3 ml double distilled water, 14 ml 2-propanol, and 1.3 gm sodium hydroxide and the mixture was heated at 70^{0}C for 30 min under continuous stirring. 1.5 g chloroacetic acid was added. Stirring at 70 ^{0}C was continued for 4 h. It was kept overnight at room temperature to get a semisolid mass. This was referred to as WsChitosan and was directly used for preparation of tablets.

Designing of experiment and optimization of sustained release matrix tablet:

Mixture design was used for evaluating the effects of WsChitosan and HPMC (total mass 350 mg) on hardness and release of diclofenac sodium from 650 mg matrix tablet. Drug content was 50 mg. Design Expert® 10 was used for designing experiments and analysis of data. Granules were prepared with wet granulation technique. Dissolution studies were performed at 37 ^{0}C using USP type II apparatus. Phosphate buffer (pH 6.8) was used as dissolution medium. Drug was estimated using UV spectroscopy.

Results & Discussion: As the content of WsChitosan was increased from 50 mg to 200 mg per tablet, the hardness of tablets was proportionately increased from 2 kg/cm^2 to 4.2 kg/cm^2. But, there was a dramatic effect on the rate of drug release. The t_{50} (min) remained constant (~310 min) beyond the WsChitosan content of 125 mg. Interestingly, 50 mg chitosan with 300 mg HPMC also had the same effect. But, WsChitosan content within 75 mg to 90 mg caused a dramatic decrease in $t_{50.}$ The tablet with 200 mg WsChitosan was considered an optimized product having 4.2 kg/cm^2 hardness and t_{90} value of 630 min. The drug release kinetics was best fitted to Korsmeyer-Peppas model. The initial burst release was only ~4.573%. The release rate constant was 0.00223. The value of n = 0.984 implies that the release kinetics followed super case-II transport where drug release occurs both by diffusion & relaxation of polymer chain.

Conclusion: Carboxymethylated chitosan is an excellent excipient for preparation of matrix tablet.

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------ ☺ ------

Effect of beta cyclodextrin on buccal permeation of bilayer ketoconazole tablet: *in vitro - ex vivo* correlation

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Background & Rationale: To improve oral bioavailability, buccal mucosa has been identified as a potential site for effective delivery of therapeutic agents to elicit prompt therapeutic action. This study focuses on the fabrication and evaluation of mucoadhesive bilayer matrix system containing β-cyclodextrin (BCD) /hydroxyl propyl β-cyclodextrin (HPBCD) as the complexing agent for improved buccal permeation.

Method: Direct compression technique was used for the production of experimental tablets, which were then evaluated for various physicochemical properties. *In vitro* drug release along with drug permeation studies (*ex vivo* in goat buccal mucosa) were performed in phosphate buffer saline (pH 6.8).

Results: Fourier transform infrared spectroscopy and differential scanning calorimetry data confirmed absence of any significant incompatibility between the drug and excipients. However, minor shifting of some peaks could be assigned to the formation of the KTZ-cyclodextrin complex. X-ray diffraction analysis showed no major changes in crystalline behaviour, however, broadening of some peaks and change in peak heights could be attributed to the formation of weak bonds and inclusion of KTZ into the cyclodextrin cavity. Among the formulations, KHPCD (KTZ with HPBCD) showed higher amounts of drug release than plain KTZ tablets. Correlation between *in vitro* drug dissolution was established with *ex vivo* permeation data.

Conclusion: Improvement in the dissolution rate for the optimized formulation suggested its higher bioavailability potential. After establishing *in vitro ex vivo* correlation, we can predict buccal permeation from the *in vitro* dissolution data. Additional *in vitro-in vivo* correlation studies are needed for future clinical translation.

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------ ☺ ------

Effect of hydrophilic polymers on crystal behaviour and dissolution rate of furosemide with correlation study

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Background & Rationale: Crystallization in presence of polymer(s) has been recognized as one of the vital tools in alteration of the physicochemical properties to improve solubility and dissolution profile of poorly soluble drugs. Objective of this study was to prepare furosemide (a low soluble/low permeable drug) crystal products from different polymeric solutions and to evaluate their crystal properties and dissolution characteristics.

Method: Furosemide crystal products were produced by conventional solvent change technique with required modifications in presence of selected hydrophilic polymeric solutions like hydroxypropylmethyl cellulose, methyl cellulose, carboxymethyl cellulose and poly vinyl alcohol. The changes in physicochemical properties of drug-crystal products were identified by X-ray powder diffraction (XRD), Fourier Transform Infra-red (FTIR), Differential scanning calorimetry (DSC) techniques. The cumulative % rate of drug release was determined by USP dissolution (paddle type).

Results: FTIR study showed minor shifting of characteristic peaks of the recrystallized furosemide but absence of specific peaks for polymers, which were further confirmed from XRD data. Correlation of *in vitro* dissolution with crystal imperfection parameters such as grain size, dislocation density, lattice strain and Full Width at Half-Maximum (FWHM) has also been attempted. Changes in crystal characteristics like dislocation density, strains etc. signified slight amorphization in the polymer-treated crystal products. Among the experimental crystals, HPMC treated crystal products showed a higher percentage of cumulative drug release than other formulations and pure drugs.

Conclusion: In the work, dissolution at 60 min has been linearly correlated with grain size, dislocation density, lattice strain and FWHM. Higher dissolution rate for the selected drug crystal product signifies its improved absorption and oral bioavailability characteristics, which demands further *in vivo* studies for its clinical application.

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------ ☺ ------

Enhancement of dissolution profile and release kinetic study of Atorvastatin in Pharmacosomes

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Background & Rationale: The vesicular systems are the concentric lipid bi-layer assemblies that are formed when certain amphiphilic building blocks are confronted with water. It prolongs the presence of drug molecules in systemic circulation and reduces the toxicity which in turn results in the modification of pharmacokinetics and biodistribution of drugs. Pharmacosomes serve as an alternative to conventional vesicles, have unique advantages over liposome, noisome, transfersomes etc. and may exist as ultrafine vesicular, micellar or hexagonal aggregates. Hence phospholipid complex of drug can be used as a potential tool for improving dissolution rate and bioavailability

Methods: The Pharmacosomes of atorvastatin calcium were prepared using two different ratios (1:1 and 1:2) of drug and phosphatidylcholine in the presence of dichloromethane by solvent evaporation technique. To determine the change in solubility due to complexation, the apparent solubility of atorvastatin calcium and atorvastatin calcium pharmacosomes were determined by adding an excess amount of drug and pharmacosomes to 5 ml distilled water in centrifuge tubes. After attaining equilibrium, the saturated solutions were centrifuged to remove excess drug. The supernatant was filtered, and suitable dilutions were made with the same solvent and then analyzed spectrophotometrically at 247 nm. *In vitro* dissolution studies for atorvastatin calcium pharmacosomes as well as pure atorvastatin calcium were performed in USP dissolution test apparatus II at 50 rpm and at 37±0.5℃ An accurately weighed amount of pharmacosomes equivalent to 20 mg of drug and 20 mg pure drug were placed in 900 ml media (distilled water). Samples (5 ml each) of dissolution fluid were withdrawn at different time intervals and replaced with the equal volume of fresh medium to maintain sink conditions. Withdrawn samples were filtered and diluted suitably and then analyzed spectrophotometrically (Shimadzu UV-1700, Japan) at 247 nm.

Results and Discussions: The drug-soya lecithin compatibility was ascertained by FTIR study. The results of the solubility study showed an almost tenfold increase in solubility of drug in the pharmacosome formulation as compared to pure drug. The free atorvastatin calcium showed only 83.14% drug release at the end of 1.25-hour dissolution study while atorvastatin calcium pharmacosome (1:1) showed 98.11% and atorvastatin calcium pharmacosome (1:2) showed 95.49 % at the same time. The release data was fit into different kinetic models and it has been found to follow Higuchi model with a Fickian release mechanism in all the formulations.

Conclusion: The solubility and dissolution profile of atorvastatin calcium can be enhanced in pharmacosomes formulation and the drug is released following diffusion mechanism from the formulation.

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------ ☺ ------

Evaluating the drug release behavior of terbinafine loaded mesoporous silica nanoparticles (MCM41)

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Background & Rationale: Mesoporous silica nanoparticles (MSNs) have superiority over other nanoparticles owing to their high and tunable surface area (>1000 m^2/g), good biocompatibility, monodisperse particle size, greater pore volume, good thermal stability, tunable pore size, and ease of surface functionalization. Additionally, there has been notable work using MSNs to improve oral delivery of smaller hydrophobic drugs and macromolecules. It is known that the MSNs contain crystalline hydrophobic drugs into their nanometric size pores in an amorphous state during its loading procedure, without bringing any alteration in their lattice energy. In this study, MCM-41 type has been synthesized, followed by determining the effect of encapsulating a BCS class II model drug Terbinafine hydrochloride (TBF) on its *in vitro* release profile.

Methods: Cetyltrimethylammonium bromide (0.25g) was mixed with 125 mL Milli Q water in a round bottom flask and further heated to 80 °C with stirring at 1000rpm on a magnetic stirrer. Sodium hydroxide (0.5mL) was added to the above mixture, followed by tetraethyl orthosilicate (1mL) in divided additions, and the reaction was further heated for the next 2 h. The white precipitates were collected by centrifugation for 15 minutes at 10000 rpm, washed with ethanol and water to remove the unreacted components, dried under vacuum for 12 h, and the final product was calcinated in a muffle furnace by heating at 550 °C for 6 h to remove the surfactant template. The *in vitro* release study was carried out in phosphate buffer saline (PBS) pH 7.4 containing 0.1% tween 80, using a dialysis bag. TBF-MSN equivalent to 1 mg of the drug, and 1 mg pure drug were dispersed in 1mL dissolution media in dialysis bag. The bags were put inside 50 ml of the dissolution media, stirring at 200 rpm using a magnetic stirrer and temperature maintained at 37 °C. The study was carried out for 24 h. The samples were withdrawn at time specific time intervals and analyzed for the drug content using a UV-Vis Spectrophotometer at 282 nm wavelength.

Results and Discussion: The *in vitro* release study data shows that the MSNs could retain the drug in an amorphous state, as seen in the release pattern. From the TBF-MSN, after an initial burst release of 45% of the drug, the cumulative drug release of 99% was seen in a 24 h study, whereas from the plain drug solution, only 68% of the drug release could be seen. The release pattern follows the Korsmeyer-Peppas kinetic model and shows a non-fickian diffusion mechanism (R2=9793 & n=0.765). This indicates that after an initial burst release, the dissolution media penetrated the pores and dissolved the mesoporous silica structure, slowly releasing the drug present inside the pores and giving a controlled drug release.

Conclusion: The synthesized MSNs showed controlled release for the hydrophobic drug terbinafine; also, the encapsulation of the drug inside the mesopores of the MSNs retained the drug in an amorphous state, as evident from the *in vitro* drug release study where almost complete release of the TBF-MSN was obtained. In contrast, the plain drug could not release up to the maximum extent as limited by its hydrophobicity.

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------ ☺ ------

Felodipine crystals produced from hydrophilic polymeric solutions showed improved drug release property: *In vitro* evaluation and correlation with crystal parameter

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Background & Rationale: Poor water solubility and extensive first-pass metabolism of felodipine are major challenges in developing an effective oral delivery system. To overcome this problem, present work was intended to develop crystal products of felodipine from selected hydrophilic polymer solutions to improve its solubility and dissolution rate.

Methods: Experimental crystal products were synthesized by controlled crystallization method using solvent change technique in presence of various hydrophilic polymers like hydroxypropylmethyl cellulose, methyl cellulose, carboxymethyl cellulose, poly vinyl alcohol etc. These were subjected to dissolution studies.

Results: Results from fourier transform infrared spectroscopy revealed absence of specific peaks for the polymers in the recrystallized felodipine. Optical microscopy showed visible morphological changes in the crystal products produced in presence of polymers. Diffraction scanning calorimetry and X-ray diffraction analysis further confirmed absence of polymers in the final crystal products of felodipine. Dissolution rate of the experimental polymer treated crystal products was higher than that of pure drug and among the polymers, HPMC treated crystal showed higher dissolution rate. Data of *in vitro* drug dissolution was correlated with critical crystal parameters like grain size, dislocation density, strain etc., which showed that among all the selected polymers, hydroxypropylmethyl cellulose (HPMC) could bring highest variation in dislocation density with smallest grain size.

Conclusion: In the study, correlation between crystal parameters like crystal grain size and lattice strain (arising from crystal imperfections) and *in vitro* dissolution has been established. Improved dissolution profile of the experimental felodipine crystal products could be the indication of its improved bioavailability for better clinical outcomes.

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------ ☺ ------

Formulation and Release Studies of Gastro-retentive Floating Beads Loaded With Metformin Hydrochloride

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Background and Rationale: Metformin hydrochloride is generally used to regulate blood glucose level. It is basically used for Insulin dependent mellitus or Type II diabetes. Following oral administration, the drug is mainly absorbed from the upper small intestine and has a relatively low bioavailability (50-60%) and an elimination half life of 2-5hrs. Therefore, floating beads of metformin hydrochloride were developed and evaluated to increase the availability of drug at the absorption window by increasing gastric emptying time and continuous release of the drug in a controlled manner up to a predetermined time. So, the aim of this study was to prepare and characterize floating beads of metformin for controlled delivery for an extended period.

Method: A. **Formulation of floating beads by inotropic external gelation method:** The beads were prepared by adding metformin hydrochloride in sodium alginate solution then added calcium carbonate to it. After this solution was dropped through a syringe containing a 24G needle into the solution which contains 10% acetic acid in 1% calcium chloride solution. The formed beads were washed with distilled water on filter paper and dried at room temperature. The beads were stored in desiccators over dried silica gel for further evaluation.

B. **Characterization and release studies of floating beads containing Metformin**. The prepared beads were evaluated for particle size, drug entrapment efficiency, percentage yield, *in vitro* buoyancy and *in vitro* drug release. The release studies were performed using 900 ml of 0.1N HCl at 37±0.5°Cand 100 rpm for 8 hrs. The sample was withdrawn at different time intervals, absorbance was measured at λ-max of 233 nm using a Shimadzu-1800 UV/Vis- spectrophotometer and cumulative percentage drug released was plotted against time.

Results and Discussion: The average particle size of beads was determined using microscopic method and found in the size range of 1.043±0.034 mm, the drug entrapment efficacy was found in the range 64± 4.6% and the percentage yield of the beads was calculated as 57.72±7.28%. All beads were tested for in-vitro buoyancy and they floated up to 24 hr with a very short lag time. The floating beads of metformin were found to release 84±5.67% drug up to 8 hrs.

Conclusion: The floating beads of Metformin were successfully prepared by inotropic external gelation method, found to give the sustained release of drug in the simulated gastric media.

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------ ☺ ------

Formulation and Evaluation of Gelatin based Melatonin Wound Healing Sponge

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Background and Rationale: The neuroendocrine hormone Melatonin which is secreted from pineal gland[1] promotes angiogenesis and thus has a positive effect on wound healing[2]. Nearly 90 percent of the world population has suffered from different types of injuries at some point of their lifetime; therefore, a good and promising wound healing dressing material, which is biocompatible, is very much required so that it can repair the wound or damaged skin rapidly. To achieve this objective, biocompatible gelatin based melatonin sponge was prepared by using fructose as a cross-linking agent. Due to the porous nature of the sponge, it traps platelets and blood plasma in it which in turn activates the coagulation factors. The main objective was to formulate a cheap, inexpensive and mechanically and biologically stable wound dressing material.

Methods:

A) Formulation of Gelatin based Melatonin sponge: Surfactant foaming method was used to formulate the Gelatin sponge. Tween 80 was used as the foaming agent in which melatonin was added by crosslinking with fructose. Further homogenization and lyophilization was carried out.

B) *In-vitro* release study: The *in vitro* release studies were carried out for different formulations of sponges in phosphate buffer pH 7.4 as dissolution medium at different time intervals ranging from 0 min to 210 mins. All of the prepared formulations showed high drug release but among them, the formulation showing highest cumulative release that is 93% at 2nd hour was chosen for further *in-vivo* study.

C) Characterization of Gelatin based Melatonin sponge and *In-vivo* study: The developed formulation was evaluated for different parameters like water uptake, porosity, moisture uptake, digestibility, tensile strength, adhesion, folding endurance, drug entrapment efficiency using SEM and FT-IR techniques. *In vivo* study was carried out using incision and excision methods in albino rats.

Results and Discussion: Gelatin based melatonin sponge was found to be suitable in terms of the above parameters evaluated and it was able to provide a faster wound healing activity in the albino rats. Melatonin was found to improve the scarring quality and helped in synthesis of collagen by activation of proline.

Conclusion: From the above study, conclusion can be drawn that the sponges of gelatin based melatonin were found to be good in terms of evaluation parameters and the formulation was efficient in rapid wound healing while maintaining the biocompatibility.

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Formulation and evaluation of Ginger transdermal patch using natural penetration enhancers.

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Background and Rationale: Ginger or *Zingiber officinale*, Roscoe of the Zingiberaceae family is a rhizome that is broadly found and most devoured in Southeast Asian nations; additionally utilized as a conventional solution for treating different infirmities. Several preparations have been formulated based on ginger extracts; extracted by hydro-alcoholic or by using the CO_2 supercritical fluid method. 6-Gingerol which is the main constituent of ginger has a very low oral-half life ($t_{1/2}$ is 7.23 min) which is a major drawback for its oral delivery[1]. A transdermal delivery system can be used to overcome this problem. Hence, the present study aimed to deliver the 6-gingerol or ginger extract as a whole through the skin to avoid metabolism of the drug before exerting its therapeutic effects.

Method: a) Extraction and formulation: The ginger extract was extracted by using 70% ethanol and the extract was formulated into a transdermal patch with natural penetration enhancers and other polymers.

b) *In vitro* release study of the prepared ginger transdermal patch: This study was performed using a cellulose dialysis membrane (molecular weight 12000–14000) which was placed between the compartments of the diffusion cell. PEG 400, 40% v/v in phosphate buffer pH 7.4 was used in the receptor compartment and was stirred at 400 rpm[2]. The entire assembly was maintained at a temperature of 37±0.5°C. Samples of 3ml were collected at preset time points up to 24hrs and replaced with fresh medium. The samples were filtered and drug content was estimated using a UV/visible spectrophotometer. The percentage drug permeated was plotted against time.

Results and Discussion: The ginger transdermal patch with Eucalyptus oil as a penetration enhancer showed better release than that with menthol. The release study was carried out up to 24hrs, even though a similar release pattern was seen but the one with eucalyptus oil as penetration enhancer shows a significant release of 91.64% and that of menthol shows a release of 81.02% at 24hrs time.

Conclusion: The ginger transdermal patch with eucalyptus oil as a penetration enhancer shows a promising result in the drug delivery and penetration of the drug from the skin membrane to reach the systemic circulation and can be used for treatment of different infirmities like inflammation, nausea, vomiting, and rheumatoid arthritis.

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------ ☺ ------

Formulation, Physicochemical Characterization and Release profile studies of Metformin from Transdermal Matrix Patches.

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Background and Rationale: Diabetes mellitus is one of the most common diseases throughout the world. One out of six diabetes patients in the world is from India. Metformin hydrochloride is generally used to regulate blood glucose level. It is used in insulin dependent mellitus or Type II diabetes and is preferable to administering insulin injections multiple times daily. However, metformin HCl has a relatively low bioavailability (50-60%) and an elimination half life of 2-5hrs. Transdermal delivery may be a suitable option in terms of patient preference since it is non-invasive, reduces the frequency of dosing and provides a controlled release of the anti diabetic active pharmaceutical ingredient. For these reasons antidiabetic transdermal patches containing Metformin were developed.

Methods: A) Preparation of Transdermal Patches: The matrix type transdermal patches containing metformin hydrochloride have been formulated using different ratios of Polyvinyl Pyrrolidone (PVP) and Ethyl Cellulose (EC) by solvent casting method over backing membrane of Polyvinyl alcohol.

B) Physicochemical Characterization and Release profile studies: Physicochemical characterization like weight variation, drug content, moisture content, moisture uptake, flatness and folding endurance studies were done for the prepared patches. *In vitro* drug release study was carried out using USP dissolution type-II apparatus using 900 ml of phosphate buffer 6.8 at 50 rpm and 34±0.5°C temperature. The study was carried out for 12 hrs and 5ml samples were withdrawn at different time intervals and analyzed for drug released by UV-VIS Spectrophotometry.

Results and Discussion: The physicochemical characterization of prepared transdermal patches shows the uniformity in weight and the variation found in the range of 461.18±11.49 mg, the thickness of the patches varies from 0.055±0.004 mm. The percentage drug content was assayed for each type of formulation and found in the range of 97±2.43%. The patches contain 6.57±0.14 % moisture and they can uptake up to 9.58± 0.24% moisture in high humid conditions. The patches were found 100% flat and high folding endurance (167±5.67). When the cumulative % of Metformin released was plotted against time in hr it was found that the 78.85±3.43 % drug has been released from the formulation containing PVP:EC=1:1. The drug release was found to be retarded as the proportion of EC is increased in the patches (65.78±3.58% PVP:EC=1:2).

Conclusions: Hence the matrix type transdermal patches of Metformin hydrochloride can be successfully formulated which is having very suitable physicochemical characteristics for stabilization of patches and the drug release also can be controlled by changing the proportion of hydrophilic and hydrophobic polymers.

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Nanoliposomes based brain targeting of Donepezil Hydrochloride for Treatment of Alzheimer's disease: *In vitro* drug release and Cell penetration study

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Background and Rationale: Alzheimer's disease is the most common type of senile dementia, affecting the world's population. Alzheimer's disease treatment strategies are mainly directed towards the inhibition of the formation of acetylcholinesterase. Among all, donepezil hydrochloride is widely used in treating Alzheimer's disease because it has a high selectivity for the target tissues. Commercially, donepezil is available in solid oral dosage form, however, this route of drug delivery has several drawbacks, most predominantly, very poor blood brain barrier penetration. Thus, it is evident that an alternative method of drug delivery is highly recommended for targeting a hydrophilic drug like donepezil hydrochloride to the brain. Hence in this study efforts were made to deliver the drug across the blood brain barrier by developing donepezil hydrochloride loaded liposomal formulation.

Methods: a) Preparation of drug loaded liposomes: Donepezil loaded liposomes were prepared using required quantities of cholesterol and soya lecithin by thin film hydration method and the prepared formulation was lyophilized and stored for further evaluation.

b) *In vitro* drug release and Cell penetration study: *In vitro* drug release from freeze dried liposomes was carried out by dialysis method and analyzed by UV-VIS spectrophotometer at 228 nm. In order to determine the *in vitro* drug release kinetics from drug loaded liposomal formulations, the drug release data was fitted to different release kinetic models for determination of the highest correlation coefficient value (R^2).To ascertain brain uptake, donepezil hydrochloride loaded liposomes were tagged with fluorescent material and its *in vivo* images were obtained.

Results and Discussion: Primarily, FTIR data showed chemical compatibility among the ingredients and Field Emission Scanning Electron Microscopic (FESEM) images obtained showed both spherical and oval shaped particles with smooth surface morphology and homogeneous distribution. *In vitro* drug released from the prepared formulation was in a sustained manner for 48hrs; best fitted with the Korsmeyer–Peppas kinetics and clearly demonstrated the involvement of Fickian diffusion in the release of the drug. Finally, *in vivo* imaging of the drug loaded liposomes tagged with fluorescent material proved enhanced brain uptake of donepezil hydrochloride.

Conclusion: Thus from the aforementioned points we can say that the donepezil hydrochloride loaded liposomes prepared can easily penetrate through the blood brain barrier and give a better therapeutic efficacy for a prolonged period of time and in a sustained manner.

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In Vitro Release and Kinetics Studies of Diflunisal from Nanostructured Lipid Carrier prepared by Hot Emulsification Method

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Background and Rationale: The safe and effective delivery of drugs to the site of action is of prime importance but is often challenging. Nanostructured lipid carriers (NLCs) have been explored and studied to deliver drugs and vitamins via several routes including for topical administration. In recent years, NLC has gained particular attention because of its advantages viz: affinity for the skin; ability to mimic skin layer lipid, propensity to boost the penetration of drugs in the stratum corneum layer, shielding of the encapsulated ingredient against degradation provoked by the external medium, ability to enhance entrapment efficiency of drug and control of drug release in the desired pattern. The goal of the present study was to prepare and characterize diflunisal loaded NLC.

Method: A) Preparation of NLC " Hot Emulsification Method," followed by ultra-probe sonication was employed for preparation. Briefly, 200 mg of lipid phase was melted followed by addition of 10 mg diflunisal to the melted lipid. Hot surfactant solution (10 ml) containing Tween 80 (1%) and co-emulsifier PEG 200 (0.5%) was prepared. Subsequently, hot surfactant solution (85ºC) was added drop by drop to the melted lipid-drug phase with stirring at 900 rpm for 20 min. Then resultant nanoemulsion was subjected to ultra probe sonication to reduce globule size. After that, the nanosized emulsion was kept in a refrigerator to form Nanostructured Lipid Carrier (DIF-NLC). NLC was characterized for particle size, PDI, zeta potential (ZP) and evaluated for *in-vitro* drug release.

B) *In-vitro* Drug Release: The *in vitro* release study was carried out in phosphate buffer saline pH 7.4 containing 0.1 % tween 80, using a dialysis bag having a molecular weight cutoff of 12-14 KDa. DIF-NLC dispersion equivalent to 2 mg of the drug was transferred to the previously activated dialysis bag and tied from both ends. Plain diflunisal was also similarly enclosed in another dialysis bag. The bags were immersed into 20 ml of the dissolution medium, temperature maintained at 32 ± 1 °C, and stirred at 200 rpm using a magnetic stirrer. The study was carried out for 48 hours; the aliquots of about 1 ml were collected in fixed period points. Concurrently the same quantity of fresh medium was added to maintain sink condition. The samples were analyzed for drug content using a UHPLC.

Result and Discussion: The fabricated NLC exhibited a particle size of 123 nm and a Zeta Potential of -18 mV. Diflunisal NLC showed extended *in vitro* drug release, with more than 90 % diflunisal released up to 48 hours. In contrast, free Diflunisal showed fast release, around 90 % within the 8 hr; Release of diflunisal from NLC demonstrated an initial burst release followed by a sustained release. As per the Akaike Information Criterion, DIF-NLC follows the logistic kinetics model of drug release.

Conclusion: The result suggests that nanostructured lipid carriers can enhance the solubility of diflunisal and reflect sustained drug release and hence may improve the efficacy of the formulation.

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Valacyclovir loaded polycaprolactone nanoparticles for improved efficacy against Herpes Zoster virus infection: *In vitro* release

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Background & Rationale: Valacyclovir (VAL) loaded polycaprolactone (PCL) nanoparticles were prepared for the treatment of genital herpes, cold sores, and shingles in adults caused by Herpes Zoster Virus (HSVII). In spite of having a good antiviral effect, VAL suffers from various disadvantages such as poor oral bioavailability, significant protein binding (15-20%) and very short elimination half-life of less than 30 minutes. The drug loading in the nanoparticles was found to be poor owing to high aqueous solubility (>174 mg/ml).

Method: A) Formulation of nanoparticles by multiple emulsion solvent evaporation technique: The nanoparticles were prepared using different stabilizers including polyvinyl alcohol (PVA), tween 80, span 20, poloxamer with the aim of maximizing the drug loading. The drug-excipient interaction was studied using Fourier transform infrared (FTIR) spectroscopy; surface morphology was evaluated by field emission scanning electron microscopy (FESEM); and the zeta potential and particle size and particle size distribution were measured using a Litesizer.

B) *In vitro* drug release study: *In vitro* drug release study was performed using dialysis membrane in phosphate buffered saline (PBS) pH 7.4 with the temperature maintained at 37±2°C for 15 days.

Results and Discussion: No chemical interaction was observed between the drug and excipients used in this study. Valacyclovir nanoparticles were found to have a smooth surface and were within a nanosized range (250–700 nm) with a negative surface charge of -13.5 mV. Drug loading in the prepared particles was found to be low (0.871±0.09%). A sustained drug release pattern from the nanoparticles is observed for the entire period of study, i.e., up to 15 days. Thus, the valacyclovir-loaded PCL nanoparticles can allow for gradual release of drug up to 15 days and may serve to overcome the problem of poor bioavailability.

Conclusion: The preparation of valacyclovir loaded PCL NPs was done successfully. Further work is required to enhance the drug loading value so that the formulation could gain the potential to come to market in near future against Herpes Zoster virus infection.

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In silico Pharmacokinetic profiling of ciprofloxacin HCl after administration as oral tablet, intravenous solution and microparticles through pulmonary route

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Background and Rationale: PBPK provides a mechanistic approach to study and predict the PK of drugs based on physiologic and anatomic characteristics, as well as the physicochemical properties of a given drug. The basic pharmacokinetic parameters of a drug molecule defined with the absorption, distribution, metabolism, and excretion, establishes the relation among the dosage regimen and therapeutic or toxicological responses. Ciprofloxacin is a fluoroquinolone derivative that is clinically effective against a broad spectrum of bacteria. Ciprofloxacin is the drug of choice for the treatment of lung infection. But this drug is hepatotoxic. The aim of this simulation study was to predict the dosage regimen of ciprofloxacin after administration through the pulmonary route in the form of 5 µm particles.

Method A-Prediction of pharmacokinetics parameters: PK-SIM® software was used for PBPK studies. Based on the varying dosage regimen and different routes of administration of ciprofloxacin, the different PBPK parameters are assessed and computed for individual and population species. The data are incorporated as per the physicochemical properties of the drug, the volumes of various organs, the metabolizing enzymes and factors related to the formulation and administration protocol of the drug. At first the model was validated with the data available in literature for administration of 250 mg as intravenous infusion. Then, the PK model was developed for pulmonary administration of 5 µm ciprofloxacin particles. Dose was varied from 25 mg -150 mg. PK profiling after administration as oral tablet and i.v bolus were also done.

Method B- Establishment of IVIVC: The *in vitro* dissolution data and *in vivo* data of oral and intravenous bolus routes were used for IVIVC studies using R-package (ivivc).

Results and Discussion: The PK profile of 150 mg pulmonary administered dose was found similar to 250 mg intravenous infusion. The half-life of the formulations was maximum; 8.85 hours for infusion and was found to be 5.68 hours for the pulmonary route. The tmax was found to be 1 hour for all formulations and the MRT ranged from 1.17-1.76 hours. The 150 mg pulmonary dose had a Cmax of 12.73 µmol/l. The C_{max} after intravenous infusion was 18.31 µmol/l. The Vd of the formulations ranged from 2.8 L/kg to 4.5 L/kg approximately. The *in-vitro* drug release profile was utilised for the investigation of IVIVC. No good correlation was found between drug dissolution and absorption.

Conclusions: It was found that 150 mg pulmonary dose of ciprofloxacin was equivalent to 250mg dose of intravenous infusion. Thus, pulmonary administration requires less dose leading to enhanced safety and better therapeutic efficacy. But no good correlation was found between dissolution of ciprofloxacin and it's absorption through oral route. This is quite expected as ciprofloxacin is a BCS class III drug.

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In-vitro release study of Diltiazem Hydrochloride from sustained release hydrogel beads

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Background and Rationale: Gellan gum hydrogel beads was prepared by ionotropic gelation technique using $CaCl_2$ as cross-linking agent for sustained delivery of diltiazem hydrochloride in order to increase the bioavailability of the drug with short biological half-life and also to reduce dose-related toxicity, frequency of dosing, and patient noncompliance [1]. Diltiazem hydrochloride undergoes extensive first-pass hepatic metabolism with very low absolute bioavailability and frequent dosing is required [2]. In recent times, various naturally derived polysaccharides have been used in sustained drug delivery systems as they do not need organic solvents for processing like synthetic polymers. Gellan gum hydrogel beads are mainly used as carriers for targeting the intestinal region as their swellability and drug release is highest in the basic region. The development of these beads may sustain the drug release for a prolonged period of time as it will be entrapped inside the polymeric core and released slowly.

Methods: A) Development of Diltiazem hydrochloride loaded hydrogel beads: Gum solution in varying concentrations were dispersed in water and kept overnight. Required quantity of drug was dispersed into the gellan gum solution and agitated thoroughly. The resultant drug-polymer dispersion was dropped through a 23G hypodermic syringe needle into calcium chloride solution with mild agitation. The prepared beads were allowed to stand for 15mins and were then filtered & air dried overnight. The beads were again dried at 45°C for 2 h and kept in a sealed container for further use.

B) The *in-vitro* release from beads: The *in-vitro* drug release study was carried out using 250 ml amber colored bottles at 37°C ± 0.5°C with 50 r.p.m in two stages. Initially 100 ml pH-1.2 HCl buffer was poured into the bottle and to it 30mg beads were added. After 2 h, acid stage was immediately converted into basic stage by adding specific amount of tri-sodium phosphate and the study was carried out upto 10 h. From the beginning 5ml aliquot of the release medium was withdrawn and replaced with equal volume of dissolution medium to ensure a constant volume of the release medium. The samples were analyzed using U.V. spectrophotometer at specific wavelengths for the different buffer systems and the cumulative percentage of drug released was calculated. All experiments were performed in triplicate.

Results and Discussion: The drug entrapment efficiency of the prepared hydrogel beads was in the range between 8.63±0.59 and 13.86±0.446. It was observed that with an increase in polymer concentration, the swelling ratio also increased. The prepared hydrogel beads showed high swelling ratio and drug release in pH 7.4 buffer solution when compared to the release in pH 1.2 buffer solutions. The formulation F3 showed minimum drug release i.e., 34.18% in pH-7.4 in 10 h. The drug release from the hydrogel beads increased with the increase in pH. The release kinetics study showed that all the formulations followed the Fickian diffusion mechanism.

Conclusions: These hydrogels beads can be successfully formulated for the sustained release of hydrophilic drugs having lower bioavailability.

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Lipid based nanocarrier showed sustained drug release and improved anticancer potential for lomustine: A strategy for effective glioma therapy

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Background and Rationale: Effective treatment of glioma remains a challenging task in drug delivery research till now. Lipid based nanocarriers, owing to their extremely small size and lipophilic nature could solve the problems of drug delivery issues for glioma therapy. The present work is aimed at the development and evaluation of lipid nanostructures for successful delivery of lomustine (an established anticancer drug) to brain tumor cells.

Methods: Conventional lipid layer hydration technique was employed to yield the lomustine experimental lipid nanostructures (LNLs). Experimental formulations were evaluated for different *in vitro* characteristics like particle size analysis, surface charge, surface morphology, internal structure, *in vitro* drug loading, *in vitro* drug release profile etc. *In vitro* drug release study was carried out at physiological pH of blood (i.e. pH 7.4) as well as endocytotic vesicular pH (pH 5) to simulate different *in vivo* environments. Anticancer potential of selected LNLs was tested *in vitro* on C6 glioma cell lines.

Results: Scanning and transmission microscopic study depicted a size of around 50 nm for the selected formulations. A sustained release of lomustine over the 48 h experimental time period was observed in both the drug release media. Confocal microscopy revealed extensive internalization of the selected LNL in C6 cells. LNLs were found to be more cytotoxic than free drug and blank nanocarriers as depicted from MTT assay.

Conclusion: Satisfactory anticancer potential along with sustained release profile for the selected LNLs warrants its *in vivo* investigations for further development.

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PBPK modelling for prediction of pharmacokinetic profile of ciprofloxacin in children after administration as oral suspension and intravenous solution.

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Background and Rationale: PBPK modelling combines the information on ADME and physicochemical properties of the drug molecule with the physiology and biology of a particular human population to simulate the drug concentration-time profile [1]. The broad-spectrum antibiotic, ciprofloxacin, is a fluoroquinolone derivative that is used in the treatment of both Gram-positive and Gram-negative bacterial infections [2]. In children ciprofloxacin is used in bronchopulmonary infections, complicated urinary tract infections, pyelonephritis, and inhalation anthrax. But ciprofloxacin is associated with hepatotoxicity [2]. The aim of this study was to predict the pharmacokinetic profile of ciprofloxacin in children of 7 yr age (1-15 yr) after administration of ciprofloxacin through parenteral route (i.v, solution) and oral route (suspension).

Method: The individual of adult (age- 39.1yrs, height- 179.6cm, weight- 87kgs) and child (age- 7yrs, height- 112cm, weight- 24.6kg) and the population group of adults (age range- 32- 46yrs, height- 168- 196cm, weight- 65-99kgs) and children (age range- 1-15yrs, height- 70- 150cm, weight- 8- 45kgs) were created in PK-Sim software from the literature data and organ weights, organ blood flow rate and other physiological parameters were auto-generated by the software. Ciprofloxacin molecule was generated by gathering all physicochemical and ADME information in the software then the formulation kinetics was generated for both adults and paediatrics population for parenteral (i.v. solution) and oral (suspension). Then the different administration protocol for adults (400mg i.v. infusion, 500mg/ml oral suspension) and children (200mg i.v. infusion, 150mg i.v. infusion 140mg i.v. infusion, 250mg/5ml oral suspension, 200mg/5ml oral suspension) were generated. All the pharmacokinetic parameters were examined by the simulation of both population groups of adults and children using respective administration protocols.

Results and Discussions: After performing the simulation by using all the given parameters for the adult individual and population and the paediatric individual and population, pharmacokinetic parameters such as AUC, Cmax, Tmax, MRT, half- life were obtained from the PKSim software. In case of adult population of 400mg iv infusion the values of AUC= 3541.99 µmol*min/l, Cmax= 25.19 µmol/l, Tmax=1h MRT= 3.97h, half- life= 3.75h and in case of 500mg/5ml oral suspension the values of AUC= 7921.01µmol*min/l, Cmax= 35.16 µmol/l, Tmax= 0.45h MRT= 7.41h, half- life= 6.08h. In case of child population of 200mg iv infusion the values of AUC= 9512.12 µmol*min/l, Cmax= 40.30 µmol/l, Tmax= 1h MRT= 5.91h, half- life= 5.58h and in case of 150mg i.v. infusion the values of AUC= 7135.11 µmol*min/l, Cmax= 30.23 µmol/l, Tmax= 1h MRT= 6.41h, half- life= 5.57h and in case of 140mg i.v. infusion the values of AUC= 4296.58 µmol*min/l, Cmax= 25.04 µmol/l, Tmax= 1h MRT= 4.33h, half- life= 4.06h. In case of 250mg/5ml oral suspension the values of AUC= 10463.22 µmol*min/l, Cmax= 48.55 µmol/l, Tmax= 0.4h MRT= 6.29h, half- life= 5.62h and in case of 200mg/5ml oral suspension the values of AUC= 8905.87 µmol*min/l, Cmax= 44.45 µmol/l, Tmax= 0.4h MRT= 6.20h, half- life= 5.63h.

Conclusion: From this study, we can conclude that 400mg i.v. infusion dose in adults is close to paediatric 140mg i.v. infusion dose and adult 500mg/5ml oral suspension is close to paediatric 200mg/5ml oral suspension. This study can predict all the pharmacokinetic parameters of children along with the appropriate dose from the adult pharmacokinetic parameters for parenteral (i.v. solution) and oral (suspension). This PBPK model can be a useful tool for increasing the efficacy of paediatric therapy.

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PREPARATION AND *IN VITRO* EVALUATION OF PLGA NANOPARTICLES OF ESOMEPRAZOLE FOR ORAL DELIVERY

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Background and Rationale: Esomeprazole magnesium trihydrate (Eso) is a proton pump inhibitor which acts by irreversibly blocking the (H+K+)-ATPase enzyme system of the gastric parietal cell. The poor absorption of esomeprazole may be because of the degradation in gastric acid which can be prevented by incorporation of HPMC by acting as a coating to the NPs. This study was conducted to prepare and evaluate the poly(D,L-lactide-co-glycolide) (PLGA) nanoparticles (NPs) of Eso as a model drug for prolongation of the gastric retention time after oral delivery.

Methods: The Eso-PLGA NPs were prepared by solvent evaporation method by using non-solvent aqueous phase containing HPMC and organic solvent system (mixture of dichloromethane and acetone) to dissolve drug and PLGA. The experimental NPs developed were evaluated for %yield, particle size, zeta potential, FT-IR study, surface morphology, drug loading (%) and drug encapsulation efficiency (%).

***In-vitro* drug release and drug release kinetics:** *In-vitro* release study was performed using dialysis membrane in phosphate buffer solution (pH 7.4) as release medium in a magnetic stirrer with temperature maintained at 37±2°C. The drug release study was performed for 120 h. The release data was fitted into different release kinetic models to assess the drug release mechanism.

Results and Discussion: The prepared nanoparticles were found to be in the range of 300 nm to 400µm as observed from data obtained from particle size analyser and SEM study. Encapsulation efficiency was found in the range of 26.16%. FT-IR studies did not show any chemical interaction between drug and polymers used in the formulation. The drug was found to be released in a sustained manner and about 74-95% of total drug was released within 120 h. Drug release kinetic data show that data were best supported by the Korsmeyer–Peppas kinetic model, which clearly demonstrates the involvement of anomalous diffusion which is controlled by more than one parameter.

Conclusions: The results of the Eso-PLGA NPs reveal that the nanoparticles are of required specification. Thus, the developed Eso-PLGA NPs can protect the drug from degradation in gastric acid and prolong its duration of action as supported from the *in vitro* release studies.

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ROS generation by curcumin and its application in cancer treatment: Formulation and drug dissolution kinetics

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Background & Rationale: Cancer is the abnormal growth of the cells in different body organs, leading to benign and malignant tumours. The advances in cancer treatment to provide painless treatment with less discomfort to the patients lead to new therapies. One such therapy is photodynamic therapy (PDT). PDT combines light, photosensitizers and oxygen to induce oxidative stress on the cancer cells by enhancing the release of reactive oxygen species (ROS). Photosensitizers is the compound that can generate ROS in the cells which in turn leads to apoptosis of the cells. Curcumin is one of the proven natural photosensitizers used in PDT with effective results.

Methods: The methods used for the preparation and dissolution of liposomes are described below

A) Preparation of Liposomes: Required amount of SPC, DSPE-$PEG_{2000,}$ and cholesterol lipids were weighed and dissolved in 2mL chloroform, 1mg of curcumin is dissolved in 1mL methanol. The mixture of the solutions was then evaporated under vacuum in the rota evaporator at 45°C with 100 rpm speed, which forms a thin film. 10 mL of 7.4 pH buffer was added to the round bottom flask, and the dispersion was then hydrated for 15 minutes at 120 rpm, followed by 10 minutes of sonication.

B) *In vitro* release study: Dialysis bag (MWCO 12KDa) was activated the night before with 7.4 pH buffer, and liposomal solution of 4mL was taken in the dialysis bag. The bag was then dialyzed against 40 mL of pH 7.4 phosphate buffer with 10% ethanol and stirred at 100 rpm. At predetermined intervals, 1 mL of sample was taken and replaced with fresh 1mL of pH 7.4 phosphate buffer. The samples were then analyzed using a multimode reader in fluorescence spectroscopy with an excitation wavelength of 420 nm and an emission wavelength of 550 nm.

Results and Discussion: Liposomes exhibited a size of around 105 nm with more than 70% entrapment efficiency and more than 1.5% drug loading. The drug from the liposomes shows around 55% release in 72h while the free drug exhibited around 90% release in 72h. Based on the Akaike information criterion, drug dissolution kinetics followed the Weibull model. The ROS generation studies proved that the formulation has more ROS generating capacity than the free drug. Additionally, the liposomes exhibited more cytotoxicity to the cancer cells than the free drug, proving the formulation's effectiveness.

Conclusion: The result suggests that liposomes can be used to deliver drug in a controlled manner, enhancing the efficacy of the curcumin-loaded liposomes. The liposomes were more effective than the free drug, and the liposomes can be used in combination with PDT.

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Synthesis and *in vitro* release kinetics of Berberine chloride loaded Mesoporous silica nanoparticles (MCM-41)

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Background and Rationale: Inflammation is a primary response from the immune system to any infection or irritation. Inflammation is a complex reaction that occurs in systemic or local organs due to exogenous or endogenous injuries, which ultimately results in redness, pain, swelling, and tissue damage. Berberine Chloride (BBR) has an excellent anti-inflammatory effect but, due to its low aqueous solubility and poor permeability, it has limited applicability. On oral administration, it has low intestine absorption, less bioavailability (5%), short half-life, undergoes high first-pass metabolism, and also causes gastric damage. The loading of berberine chloride into the MSNs leads to sustained release of BBR, so the BBR remains for an extended period at its site of action. This study aimed to assess the suitability of MSNs to control the release of BBR for its local anti-inflammatory effect.

Methods: Synthesis of MCM-41 was carried out using the modified Stober's method, using Cetyltrimethylammonium bromide (CTAB) and Triethoxysilane (TEOS) structure-directing agent and silica source, respectively. There is subsequent hydrolysis and condensation of silane in the basic condition (1N NaOH). Optimization of MCM-41 was done with the help of various process parameters like temperature, stirring rate, rate of addition of TEOS, time of reaction, and output was particle size and PDI. The optimized MSNs were allowed for drug loading and other characterization such as particle size, PDI, FTIR, DSC, X-ray, SEM and FETEM analysis, *in vitro* drug release study.

***In vitro* drug release kinetics:** The *in vitro* drug release was carried out in PBS pH 7.4. The donor compartment consisted of a dispersion of free BBR or BBR-MSNs in phosphate buffer 2 mL (pH 7.4), and the receiving chamber consisted of pure phosphate buffer 30 mL (pH 7.4). The receptor compartment was maintained at 36 ± 1ºC with circulating jackets and stirred at 100 rpm. The sample of 1 mL was collected from the receptor phase at predetermined time points for of 24 h, and the receptor compartment was instantly refilled with the same amount of pH 7.4 phosphate buffer and analyzed using an UV spectrophotometer at λmax (266 nm).

Results and Discussion: The average particle size and PDI of optimized MSN were 150 (±6) nm and 0.2, respectively. The drug loading and entrapment efficiency of BBR were found to be 30 and 50 %, respectively. The image obtained by FETEM indicates the prepared MCM was spherical and porous in nature. The results of solid-state characterization confirm the transformation of BBR from crystalline to amorphous. The *in vitro* drug release data shows the biphasic release of BBR from the BBR-loaded MSNs, i.e., initial burst release (55%) within 4 h due to the dissolution of BBR present on the surface of MCM-41 followed by sustained release (90%) up to 36 h because of BBR diffusion from pores of MSNs. The results indicate a 3 fold controlled release of BBR from loaded MSNs when compared to free BBR. The drug release was best fitted to the Korsmeyer Peppas model of release kinetics.

Conclusion: Berberine chloride-loaded MCM-41 MSNs were prepared, and it is a suitable nanocarrier to overcome the solubility and permeability problems of berberine chloride. The loading of BBR into MSNs provides sustained drug release; therefore, the problems due to the short half-life of BBR are overcome.

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------ ☺ ------

Understanding the *in vitro* release behavior of voriconazole-loaded mesoporous silica nanoparticle (SBA-15)

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Background and Rationale: Mesoporous silica nanoparticles (MSN) have gained much attention in recent years due to their fascinating properties like tunable particle size, high drug loading, and accessible surface functionalization. The word mesoporous refers to the pore size ranges from 2 to 50 nm [1]. Voriconazole has poor aqueous solubility and is highly vulnerable to the first-pass effect. Additionally, it is associated with various side effects such as diarrhoea, nausea, vomiting, fever, headache, and appetite loss. Parenteral administration of Voriconazole results in untoward effects such as neurotoxicity, hepatotoxicity and drug-drug interactions. These kinds of adverse effects restrict its utilization in fungal infection management. In this study, MSNs-loaded voriconazole was prepared to overcome the problems associated with its delivery [2].

Methods: A) Synthesis of SBA-15 MSNs template: In the preparation of SBA-15 MSNs template, TEOS was used as silica source and Pluronic P123 was used as a structure-directing agent (SDA). Initially. 2.0 g of Pluronic P123 copolymer was gently mixed with 15 g of water and 60 g of 2 M HCL at 35^0C and this mixture was stirred for 20 h. After 20 h, the mixture was kept for a day at 80^0C in the absence of stirring. Finally, the dried sample was subjected to calcination to remove SDA. **B) Loading of voriconazole into SBA-15:** The solvent evaporation method is widely used for drug loading in SBA-15 silica carriers. Voriconazole was dissolved in 10 ml methanol (5mg/mL) followed by addition of SBA-15. The dispersion was subjected to stirring for 24 h in a closed container. Later, the solvent was discarded by using the solvent evaporation method. The obtained product was dried in a vacuum oven at 40^0C overnight. After 24 h. The MSN-loaded mixture was subjected to centrifugation at 14500 rpm for 15 min. and later washed with Milli Q water and dried at room temperature. **C) *In vitro* release experiment:** Dialysis bag was soaked 12 h before experiment in respective selected release media. The VRC-MSNs dispersion was enclosed in a dialysis bag and incorporated in 50 ml of release medium. Aliquots were collected at fixed time points (0.083,0.16,0.25,0.5,1,2,4,8,12,24h) and the same amount of new release medium was returned after every time point. Similarly, a free VRC solution was tested as a control.

Results and Discussion: In SBA-15, silica as a matrix shows enhanced solubility and suitable drug release profile. Voriconazole-loaded SBA-15 showed a burst release due to the surface adsorption phenomenon. Within initial 2 h, almost 70% of drug was released from the silica matrix compared to only about 38% from the plain drug. The release from the formulation follows the Weibull model. Voriconazole-loaded MSN exhibited a 24 h-controlled release pattern while 75% of drug was released from plain voriconazole in 24 h.

Conclusions: Voriconazole loaded SBA-15 MSNs were prepared and exhibited controlled release for 24 h**.** SBA-15 is a promising nanocarrier for enhancing the solubility and *in vitro* release of voriconazole which has poor aqueous solubility.

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Aptamer functionalized betulinic acid analogue nanotherapy deciphering therapeutic efficacy towards human colon cancer: A promising alternative chemotherapy

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Background and Rationale: Chemotherapy is still far from producing a satisfactory result due to its adverse side effects. The development of novel plant derived natural products and their analogues for anticancer activity are increasing day by day. On this rationale, some new analogues of natural triterpenoid compound (Betulinic Acid - BA) were synthesized in our previous study. The lead molecule (2c) was found to be cytotoxic against human colon carcinoma cell line, HT-29. We have earlier reported that 2c was capable of inducing apoptosis [1] as well as another mode of programmed cell death, autophagy[2], in HT-29 cell line. Despite its impressive biological activity, poor water solubility and low bioavailability creates difficulties in its pharmacological activity. To overcome these lacunae and make it a promising drug candidate, PLGA [Poly (D, L-lactic-co-glycolic acid)] encapsulated 2c (2c-NPs) was prepared which showed significantly enhanced antiproliferative activity than free drug, 2c[3]. However, a common problem to use this nanoparticulate drug delivery system is, its non-specific distribution in cancer tissue as well as normal tissue. Thus, to enhance the therapeutic efficacy and reduce off-target cytotoxicity towards normal cells, in this present study we focus to target the nanoencapsulated lead BA analogue to colon. This procedure involves the preparation of aptamer (Epithelial Cell Adhesion Molecule, EpCAM) conjugated PLGA nanoparticles loaded with the lead BA analogue (Apt-2c-NPs) and evaluation of *in vitro* and *in vivo* efficacy of the formulation in targeting human colon carcinoma.

Methods: Apt-2c-NPs nanoformulation was developed by modified multiple emulsion solvent evaporation method followed by aptamer conjugation. After determination of particle size and surface charge, particle morphology was determined by SEM, TEM and AFM. *In vitro* antiproliferative activity was measured by MTT assay, Annexin V assay, JC1 analysis, cell cycle, western blotting, and study of autophagic signalling pathway. Alteration of pro and anti-apoptotic gene expression *in vivo* was measured by rtPCR. Effect of Apt-2c-NP to modulate pro and anti-inflammatory cytokines in tumor microenvironment was measured by FACS analysis. *In vivo* distribution of Apt-2c-NP was determined by pharmacokinetics study using LC-MS-MS and *in vivo* live imaging by gamma scintigraphy camera. *In vivo* therapeutic potential after Apt-2c-NP treatment was measured in colon cancer bearing experimental model animals (Swiss Albino mice and Sprague Dawley rat) by histopathological observations.

Results and Discussion: An improved *in vitro* antiproliferative activity against cancer cells and no off-target cytotoxicity toward normal cells were observed. *In vivo* live imaging in colorectal cancer animal model, biodistribution study deciphered a significantly higher accumulation of aptamer-conjugated drug-encapsulated nanoparticles (Apt-2cNP) in cancer regions as compared to non-targeted BA analogue nanoformulation (2c-NPs) and free drug. Pharmacokinetic profiling revealed that Apt-2c-NP enhanced biological half-life by 7 h, increased AUC by 153.7%, and MRT by 40 % compared to free drug. Furthermore, gene expression study, histopathological analysis and immunological profiling of tumor microenvironment suggest enhanced immunological response (increase in mDC/pDC ratio, expression of TNFα and increase in macrophage population in tumor microenvironment (TME)) and predominantly greater therapeutic potential of aptamer conjugated nanoparticles.

Conclusions: Aptamer conjugation enhanced potential *in vitro* and therapeutic efficacy of the BA analogue nanoformulation, Apt-2cNP with better immune activation at TME. Thus, the translation of this aptamer functionalized nanoformulation from bench to bedside can be a promising alternative to cancer chemotherapy.

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Combinatorial delivery of nanoencapsulated active constituents embedded in 3D printed wafer for both drug and particle release applications

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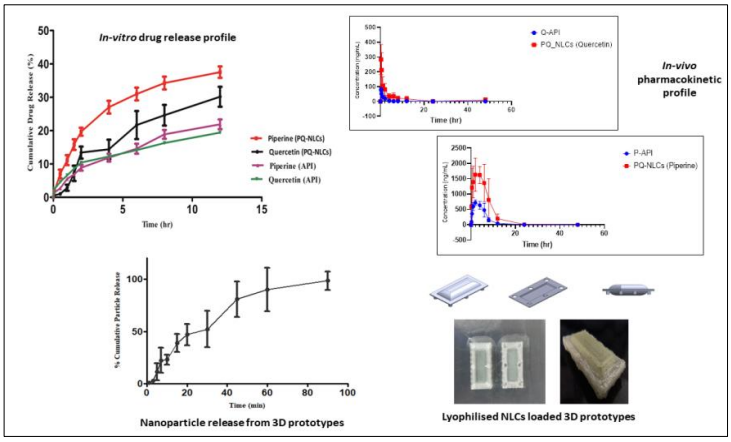
Background and Rationale: The need for localized drug delivery of plant-based active constituents as a particulate system against oral cancer is desired to ensure not only the delivery of particulates but also the release of the drug at the diseased site. Hence, active constituent enriched nanoformulations embedded in 3D printed wafer could be a holistic approach to address the unmet localized drug delivery needs.

Methods: Co-encapsulation of both piperine and quercetin in nanostructured lipid carriers (PQ- NLCs) was carried out through solvent evaporation technique and the product was evaluated for *in-vitro* drugs release through dialysis sac method using ethanolic solution (35% v/v) as release medium [1], followed by *in-vivo* pharmacokinetic profiling in rats. On a translational basis, PQ-NLCs were further evaluated for an *in-vitro* particle release study from the prototyped 3D printed mouth-dissolving wafers. Particle release quantification was performed using *Derived Kilo Counts Per Second (Derived KCPS)* from dynamic light scattering (DLS) technique as it is directly proportional to particle concentration [2].



Results and Discussion: The *in vitro* release studies showed that 30% quercetin and 37.5% piperine were released, which is more than pristine drug dispersion, following Higuchi release kinetics. The pharmacokinetic profile showed the enhancement in relative bioavailability of 6.33 and 3.56 folds of quercetin and piperine, respectively. It can be considered owing to increased solubility, absorption, and residence time of drug delivered at the nanometric scale. After this, lyophilized PQ-NLCs in the powdered form were loaded inside Fused Deposition Modelling (FDM) mediated 3D printed polymeric wafers. The complete nanoparticle release from the designed 3D wafers occurred within 90 minutes. Used polymeric matrix was exhausted and started dissolving in presence of artificial saliva, leading to the release of nanoparticles from the designed prototype.

Conclusion: Improved *in-vitro* drug release profile along with enhancement in the relative bioavailability and pharmacokinetic profile was achieved through NLCs as compared to pristine drugs. NLCs delivery through fabricated 3D printed wafers systems at the desired site of action can be considered as the latest additive manufacturing-driven treatment approach against oral cancer.

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Design, formulation and *in vitro* and *in vivo* evaluation of novel herbal antihypertensive regioselective bilayered tablet.

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Background & Rationale: Cardiovascular disease (CVD) is the primary reason for morbidity and mortality worldwide. Plants rich in phytosterols like phenolic and flavonoid compounds are known for anti-hypertensive effects. Bilayer tablet technology can be employed in the development of controlled release formulations. The present study was aimed at the formulation of novel regioselective bilayer tablets containing natural antihypertensives from *Clerodendrum colebrookianum* Walp (CCE) and *Centella asiatica* Linn (CAE) for dual release and to sustain an effective plasma level for an extended span of time. Studies to determine the *in vitro* and *in vivo* pharmacokinetic parameters in comparison to quercetin and gallic acid were also carried out.

Methodology: The formulations were prepared by direct compression method. A 3-factor, 2-level BBD (Box-Behnken Design) was applied for exploring and optimizing the main effects, quadratic effects as well as interaction effects of the ingredients. Prepared formulations were physico-chemically characterized, *in vitro* drug release study was done and evaluated for its *in vivo* antihypertensive activity by 2K1C hypertension induction method and DOCA induced hypertension model. The release of drug from different batches of prepared tablets was studied using USP type II dissolution apparatus . The dissolution medium used was 500 ml of simulated gastric fluid pH1.2 for first 120 minutes for immediate release layer and then 900 ml of phosphate buffer pH6.8 with 0.5% w/v SLS was used up to 12 hours for sustained release layer. In-vivo pharmacokinetic parameters were determined in Wistar albino rats. Blood samples (2 ml) were obtained by retro orbital puncture at 0, 0.25, 0.5, 1, 2, 3, 4, 6, 8, 12h after drug administration. The plasma drug was extracted and levels were estimated by HPLC with UV detection. Pharmacokinetic parameters such as C_{max}, t_{max}, AUC, $t_{1/2}$ etc were evaluated from plasma concentration time profile using the software Kinetica (version 4)[1-3].

Results and Discussion: Bilayer tablets had a hardness of 7.94±0.234 kg cm^{-2} and complied with the USP friability test. The drug content was found to be 92.2±2.65 mg for CCE and 86.92± 2.70 for CAE. From the *in vitro* study, drug release from CAE immediate release layer was found to be 93.83% in 120 min and that of the CCE sustain release layer was 92.47 % at the end of 12 h and % release of CCE in first 120 min was found to be 35.82 %. Anomalous non Fickian transport mechanism was followed by SR layer with regression coefficient (R^2) of 0.997 and super case-II transport was followed by IR layer with R^2 of 0.988. Pharmacodynamic study reveals significantly good antihypertensive activity compared with the standard drug. In DOCA-salt hypertensive rats, formulation treated group showed significant reduction of HR at 30 min. From *in vivo* pharmacokinetic study the average peak plasma concentration (C_{max}) of quercetin was found to be 0.185± 2.35 μgmL^{-1}, which was more than that of the bilayer tablets (0.09 ± 0.29 μgmL−1). The time to peak plasma concentration (t_{max}) of both quercetin (180 ± 1.35 min) and CCE (180 ± 12.25 min) was found to be similar, indicating that rate of absorption from both the formulations was identical. The $AUC_{0-\infty}$of quercetin and bilayer tablets was found to be 16.43 ± 26.35 mg·min·$L^{-1}$and 18.05 ± 2.35 mg·min·L^{-1},respectively. The CL value for bilayer tablet was found to be 0.07 ± 0.06 L·(hr·kg)$^{-1}$, which was similar to the CL value for quercetin that is 0.09 ± 0.08(hr·kg)$^{-1}$. T ½ of bilayer tablet and quercetin were found to be 176.01 ± 3.97 min and 178.01 ± 8.13 min respectively. The C_{max} of gallic acid was found to be 1.75 ± 0.29μgmL^{-1}, which was more than that of the bilayer tablets (.0.80 ± 0.15μgmL^{-1}). The t_{max} for gallic acid was 90.00 ± 2.25 min which is more than that of *Centella* extract (60.00 ± 2.21 min) of bilayer tablet which indicates that CAE is immediately released as it needed less time to reach maximum concentration. The AUC $_{0-\infty}$of gallic acid and bilayer tablets were found to be 18.05 ± 16.35mg·min·$L^{-1}$and 14.05 ± 6.35mg·min·L^{-1}, respectively. The CL value for bilayer tablet (0.24 ± 0.08 L·(hr·kg)$^{-1}$), and for gallic acid (that is 0.45 ± 0.06(hr·kg)$^{-1}$) were found to be similar.

Conclusions: Overall research work concluded that novel antihypertensive formulation of regioselective bilayer tablets by combining traditional health practices and novel drug delivery system was successfully done and it was well demonstrated from in vivo pharmacokinetic study and release study.

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Enhanced paclitaxel loading and improved pharmacokinetic parameters of a novel TLS 9a functionalized nanocarrier for a safer therapeutic management of hepatic carcinoma

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Background & Rationale: Chemotherapy, so far the sole therapeutic option to treat hepatocellular carcinoma (HCC), has severe toxicity in healthy tissue that greatly compromises the therapeutic outcome, causing high incidence of mortality [1]. Thus, neoplastic cell-specific delivery of chemotherapeutics is the golden option to control HCC more efficiently, avoiding the cytotoxicity in the normal cells. The aptamer TLS 9a with phosphorothioate backbone modification (L5) remains unexplored so far for preferential delivery of therapeutics in neoplastic hepatocytes to induce apoptosis. Thus, the objective of the present investigation was to compare the therapeutic potential of L5-functionalized paclitaxel nanocarrier (PTX-NPL5) with those of the other experimental drug nanocarriers functionalized by previously reported HCC cell-targeting aptamers and non-aptamer ligands, such as galactosamine and apotransferrin. Further, enhancement of solubilisation of paclitaxel for better drug loading and comparison of pharmacokinetic properties of the formulations are also the important focus of the study.

Methods: The multiple emulsion solvent-evaporation technique was performed to prepare PTX-loaded polymeric nanoparticles. A myriad of well-defined investigations such as cell physicochemical characterizations and *in vitro* drug release of PTX from experimental formulations by HPLC, studies related to apoptosis, histopathology, pharmacokinetic analysis via LC-MS/MS, immunoblotting and molecular modelling study were conducted.

Results and Discussion: The release patterns of PTX from PTX-NP and different ligand-functionalized nanoparticles exhibited initial burst release for a period of 24 h followed by sustained release of the drug for 60 days. The cumulative percentage of drug released from PTX-NP (ligand-free nanoparticle) and PTX-NPL5 were found to be 72.79 and 77.77%, respectively, for a period of 60 days. Further, fitting of the release data of PTX from PTXNPL5 into the different kinetic models revealed that drug release pattern was best fitted in Korsemeyer-Peppas kinetic model as evidenced by the value of the regression coefficient (R^2) and release exponent (n). PTX-NPL5 had the highest potency among the different ligand-attached experimental formulations in inducing selective apoptosis in neoplastic hepatocytes via a mitochondrial-dependent apoptotic pathway. Predominantly greater uptake of PTX-NPL5 in the liver of carcinogen-treated rats treated with PTX-NPL5 suggests that accumulation of nanoparticles was more in hepatic tissues than the other vital organs of cancerous rats. Further, when we compared the uptake of PTX-NPL5 in livers of normal rats and carcinogen-treated rats treated with PTXNPL5, it showed that the nanoparticle uptake was predominantly greater in carcinogen-treated rats treated with PTXNPL5. This could be possible because of the greater affinity of L5 towards specific binding protein(s) expressed/overexpressed specifically on the neoplastic hepatocytes.

Conclusion: The potential of PTX-NPL5 has provided enough impetus for its rapid translation from the pre-clinical to clinical domain to establish itself as a targeted therapeutic to significantly prolong survival in HCC patients.

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Evaluation of Glibenclamide-loaded PLGA Controlled Release Biocompatible Nanoparticles

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Background and Rationale: Nanoparticles have emerged as suitable means to improve and optimize the delivery of conventional therapeutic drugs. This targeted strategy results in the controlled administration of medications in low doses for efficient activity within the body.[1,2] The goal of the work was to make glibenclamide-containing poly (D, L-lactic-co-glycolic acid) (PLGA) nanoparticles and evaluate them *in vivo* and *in vitro*.

Methods: A) Preparation of Glibenclamide loaded nanoparticles: The emulsification solvent evaporation process was used to make glibenclamide-loaded PLGA nanoparticles. Using a modified emulsification solvent evaporation technique, an attempt was made to optimize the nanoparticle formulation by changeable drug/polymer ratio, organic solvent (methanol/dichloromethane) ratio, surfactant ratio (PVA/polysorbate-80) in a fixed concentration (0.5 %w/v), and stirring speed (300 to 3000 rpm).

B) *In-vitro* drug release studies: The *in-vitro* release of glibenclamide from loaded nanoparticles were carried out by USP type II dissolution test apparatus in 900 ml of media (0.1N HCl) for the first two hours and then in phosphate buffer (PH 7.5) from 3 to 72 h at 37± 0.5^0C and stirring rate of 100 rpm. 5ml samples were taken on a regular basis and replaced with an equivalent volume of fresh dissolving medium. The concentration of glibenclamide was evaluated spectrophotometrically at 300 nm using a UV-Visible spectrophotometer after filtration through Whatman Grade No. 41 quantitative filter paper (pore size 25 µm). In order to decide the drug release mechanism, different kinetic models (first order, zero order, and Higuchi) were used to examine the *in vitro* release profile.

Results and Discussion: The *in-vitro* release profile and release kinetics of glibenclamide via glibenclamide loaded PLGA nanoparticles revealed that drug release reduces as polymer concentration increases. However, drug release has risen in formulations with higher drug concentrations. Formulation release behavior *in vitro* follows zero-order kinetics. DSC analysis revealed that stable glibenclamide loaded PLGA nanoparticles were successfully produced using the solvent evaporation process with no incompatibility.

Conclusions: The emulsification solvent evaporation process was used to produce stable glibenclamide loaded PLGA nanoparticles with varied glibenclamide PLGA ratios. With appropriate drug content, the encapsulation efficiency of the produced nanoparticles was significantly increased. The drug release was also sustained as the polymer concentration increased, demonstrating its potential use in drug delivery.

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Nuclear Imaging and *in vitro* assessment of starch Microsphere of Gliclazide Hydrochloride

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Background & Rationale: Microspheres or microparticles, are small spherical particles with a size ranging from 1 µm to 1000 µm. They may be made up of either natural or synthetic polymers [1] . Gliclazide is mainly categorized as an antidiabetic drug used to manage type II diabetes and is taken orally. In relation with the previously available study data, good general tolerability of this drug among the individuals can be predicted along with a minimum rate of secondary failures. However, gliclazide is found to have a slow and variable absorption pattern which can be related because of its hydrophobic nature that limits its dissolution or its poor permeability across the gastrointestinal tract [2]. In order to control the drug release, the study approach involves incorporating gliclazide in mucoadhesive microspheres using starch isolated from *Musa babisiana* species.

Methods:

A) Formulation of mucoadhesive microspheres: In total nine formulations of gliclazide loaded microspheres were prepared using ionic gelation. The starch from the banana species was extracted out following some modifications. Finally, the drug along with the starch and sodium alginate were mixed together and microspheres were prepared using calcium carbonate as a cross linking agent in presence of deionized water.

B) *In vitro* release, Bioadhesion and Gamma scintigraphic study:

The *in-vitro* release study of the prepared Gliclazide-loaded mucoadhesive microspheres was carried out in both gastric and intestinal pH for 12 hours using paddle type dissolution apparatus. At different time intervals samples were withdrawn and the amount of drug was measured using spectrophotometric techniques. Bioadhesion study was carried out using goat intestinal mucosa both in gastric and intestinal pH for 12 hours. Furthermore, the optimized formulation was evaluated for its site specificity using 99mTc as the radiolabeling agent by the technique of gamma-scintigraphy in rabbits.

Results and Discussion: The *in-vitro* release data from all the batches of prepared microspheres indicates that cumulative percentage release of microspheres is significantly impacted by the increase in concentration of polymers. The increased density of the polymer matrix at higher concentration results in an increased diffusion path length. Further studies also suggested that the prepared microspheres possess good mucoadhesiveness. The *in vivo* biodistribution study of the optimized formulation in rabbits using the technique of Gamma Scintigraphy justified the design concept and related the potential of this developed system for stomach-specific targeting.

Conclusion: From the above study, conclusion can be drawn that this *Musa babisiana* starch is a potential mucoadhesive agent available from a natural source and can be utilized to formulate site-specific controlled release mucoadhesive microsphere orally, thereby enhancing the bioavailability of drugs.

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Skin penetration and retention profiles of a dermal cosmeceutical intended for use in high altitude areas for UV radiation protection

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Background and Rationale: Solar ultraviolet (UV) radiation increases at higher altitudes and snow covered areas possess a far greater risk, as UV radiation is reflected by snow causing a 2-fold increase in radiation intensity. Upholding the sanction directive of the Ministry of Defence, Government of India; the Hygiene Chemical Standing Technical Committee, proposed the introduction of a sunscreen formulation into the Indian Army for troops deployed at 6000 feet above sea level or higher. Therefore, a formulation was designed which contained a synergistic combination of USFDA approved sunscreen ingredients and two antioxidant compounds which results in a 50+ SPF value and added antioxidant activity to reduce the detrimental effects of reactive oxygen species generated due to UV exposure. The formulation was designed to be stable at subzero conditions and provided optimum photoprotective activity with ability to modulate TGF-β-Smad mediated oxidative collagen degradation pathway; NF-κB and MAPK inflammatory pathways. This research work was aimed at establishing the skin permeation and skin retention profiles of the UV filters used in the synergistic formulation.

Methods: (A) *In vitro* skin penetration study: The study was performed using freshly dissected Wistar rat abdominal skin mounted on a vertical Franz diffusion cell with 1.77 cm2 donor surface area and 7 mL receptor volume. The stratum cornem was faced down and dermis was facing the receptor compartment. Each diffusion cell contained 4% (w/v) bovine serum albumin (BSA) in 0.1M phosphate buffer (pH 7.4) maintained at 32°C by a circulating water bath and stirred at 300 rpm using magnetic stirrer bars. According to the COLIPA standard procedure, 2.0 mg/cm^2 of the sunscreen formulation was applied on the skin surface. Samples were withdrawn at 0h, 4h, 8h, 12h and 24h and replaced with an equal volume of receiving solution pre-thermostated at 32°C. Each sample was subjected to HPLC analysis to determine the amount of UV filters absorbed [1].

(B) *In vitro* skin retention study: At the end of the 12-hour exposure time, SC was stripped from the skin samples using 16 cuts of cellophane tapes (3M, Scotch, St. Paul, MN, US)[2]. Discarding the first one, the remaining tapes were cut and sonicated for the extraction of epidermis and dermis (E+D). Each sample was subjected to HPLC analysis to determine the amount of UV filters retained on rat skin.

(C) Human skin penetration study in real-life conditions: The study was carried out on 10 healthy subjects between the ages of 20–40 years with undamaged skin and no history of cutaneous disease. The method of tape-stripping was used for the study which was carried out in real-life conditions at an altitude of 13200 feet above sea-level. The amount of UV filters remaining on the skin after 6h of application and exposure to real-life conditions was determined by subjecting the pooled samples of 20 tape-stripping to HPLC analysis[3].

Results and Discussion: It was found that the cumulative amount of UV filters permeated through abdominal skin of Wistar rats was below 1%. Similarly after washing of the skin at the end of the experimental period, the quantity of UV filters retained on the stratum corneum and E+D were found to be below 1% which indicated that the actives did not diffuse into the skin even after 24h exposure. It was also observed that over 90% of the UV filters were recovered in the skin tape-stripping samples which indicated that very little UV filters penetrated the viable epidermal layer of the skin. This suggested that the UV filters were retained on the skin for an adequate amount of time for optimum photoprotective activity.

Conclusion: Applied sunscreen must be retained on non-viable epidermis to provide maximum photoprotection and minimum systemic absorption. The skin penetration and skin retention profile of this sunscreen formulation was found to satisfy these requirements, making it suitable for use in high altitude regions by Army personnel.

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Acknowledgements

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Development Of Novel Discriminating Dissolution Model For Osmotic Drug Delivery System

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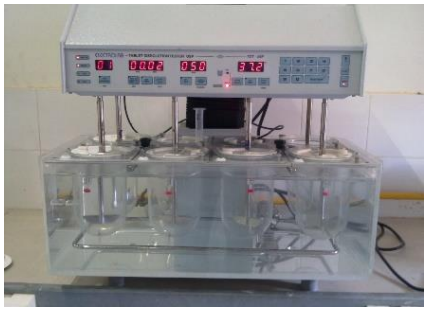
Background and Rationale: Dissolution profile has the power to guide during the development of new extended-release formulations. In the osmotic dosage forms, drug releases from pinch size of orifice while rest of the dosage form area is covered by water insoluble coating membrane through which media penetrates inside the dosage form, which in turn, critically governs the release mechanism by generating osmotic difference across inner and outer side of the dosage form. A major issue with the osmotic dosage form is that while subjecting osmotic tablets to the dissolution process, it is always ensured that the top of the tablet having orifice is not covered by the inner bottom part of the dissolution vessel. But, in order to follow this, the bottom side of the tablet (opponent to orifice side and at least 40% surface area of the tablet) is covered by the inner bottom part of dissolution vessel which ultimately affects rate of penetration of media into the dosage form, ultimately affecting release of drug from it. Therefore, the aim of this study was to develop discriminatory dissolution model for an osmotic drug delivery system to detect impact of critical formulation changes on the product performance that will potentially help to predict in-vivo behaviour during the development stage of new formulation.

Methodology: As a general procedure, tablet core of model drug, i.e. sertraline HCl, comprising of osmogent, osmopolymers, surfactant and lubricant was prepared by direct compression. The prepared tablets were coated in lab scale coater using non-aqueous solution comprising cellulose acetate and PEG. Each tablet was mechanically drilled on one side to give a 0.8mm diameter aperture. Dissolution study was carried out at 37 ± 2°C in USP II apparatus using 900 ml in three different dissolution media, 0.1N HCL, phosphate buffers pH 4.5 and pH 6.8, at three different agitation speeds, i.e., 50 RPM, 100 RPM and 150 RPM, in 2 situations (1) free tablets as per normal dissolution condition, and (2) stationary tablets. To make the tablet stationary, each tablet was glued to the barrel stub of a 5-cc plastic syringe and the syringe-mounted tablets were attached to the sippers of dissolution baths. The height of the syringe mounted tablets was adjusted so that the tablets were below the media and above the paddle.



Results and Discussion: In stationary tablets situation, variation of % drug release at each time point interval was found within ±5% across the all 3 media, i.e. 0.1N HCl, PB pH 4.5 and PB pH 6.8, at the different agitation speeds, i.e. 50, 100 and 150 RPM. While in free tablets situation, variation of % drug release increase upto ±15% within the same dissolution media depending on the incremental speed of agitation i.e. from 50 RPM to 100 and 150 RPM except that the variation was within ±8% at each time point interval at the same agitation speed in different dissolution media. We found that the main cause behind variation in dissolution profile at different agitation speed with free tablets is due to the fact that the bottom side of tablets (opponent to orifice side) (~ 40% surface area of tablet) is covered by the inner bottom part of dissolution vessel which ultimately affects penetration rate of media inside the dosage form resulting into varying release profile of drug from the tablets. As agitation speed increases, free tablets start rotating inside the dissolution vessel and even open up at the bottom side, ultimately increasing media penetration rate inside the dosage form which results in variation in dissolution profile at different agitation speed in case of the free tablets.

Conclusion: We conclude that dissolution studies with a stationary tablet that makes all sides of the tablet available for direct contact with the dissolution media could be a discriminating method for detecting impact of critical formulation changes on the product performance during the early product development stages.

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Evaluation of targeted and controlled drug release multi-particulate formulation with dual release mechanism through *in-vitro* and *in-vivo* approach

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Background and Rationale: SMD-24-80 is a glucocorticosteroid with a high local anti-inflammatory effect. Absorption of this compound is rapid and seems to be completed after oral dosing of plain micronized compound. However, the systemic bioavailability needs to be low, allowing high amounts of the drug to become available in the gut at specific site that produce anti-inflammatory actions. For this, the formulation needs to be developed in such a way to keep the drug available at the specific site in the gut to generate the maximum local actions similar to the innovator formulation. So, the formulation was developed and evaluated through a variety of *in-vitro* experiments and *in-vivo* through BE study.

Methods: (A) *In-vitro* (Dissolution) Experiments: As the formulation is having dual release mechanism throughout the gut, the *in-vitro* assessment of drug release is challenging and to be evaluated at a narrow interval of pH. Hence, the dissolution medium was selected across the range from pH 1.2 to pH 7.5 using conventional and simulated fluid, covering the entire biological pH range in the gut. The apparatus used was paddle with sinkers. The capsules were inserted in acidic medium for initial 2 hours and then the pellets were precisely and accurately transferred to the subsequent medium. The drug release of the test formulation was matched with that of the innovator formulation using similarity factor (f2). The simulated fluid was prepared in such a way to evaluate the rate of drug release through the second release mechanism, very effectively.

(B) *In-vivo* (Bioequivalence) Studies: Based on the nature of the formulation, the in-vivo performance was evaluated through bioequivalence studies using 16 healthy volunteers with two-way crossover study design in fasting and fed conditions containing enough and mandatory time points thoroughly.

Results and Discussion: Regarding *in-vitro* results, the first release mechanism had shown completely similar performance between the formulations in acidic pH as well as pH range below pH 5.5. The *in-vitro* results above pH 5.5 showed the similarity between formulations as the f2 values were above 50 in the dissolution media over the entire pH range involved in the study including the simulated fluid. Regarding *in-vivo* results, the fasting and fed studies had shown the acceptable results to represent the test formulation as bioequivalent to innovator formulation.

Conclusions: Based on *in-vitro* drug release similarity and *in-vitro* similarity of both formulations it was concluded that the test formulation is bioequivalent to the innovator formulation.

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In-vitro Dissolution vs *In-vitro* Lipolysis: Which is Better to Predict the *in-vivo* Performance of Lipid Formulations?

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Background and Rationale: Lipid Based Formulation Systems (LBFs) are widely used to enhance solubility and bioavailability of poorly water-soluble drugs. Generally, it is difficult to predict *in vivo* performance and clinically correlate the formulation performance due to lack of simulation of physiological conditions in dissolution testing. *In vitro* lipolysis technique is a promising alternative tool to predict the *in vivo* performance of LBFs. In present work we evaluate solubilization capacity of lipid-based formulations of curcumin and ticagrelor using *in vitro* lipolysis technique. Selected formulations were further evaluated for *in vivo* pharmacokinetic study in suitable animal model to correlate the *in vitro- in vivo* performance.

Methods: Various formulations of curcumin and ticagrelor were prepared using different composition of lipid excipients. Three variants of 30 mg curcumin capsules with fill weights 495 mg, 750 mg and 900 mg were prepared; similarly two variants of 90 mg ticagrelor capsules with fill weights 750 mg and 900 mg were prepared. The developed formulations of both the drugs and marketed reference were evaluated for *in vitro* dissolution using USP Type II apparatus in various dissolution media and via an *in vitro* lipolysis study. In vitro lipolysis study was performed on pH-stat apparatus (Metrohm AG, Switzerland), by adding the formulation to 36 ml of lipolysis medium at 37°C. After 10 minutes, 4 ml of pancreatin solution was added. To determine the solubility of the drug in the micellar phase aliquots of 1 ml were sampled at various time points up to 1 h. Each sample was immediately treated with inhibitor solution to stop lipolysis followed by centrifugation and analysis of supernatant using a validated HPLC method. Based on the performance of these formulations in lipolysis study the best formulations of both the drugs were selected for *in vivo* studies in Wistar rats.

Results and Discussion: The dissolution profiles for curcumin formulations matched with that of the market reference in all the biorelevant media i.e. HCl buffer pH 1.2; acetate buffer pH 4.5 and phosphate buffer pH 6.8; and in distilled water. The ticagrelor formulations showed remarkable increase in the dissolution in above dissolution media compared to market reference. In both the cases all lipid formulations produced up to 100% dissolution therefore it was difficult to select a formulation which could give similar *in vivo* performance. Therefore, *in vitro* lipolysis study was performed and the solubilization capacity of each formulation was estimated (Fig. 1). The capsule formulations with 750 mg and 900 mg filled weight of both the drugs showed superior solubilization in in vitro lipolysis study, therefore these were selected for animal studies and compared with market reference (Fig. 2).

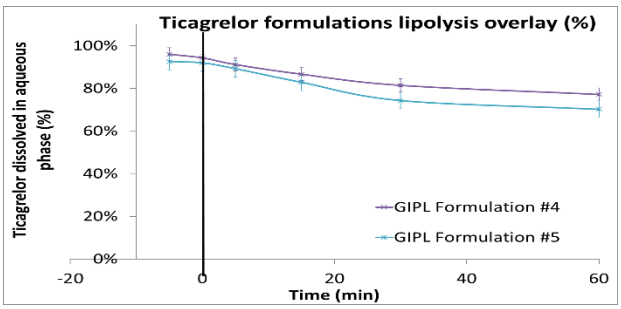

Fig. 1: *In vitro* lipolysis of Ticagrelor formulations.

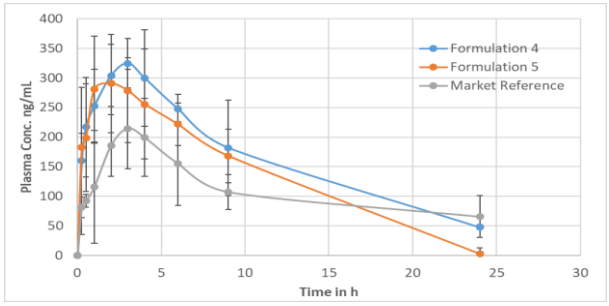

Fig. 2: *In vivo* PK study of Ticagrelor formulations

Conclusions: The *in vitro* dissolution profiles for all the formulations showed good drug dissolution, but the test was not sufficient to discriminate an optimum formulation for pharmacokinetic studies. *In vitro* lipolysis test proved to be an excellent discriminatory tool to evaluate the solubilization capacity of lipid-based formulations and to establish *in vitro* - *in vivo* correlation and can enable selection of the right LBFs prior to clinical studies to save time and expenses.

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Authors are thankful to Gattefosse SAS, France for carrying out *in vitro* lipolysis studies and also to ACG worldwide for providing gift samples of Capsule shells.

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Application of Dissolution for Evaluation of Taste Masking Effect of Primaquine Phosphate Complex Developed with Ion Exchange Resins

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Background and Rationale: Taste masking of primaquine phosphate (PP) using ion exchange resins (IERs) and subsequent solid oral formulation development was carried out. A simple and reliable *in-vitro* dissolution testing was employed to evaluate taste masking capability by quantifying release of the drug in simulated salivary fluid (SSF). Human sensory panel is usually employed to evaluate palatability of oral formulations. However, the use of human volunteers could involve ethical issues and higher costs. Electronic tongue, an alternative *in vitro* option is convenient, but it comes with a disadvantage of non-reproducibility owing to sensitivity to smallest environmental changes. Dissolution testing to potentially predict or quantify the effect of the taste masking is a simple, cost-effective, facile approach that can be used during the early stages of formulation development, optimization as well as a QC tool during commercial manufacturing of a taste masked formulation[1]. The current work involved taste masking of a highly bitter drug, PP using a popular and commercially viable approach of complexation with ion exchange resins (IERs). Dissolution testing was used as a tool to evaluate the taste masking efficiency of the complexes.

Methodology: PP and cation exchange resins namely IER 64, IER 69 and IER 88 (Amberlite IRP 64, 69 and 88 resp.) were subjected to complex formation in 1:1 and 1:2 weight ratios using shake flask method at ambient temperature. The resulting drug resin complexes (resinates) were filtered and dried at 50°C and the filtrate was evaluated for uncomplexed drug. The resinates were subjected to evaluation of drug loading and *in vitro* drug release studies. USP type II apparatus was employed and 900 ml of buffer (0.1N HCl containing 30% 2M NaCl) maintained at 37°C, stirred at 50 rpm was used as a dissolution medium. Resinates containing PP and IER 69 in 1:2 ratio {Resinate 69(1:2)} equivalent to 15 mg dose of primaquine was added to 10 ml of simulated salivary fluid (SSF) maintained at 37°C under gentle agitation. Aliquots (150 µl) were withdrawn at 15, 30, 45, 60 and 120 sec and analyzed for free PP concentration using validated RP-HPLC. The resinate was further formulated into orally disintegrating tablets using excipients like Pearlitol, Startab,Starch1500, Prosolv, Pruv and vanilla flavor. The tablets were subjected to *in vitro* drug release studies using aforementioned conditions.

Results & Discussion: *In vitro* drug release from resinate 69 (1:2) was found to be more than 88% within 1h indicating that complexation did not affect the drug release and would allow quick dissolution of drug in gastric fluid leading to its faster absorption. The resinate showed <0.5% drug release in SSF at the end of 2minutesof study period. This indicated excellent *in vitro* taste masking efficiency of the resinate. Optimized orally disintegrating tablet formulation of the resinate exhibited more than 90% drug release within an hour.

Conclusion: The orally disintegrating tablet formulation prepared with the resinate showed acceptable organoleptic, physical and *in vitro* release characteristics. The developed taste masked formulation is a better and commercially viable alternative to the conventional PP formulations .Dissolution test can be a simple, feasible approach for analyzing the taste masking during the formulation development and optimization as well as a Quality Control test for evaluating taste masking of batch production of the complexation.

Reference: 1. Gittings S.et al., *Dissolution methodology for taste masked oral dosage forms*. J. Control. Rel. 2014. 173(1) p.32-42.

Acknowledgements

Authors are thankful to Colorcon Asia Pvt. Ltd. for providing the samples of IERs and tableting excipients like Pearlitol, Startab, Starch 1500, HPMC E5. ; JRS Pharma Ltd. for providing samples of Pruv & Prosolv

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Artemether Solid Dispersion in Fast Disintegrating Tablet to Enhance Dissolution Rate and Oral Bioavailability

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Background & Rationale: Artemether (ART), an antimalarial drug, has poor solubility and low bioavailability[1]. Soluplus® (SOP)is a graft copolymer consisting of polyvinyl caprolactam, polyvinyl acetate and polyethylene glycol. It is amphiphilic in nature and thus can be effectively used as a solubilizer and as a carrier matrix. Therefore, solid dispersion (SD) of the drug was formulated using Soluplus and the SD was incorporated in the fast disintegrating tablet[2].

Methods: A) Preparation of Solid dispersion: The SD was prepared using the solvent evaporation method using a rotary evaporator. Fast disintegrating tablet of ART SD was produced by using directly compressible excipients such as Ludiflash (AFT1) and Ludipress (AFT2).

B) *In vitro* release and pharmacokinetic study of solid dispersion tablet: The ART SD was compared with the plain ART, marketed tablet, AFT1 and AFT2. The *in vitro* dissolution was performed in 0.1 N HCl + 0.5 % Myrj 52. Sample aliquots of 5 mL were drawn at different time points up to 120 minutes. After each withdrawal, an equal volume of dissolution medium was added to each vessel. The samples were filtered and analyzed by UV spectrophotometry at 210 nm and the percent drug release at each dissolution time point was calculated. Pharmacokinetic study was performed in mice for bioavailability enhancement.

Results: The drug release from plain ART was only 57.46 at the end of 2 hours which suggested the slower rate of dissolution due to poor aqueous solubility while the ART SD and the tablets (AFT1 and AFT2) showed improved dissolution rate. The drug release from AFT1 and AFT2 tablets after 2hours was 96.21% and 94.26% respectively. The ART SD and the tablets were superior in the dissolution rate from the marketed tablet [H1] as well as plain ART. The pharmacokinetic study in mice showed increased C_{max} and AUC_{0-24} for AFT1 tablet by 1.88 and 3.19-fold as compared to the marketed tablet indicating–improved bioavailability of ART.

Conclusions: The Artemether solubility was improved with the Soluplus by preparing solid dispersion in fast disintegrating tablets that resulted in improved dissolution rate and bioavailability after oral administration in mice.

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Bioadhesive colon targeted pellets of Curcumin and Cyclosporin for improved management of Inflammatory bowel disease

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Background and rationale: Inflammatory bowel disease (IBD) is an intestinal disorder characterized by aggravation of intestinal mucous layer leading to bloody and mucous diarrhoea causing variations in the intestinal pH, intestinal microbial flora and mucosal integrity[1]. Multiparticulate mucoadhesive formulations showing better mucoadhesion and a higher intestinal residence time are preferred to mitigate this issue[2]. Hence, the main objective of this work was to develop multiparticulate pH-dependent, sustained release mucoadhesive pellets of curcumin and cyclosporin for targeting the affected site for an improved therapeutic effect. The pellets were coated with a pH sensitive polymer for targeted drug delivery in the colon. Combination of curcumin and cyclosporin have been proven to exhibit a synergistic effect in management of IBD in low dose as compared to individual high dose. Therefore, curcumin and cyclosporine-loaded bioadhesive pellets may act as a promising targeted system in the management of IBD.

Methods: A) Formulation of Bioadhesive pellets: Extrusion-Spheronization technique was used for preparation of pellets. All excipients were mixed in a mortar and then wetted using purified water as a granulating liquid until a wet mass was obtained. The plastic mass was fed to the extruder followed by spheronizer for pellet formation. Pellets were coated with pH sensitive polymer Eudragit® S100 for targeted delivery in the colon.

B) In-vitro Dissolution studies: *In vitro* dissolution studies were performed on pellets with 5%, 10% and 20% weight gain after coating with Eudragit® S100. The dissolution was carried out in 250 ml of 0.1 N HCL with 2% SLS (sodium lauryl sulphate) for 2 h followed by 250 ml of a phosphate buffer pH 6.8 with 2% SLS for additional 4 h (total 6 hours) followed by a phosphate buffer 7.4 with 2% SLS for additional 18 hours. Aliquots were withdrawn at periodic time intervals, filtered through a 0.45-µm syringe filter and analysed by HPLC.

Results and Discussion: The formulations with 5% and 10% Eudragit® S 100 coating released more than 10% curcumin and cyclosporin at pH 1.2 whereas more than 70% cyclosporin was released at pH 6.8. In contrast, in case of the formulation with 20% Eudragit® S 100 coating both the drugs, curcumin and cyclosporine, showed no drug release at pH 1.2 (stomach pH), less than 15% release at pH 6.8 (intestinal pH) and almost 80% release at pH 7.4 (colonic pH) at the end of 24 h which was desirable. The *in vitro* release results of 20% Eudragit® S100 coating proved that curcumin and cyclosporine showed a gradient of pH-sensitive release characteristics.

Conclusion: Bioadhesive pellets of curcumin and cyclosporine coated with Eudragit® S100 is a promising approach for targeting both the drugs to the intestinal region for efficient management of IBD.

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Comparative drug release studies of Disulfiram from lipid nanocarriers in management of Cervical Cancer

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Background and Rationale: Cervical cancer is a significant cause of mortality and morbidity amongst women globally. Parenteral administration of chemotherapeutics like cisplatin are associated with drawbacks including lack of localization and unwanted systemic distribution of drug in the body causing systemic side effects like thrombocytopenia, neutropenia, nephrotoxicity, neurotoxicity, anaemia due to haematological toxicity, and bone marrow depression. Therefore, there is a dire need to search for new molecules or repurpose molecules. Disulfiram is currently used as an anti-alcoholic drug. However, it has shown potential anticancer activity by inducing apoptosis in some cell lines and reducing tumour growth and has potential in treatment of cervical cancer. However, the lipophilicity of disulfiram restricts its clinical use by its inability to cross physiological barriers. Therefore, we have attempted to formulate disulfiram using nanocarrier delivery system for effective delivery of anticancer molecules into the tumour tissues by exploiting the pathophysiology of tumour microenvironment. The aim of study was to do a comparative evaluation of release behaviour of disulfiram from two nanocarrier delivery systems- nanoemulsion and nanostructured lipid carrier (NLC).

Methods:

1) Formulation development- Disulfiram was incorporated in a conventional gel, nanoemulsion gel and nanostructured lipid carrier (NLC) gel.

2) *In vitro* release and *Ex vivo* release of drug- The optimised formulations were subjected to diffusion study to quantify the amount of drug release through PVDF membrane. Study was conducted on a Franz diffusion cell using 22 ml of receptor compartment filled with 3% Tween 80 + 50 % ethanol+ Phosphate Buffer pH 4 and pH 7.5. The temperature of the cell was maintained at 37°C ± 0.5°C with constant stirring at 100 rpm. Samples were withdrawn at regular intervals (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 hours), filtered and analyzed for drug content by UV spectrophotometry. The receptor compartment was replenished with fresh medium to maintain sink conditions after each sampling. Percent cumulative drug release was plotted as a function of time. For *Ex vivo* release studies, the above procedure was repeated using porcine vaginal membrane.

Results and Discussion: Drug release from NLC gel at the end of 12 hours was 84.49% in phosphate buffer pH 4 and 82.62% in phosphate buffer pH 7.4. The drug release from nanoemulsion gel was 87.17% in phosphate buffer pH 4 and 89.28% in phosphate buffer pH 7.4 at the end of 12 hours. *Ex vivo* studies showed that 61.29% drug released from NLC gel and 65.21% drug released from Nanoemulsion gel at the end of 12 hours each. Kinetic studies revealed that both formulations followed zero order drug release pattern.

Conclusion: Disulfiram was formulated into Nanoemulsion gel and NLC gel for treatment of cervix cancer stage 1. Both the formulations showed satisfactory drug release rate and can be explored for anticancer effect in cervical cancer.

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Comparative *in vitro* dissolution of itraconazole marketed formulations: cause and effect analysis

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Background and Rationale: Itraconazole is a synthetic triazole antifungal agent, which has recently also demonstrated anti-cancer activity. Owing to poor solubility and permeability, it exhibits low bioavailability (F~50%). The RLD, Sporanox® capsules also show significant inter and intra-subject variability. Several generic formulations of itraconazole capsules available in the Indian market have shown highly variable therapeutic outcomes. The current study aims to compare the *in vitro* dissolution of marketed formulations of itraconazole and establish cause-and-effect relationship between variability in drug release and various formulation aspects.

Methods: The *in vitro* dissolution studies of 10 marketed formulations of itraconazole were performed using the method described in the USP (Test 2). The % drug release was calculated at the end of 60 minutes after analyzing by UV-Visible spectroscopy (Cary60- Agilent). The formulations were also characterized for pellet size, size distribution, surface area, coating thickness, etc. (Leica Microscope APOS8).

Results and Discussion: Only 3 (including RLD) out of 10 marketed formulations passed the dissolution test as per USP monograph. The absence of surfactant in the dissolution medium as recommended by USP (Test 2) offered good discriminatory power to the medium. A larger pellet size (> 100 µ), lower number, and lower effective surface area of pellets per capsule could be responsible for lower dissolution in failing formulations. Wider size distribution range, as well as larger variation in surface area, could have led to % RSD as high as 67.59 (MF-A100) and 45.78 (MF-F100) among many formulations (Table 1). Photomicrograph images of formulations confirmed coating of placebo pellets with the drug as the method of pellet manufacturing and coating thickness influenced the drug dissolution. However, formulation MF-B100 (D_{60} - 5%) did not show drug layer on the pellets; indicating a different method of manufacturing, possibly extrusion- spheronization. The presence of the drug in the pellet matrix could have affected the dissolution of the drug in this case.

Formulation code	%DR	%RSD	Pellets count (Nos.)	Diameter (µm)	%RSD	Particle size range (µm)	Area (µm²)	%RSD	Coating thickness (um)
MF-A100	59	67.59	572	107.89	7.16	93.87-122.09	9184.86	14.34	38.37
MF-B100	5	12.64	387	120.1	8.86	99.56-133.20	11410.78	17.18	uncoated
MF-C100	21	46.43	145	166.59	5.52	153.03-179.6	21858.44	10.98	46.5
MF-D100	15	4.22	615	106.17	9.79	90.95-125.28	8932.87	19.64	39.79
MF-E100	**93**	3.99	825	92.65	3.44	88.105-97.89	6749.31	6.88	37.32
MF-F100	62	45.78	155	176.54	5.29	164.01- 95.29	24543.04	10.69	47.2
MF-G200	10	41.31	697	107.3	9.73	86.05-122.11	9123.22	18.6	57.02
MF-H200	67	13.32	890	108.91	4.72	101.7-114.88	9334.38	9.36	50.96
MF-I100	**95**	1.45	976	91.26	8.5	77.87-103.13	6586.24	16.73	35.39
MF-J200	**95**	0.79	1414	92.39	7.09	77.50-100.99	6736.96	13.69928	45.76

Conclusion: Comparison of itraconazole marketed formulations using discriminatory USP method revealed a failure in the dissolution for most of them. The method of manufacturing, pellet size, size distribution, surface area and drug coating thickness were observed to be critical factors influencing the dissolution. The low and variable dissolution could be one of the major reasons for the poor and variable oral bioavailability. .

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Cyclodextrin-based binary and ternary complexes of Zaltoprofen for solubility and dissolution enhancement

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Background & Rationale: Zaltoprofen (ZPF) is an important non-steroidal inflammatory drug having powerful inhibitory actions on acute and chronic inflammation by suppressing the prostaglandin synthesis and bradykinin responses[1]. However, ZPF is poorly water soluble and thus its absorption in the body is compromised. Cyclodextrins (CD) are cyclic oligosaccharides consisting of D-glucopyranoside units connected by glycosidic bonds [2]. CD due to their hollow cone structures, can entrap hydrophobic drug molecule into CD cavity through various intermolecular forces. The present study was aimed at formation of binary and ternary complexes of ZPF for its solubility and dissolution enhancement. The effect of L-Arginine (L-Arg) on solubilizing and complexation abilities of cyclodextrins namely, β-CD and HP-β-CD were assessed. Complexes were characterized by saturation solubility and *in vitro* dissolution studies. Change in crystallinity was evidenced by DSC study. Interaction of drug with CD and L-Arg was established using FTIR and ^{1}HNMR studies. Thus, ternary system of ZPF could be an innovative approach for its solubility and dissolution enhancement.

Methodology: A. Preparation of inclusion complex: Phase solubility study was carried out as per Higuchi-Connors method for prediction of possible molar ratios of inclusion complexes and selection of ternary agent. The binary (ZPF: β-CD and ZPF: HP-β-CD) and ternary inclusion complexes of drug (ZPF: β-CD: L-Arg and ZPF: HP-β-CD: L-Arg) were prepared by physical mixing, spray drying and co-evaporation method.

B. Characterization: Solubility of ZPF inclusion complex in water and HCl was determined by shake flask method. *In vitro* dissolution study was done to explicate the influence of complex formation on drug release, which was performed using USP Type II paddle type dissolution apparatus and HCl buffer (pH 1.2) dissolution medium. On the basis of saturation solubility and dissolution studies, binary and ternary complexes chosen for further characterization studies by FTIR, DSC, and ^{1}HNMR.

Result & Discussion: L-arginine was selected as an auxiliary agent for phase solubility studies and preparation of inclusion complexes. The ternary complexes showed greater increase in solubility and dissolution of ZPF than binary complexes of ZPF with β-CD and HP-β-CD. Formation of amorphous solid system are responsible for increased solubility. DSC study demonstrated strong interaction between pure ZPF and HP-β-CD or β-CD during the complex formation process along with higher negative enthalpy (ΔH) values which were indicative of stable complex formation. In NMR spectra, the chemical shift values of L-Arg have altered remarkably which is indicative of interaction of ZPF with CDs.

Conclusion: The apparent stability constant (K_c) and complexation efficiency (CE) of β-CD and HP-β-CD were enhanced due to addition of promising auxiliary agent L-Arginine in ternary complexes. Thus, inclusion complexation of ZPF with β-CD/ HP-β-CD and L-Arginine can be used as a promising method to improve its solubility for achieving better dissolution and oral bioavailability.

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Design and evaluation of multiparticulate extended release drug delivery system of an antihypertensive agent

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Background and Rationale: This study relates to the development of pellet formulation of an antihypertensive agent (AH) for oral administration as a controlled release formulation suitable for once a daily administration. This antihypertensive agent classified under BCS Class-I drug with pH dependent solubility, with maximum solubility at low pH. Thus, the aim of this study was to develop pellets which give the release in acidic as well neutral medium and further compare in-vitro dissolution with the innovator product. The specific objective was to optimize dissolution of ER coated pellets in 0.1 N HCl as well as pH 6.8 phosphate buffer by using the different strategies. Pellets were prepared with addition of excipients like pH regulator (strategy-I) and in-situ base former (Strategy-II) with controlled release polymer coating as well as enteric coating.

Methods: The solution layering technique was used for pellet formation with the help of a fluidized bed processor (GPCG 1.1, ACG, India). First the drug solution was prepared and sprayed onto the blank pellets i.e. sugar sphere, followed by extended release coating with different polymers. These ER coated pellets were filled into suitable size capsule.

***In vitro* Release Study of Extended Release Pellets:** These studies were performed in dissolution Type-II paddle apparatus (Make- Lab India, Model-DS8000) for 24 Hrs. Dissolution medium 0.1 N HCl and 6.8 Phosphate buffer; 900 mL at 100 rpm with the use of wire helix sinker.

Results and Discussion: In the strategy-I pellets were prepared with pH regulator in order to achieve drug release in both media as that of innovator but the drug release was achieved only in 0.1 N HCl, whereas in pH 6.8 phosphate buffer the release was found to be faster as compared to the innovator. Hence, the second strategy using in-situ base former was used to retard the drug release in pH 6.8 phosphate buffer. By applying strategy-II it was noticed that the drug release was controlled in pH 6.8 phosphate buffer but in 0.1 N HCl release was found to be faster than innovator. To control the drug release in 0.1 N HCl the enteric coat of polymer was applied on ER coated pellets. By performing enteric release coating dissolution was achieved in both media as that of innovator product.

Conclusion: Present work was carried in order to design and evaluate antihypertensive agent capsule containing extended release pellets. It is confirmed that optimized pellets give the identical release in 0.1 N HCl and pH 6.8 Phosphate buffer as that of innovator. With the use of *in-situ* base former and enteric polymer coating the drug release was successfully optimized in both dissolution media.

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Design and evaluation of osmotic controlled release oral drug delivery system of BCS class II drug by QbD approach

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Background & Rationale: Osmotic controlled release oral drug delivery system (OROS) was prepared for BCS class II drug antiepileptic drug (AED) which is a drug of choice for the treatment of partial and tonic-clonic seizures. It has low aqueous solubility, thus dissolution dependent bioavailability. Also, there is a need to achieve a controlled release of the drug due to its narrow therapeutic window (4-12 µg/mL) and possible side effects. The rationale of designing the osmotic drug delivery system of AED was its ability to maintain the plasma concentration of the drug within its therapeutic window, while reducing the incidence of adverse effects as well as offering the advantage of once daily dosing and thereby improving patient compliance. The QbD approach was applied and control strategy was proposed for critical formulation components which are elements of semipermeable coating membrane polymer, plasticizer and pore former to ensure defined targeted drug release pattern each time, and thus pharmacokinetic fate of the formulation.

Methodology: (A) Development of OROS: Unitary core tablets (400 mg) were prepared by wet granulation method in RMG using purified water as a binder. Granules were compressed using 12.00 mm (D-tooling, round, standard concave, beveled edge) punch on rotary compression machine. ER coating (700 mg) was added using an auto coater. In total, 09 experimental runs were conducted with four factors which are coded at 2 levels, Low (-) and High (+). Tablets were drilled to have 0.6 mm orifice size using a manual drilling machine.

(B) *In Vitro* dissolution testing: Performed in a USP type I, basket apparatus with cage sinker using deaerated purified water as a dissolution medium (1800 mL) at 100 RPM, 37^0C ± 0.5^0 C. Test was performed for 24 h. Aliquots were withdrawn at predetermined time points, diluted as required and the dissolved drug was quantified using UV-Vis Spectrophotometry at 284 nm.

Results and Discussion: All formulation trials showed drug release within specifications as per USP. (More than 75% at the end of 24 hrs). The proposed control space for critical material attributes of ER membrane coat showed desired drug release within the limits and thus the range defined for all the polymers; CA320 S, CA 39810 NF, HPMC 15 CPS and PEG 8000 was suitable to develop a dosage form which would maintain drug release within the therapeutic window while avoiding the peak-valley fluctuations. Also, optimized formulation had drug release comparable to that of the reference product.

Conclusion: OROS is a suitable DDS for BCS class 2 drug in order to achieve improved dissolution, therapeutic levels of drug between MEC and MSC to give a safe drug product which would improve the patient compliance.

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Design, development and evaluation of artesunate loaded solid lipid nanoparticles

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Background and Rationale: Artesunate is listed as essential medicine by WHO. It is included as therapy for serious malarial infection caused by *Plasmodium falciparum* with anti-infective, antimalarial, antiparasitic, and repellent properties. The challenging part of the drug profile is its poor solubility, poor permeability with a lower half-life that leads to higher and frequent dosing with poor patient compliance. The research aims to resolve the underlying problems of artesunate therapy by designing and developing solid lipid nanoparticles.

Methodology: Based on preliminary observation of entrapment efficiency, drug loading, and size the solvent injection method was selected for formulation of artesunate SLN. Here, cetyl palmitate was used as lipid, span 60 as a lipophilic surfactant, and tween 80 as hydrophilic surfactant. The prepared SLN were evaluated for drug entrapment, size and *in vitro* drug release.

Results and Discussion: The entrapment efficiency and drug loading of the final selected batch were found to be 83.4% and 5.38% respectively. Zetasizer study of SLN batch revealed the formation of nanoparticles of approximately size 278.1 nm which indicated SLN that was formed was in nanoparticle range of 10-1000 nm. The FE-SEM study of SLN has revealed the formation of nanoparticles of approximately size 246 nm which also indicated the formation of SLN in the range of 10-1000 nm. The drug release from SLN dispersion at the end of 2 hours was 97.5% and 73.34% respectively.

Conclusion: A factorial design study proved that drug release and entrapment efficiency values are strongly dependent on the concentration of span 60 and tween 80 respectively. Na CMC has shown a positive effect on drug release whereas; Carbopol 940 has a greater linear effect on viscosity and bio-adhesive strength of formulations as it has a high degree of gelling capacity. Also, the solubility study data indicate up to 50 fold increase in solubility for both the methods.

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Design, Optimization and Evaluation of SNEDDS for oral delivery in the management of Gout

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Background and Rationale: Gout is the commonest form of attenuated rheumatological disorder and a type of inflammatory arthritis. Febuxostat (FXT), a xanthine oxidoreductase inhibitor (BCS Class II) widely prescribed for the treatment of gout and hyperuricemia has variable pharmacokinetic parameters following oral administration (bioavailability: 40-50%, plasma half-life: 5-8hrs) [1]. Self-nano emulsifying drug delivery systems (SNEDDS) are characterized by small particle size, excellent stability, enhanced permeation across the intestinal membrane, reduced or eliminated food effects and enhanced drug bioavailability by reducing the hepatic clearance of the drug[2]. Novel approaches in SNEDDS have emerged with the advantage of improvement of stability. The aim of current research work is to formulate, optimize, and develop stable FXT-SNEDDS for improving the solubility and bioavailability with the objective to assess *in vitro* release of optimized batches of SNEDDS.

Methods: (A) Preparation and characterization of L-SNEDDS & S-SNEDDS: Pseudo ternary phase diagram and D-optimal design were used for optimization of L-SNEDDS. The optimized formulation of L-SNEDDS was adsorbed onto Aerosil 200.

(B*) In vitro* release of optimized batches of L-SNEDDS & S-SNEDDS: Optimized batches of L-SNEDDS were filled in size 00 hard gelatin capsules. *In vitro* dissolution profile was done in USP apparatus II and compared to marketed and pure drug. The test was done at 37 ±0.5^{O}C at 50 rpm in dissolution media - pH 1.2 HCl, pH 6.8 and 7.4 phosphate buffer. 5ml of aliquot was withdrawn at specific time periods. The amount of the drug was determined by UV spectroscopy at 315 nm.

(C) *In vitro* diffusion studies using Dialysis Bag method**:** Dialysis membrane method was used for permeation studies in pH 1.2 HCl, pH 6.8 and 7.4 phosphate buffer. 1ml of SNEDDS was kept in one end sealed dialysis membrane along with dilution by buffer used. The pouch was rotated at 50 rpm at 37±0.5^{O}C. 5ml of aliquot was withdrawn at specific time periods. The amount of the drug was determined by UV spectroscopy.

Results and Discussions: First, various oil, surfactants and co surfactants were screened for formulation of FXT loaded L-SNEDDS and their concentration was optimized by QbD approach using D-optimal design. The optimized batches were thermodynamically stable and had particle size of 97.25 nm with zeta potential of -21.4mV and drug content in the range of 95-100%. The optimized batches of L-SNEDDS demonstrated approximately 75% drug release in 0.1N HCl pH 1.2 and 92% drug release in phosphate buffer pH 6.8 and 7.4 in 60 mins. S-SNEDDS were formulated and showed sustained and controlled drug release for 10hrs and drug was released completely within 24hrs. The formulations were stable at refrigerated and room temperature for 3 months.

Conclusion: The optimized formulations were suitable for enhancing solubility and bioavailability of FXT for oral administration. Also, it can be concluded that release was independent of pH.

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Development of a biorelevant dissolution medium mimicking South Indian staple Breakfast Meal (SIBM) – Feasibility studies

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Background and Rationale: Biorelevant *in vitro* dissolution media are useful for qualitative prediction of formulation as well as food effects on the dissolution and availability of orally administered drugs. Currently available biorelevant media like FaSSIF and FeSSIF are based on western food [1]. Indian cuisine differs markedly across various regions of the country and can have variable effects on drug dissolution and bioavailability. There are limited studies in this area. Aim of this study was to a)Investigate the effect of a typical SIBM (Idli, Chutney and Sambar) on dissolution rate of model drug, Levofloxacin Hemihydrate (LV), and b) Develop a biorelevant medium mimicking fed state after a typical SIBM. LV is an antibacterial drug belonging to BCS Class I (High Solubility, High Permeability) and is a widely used broad-spectrum oral quinolone antibiotic.

Methods: (A) Protein, Carbohydrate and Fat content in a typical SIBM: By Lowry method, Anthrone method and Soxhlet extraction method respectively.

(B) *In vitro* release studies: were carried out on plain drug LV (250 mg) and marketed preparation using USP-II Apparatus; 900 mL medium, at 37±0.5°C and 75 RPM. Aliquots (5 mL), withdrawn at periodic intervals upto 45 min were analysed by UV Spectrophotometry. The media used were: a) Compendial Media - 0.1N HCl and Phosphate Buffer pH 6.8; b) South Indian staple breakfast diet-based Medium (SISBM)- SIBM was crushed and slurry transferred to dissolution vessels containing 0.1 N HCl (pH 1.2)/ Phosphate buffer (pH 6.8) and volume adjusted with the respective medium; c) SIBM specific enriched medium (SIBMSpEM) –Calculated amounts of Protein (Albumin 0.51 %), Carbohydrate (Glucose 0.24 %), Fat (Lecithin 0.44 %) were taken in separate dissolution vessels and Simulated Gastric Fluid (SGF) pH 1.2 or Simulated Intestinal Fluid (SIF) pH 6.8 were added to prepare Protein enriched, Carbohydrate enriched & Fat enriched media, respectively; d) Combined South Indian enriched medium (CSIBM) - Calculated amounts of Albumin, Glucose and Lecithin (as above) were mixed and added to SGF pH 1.2/ SIF pH 6.8.

Results and Discussion: Plain LV dissolved rapidly in 0.1 N HCl (100% in 15 mins), compared to 94% in 45 mins in pH 6.8 Phosphate buffer; pattern of release from marketed formulation was similar. In SISBM and CSIBM, an increase in dissolution/release rate of plain LV and from marketed preparation was evident, particularly in SGF medium (2 fold increase). Studies in SIBMSpEM revealed that the enhancement of LV dissolution/release is mainly in the protein enriched medium, effect being more pronounced in pH 1.2 buffer enriched medium. This may be attributed to hydrogen bonding between His 241 part of protein albumin and piperidone carbonyl of LV, Ser 191 part of protein albumin and carboxylate site of LV; Glu 291 part of protein albumin and morpholinyl ring protons of LV[2].

Conclusions: A Simulated Medium mimicking typical SIBM was successfully developed. An increase in rate and extent in dissolution/release of LV was evident. However, more extensive studies are warranted and similar studies to be extended to other types of Indian meals and for more drugs of different categories and BCS classes.

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DEVELOPMENT OF CAROTENOID BASED LIPOSOMAL FORMULATION FOR OCULAR DRUG DELIVERY SYSTEM

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Background and Rationale: Age-related macular degeneration (AMD) is a painless eye disorder in which the macula is damaged, causing visual loss. Pathophysiology starts with oxidative stress which further leads to inflammation of the macula and neovascularization. Oxidative stress, inflammation, neovascularization are implicated in the onset and progression of AMD. Carotenoid of the xanthophyll class, used in present study; is abundant in the fibrous layers of the fovea, where it forms the macular pigment. It functions as an antioxidant and protects the body from photooxidative damage to macula, making it a potential candidate in reducing risk of AMD. The usage of lutein is restricted due to its low oral bioavailability, which is caused by its poor water solubility and stability. Liposomes are preferred carriers for enhancement of bioavailability and stability. Liposomes are non-toxic and biocompatible vesicular nanocarriers which can be used to encapsulate carotenoid to enhance its solubility and deliver it in a sustained manner with potential targeted delivery.

Methods: Excipients selected included L-alpha phosphatidylcholine as lipid, cholesterol as stabilizer and phosphate buffer saline 7.4 pH as a solvent. For the liposome based ocular delivery of carotenoid, ideal particle size was targeted between 50-200nm. Ethanol injection was selected for preparation of liposomes used in present study and batches were evaluated for particle size, zeta potential, %drug loading, entrapment efficiency and *in vitro* drug release.

***In Vitro* drug release from formulation and API:** The *in vitro* drug release was performed using two dialysis membranes. Dialysis membrane was soaked in distilled water for 12 hours at room temperature. The initial length was 8 cm and 5.4 mm was the diameter. In one case, 5 ml liposomal suspension was placed in the dialysis membrane equivalent to drug concentration (0.6mg/ml) and the other membrane was filled with 3 mg API. Both sides were closed by the clips and tested for leakages, Final length was 6cm. These dialysis membranes were placed into 75 ml PBS buffer saline pH 7.4 at 37^0C with 75 rpm. A 3 ml aliquot of the release medium was withdrawn for analysis at different time intervals and replaced with fresh 3ml medium. Drug release was determined by UV-visible spectrophotometer (2).

Results and Discussion: The initial release of API and optimized formulation was found to be similar, after that the drug release in formulation was found to be increasing, while in API drug release was found to be slower during the 36hr test period. Optimized liposomal formulation showed 96% drug release while the API only 54% drug release. This suggested that the liposomal formulation of selected carotenoid enhanced the solubility approximately 2-fold when compared with the API.

Conclusion: *In Vitro* drug release study shows the solubility enhancement with continued drug release of the liposomal formulation compared to the API. Thus, it can be concluded that solubility enhancement of drugs can lead to good retinal absorption of drugs with potential to increase the bioavailability of the drug in formulation.

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------ ☺ ------

Dissolution studies of Olanzapine Solid Self Micro Emulsifying Drug Delivery System.

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Background and Rationale: Olanzapine is an atypical antipsychotic agent. Being a BCS Class II drug it has poor aqueous solubility and high permeability, also it undergoes high hepatic metabolism. The bioavailability of BCS Class II drug is rate limited by dissolution. Hence, increase in bioavailability can be obtained by increasing the rate of dissolution. Self Micro Emulsifying Drug Delivery System (SMEDDS) is a novel lipid based drug delivery system. It is an isotropic mixture of oil, surfactant, and cosurfactant that can influence drug absorption by increasing its solubilisation capacity, enhance permeation of the drug, and is easy to formulate. Further lipid based drug delivery system will aid in lymphatic uptake avoiding first pass metabolism. The liquid SMEDDS formulation can be converted into a solid dosage form in order to improve the handling of liquid SMEDDS.

Methods: (A) Preparation of formulation: In the present study, Olanzapine SMEDDS was prepared using Capryol 90 as oil and Kolliphor ELP:Transcutol HP as Smix. SMEDDS was prepared by dissolving the drug into the lipid to aid its complete dissolution, followed by addition of surfactant and cosurfactant. From the microemulsion region, points were selected in such a way that mix concentration was minimum. Trials were conducted by varying the surfactant concentration and oil concentration. From this trial six best formulations were selected (FI, FII, FIII, FIV, FV, and FVI). The liquid SMEDDS were then converted into solid SMEDDS by adsorption technique using Neusilin US2 as adsorbent.

(B) Dissolution study: It was performed on selected formulations (NFI, NFII, NFIII, NFIV, NF V, and NFVI) and marketed tablets using USP type 2 apparatus. The dissolution medium consisted of 900 ml of 0.1 N HCl. The paddle speed and bath temperature were set at 50 rpm and 37 ± 0.5°C, respectively. Aliquots of samples were withdrawn at 5,10,15,30,45, and 60 mins. The withdrawn samples were filtered and analysed using UV spectrophotometry.

Results and Discussion: All the dry adsorbate SMEDDS showed 50% release in the first 10 mins as compared to 85% release from marketed tablet formulation. Marketed tablet formulation showed maximum release at the end of 10 mins whereas, the dry adsorbate SMEDDS showed a maximum release of 80% at the end of 60 mins.

Conclusion: The SMEDDS containing Capryol 90 as oil with Kolliphor ELP and Transcutol HP as surfactant and cosurfactant were prepared successfully. Dry adsorbate SMEDDS prepared using Neusilin US2 retarded the release of drug over 1hr. Formulation of olanzapine in SMEDDS form will aid in lymphatic uptake avoiding its first pass metabolism. This will result in improved bioavailability of the drug.

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Dissolution study of lipid-based drug delivery systems of primaquine

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Background and Rationale: Limitations of primaquine therapy include its risk of hemolysis and the need for repeated administration for preventing the relapse of malaria. The present investigation aims to explore different lipid-based formulation strategies for the sustained release of primaquine (PQ) and to reduce its hemolytic toxicity. There is no artemisinin combination therapy (ACT) with primaquine available to cure and also prevent relapse and further transmission. Hence the research work also aims to formulate primaquine in combination with artesunate as dual drug liposomes. Artemisinin acts as a blood schizonticide for both *P.vivax* and *P.falciparum*, and primaquine as hypnozoiticide for the prevention of relapse[1]. In the present study, various formulation strategies for sustained delivery of primaquine were explored *viz.* (i) combination of primaquine salt (PQ_{salt}) - primaquine base (PQ_{base}) in liposomes (ii) combination of artesunate - primaquine salt (PQ_{salt}) in liposomes, and (iii) primaquine base (PQ_{base}) solid lipid nanoparticles (SLNs).

Methods: (A) Preparation of formulations: 1. Liposomes were prepared using the thin-film hydration method. Drug loading in the core was done by the active pH gradient method. **(**i). PQ_{base} - PQ_{salt} liposomes: The PQ_{base} being lipophilic is entrapped in the lipid bilayer while the PQ_{salt} is encapsulated in the core. (ii). PQ_{salt} - Artesunate liposomes: To incorporate PQ_{salt} along with artesunate in liposome for ACT regimen. Here, the salt form stays in the core while artesunate stays in the lipid bilayer.

2. PQ_{base} is dissolved in the melted lipid, emulsified, and cooled under sonication to form SLN.

(B) *In vitro* drug release: Each formulation was filled in a dialysis sac and studied for *in vitro* drug release in 50 ml of pH 7.4 phosphate buffer at 100rpm maintained at 37±0.5°C. Aliquots withdrawn at specified time intervals were centrifuged and the supernatant layer was analyzed for drug content using HPLC.

Results and Discussion: The PQ_{base} - PQ_{salt} combination showed a sustained release profile releasing 80% of PQ after 6 hours. Artesunate and PQ were also released in a sustained manner in the case of dual drug liposomes. The % entrapment efficiency (EE) of PQ was more than 35% in both liposome preparations. The SLN with 65% EE exhibited a sustained release profile. All these formulation strategies were effective in entrapping a sufficient amount of drug in the system and exhibited reduced hemolytic potential as compared to the unprocessed drug.

Conclusions: Dual drug liposomes are beneficial for delivering drugs as ACT to prevent both relapse and transmission. The result from this investigation is indicative of the feasibility of dual drug liposomes for better control of malaria. The lipid-based sustained-release SLNs showed a better reduction in the hemolytic potential of PQ as compared to the liposomal formulations.

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Drug Release Studies Of Azithromycin Dihydrate Loaded Polymeric Micellar Systems

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Background & Rationale: The delivery of ophthalmic drugs is one of the most fascinating and demanding tasks faced by the pharmaceutical scientist. Azithromycin dihydrate (AZN.2H2O); a BCS Class II drug exhibits poor solubility in tear fluid that results in poor bioavailability after topical administration. Polymeric micelles as drug delivery systems have been explored in order to enhance the retention time of the formulation and thus the resultant bioavailability of drug. Polymeric micelles are used in drug delivery because of their interesting characteristics, like biocompatibility, low toxicity, core–shell arrangement, micellar association, morphology, nano size, and relatively high stability. The objective of the present study was to evaluate the release of AZN.2H2O from polymeric micelles and ascertain the modulation in its release by incorporation in polymeric micelles.

Methods: A)Formulation of drug loaded polymeric micelles : Thin film hydration method was used for the preparation of polymeric micelles. A thin film was prepared in rotary evaporator using solvent evaporation method after optimization studies utilizing ethanol as a solvent with different ratios of 1:5, 1:7, 1:10, 1:12, 1:15 for AZN.2H2O : Soluplus®. The obtained polymeric micelles were evaluated for particle size and efficiency, *in vitro* release studies and *ex vivo* permission studies.

B) *In-vitro* release study of AZN.2H2O loaded micelles: Release study was carried out for drug solution as well as polymeric micellar formulation by the dialysis bag method. The dialysis bags containing drug solution and polymeric micellar formulation were placed in 50 ml of STF pH 7.4 used as a release medium, at 37 ± 0.5℃ and the medium was stirred on the magnetic stirrer. 1ml aliquots were withdrawn from the release medium at 0, 5, 10, 15, 30, 45 minutes as well as for 1, 2, 4, 6, 8, and 10 hours and were replaced with 1ml of fresh release medium. The aliquots were then analysed by UV spectroscopy for release of AZN.2H2O at absorption maxima of 546 nm and its cumulative release was calculated using standard plot developed for the drug. The measurements were performed in triplicate for each sample**.**

C)*Ex vivo* permeation study: The trans-corneal permeability of developed micellar formulation was studied on excised goat corneas. The study was conducted using Franz diffusion cell where the upper chamber served as a donor compartment and the lower chamber served as receiver compartment that contained STF. The assembly was maintained at 37℃±0.5℃. The concentration of drug in aliquots was quantified using UV spectroscopy. Amount of drug permeated through goat cornea from plain drug suspension, aqueous dispersion of polymeric Micelles, was determined and evaluated as flux and permission. The obtained release data was fit into kinetic models and the best fit model was selected.

Results and Discussion: A clear polymeric dispersion of micelles was obtained. The polymeric micelles exhibited a particle size of 62.81 nm and entrapment efficiency of 89.73%. The polymeric micelle formulation was found to show a flux of 55.56 $\mu g/cm^2/hr$ and permeation of 0.05556 cm/hr x 10^{3}. The % cumulative release for the drug was 27.03±3.37.

Conclusion: From the *in vitro* drug release and *ex vivo* permeation studies it was observed that AZN.2H2O loaded polymeric micelle formulation with potential for improved delivery was successfully formulated.

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Evaluation of Terbinafine Hydrochloride release from Solid lipid nanoparticle gel

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Background and Rationale: Terbinafine hydrochloride is an active substance used for treatment of onychomycosis. It has high permeability with log P value of 5.5, can diffuse through the thick layers of dead skin and is retained in the skin for a longer time without systemic absorption. Conventional topical formulations penetrate the skin to a lower extent and hence necessitate longer treatment duration or have to be supplemented by oral therapy. Solid lipid nanoparticles show numerous advantages associated with this carrier system when delivered topically. The rationale of the current study is to develop a gel formulation of SLN loaded with terbinafine which gives long term release of the drug as compared to marketed formulation.

Methods: A) Preparation of formulations: In this study, Terbinafine hydrochloride SLNs were prepared by hot emulsification method, where solid lipids were glyceryl monostearate (GMS) and Compritol and emulsifier was Cremophor RH40. The lipid phase and water phase were separately heated. Once the added terbinafine hydrochloride was dissolved in the lipid phase, the water phase was mixed into it. It was mixed well on the vortex and then subjected to a probe sonicator.

B) *In vitro* diffusion: *In vitro* diffusion studies of marketed cream and developed SLNs were carried out using Franz diffusion cell using cellophane membrane of molecular weight (12-14 kDa). From the solubility studies it was decided to use a mixture containing phosphate buffer pH 6.8 and Tween 80 (0.8%) as diffusion medium. Aliquots were withdrawn and replaced with fresh medium at predetermined time intervals of 0.5, 1, 2, 4, 6, 8 and 24 hours.

Results and Discussion: The particle size of the formulation was found to be 262 nm and PDI was 0.3 which can be considered in the acceptable limit. Entrapment efficiency was determined by indirect method and was found to be 96.88%. Amount of drug diffused from the marketed cream is faster at most of the time points with complete release occurring at the end of 24 hours. The developed SLN gel showed 85.34% drug diffusion. It showed initial burst release followed by a sustained pattern up to 24 hours.

Conclusion: Higher entrapment would result in prevention of degradation of the drug and would ensure better release over longer time duration. SLN based gel showed sustained release as compared to marketed cream. Thus, the developed formulation can be used for sustaining the release of the drug.

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Exploring supramolecular synthon approach for solubility modulation of poorly-soluble Clotrimazole drug

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Background & Objectives: Crystal engineering technique has been widely investigated recently in order to tailor make drug properties at the crystalline level thus aiding to manoeuvre drug properties like solubility, stability etc.. In this approach an API and the conformer are non-covalently associated by hydrogen bonds in order to yield multicomponent cocrystalline compound with crystallinity different from the original active.[1] Clotrimazole (CMZ) is a broad-spectrum topical antifungal drug belonging to BCS class II drug showing poor solubility of 0.49 mg/L and instability in water. The objective of current research was to develop and characterize CMZ cocrystals, including saturation solubility and *in vitro* dissolution studies.

Methods : A) Development of of Cocrystals -GRAS listed coformers like Resorcinol, Fumaric acid, Salicylic acid, Benzoic acid, Itaconic acid, Methyl paraben, Succinic acid, p-Amino benzoic acid, Citric acid and Sucralose were screened using Cosmo Quick-18 Demo software. The cocrystals were prepared by three techniques- Solvent Evaporation, Ultrasound cocrystallization and Antisolvent cocrystallization, wherein various stoichiometric ratios of CMZ and the coformers were tried. **B) Characterization of cocrystals:** The obtained cocrystals were evaluated for different attributes like visual morphology, melting point, fourier transform infrared spectroscopy, saturation solubility and *in vitro* dissolution in Phosphate Buffer PBS 7.4 and distilled water, DSC, PXRD and SEM.

Results and Discussion: From the coformer scrutiny, Resorcinol and Fumaric acid were found to be most suitable and hence considered for further cocrystallization studies. All the 3 techniques were found to be successful in yielding cocrystals. A distinct difference in the visual morphology of cocrystals was observed as compared to plain CMZ (visually and SEM); and a distinct difference in chemical structure was confirmed by FTIR. The solubility of cocrystals was enhanced compared to that of pure drug and this in turn led to enhancement of dissolution rate. However, the solubility of physical mixtures was observed to be much higher than that of cocrystals and pure drug, indicating the enhanced probability of intimate contact with the drug and coformer during physical mixing, resulting in increased solubility.

Conclusion: The saturation solubility and *in vitro* dissolution rate of the physical mixture in Phosphate buffer PBS pH 7.4 and distilled water were found to be higher as compared to cocrystals and drug. This may be attributed to higher degree of interaction between drug and co former by physical mixing as compared to the 3 techniques utilizing solvent medium.

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Fabrication and characterization of CDI cross-linked β-cyclodextrin nanosponges of Paliperidone

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Background and Rationale: Schizophrenia is a mental disorder with symptoms such as diminished cognition, depression, reduced thought process, psychotic episodes, poor quality of life, etc. Antipsychotics are the drugs of choice in treatment of schizophrenia. Paliperidone (PLP) is an antipsychotic drug indicated for treatment and management of schizophrenia. PLP is practically insoluble in water and has poor oral bioavailability of about 28% (1). Inclusion complexation with cyclodextrins (CDs) is a promising method for improvement of solubility and bioavailability of poorly soluble drugs. Nanosponges (NS) are hyper cross-linked colloidal structures comprised of sub-microscopic units having cavities of nano meter size. They are synthesized by cross-linking many cyclodextrins using a suitable cross-linker. The inner cavity of NS resembles the pores of a regular sponge having ability to entrap molecules or drugs, therefore known as cyclodextrin nanosponges (CDNS) (2). Aim of this study was to develop inclusion complexes of PLP with carbonyldiimidazole (CDI) cross-linked nanosponges for enhancement of solubility and dissolution.

Methods: A) Synthesis of blank CDNS and PLP-loaded nanosponges: The CDNS were synthesized by polymer condensation method using CDI as a cross-linker in 1:4 (NS1) and 1:8 (NS2) molar ratio of β-CD: CDI. The nanosponges containing PLP were prepared using sonication method. The supernatant was separated and lyophilized. The lyophilized PLP-loaded NS namely, F1 (1:4 β-CD: CDI) and F2 (1:8 β-CD: CDI).

B) Solubility study and *in vitro* drug release study: Solubility study was carried out by adding excess amounts of F1 and F2 to 10 ml of distilled water in conical flasks. The flasks were stoppered and agitated for 24 h using a thermostatic rotary shaker maintained at 25°C and 100 rpm. The absorbance of the filtered supernatant was measured at 237 nm on a UV spectrophotometer. The *in vitro* drug release study was performed using USP dissolution test apparatus (USP type I) using 500 ml of pH 6.8 phosphate buffer as dissolution medium maintained at 37 ± 0.5 °C at 100 rpm.

Results and Discussion: The solubility of PLP, F1 and F2 was found in the order as PLP < F1 < F2, which was 98 and 105 folds higher than the pure PLP. The increase in solubility of PLP might be due to higher interaction of aromatic ring with the inner cavity of β-CD and availability of numerous pores of nanosponges for inclusion of drug. The interaction of PLP with CDNS was confirmed by FTIR, DSC, and PXRD studies. Formulation F1 and F2 showed controlled drug release over 6 h. The controlled release of PLP from formulation F1 and F2 obtained in drug release study can be owed to large degree of cross-linking which allowed inclusion of PLP in nanosponges cavities. About 73.3% and 78.35% drug release was obtained from F1 and F2 respectively. However, only 55.93% drug release occured from pure PLP after 3 h.

Conclusion: The remarkably enhanced solubility can be attributed to increased wetting property and decreased crystallinity of PLP. Thus, β-CD-based nanosponges is a novel and promising carrier for solubility and dissolution enhancement of PLP.

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FORMULATION AND CHARACTERIZATION OF PROVESICULAR TRANSDERMAL DELIVERY SYSTEM OF ITRACONAZOLE

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Background and Rationale: Itraconazole (ITZ) is an orally active triazole, synthetic lipophilic antifungal agent, used in the treatment of a broad spectrum fungal infections. Oral administration of ITZ is associated with severe side effects in the gastrointestinal tract, such as constipation, stomach pain, and exhibits low bioavailability (55%) due to its poor water solubility. Owing to these limitations, a transdermal drug delivery system of such antifungal agent was designed to improve the efficacy and bioavailability of the drug [1]. The main aim of this study was to formulate and evaluate proniosomes for transdermal drug delivery of ITZ by encapsulating the drug in various formulations of proniosomal gel composed of various surfactants like Tween and Span, with cholesterol and phosphatidylcholine.

Method: A) Formulation of proniosomal gel: Itraconazole Proniosomes were prepared by coacervation phase separation method. The optimised Proniosomal gel formulation was incorporated in Hydrogel matrices of two different polymers namely, Carbopol and HPMC.

B) Evaluation of prepared proniosomal gel and final hydrogel formulation: The optimised proniosomal gel (TF5) was subjected to *in vitro* drug release study. The final ITZ-proniosome loaded hydrogel formulation was evaluated for gel characteristics, *in vitro* drug release studies, *ex vivo* skin permeation studies, skin irritation studies, antifungal activity, and stability study.

C) Methodology of *in vitro drug release* and *ex vivo* permeation study: The *in vitro* drug release study for both gel and hydrogel was conducted by using modified Franz diffusion cell mounted with dialysis membrane-70 (Hi media). The donor and receptor compartment consisted of 1 g of gel formulation and 50 ml phosphate buffer pH 7.4 maintained at 37 ± 1°C, respectively. The aliquots of 5 ml were withdrawn at intervals of 0.5, 1, 2, 4, 6, and 8 h and analysed at 262 nm. The % CDR was calculated at the end of 8 h. The *ex vivo* skin permeation study was performed by using rat skin (Wistar albino rats) instead of dialysis membrane. The rest of the procedure was the same as that of the *in vitro* drug release study.

Results and discussion: Among all the formulated proniosomal gels, formulation TF5 containing tween 20 was found to be most efficient, with the *in vitro* release up to 35.72% after 8 hours. The final TF5-proniosome loaded hydrogel formulation (G2) complied with all the gels characteristics. The *in-vitro* diffusion study and *ex vivo* skin permeation study showed a release of 87.83 ± 0.52% and 90.89%, respectively and followed anomalous or Non-Fickian diffusion type. It showed similar antifungal activity against Candida albicans as that of marketed preparation. Skin irritation studies proved the safety of the gel. Both the TF5 and G2 hydrogel were stable at 2-8°C and room temperature.

Conclusion: It can be concluded that Itraconazole proniosomal hydrogel can significantly improve the therapy against skin fungal infection via transdermal route as proniosomes form depot in deeper skin layers and continuously release drug for a prolonged period thereby increasing the efficacy of treatment.

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Formulation and Evaluation of Telmisartan Nanosuspension and Development of solid Dosage Form.

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Background & Rationale: The dissolution rate of BCS Class II, which is a limiting factor in its bioavailability, is controlled by the surface area of the drug particles undergoing dissolution. The higher the surface area, the higher the rate of dissolution [1], as defined by the Noyes–Whitney equation. While other traditional methods for increasing drug dissolution rate are widely used, these techniques have practical limitations, and the desired bioavailability enhancement may not be achieved [2]. Hence recently, there is a lot of focus on nanosizing drugs for increasing the rate of dissolution and consequently the bioavailability.

Methods: **A)** Ultrasonication method: Nanosuspension was prepared by the precipitation–ultrasonication method. The effects of the concentration of PVA (Poly vinyl alcohol) and Poloxamer 407 in the anti-solvent and the concentration of telmisartan in the organic phase on the particle size of nanosuspension was investigated, and the optimal concentrations 0.15% w/v and 0.45% w/v were selected. Further, the nanosuspension was freeze dried to get the amorphous powder which was then converted into solid (Tablet) Dosage form.

B) Evaluation The particle size and zeta potential were determined using Malvern Mastersizer 2000 SM, Malvern Instruments Corp., U.K. Differential scanning calorimetry (DSC) was carried out to check the compatibility. The *in vitro* dissolution rate of telmisartan was performed by means of USP dissolution apparatus type II with speed 75 rpm at 37 ± 0.5ºC. Further, the liquid nanosupension was freeze dried and then converted into solid (tablet) dosage form. *In vitro* drug release of the developed telmisartan tablet was compared with marketed tablet.

Results and Discussion: Nanocrystals had mean particle size of 224 nm and zeta potential of 12.9 mV, respectively. The nanocrystals had a significant crystalline improvement as compared to pure crystals, according to the differential scanning calorimetry (DSC) study. The *in vitro* dissolution rate of telmisartan was significantly increased by reducing the particle size. Further, the *In vitro* drug release of the developed telmisartan tablet when compared with marketed tablet, was found to be more rapid. Thus, telmisartan IR tablets were formulated with good release profile.

Conclusion: The prepared tablet showed better drug release compared to the marketed tablet. Finally the effect of nano-sized telmisartan on dissolution rate, showed better results. So, Telmisartan IR tablets can be formulated with good release profile.

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Formulation and optimization of electro-spun transdermal patch of an anti-depressant drug

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Rationale: Depression is considered as a major contributor to overall global burden of disease by WHO. The selected antidepressant drug (AD) is taken orally but it undergoes extensive first pass metabolism thus shows low bioavailability (32±15%). Also, orally AD causes gastric irritation. Generally, AD therapy lasts for more than 6 weeks and thus immediate release dosage forms become less patient compliant. Controlled drug delivery can be helpful to reduce dosing frequency and thus increase patient compliance. Transdermal drug delivery can be used to provide both, controlled drug release as well as bypass first pass metabolism. In transdermal patch, uniform distribution of drug in matrix guides the release and thus formulation of patch becomes critical. Thus, a novel technique such as electrospinning technique can be employed to prepare nanofibres uniformly woven into transdermal patch. The aim of this study was to formulate electrospun transdermal patch of AD and evaluate drug release using Franz diffusion apparatus using cellulose acetate membrane.

Experimental Work : A. Preparation of Espun Transdermal patch of AD - Polyvinyl alcohol was dissolved in hot water and cooled till room temperature. Suitable plasticizer, co-solvent and AD were added under stirring to obtain a clear solution. The obtained solution was subjected to electrospinning at 0.5mL/hr flow rate, 150 rpm drum speed and voltage of 20kV and the patch was formed on a hard aluminum foil attached to the drum. The prepared nanofibre patch was characterized for folding endurance, elongation strength, thickness, drug content, Fourier transform infrared spectroscopy (FT-IR) and Differential scanning calorimetry (DSC). **B.** QbD based Optimization: A 2^2 factorial design was employed using two independent variables, concentration of polymer and concentration of plasticizer. Drug diffusion at 24 hrs and elongation strength were the dependent variables. **C.** *In-Vitro* drug release study using Franz diffusion cell: *In vitro* drug release was studied using Franz diffusion apparatus with receptor compartment capacity of 20mL. Cellulose acetate membrane with a pore size of 0.45µ was mounted between receptor and donor compartment. The receptor compartment was filled with phosphate buffer pH 7.4 and was mounted on a magnetic stirrer and temperature of media was maintained 32 ± 0.5 ºC. Sample was withdrawn at different time intervals upto 24 hrs and sink condition was maintained after each withdrawal. Samples were analyzed using UV-VIS spectrophotometer.

Results and Discussion : Quality by design approach was employed to understand the influence of critical formulation variables that affect the drug release. Increase in polymer concentration shows decrease in drug release which might be due to formation of thicker polymer nanofibers. Increase in plasticizer concentration shows increase in drug diffusion through cellulose acetate membrane. The optimized batch gave 80.57% drug diffusion at the end of 24 hours as against plain drug which gave 31.42% drug diffusion (Figure 1). The elongation strength of optimized batch was found to be 32%.

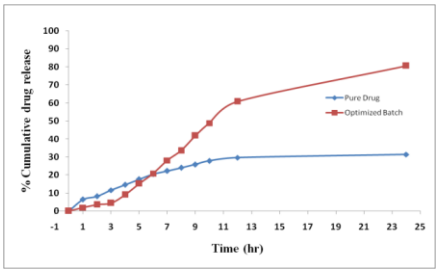

Figure 1 Drug Diffusion from pure drug and Optimized batch of transdermal patch of AD

Conclusion: This study has established the potential of developing electrospun transdermal patch of the antidepressant drug with desired sustained release and can be a better alternative to current marketed oral formulations for treatment of depression. Further studies using human cadaver skin to evaluate drug release can help understand drug diffusion through skin and thus can be helpful in further formulation development.

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Formulation, evaluation and dissolution rate enhancement of dispersible tablet for oral suspension.

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Background and Rationale: Pulmonary arterial hypertension (PAH) is a life-threatening disease, which further leads to progressive cardiac hypertrophy and right ventricular dysfunction. Though treatment strategies have improved over the past years, right heart failure still has a high mortality rate [1]. Drug X, an endothelin receptor antagonist is a class II drug with low solubility, high permeability and bitter taste. Therefore, to increase its solubility and mask the taste, dispersible tablets were formulated for easy administration of oral suspension in paediatrics [2]. The main aim of the study was to formulate and evaluate dispersible tablets with enhanced solubility for paediatric patients suffering from PAH.

Methodology:

A) Formulation of dispersible tablet for oral suspension: The dispersible tablets were prepared by wet granulation method using Glatt fluid bed processor equipment. Prepared granules were compressed and evaluated for physical properties, *in vitro* dissolution, disintegration time, assay, content uniformity and blend uniformity.

B) *In vitro* dissolution studies: Drug release profile of prepared tablets was compared with marketed formulation. The drug release studies were performed in 0.1N HCl pH1.2 with 0.5% SLS for 30 minutes at 37°C ± 0.5°C.

Results and discussion: The optimized batch showed better performance in comparison to other batches as the granules were not gritty after dispersion of tablet in water and drug release profile was found to be higher as compared to other trial batches. The dissolution profile of the developed dispersible tablet (% drug release of 97.4± 1.30% in 30 minutes) was found to be comparable with the marketed formulation (% drug release of 94.7± 1.43% in 30 minutes).

Conclusion: The developed dispersible tablet for oral suspension of drug X had a similar dissolution profile compared to the marketed formulation.

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In vitro Dissolution Study- A Critical Quality Attribute for the Optimisation of Developed Modified Elementary Osmotic Pump

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Background and rationale: Butorphanol Tartrate (BT) is a centrally acting opioid analgesic used in severe acute or chronic pains. It has short elimination half life (2.5-3.5hrs), requiring multiple dosing to achieve and maintain the therapeutic concentration, which leads to decreased patient compliance, increased incidence of side effects and tolerance. Controlled release delivery of drugs can promote extended and safe use (1). Among various oral controlled release devices, osmotically driven systems hold a prominent place because of their reliability, ability to deliver the contents at a predetermined rate for prolonged periods, ease of operation, good *in vitro in vivo* correlation and, convenience for production scale up(2). Osmotic tablets of BT based on monolithic osmotic technology were prepared and evaluated.

Methods: A) Oral controlled porosity membrane based osmotic system (modified EOP) also known as controlled porosity osmotic pump (CPOP) for delivery BT was prepared. Hydrophilic swelling polymers such as HPMC K4M and guar gum were selected for formulation development. These polymers were used individually and also in combination to arrive at an optimum formulation with desired *In vitro* release profile. Sodium bicarbonate was used as an osmogen, PEG400 and dibutyl phthalate as pore former, cellulose acetate as coating agent. The alcoholic solution of PVP K 30 M was added for granulation and granules were dried at 60ºC for 2 h, lubricated and compressed into tablets weighing 250mg using 8 mm deep concave punch on a single punch tablet machine. The batches were evaluated for studying the influence of varying osmogen, use of different types of pore formers, different concentration levels of pore former in coating solutions, effect of concentrations of cellulose acetate in coating solution, different types of coating membranes, effect of pH and effect of agitational intensity.

B) *In vitro* release study: The developed formulations were subjected to *in vitro* drug release studies using USP II dissolution apparatus at 100 rpm. Electrolab (India) Pvt. Ltd. Product code 123004 modified version was manufactured upon special request. 250ml mini jar conversion kit: 1) glass jar – (08 nos.) - capacity 250ml. 2) mini paddles – (08 nos.) 3) evaporation discs (08 nos.) 4) composite bath top plate for 250ml mini vessel 5) small centering device for 250ml mini jar 6) vernier calliper for 250ml mini jar along with new larger LCD display, Lan connectivity for central printing, storing and sharing of data. Unique timeaction™ function for media changeover and infinity test run, ideal for sustained and controlled release products adjustable sampling cannula for jar lid length 127 mm individual vessel temperature sensors. Dissolution medium used was phosphate buffer (pH 6.8, 250 ml) at 37˚C±0.5˚C. Aliquots of 5ml were withdrawn at 1, 2, 4, 6, 8, 12, 16, 20 and 24 h and the same amount of dissolution medium were replenished. The dissolution samples, after filtration through 0.45µm nylon membrane filters, were analysed using a developed validated HPLC method at 280 nm.

Results and discussion: The drug release was directly proportional to the concentration of pore formers and osmotic agents and inversely proportional to the concentration of polymer (cellulose acetate) in the coating membrane. From the *in vitro* release profiles of the formulations, it was evident that the drug release increased linearly with increase in concentration of osmotic agent and the extent of pore formation. Release was slower from dense coating proved that the drug release is directly proportional to porosity of coating membrane. From the *in vitro* study the drug release from the developed monolithic tablet was found to exhibit pH independent, agitation independent and volume independent release kinetics.

Conclusion: Drug release from monolithic tablets was linearly proportional to osmotic pressure generated. The formulation provides robust *in vitro* release over 24 hours, consistent with a once-a-day dosage form. Drug release data of controlled porosity osmotic pump formulations fitted well into zero-order kinetics, indicating the release to be drug load independent. *In vitro* studies concluded that the developed optimized formulation was independent of hydrodynamic condition. It was also concluded that optimization of formulation variables, especially the type of osmogen and its quantity and type of coating membrane formed with specific thickness, were found to be the key parameters to design and develop osmotic tablets for controlled and prolonged delivery of BT with improved therapeutic potential.

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Inclusion Complex of Curcumin With HP-β-CD and L-Arginine with enhanced solubility

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Background & Rationale: Curcumin, a naturally occurring yellow-orange polyphenolic compound derived from the plant *Curcuma longa*, has been well demonstrated to have anti-cancer, anti-inflammatory, anti-bacterial, anti-malarial properties, antileishmanial effect, antiangiogenic, antioxidant, analgesic, anti-inflammatory, and antiseptic properties [1]. Curcumin is poorly absorbed in the intestine, due to poor solubility leading to limited bioavailability [2]. Thus, the aim of the present research work was to improve the solubility and dissolution profile of Curcumin, a poorly water-soluble phytochemical by the formation of ternary inclusion complex, with hydroxypropyl β-cyclodextrin (HP-β-CD) and L-arginine.

Methods: (A) Formation of ternary inclusion complex with hydroxypropyl β-cyclodextrin (HP-β-CD) and L-arginine: The solubility of curcumin was enhanced through incorporation into cyclodextrin cavity by forming a binary and ternary complex using HP-β-CD and ternary agent L-Arginine. Physical mixing, kneading, co-evaporation, and spray drying methods were used to prepare the binary (Curcumin - HP-β-CD) and ternary complexes (Curcumin - HP-β-CD - L-arginine) in equimolar proportions. Additionally, Saturation solubility of binary and ternary complexes were evaluated.

(B) *In-vitro* release study: Dissolution studies of binary and ternary complexes were performed using USP type I dissolution apparatus at 100 RPM, in 900ml phosphate buffer (pH= 6.8) maintained at 37± 0.5°C.

Results and Discussion: L-arginine showed the highest saturation solubility and hence was used as ternary agent, which enhances solubilization efficiency leading to a synergistic effect on solubility and dissolution rate of curcumin. Saturation solubility of curcumin was found to be 0.0062 mg/ml in water. Out of the four methods used, ternary complexes of co-evaporation method were found to be 0.049 mg/ml. Phase solubility studies revealed an increase in solubility of the curcumin upon addition of HP-β-CD (with L-arginine in the case of ternary), showing AL type of graph indicating the formation of a 1:1 (binary) and 1:1:1 (ternary) stoichiometry inclusion complexes. Dissolution rate of ternary co-evaporation complex was obtained as 38.76 % in 10 minutes and 70.12% at 60 minutes. As per the result of the saturation solubility and dissolution studies, the ternary co-evaporation complex showed higher solubility and dissolution rate in comparison to other inclusion complexes and curcumin.

Conclusion: Curcumin, a poorly water-soluble phytochemical showed improved solubility and dissolution profile by the formation of ternary inclusion complex with hydroxypropyl β-cyclodextrin (HP-β-CD) and L-arginine.

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Inclusion complexes of Etodolac with hydroxypropyl-beta-cyclodextrin and auxiliary agent: Formulation and characterization

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Background andd Rationale: Etodolac (ETD) is a therapeutically important non-steroidal anti-inflammatory drug, classified as a BCS class II drug due to its low solubility and high permeability in the gastrointestinal (GI) tract. It reduces pain, swelling, and joint stiffness in arthritis, which is one of the most chronic inflammatory diseases[1]. Aim of this study was to prepare inclusion complexes of ETD with hydroxypropyl-beta-cyclodextrin (HP-β-CD) and to study the effect of L-arginine (L-Arg) [2] as an auxiliary agent on the complexation efficiency of HP-β-CD to improve aqueous solubility and the dissolution property of ETD.

Methods: A) Selection of auxiliary agents and preparation of inclusion complex (ICs): The auxiliary agents, viz., HPMC K4, PVP K30, PEG 4000, L-Arg, and glycine, were evaluated for their solubility enhancement property toward ETD. Binary inclusion complexes containing ETD−HP-β-CD (1:1 mol ratio) and ternary complexes containing ETD−HP-β-CD−L-Arg (1:1:1 mol ratio) were prepared by physical mixing (PM), co-evaporation (COE), and spray drying (SD) methods.

B) Solubility, *in vitro* dissolution and characterization: Solubility of prepared complexes of ETD was determined by classical shake flask method. Dissolution studies on the complexes were performed in (pH 1.2) HCl buffer, using a USP type II paddle type dissolution apparatus. Further the complexes were characterized using differential scanning colorimetry (DSC), Fourier transform-infrared spectroscopy (FT-IR), and powder X-ray diffraction (PXRD) studies.

Results and Discussion: The highest solubility of ETD was observed in L-Arg. The solubility of ETD increased linearly with respect to HP-β-CD concentration indicating an AL type curve. The stability constant (Kc) (2573.31 M−1) and complexation efficiency (CE) (1.209) values that were higher for ternary complex as compared to the binary system (Kc=162.11 M−1 and CE=0.078) could be attributed to addition of L-Arg and therefore suggest a more stable complex formation with improved complexation of CD with ETD. The improvement in drug release was in the order of pure ETD < PM < COE or SD. Ternary complexes of the COE and SD methods showed an increase of 19.96- and 20.73-fold, respectively, with respect to that of pure ETD. Ternary complexes prepared with the addition of L-Arg showed remarkable improvement in the dissolution profile of ETD than the binary complexes. The complexes prepared by the COE and SD methods showed greater dissolution as compared to physical mixtures.

Conclusion: The present study successfully demonstrated the formation of a ternary complex between ETD, HP-β-CD, and L-Arg, proving L-Arg as an effective auxiliary substance in solubility enhancement of ETD using a strategy of inclusion phenomena.

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Influence of Process Variables on *In Vitro* Performance of Developed Water Penetration-Controlled System Containing Poorly Soluble Drug

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Background & Rationale: Continuous suppression of pain through the use of opioid analgesics is now recommended in chronic pain treatment. Conventional or short acting opioids have shorter half-life, requiring dosing every 4-6 hours, making it non-compliant for the patient. With an aim to improve patient compliance, increase dosing intervals, provide constant plasma concentrations with less frequent peak to trough fluctuations fewer side effects improved clinical outcome, extended-release formulation was developed. The aim was to develop and evaluate water penetration controlled swellable matrices (CRSM) of butorphanol tartrate (10 mg). CRSM follow the mechanism where the drug release from the tablet matrix is controlled using a glassy polymer that hydrates rapidly to form a hydrogel layer before the tablet contents dissolve prematurely limiting media penetration into the tablet matrix. The objective was to achieve a sustained release profile i.e., 15 to 20% drug release in 2h, 30 to 35% in 6h, 35 to 45% in 8h, and 75 to 80% in 24 h and to study the effect of hydrodynamic conditions on drug release such as multi-rpm, multi-dissolution media and multiple dissolution volume. The study also investigates drug release kinetics of the developed formulation using mathematical models and compares the *In-vitro* release profiles of high (10mg) with low dose (5mg) strength of the drug.

Methodology: *In-vitro* drug dissolution is a vital component of tablet development and quality assessment. The *In-vitro* drug release studies on all the developed formulations were conducted to investigate various hydrodynamic conditions affecting the drug release from swellable matrices such as agitation, polymer grade, polymer content, tablet hardness, manufacturing procedure using a customized Electrolab TDT-08LX dissolution apparatus. The *In-vitro* release profiles of the developed formulations were investigated under following dissolution conditions. Buffers maintained at 37°C included: pH 1.2 Hydrochloric acid buffer for 2 hrs followed by pH 6.8 phosphate buffer for 24 hrs along with pH 6.8 PBS for 24 h at 50 rpm in 250ml of dissolution media and pH 4.5 acetate buffer for 24hrs at 50 rpm in 250ml of dissolution media.

Results and Discussions: From *In-vitro* release studies under various dissolution conditions, it was observed that drug release was found to be sustained with increasing pH (pH 6.8<pH4.5<pH1). There was no significant difference in the *in-vitro* release profiles at varying agitation speeds, 50 rpm and 100 rpm. Batch N1 showed comparable release profiles with Batch S12 when the dissolution studies were carried out in pH 4.5, pH 6.8 and pH change method (2).

Conclusion: There were no significant differences in the drug release profiles at 50 rpm and 100 rpm as well as in the drug release profiles when studied in 250ml and 500ml of dissolution media. However, significant differences were found in the drug release profiles when studied in 250ml and 100ml of dissolution media. Data was applied to Higuchi & Korsmeyer Peppas release kinetic models with higher value for r^2 confirmed the diffusion-controlled drug release mechanism. As the pH increases, the drug release was found to be more sustained. Drug release data from developed water penetration-controlled system formulations also fitted well into zero-order kinetics, indicating the release to be drug load independent.

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Investigations on a Dual Strategy in Dissolution Enhancement of a BCS Class 2 Drug.

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Background and Rationale: Dissolution improvement remains a mainstay strategy of formulation development of BCS class 2 drugs with a goal to improve their bioavailability. Recently, use of functional lipids as excipients is gaining impetus owing to their ability to aid solubility by emulsification and micellization. However, very few reports have appeared suggesting their use in tablet formulations. In this paper, we have developed tablets using lipidic surfactants that served a dual purpose as a binder as well as aid in dissolution. An anti-hypertensive drug, Telmisartan (TEL) from BCS Class 2 was selected. The drug has 40 % absolute bioavailability, pH dependent solubility and is reported to degrade in extreme alkaline conditions. It was therefore thought worthwhile to enhance dissolution by using a combination of lipidic excipients and alkalizers to provide basic microenvironmental pH.

Methodology: The tablets were prepared using wet granulation technique, Briefly, alkalizers in water, API dispersed in molten lipids, were mixed followed by addition of starch paste to prepare granules. Tablet was compressed using single punch (8.5mm) tablet press and characterised for drug content, weight variation, hardness and in vitro dissolution. Dissolution studies were performed on USP type 2 apparatus (LAB -INDIA) at 37°C in 900 ml of phosphate buffer (pH 7.5) as per USP and 0.1 M HCL (pH 1.2) as per IP at speed of 75 rpm. Samples withdrawn from dissolution media at specific time intervals (15,30,45,60,90,120 min) amount solubilized was determined by UV spectroscopy (SHIMADZU-UV 1900).

Results and Discussion: All the tablets were smooth in appearance, uniform in weight with hardness of 4.0-5.0 kg/cm^2. The drug content of all batches at different doses was found to be more than 90%. Preliminary studies on granules indicated improvement in dissolution of drug in presence of alkalizers and surfactants. Owing to basic nature, dissolution rate was observed to be more in pH 1.2 medium as compared to phosphate buffer. Increasing the lipid concentration reduced the dissolution rate probably due to the hydrophobic environment offered by the lipidic excipient. Furthermore, as the concentration of alkalizers in the microenvironment increased, the dissolution of drug also improved, both in HCl (54% to 82% at end of 60 min) as well as phosphate buffer (45% to 59% at end of 1 hour). Alkalizers more than lipids were observed to influence the dissolution profile of the drug.

Conclusion: Tablets using lipidic excipients could be successfully formulated. Modulation of microenvironmental pH can be a viable strategy to enhance the solubility and dissolution rate of telmisartan. This approach coupled with varying lipid excipients can be used to design IR as well as SR tablets of the drug.

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In-Vitro Blood-Brain Barrier Model: Development and Validation

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Background and Rationale: The prevalence of central nervous system (CNS) disorders is rising globally, especially due to the continuously increasing elderly population. The blood-brain barrier (BBB) protects the CNS and consequently, impedes the success of ongoing therapies by restricting the entry of drugs to the brain. Therefore, to discover newer CNS therapies, it is important to develop a BBB model where experiments can be carried out in a fast and simple way. Cell-based *in-vitro* BBB models are expensive, highly contamination-prone, have low TEER (transendothelial electric resistance) values with reproducibility & stability issues and are prone to variation in the results. Therefore, the phospholipid vesicles (or liposomes)-based BBB is a simple, promising, and alternative *in-vitro* model that mimics the lipid composition of brain endothelial cells with no contamination issues and high TEER value.

Methodology:

A) Liposomal Formulation and Barrier Development: The thin-film hydration method was used to produce liposomes containing phosphatidylcholine, phosphatidylethanolamine, sphingomyelin, and cholesterol. These mimic the lipidic composition of brain endothelial cells. Liposomes of two distinct sizes, specifically small and large liposomes, were used to establish a tight barrier. These were deposited into the pores and onto the surface of a membrane filter in a Transwell system by using centrifugation. The transendothelial electric resistance (TEER) value indicated that the tight liposome barrier was formed.

B) *In-vitro* drug permeability study: These experiments were performed in a phosphate-buffered saline (pH 7.4) using a set of standard drug compounds with different physicochemical properties such as molecular weight, log p-value, half-life, etc. Permeation studies were conducted after loading the donor compartments with the drug solution (100µl) and placing them in separate wells (24-well plates) with phosphate buffer (600µl) in the acceptor compartment. The donor compartment represents the blood side while the acceptor compartment represents the brain side. The samples (200µl) from the receiver compartment were withdrawn into 96-well, UV-transparent plates for analysis at fixed time intervals and an equivalent amount of fresh PBS buffer was then replaced. The cumulative amount of drug was plotted against the time and the apparent permeability coefficient was determined from the flux rate.

Result and Discussion: The apparent permeability coefficients from the linear flux rates were found to be 7.5×10^{-8}, 1.08×10^{-5}, 2.22×10^{-4}, and 1.12×10^{-6} cm/s for benzotropine mesylate, metoprolol succinate, tetrahydrocurcumin, and atenolol respectively. Depending on the difference in physicochemical properties, it has been found that these drug compounds have different apparent permeability coefficients.

Conclusion: The vesicle-based *in-vitro* model is a tight barrier of liposomes, representing a much simpler and easier method to mimic the BBB as compared to cell-based methods. This model used for high throughput screening of possible drug candidates for their permeability properties early in the development process, leading to a pre-selection of the best drug/nano system prior to continuing to *in-vitro* and *in-vivo* research.

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Modulation of the *in vitro* dissolution and *ex vivo* permeability of BCS Class III API

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Background and Rationale: API is an oral anticoagulant. Despite having very low aqueous solubility it falls under BCS Class III because of low dose and the highest strength of dose being soluble in 250 ml of water. Also, the API is a p-gp substrate which alters the permeability of drug and subsequently the bioavailability. Formulation of higher strength of doses is not possible because of low solubility and also high dose can induce toxicity. Several approaches such as use of surfactants, lipidic carriers, lipid- polymer carriers etc. are used to modulate the release and permeability of BCS Class III drugs(1). However, they have limited commercial use due to scalability issues. Hence a very simple and scalable method is sought after. Herein we have explored the use of mesoporous silica and soluplus to modulate the drug release and the permeability of the API.

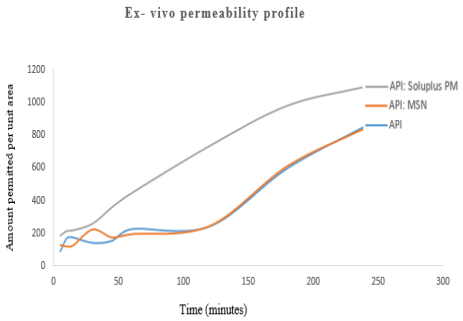
Methods: A. Preparation of API: MSN complex (API-MSN) and amp; API: Soluplus complex (API-SOL): The API-MSN complex was prepared by melt method, while the API-SOL complex was obtained by physical mixing method. The prepared samples were stored in a plastic container under room temperature.

B. Solubility studies: The saturation solubility studies of API, API-MSN complex and API-SOL complex were performed by adding an excessive amount of the samples to 50 ml of media. The solutions were placed in a shaking water bath rotating at 50 rpm and maintained at 37 ± 1 °C. After 24 hours, the dispersions were filtered through a 22-micron syringe filter and analyzed under UV-Spectrophotometer.

C. *In vitro* drug release: The dissolution studies were performed using an USP apparatus type II with a paddle rotating speed of 75 RPM and 900 ml of dissolution medium at 37 ± 1 °C. The dissolution medium used was 0.05 M sodium phosphate buffer with 0.05% SLS, pH 6.8. The collected samples were filtered through a 22-micron syringe filter and analyzed by UV-Spectrophotometry. The studies were performed in triplicate.

D. *Ex vivo* permeability studies: The permeation study was performed using a non-everted intestinal gut sac method using goat ileum. The permeation study was performed using a USP type II apparatus with a paddle rotating speed of 100 RPM and 250 ml of Ringers solution at 37 ± 1 °C. The collected samples were filtered through a 22-micron syringe filter and analyzed under UV-Spectrophotometer.

Results and Discussion: The solubility of API-MSN complex and API-SOL complex was improved 2 and 4.5 folds respectively as compared to pure drug. The dissolution profiles of pure drug, marketed formulation and API-SOL complex showed more than 85% drug release in 30 min indicating the immediate release whereas the drug release from the API- MSN complex was found to be around 48% in 30 min followed by sustained release over a period of 5 h. The ex-vivo permeability study indicated that permeation of the API across the non-everted goat ileum from the API -MSN complex was similar to that of the pure API. However, in the case of API -SOL complex the permeability was 1.28 times higher as compared to that of the pure API, possibly due to the p-gp inhibitory activity of soluplus (Fig 1). Thus soluplus, an amphiphilic carrier can be considered as a better carrier to modulate permeability of the BCS class III drug.



Conclusions: Though MSN could be used as a single component system to enhance solubility and modulate the drug release; it has no effect in modulating permeability of the BCS class III drug. Soluplus being a solubilizing agent and a p-gp inhibitor, enhances both solubility and permeability of API and hence could be preferred for enhancing the bioavailability of BCS class III drug.

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Mucoadhesive Microsphere Based Drug Delivery System for Epilepsy

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Background and rationale: Epilepsy is primarily a disorder characterised by spontaneous occurrence of seizures and involves hyper excitable neurons. Gabapentin has been found effective against simple and complex partial seizures, and it is a first-line drug for diabetic neuropathy. Gabapentin is absorbed through absorption window at duodenum via carrier-mediated transport pathway, but in case of conventional formulation, the gastric retention time is very short and most of the drug is eliminated as such. By preparing gastro-retentive mucoadhesive microspheres, the retention time of formulation can be prolonged, and using rate-controlling polymer, release of drug can be controlled so that saturation of carrier can be prevented and bioavailability of drug can be enhanced. The aim of the present study is to formulate, optimize and evaluate mucoadhesive microspheres based drug delivery system containing gabapentin for treatment of epilepsy.

Methods: (A) Preparation of Microspheres: Gabapentin microspheres were prepared by solvent evaporation method. Gabapentin was dissolved in dichloromethane: methanol (1:1) at room temperature. In the same solution ethyl cellulose and HPMC E50 were added and stirred using a magnetic stirrer to form a homogenous mixture. This solution was then poured into 100 ml of water containing polyvinyl alcohol (PVA) as an emulsifying agent and was stirred at room temperature for 3-4 hours at 500-800 rpm. The obtained microspheres were separated by filtration using Whatman filter paper and dried at room temperature.

(B) *In vitro* drug dissolution from Gabapentin microspheres: Dissolution studies for the developed Gabapentin microspheres were carried out in 0.1N HCl for a period of 12 hours. By using dissolution apparatus USP apparatus I – Basket Type apparatus. Dissolution medium and volume: 0.1 N HCl; 900 ml, Temperature: 37 ± 0.5 °C, Sample aliquots withdrawn: 5 ml, Time intervals: 2,4,6,8,10,12 hours.

Results and Discussion: Drug release gabapentin from microspheres was found to be sustained. From the result it was observed that formulation 1 (F1) gives 65.00% release in 12 hrs, and formulation 3 (F3) batch gives 78.13% release in 12 hours. Therefore, from the observed result F3 batch was selected for further evaluation.

Conclusion: Gabapentin loaded microspheres from formulation batch 3 (F3) was shown to be the suitable formulation to target the desired release. Further it is a viable alternative to costly and time-consuming encapsulation or any other nanoformulation.

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Nanoemulsion based in situ gel to improve bioavailability of poorly soluble drugs for effective management of retinoblastoma

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Background and Rationale: Retinoblastoma (RB) is the most common type of intraocular cancer of infancy that arises near the retina. There are around 8000 cases every year and in an undeveloped nation around 50%-70% children died due to RB. Treatment for retinoblastoma mainly includes radiation therapy and intra-arterial chemotherapy; however these treatments have shown serious adverse effects. The drug regimen of carboplatin, etoposide and vincristine is also given by intravenous route but has shown resistance. Hence there arises a need to improve the therapeutic effect of drugs by reducing side effects and increasing their absorption across the ocular barriers. Studies on ocular cancer found that quercetin could inhibit migration and induce apoptosis in RB cells whereas etoposide inhibits DNA synthesis. Therefore, a combination of quercetin and etoposide could provide a novel approach against retinoblastoma. However both drugs belong to BCS class IV and their clinical use is limited by bioavailability problems. In situ nanoemulsion systems are viscous liquids that form gel phase upon exposure to physiological condition. The aim of this study was to enhance ocular bioavailability of quercetin and etoposide by formulating nanoemulsion based in-situ gel to improve drug permeation and retention time in the ocular cavity.

Methods:

1. Formulation Development:- Etoposide and Quercetin was taken in ratio of (2:1) and incorporated in nanoemulsion gel
2. *In vitro* Release studies: - The optimized formulation was evaluated by diffusion studies to quantify the amount of drug released through Nylon membrane. Study was conducted using Franz Diffusion cell using 22ml of receptor compartment. The temperature of the cell was maintained at 37°C ± 0.5°C with constant stirring at 100 rpm. Samples were withdrawn at regular intervals, filtered and analysed for drug content by UV spectrophotometry. The receptor compartment was replenished with fresh medium to maintain sink conditions after each sampling. % cumulative drug released was plotted as a function of time.

Results and Discussion: The drug release was found to be 84% at the end of 12hr while drug release from gel was found to be 78% at the end of 8hr. The nanoemulsion based in situ gel effectively improved drug release.

Conclusion: Combination of quercetin and etoposide was given by formulating nanoemulsion based in situ gel for effective therapeutic management of retinoblastoma. The gel system demonstrated improved drug release and extended release. Hence it can be further investigated for retinoblastoma treatment.

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Solubility and Bioavailability Enhancement by Various Methods of B-Cyclodextrin Inclusion Complexation

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Background and Rationale: Drug X is a Phosphodiesterase-5 inhibitor belonging to BCS class II. Clinical efficacy of the Drug X is critically limited by its poor water solubility. Various solubility enhancement techniques are widely been explored to improve the solubility and bioavailability of poorly soluble drugs. The aim of this research work was to enhance the solubility and subsequently the bioavailability of the Drug X and further formulate it into a suitable dosage form. Different methods of hydrophilic (Beta-cyclodextrin (β-CD) inclusion complex[1] were explored and compared with a marketed formulation for improvement of solubility and bioavailability. With a rationale that the fast dissolving tablets (FDT) show rapid onset of action[2], the developed β-CD-Drug X complexes were further formulated as FDT system.

Method: A) Solubility enhancement approach: β-CD inclusion complexation for solubility enhancement of Drug X was explored. Complexes with Kneading, Homogenization and Dry blending method were prepared and evaluated. Complex of the drug and β-CD were prepared at a ratio of 1:1.5 according to results obtained by Job's plot and phase solubility study. The prepared complexes were blended and lubricated to prepare FDT. These were evaluated for appearance, drug content, percent yield, and disintegration time and subjected to saturation solubility and *in-vitro* dissolution studies.

B) *In-vitro* release study: The relative *in vitro* dissolution behaviour of the Drug form β-CD inclusion complexes prepared from kneading, homogenization and dry blending method were studied in 0.5% SLS as dissolution medium and were performed in triplicate (1000 ml; 37±0.5°C) using USP type II apparatus. The concentration of drug dissolved was assayed by HPLC. Similarly, *In vitro* release of marketed product was carried out and the release profiles of tablets prepared by inclusion complexation and marketed product were then compared.

Results and Discussion: On comparing the dissolution profiles of FDTs formulated with different β-CD-Drug X complexes and Marketed formulation, it was observed that all the approaches of inclusion complexation showed a better release than the marketed formulation. β-CD complex prepared from homogenization method (% drug release 92.47±1.23% in 15 min) exhibited better release as compared to kneading method (% drug release 75.16±2.16% in 15 min) and dry blending method (% drug release 75.19±1.48% in 15 min) as well as the marketed formulation (% drug release 58.74±1.57% in 15 min). The drug release from all the formulations followed Michaelis Menten kinetics.

Conclusion: The overall results lead to the understanding that the developed hydrophilic system (Beta-cyclodextrin (β-CD) inclusion complex can successfully improve the dissolution profile of the Drug X. The inclusion complex prepared via homogenization method improved bioavailability of Drug X to the greatest extent making it the most effective approach.

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Solubility enhancement of BCS Class II drug orlistat by nano-crystallization approach

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Background: Poor solubility of orlistat limits its luminal uptake and thus needs to be administered in higher doses, which leads to an increase in drug related side effects.[1] Thus, there is an unmet need to address the limited solubility of orlistat to increase its solubility in the physiological conditions, thereby decreasing the overall dose that is administered. Thus, here, we investigate use of nano-crystallization (NCs) technique to increase the aqueous solubility of orlistat.

Methods: The aim of the present research was to investigate nano-crystallization to increase the solubility of orlistat using Poloxamer 188 (P188) and Polyethyleneglycol 6000 (PEG6000) by melt extrusion and high-pressure homogenization (HPH) method. Contact angle measurement of orlistat nanocrystals was carried out using Ramé-hart contact angle telescope-goniometer to check the wettability. Saturation solubility of orlistat nanocrystals was evaluated in phosphate buffer 7.4 (with and without 3% SLS and 0.5% NaCl) using orbital shaker. The dissolution was carried out in triplicate as per the USP protocol in USP type II paddle type dissolution apparatus. The dissolution media was 900ml of pH 6 buffer with 3% SLS and 0.5% NaCl maintained at 37 ± 0.5°C and stirred at 75 rpm. Aliquots (3ml) were withdrawn at predetermined time intervals and filtered followed by HPLC analysis.

Results: The contact angle measurement showed that hydrophobicity of orlistat nanocrystals was decreased by 10-13 folds compared to pure Orlistat. A ~2-fold and 1.5-fold increase in solubility was observed in PEG 6000-orlistat nanocrystals (OPe11N) than P188-orlistat nanocrystals (OPo11N) and P188: PEG 6000-orlistat nanocrystals (OPoPe11N), respectively. OPo11N compared to pure orlistat led to a decrease in 90% of the drug release ($T_{90\%}$) (20 minutes for OPo11N and 51 minutes for marketed sample). *In-vitro* release profile of OPo11N in capsule dosage form showed $T_{90\%}$ within 24.58 ± 1.05 minutes due to the presence of glidants and diluents in the capsule dosage form.

Conclusion: Poloxamer 188 exhibited optimum increment in solubility based on the percent yield, drug content, saturation solubility, and *in-vitro* drug release. An increased solubility and *in vitro* drug release over marketed product yields promising results for solubility enhancement of poorly water-soluble drug like orlistat using NCs approach and opens further research avenues in employing NC approach to achieve a higher aqueous solubility, especially for BCS Class II drugs.

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Stavudine loaded particulates: Influence of formulation and dissolution methodology on *in vitro* release

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Background and Rationale: Stavudine has a very short half-life (1 hr) and is very hydrophilic (logDoct = − 0.84), thus necessitating frequent administration to maintain constant therapeutic drug levels. Poor drug entrapment and unfavourable release profiles are the major limitations for preparation of micro and nano-particles of stavudine. Detailed study on influence of inherent viscosity, temperature and agitation on *in vitro* release of stavudine loaded PLGA Microparticles (MPs) prepared by double emulsification solvent evaporation technique and SLNs prepared by nanoprecipitation technique was carried out.

Methods: A) Formulation of PLGA MPs and SLNs: PLGA with inherent viscosities of 0.74-0.94 dl/g (ester terminated) and 0.45-0.60 dl/g (acid terminated) and stabilizers were used in different proportions. Stavudine was dissolved in the water phase with gelatin as a leaching retardant. In case of SLNs, Glyceryl palmitostearate or GMS was used as lipid to form matrix, Gelucire 50/13 as a surfactant and transcutol HP as a solvent. **B) *In Vitro* release:** The release profile of PLGA MPs was studied in purified water at 'real time' and at different accelerated temperatures to correlate real time release with static and agitated condition using USP apparatus 2. *In vitro* drug release data were fitted to various release kinetic models. *In vitro* release profile using USP apparatus 2 at 'real time' was compared with USP apparatus 4 as well as with SLNs.

Results and Discussion: A burst effect followed by sustained release was observed from PLGA MPs indicating bi-phasic release behaviour. In case of ester terminated PLGA MPs dispersion, release at 2 h and 48 h was 53% and 54% respectively under static condition, and 48% and 53% respectively under agitated condition. In case of acid terminated dried PLGA MPs, release at 2 h and 48 h was 35% and 52% respectively under static condition and 44% and 55% respectively under agitated condition. Higher temperatures increased the release due to accelerated degradation of PLGA without alteration in release pattern. Similar release rate and pattern was observed on USP apparatus 4 as on USP apparatus 2. *In vitro* drug release data was found to be best fitted to Higuchi's kinetic model. SLN released the drug faster as compared to PLGA MPs owing to smaller particle size, large surface area and faster diffusion.

Conclusion: PLGA MPs formulations were found to be superior with respect to EE (%) and release rate compared to SLNs system. Model fitting indicated diffusion as the mechanism for drug release from MPs. Accelerated *in vitro* release tests at elevated temperatures indicated good correlation of the "real-time" release using the Arrhenius equation.

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Studies on *in-vitro* release of Glimepiride loaded Microemulsion

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Background and Rationale: Poor solubility and rapid first pass metabolism contributes to low bioavailability of glimepiride. The molecular weight and its log P value (3.5) increases its potential to be formulated as a topical microemulsion preparation. Microemulsion formulation improves solubility, enhances penetration power, minimizes side effects and is easy to prepare. Further, use of excipients can increase the penetration of active across skin.

Methods: Glimepiride microemulsion was prepared by using Capryol 90 as a vehicle and Kolliphor ELP: DMSO as a Smix (surfactant and co-surfactant combination) by the water titration method. The Franz diffusion cell was used for determining the permeability and flux. Cellulose membrane with a mol wt cut off 12000- 14000 Da was used as the dialysis membrane. To maintain sink condition, receptor compartment was filled with a methanol water system in the ratio of 80:20 and microemulsion was placed in the donor compartment. Aliquots of 3 ml were withdrawn at 30 min, 1hr, 2hr, 3hr, 4hr, 5hr, 6hr, 7hr, 8hr from the receptor compartment, filtered and analyzed at λmax . Microemulsion was also evaluated for assay, particle size, and zeta potential.

Results and Discussion: Formulated microemulsion was evaluated with respect to different physiochemical parameters such as assay, particle size, zeta potential, *in vitro* drug release, flux and stability studies. The assay and particle size of microemulsion was 97.64 % and 117 nm respectively. The flux and drug release of microemulsion was found to be higher than control formulation at 8 hr.

Conclusions: It was concluded that physiochemically stable GLP microemulsion formulated and the drug release increased with increase in concentration of penetration enhancer which is suitable for topical application. Data shows that the antidiabetic activity of GLP was significantly improved following transdermal application of optimized microemulsion.

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SUPRAMOLECULAR COMPLEXES OF IRBESARTAN NANOSPONGES WITH ENHANCED DISSOLUTION

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Background and Rationale: Hypertension is a predominant health problem of both, developed and developing countries (1). Irbesartan (IRB), one of the extensively prescribed drugs, for treatment of hypertension has limited therapeutic potential attributed to its slow dissolution rate and poor bioavailability. Cyclodextrin based nanosponges (NSs) are novel nanosized delivery systems comprised of hyper-crosslinked solid nanoparticles with nanosized cavities (2). The aim of this study was to investigate the influence of crosslinkers: pyromellitic dianyhydride (PMDA) and Diphenyl carbonate (DPC), used in fabrication of nanosponges, on solubility and dissolution profile of Irbesartan.

Methods: A) Synthesis and Characterisation: Two nanosponges, both, blank and drug loaded, were prepared using two cross linkers namely pyromellitic dianhydride (PMDA) and diphenyl carbonate (DPC). Solubilization efficiency studies were carried out to examine the extent to which various ratios of synthesized PMDA and DPC cross-linked CDNS could solubilize Irbesartan in comparison to plain β-CD. Characterization studies such as Differential Scanning Calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), Powdered X-ray diffraction (PXRD), Scanning electron microscopy (SEM) and Nuclear Magnetic Resonance (NMR) studies, to confirm the complexation of IRB with nanosponges were carried out. **B)** *In vitro* release study: *In vitro* drug release studies for Irbesartan and drug loaded nanosponges were conducted in triplicates using USP Type II dissolution apparatus at 75 RPM, in 900ml HCl buffer (pH= 1.2) maintained at 37± 0.5°C.

Results and Discussion: Saturation solubility of Irbesartan was found to be 0.007 mg/ml in water. The PXRD studies revealed the shift from crystalline nature of Irbesartan to amorphous form in nanosponges. Complexation of IRB with β-cyclodextrin based nanosponges, as IRB-PMDA-CDNS and IRB-DPC-CDNS, resulted in significant enhancement of 81.86 and 23.35 folds, in aqueous solubility and 1.91 and 1.96-folds enhancement in its percent dissolution efficiency (% D.E.), respectively. The average particle size of IRB-PMDA-CDNS and IRB-DPC-CDNS were 471.5nm and 382.7nm respectively.

Conclusions: The study proposed cyclodextrin nanosponges fabricated with PMDA crosslinker, as an effective nanocarrier for the delivery of Irbesartan. The IRB loaded nanosponges were characterized using mean particle size and zeta potential, DSC, FTIR, PXRD, and SEM which confirmed the formation of inclusion and non-inclusion complexes.

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Design and development of mucoadhesive delivery system of Ciprofloxacin HCL

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Rationale: Ciprofloxacin hydrochloride USP used in this research work is a first-generation fluoroquinolone and has a broad-spectrum antibacterial activity. Solubility of drug is pH dependent as it is mainly absorbed from proximal areas of GIT and has high solubility in lower pH and degraded at the alkaline pH at the lower part of GIT, it is preferable to develop a stomach specific drug delivery system i.e. gastroretentive drug delivery system for achieving desired therapeutic effect. There is no marketed mucoadhesive formulation having ciprofloxacin hydrochloride as an active ingredient, based on these reasons the present study has aimed to develop a mucoadhesive drug delivery system of ciprofloxacin hydrochloride which will resolve the problem of instability of ciprofloxacin in alkaline pH.

Methods: 1. Preparation: Direct compression method was used because the formulation contains POLYOX which has excellent binding property and good lubricity. All the API and the excipients like HPMC, POLYOX were sifted through 60# sieve and mixed together. Mg stearate and Aerosil was added as lubricant and glidant respectively and mixed. Further the blend was compressed and mucoadhesive tablets were obtained (1**) 2**. Evaluation: Precompression studies were done. Interaction between the drug and the excipient was checked. A)*In-vivo*, B)Ex-vivo (Mucoadhesive force measurement) and C)*In-vitro* i) residence time (Using the Dissolution as well as disintegration apparatus by tying the goat stomach mucosa to a glass slide and it with the paddle and the base of the tube apparatus respectively), ii) Dissolution studies (USP type II (paddle) apparatus at 100 rpm.) studies of the were done. Force of adhesion was also measured. The stability studies were done of the prepared capsule in normal and accelerated conditions. (2)

Results and Discussion: After screening different grades of Polyox and HPMC, Polyox 303, HPMC K15M were chosen because of its controlled drug release and better mucoadhesive property. The appropriate amount of polymer to be used was determined by using 3^2 factorial design. No interaction was observed between the drug and the excipient from the FTIR and DSC studies. The formulation was found to be stable at normal and accelerated stability conditions. In the in-vitro studies the retention time of the tablet was approx. 8 to 12 hrs and the drug released was found to be 98 to 60% in the respective batches. The force of adhesion was found to be significant.

Conclusion: Gastroretentive mucoadhesive matrix tablets of Ciprofloxacin HCl with the desired mucoretention time and drug release profile were developed using a combination of Polyox 303 and HPMC K15M. The results of in vivo X-ray imaging indicated that developed mucoadhesive tablets retained in the stomach for a prolonged period of time. Such a formulation will reduce the dosing frequency and will increase patient compliance.

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A Predictive Pulmonary Pharmacokinetic Modeling of Inhaled Nanotherapeutic Formulation for Pulmonary Hypertension: Correlation with the *In Vitro* Drug Release

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Background and Rationale: Pulmonary hypertension (PH) is a rise in resting pulmonary arterial pressure i.e greater than 20 mm Hg. Current treatments provide symptomatic treatment and the underlying progress of PH continues leading to higher mortality rates due to non-reversal of the disease. This warrants the need for drug therapies targeted at the mechanisms leading to the progression of the disease, especially angiogenesis and vascular remodelling. Given that, we have hypothesized liposomal dry powder inhaler formulation of the anti-proliferative and anti-angiogenic drug, Resveratrol (RSV), using Quality by Design (QbD) approach for the therapeutic management of pulmonary hypertension and characterized it successfully. Resveratrol, SIRT 1 activator, alters various signalling pathways, inhibits apoptosis, and negatively regulates angiogenesis either, by increasing the production of anti-angiogenic factors or inhibiting pro-angiogenic factors.

Methodology: The QbD based RSV liposomal DPI formulation was developed and characterized for physicochemical and aerodynamic properties required for DPI. in vitro RSV release from the DPI formulation was calculated in simulated lung fluid pH 7.4 and the concentration vs time graph was plotted for the release study. Following the in vitro release study, the final DPI formulation was evaluated for in vivo lung pharmacokinetic study in rats over 24 hr period. Concerning lung pharmacokinetics, we have customized an empirical compartmental model for the predictive RSV profiling in the lung tissues from the inhaled nanoliposomal DPI using Phoenix 64 WinNonlin version 8.2 (Certara, NJ).

Results and Discussion: The % cumulative RSV release graph highlighted the controlled release of the drug from liposomes with approximately 40% drug released for 24 hrs. A custom PK Model was built to analyze PK of inhalation formulation and certain important plots were analyzed. Various analytical plots like observed vs predicted concentration denoted as dependent variable (DV) vs individual predictions (IPRED) and DV, IPRED vs time as independent variable (IVAR) plots were generated and analyzed. From these analyzed parameters, we summarized that the customized PK model fits for the inhaled RSV DPI formulation pulmonary delivery. These simulated PK predictions were correlated strongly with the in vitro release of RSV and conclude the sustained release of the drug from the DPI formulation.

Conclusion: From the analysis, it is conclusively evident that RSV was released in a controlled manner from the liposomal DPI formulation and the predictive pulmonary pharmacokinetic modelling can be correlated with the in vitro release of the drug from the DPI formulation.

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Development and *in vitro* release studies of Iloperidone nanoformulations for nasal delivery

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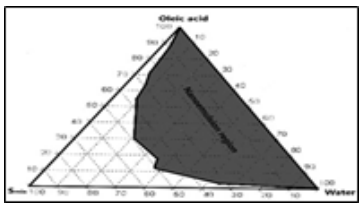
Background and Rationale: Iloperidone is a second generation, antipsychotic BCS class II drug, used in treating Schizophrenia. It is likely to show irregular bioavailability following oral administration due to low water solubility.(1) Hence, an attempt has been made to develop Iloperidone nanoemulsions containing chitosan for nasal delivery wherein the nanoemulsions would help in enhancing drug solubility and permeability across nasal mucosa and presence of mucoadhesive chitosan can reduce mucociliary clearance and prolong nasal residence time of the drug. Intranasal route as non-invasive approach can help improving drug bioavailability with potential for direct brain delivery. (2)

Methodology: UV spectrophotometric method for Iloperidone in methanol AR and simulated nasal fluid, pH 6.4 was developed for quantification of drug from formulations and during *in vitro* release studies respectively and validated. Development of nanoemulsions involved screening of oils, surfactants and cosurfactants for their solubilizing capacity for Iloperidone. Further optimization was based on emulsification ability of surfactants and cosurfactants for selected oils and then by constructing pseudoternary phase diagrams using water titration method. Nanoemulsions of Iloperidone (4 % w/v) were optimized by response surface methodology using DESIGN EXPERT 13 and evaluated. Varying concentrations of Chitosan (0.1% - 0.8% w/v) were included in Iloperidone nanoemulsions. *In vitro* release studies of developed nanoformulations were performed for 6 hours in 100 ml, simulated nasal fluid, pH 6.4, 75 rpm, 32 ± 0.5°C.

Results and Discussion: The absorbance values of Iloperidone in methanol AR and simulated nasal fluid, pH 6.4 were found to be linear in the range 4 – 14 µg/mL with R^2 = 0.9998 respectively. The composition of optimized nanoemulsions was Oleic acid (20% w/w) as oil phase, Tween 80 and Transcutol (40% w/w) as S_{mix} (1: 1) and water. (Fig. 1) The optimized nanoemulsions were translucent, stable to freeze thaw cycles with pH 5.5 ± 0.5 and drug content 98.23 ± 0.03%. 0.1 % w/v Chitosan could be incorporated in the Iloperidone nanoemulsions while higher concentrations of Chitosan led to phase separation in the nanoemulsions. *In vitro* release studies showed that as compared to pure drug, Iloperidone nanoemulsions showed improved solubility while the presence of Chitosan in the Iloperidone nanoemulsions showed sustaining effect over 6 hours. (Fig. 2)



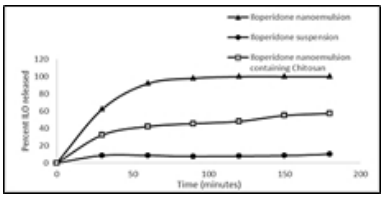


Fig.1: Pseudoternary phase diagram Fig. 2: *In vitro* release studies

Conclusions: Iloperidone nanoemulsions were successfully prepared by low energy emulsification method and chitosan could be incorporated in the nanoemulsions. *In vitro* release studies showed sustained release of Iloperidone from the nanoemulsions in the presence of chitosan which can be proposed to increase the residence time of developed nanoformulations in the nasal cavity.

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DISSOLUTION STUDY OF HERBAL TABLET

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Background & Rationale: Dissolution test can be considered as vital evaluation parameter to prove rational of herbal tablet formulation (1). Herbal tablet contains herbal extracts of complex nature and hence, dissolution test of herbal tablet is challenging. *Salacia chinensis*, a vital herb with multiple effects is used to treat various diseases and disorders like diabetes and hyperlipidemia, was selected for the study (2). Herbal tablet (ST) which contains dried aqueous extract of *Salacia chinensis* was formulated and dissolution test was developed to study the release profile.

Methods: A) Preparation of ST: Herbal tablets (ST) were prepared by wet granulation. ST contains a single herbal extract of *Salacia chinensis.* UV method for dissolution study of ST using Salacinol (SAL) analyte marker was developed and validated. **B) Dissolution Method:** The dissolution study of ST was carried out in 0.1M HCl and USP type-2 (Paddle) apparatus was used. 900 ml volume of dissolution vessel, 37.5 ± 0.5 ºC temperature, stirring speed of 50 rpm and 5 mL sample aliquots withdrawn at 0, 5, 15, 30, 60, 120, 180, 240, 300, 360 minutes with replacement. Six tablets were placed in six different vessels. Absorbances of collected samples were measured at 254 nm by UV spectrophotometer at each time point. The drug release was predicted by using kinetic modelling**.**

Results and Discussion: The method validation parameters were checked as per the ICH guidelines. The soluble portion is released through diffusion while bound portion is released through erosion. There was a synergistic effect of gum acacia and gelatin along with HPMC found on drug release for a longer duration as a sustained release. The model that best fitted the release data was evaluated by the correlation coefficient (R^2).

Conclusion: The linear increase in drug release was observed over a prolonged period and is significant as a sustained release tablet dosage form. The results of validation show that the method is precise and robust. The release profile of ST is best fitted to the zero order and Korsemeyer- Peppas model with coefficient of determination (for both R^2 = 0.96) indicating non-Fickian diffusion or anomalous transport with the release by diffusion and erosion mechanism with the combination of both diffusion and erosion sustained release.

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Evaluation of isoniazid loaded hyaluronic acid coated chitosan nanoparticles

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Background and Rationale: Chitosan, a partially deacetylated chitin composed of N-acetylglucosamine which is polycationic, biocompatible, low immunogenic and low cost polymer. Hyaluronic acid (HA) is a biocompatible, biodegradable and has a variety of modification sites; it is a promising candidate for use as a carrier or as a targeting ligand on the surface of nanoparticles for treatment of tuberculosis. To enhance the concentration of isoniazid at target site, isoniazid loaded chitosan nanoparticles were coated with hyaluronic acid and studied effect of concentration of hyaluronic acid on rate of dissolution of isoniazid from hyaluronic acid (HA) coated chitosan nanoparticles.

Methods: A) Coating of isoniazid loaded chitosan nanoparticles with hyaluronic acid: Isoniazid loaded chitosan nanoparticles were coated by hyaluronic acid (0.5mg/ml, 1mg/ml, and 1.5mg/ml). Isoniazid loaded chitosan nanoparticle suspension (10ml) was stirred on a magnetic stirrer. Required quantity of hyaluronic acid was dissolved in 10ml of 1% acetic acid. In a beaker, hyaluronic acid solution and nanoparticle suspension were added simultaneously and vigorously stirred for 1 hour. The hyaluronic acid-coated nanoparticle suspension was centrifuged, and the resulting nanoparticles were washed in purified water. **B) *In-vitro* drug release studies:** For this, 2ml of nanoparticles suspension was inserted in a dialysis bag with a molecular weight cutoff of 1000. After that, the dialysis bag was soaked in 60 ml of 7.4 phosphate buffer solution and shaken at 60 rpm at 37°C on a rotary shaker. A sample was withdrawn at different time intervals of 0, 1, 3, 5, 10, 16, 24hrs and analyzed simultaneously by UV spectroscopy at 263.2nm

Results and Discussion: Hyaluronic acid coated nanoparticles were found to have a slower release than uncoated chitosan nanoparticles which indicates that surface modification of nanoparticles further retard the release of a drug. As the particle size of hyaluronic acid coated chitosan nanoparticles was found higher compared to the chitosan nanoparticles, increases the thickness of nanoparticles in turn leads to increase in diffusion distance of drug and hence slower release of isoniazid from hyaluronic acid coated chitosan nanoparticles.

Conclusion: The isoniazid loaded hyaluronic acid coated chitosan nanoparticles shows a prolonged release profile, which indicates the ability of a nanoparticulation method to effectively encapsulate the isoniazid.

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Evaluation of Safer Monomer Release from Super-aggregated Amphotericin B Nanosuspension

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Background and Rationale: Amphotericin B (AmB) remains the gold standard for the treatment of life threatening infections like systemic fungal infections, visceral leishmaniasis and currently mucormycosis. The toxicity of AmB is attributed to strong binding to cholesterol in the host cells, specifically in the kidney, causing severe and often near fatal renal toxicity. High nephrotoxicity which is attributed to the aggregated state of AmB in the conventional AmB formulations, can be decreased by maintaining AmB in the monomeric form as in this state AmB affinity for cholesterol is lacking. Further AmB in super-aggregated form is claimed to demonstrate comparable safety to the monomeric form. This is achieved as AmB super-aggregated form serves as depots which slowly release the safe monomeric form. In the present study we report a AmB nanosuspension with AmB in the super-aggregated form. The aim of the study was to evaluate role of excipients in enabling the super-aggregated state of AmB. The objective of the study was to evaluate drug release of AmB from the nanosuspension with the specific objective of confirming release of AmB in the monomeric form in the dissolution medium.

Methods: AmB Nanosuspension (~5mg AmB/mL) was prepared by Nanoprecipitation method. Various excipients particularly fatty acids/esters were evaluated based on the thermodynamic parameters for the preparation of AmB nanosuspension comprising AmB in the super aggregated state. Nano Brook 90 Plus Particle size analyser was employed to monitor Particle size and PDI and morphology of Nanosuspension was determined by Transmission Electron Microscopy (TEM). The excipient drug interaction was evaluated by FTIR spectroscopy and Raman Spectroscopy. The superaggregated form was confirmed by recording UV spectra. AmB release was evaluated by sample and separate method using USP dissolution apparatus II. The dissolution medium was PBS pH 7.4. AmB released in the medium was characterised for the aggregation state by scanning in the UV region 300-450 nm, at different time points. Safety of AmB nanosuspension was monitored by in vitro haemolysis study, using rat plasma and compared with the liposomal formulation and Micellar Amfocare.

Results and Discussion: AmB Nanosuspensions exhibited average particle size in the range ~150 nm with PDI <0.3, while TEM revealed spherical shape. Increase in the thermodynamic parameters Δ δtotal, ΔHm, Δ Pol, with increase in the fatty chain length reflected higher affinity with shorter chain length. FTIR Spectroscopy and Raman Spectra revealed presence of intermolecular hydrogen and hydrophobic specific interaction between excipients and AmB. Nevertheless, longer fatty chain containing excipients surprisingly providing stable super-aggregated form of AmB. AmB nanosuspension exhibited slow release of AmB in the monomeric form, confirmed by the UV spectra. While micellar AmB revealed extensive hemolysis (>90%), as anticipated, AmB nanosuspension exhibited low hemolysis (<10%) comparable to Marketed Liposomal Amphotericin B, proposing safety.

Conclusion: Super aggregated AmB Nanosuspension presents great promise as a safer, affordable and efficacious alternative, which can exhibit slow release of AmB in the monomeric form.

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Exploring Lipid Nanocarriers for Sparingly soluble drug in treatment of loco-regional therapy of oral cancer: An *In-vitro* perspective

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Background: Sparingly soluble drugs pose significant hindrance in release within oral cavity when administered locally. In disease conditions like oral cancer the permeability of anticancer drugs is significantly varied. Efficacy of locally administered drugs at the site of disease may be enhanced by prolonging its duration at the site by creating mucoadhesive formulations, as compared to conventional oral and parenteral chemotherapeutics. Sparingly soluble or lipophilic drugs follow transcellular route of absorption across oral mucosa [1] which can be exploited to release drug inside cancer cells. Since release of drug in oral cavity is critical and has been scarcely researched upon this study is preliminarily focused on developing lipid nanocarriers containing sparingly soluble lipophilic anti-EGFR agent and evaluating its *in vitro* release in loco-regional therapy.

Method: (1). Preparation of drug entrapped lipid nanocarriers: Lipid nanocarriers entrapping drug were prepared by melt-emulsification followed by homogenization technique [2]. The batches were characterized for particle size, zeta potential, entrapment efficiency, drug loading and in-vitro release. Lipid Nanocarriers were purified by passing through a sephadex column and were used for further characterization.

(2). *In vitro* release studies: *In vitro* release studies were performed in PBS pH6.8 having 1% surfactant. 1ml of purified formulation containing 0.2mg drug was placed in pre-treated dialysis bag membrane and was placed in PBS-surfactant mixture. The medium was stirred at 100 rpm for a period of 48 hours. Samples were withdrawn at different time intervals to check for release of drug.

Results and Discussion: The hydrodynamic size observed for this formulation was around 100nm with zeta potential around -30mV. Drug entrapped was upto 80% and drug loading was upto 2%. The *in vitro* release was observed to be around 50% by the end of 24hrs. This is due to the fact that the drug is sparingly soluble and is also encapsulated in lipid nanocarriers.

Conclusion: Due to slow release of drug, it is essential to prolong the residence time of formulation at the site of disease. Suitable mucoadhesive formulation with ease in application needs to be developed to increase its residence time and improve release at the site of disease for effective therapeutic outcome. In-depth optimization, its characterization and evaluation shall give better insight into its release profile and effectiveness.

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Formulation and Evaluation of Highly Ordered Three-Dimensional Mesoporous Silica Nanostructure (3D MCM-48) For Solubility Enhancement of Poorly Soluble Antifungal Drug

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Background and rationale : Most of the present and newly synthesized antifungal drugs are poorly water-soluble candidate which results in low absorption and poor pharmacological responses[1]. Among the available nanosystems, ordered 3D Mesoporous Silica Nanoparticles (MSNs) comes out as the inventive nanocarrier for drug delivery due to highly porous structure with large surface area for drug loading, tunable pore size, smooth molecular diffusion, excellent biocompatibility, flexibility in surface functionalization for further improving the site targeting, release and bio-adhesion properties and their ability to keep the drug in amorphous form. Aim of the present research investigation was to formulate and evaluate the mesoporous silica nanoparticles for the treatment of skin candidiasis as well as to improve the solubility of the azole category drug.

Method and Evaluation: Mesoporous silica nanoparticles (MCM-48) with molecular sieves were synthesized by modified Stober's method. 3 In 2.9 % of ammonia solution cetyltrimethylammonium bromide (CTAB) as surfactant or template, Polaxamer-407 as particle size controller and ethanol as solvent was added. Tetraethylorthosilicate (TEOS) was added as silica source. A 3D pore structure of MCM -48 was obtained on which drug loading was done by Incipient Wetness Impregnation technique in which concentrated solution of drug in solvent was prepared and rotary evaporated till complete solvent removal. The drug loaded 3D MSN particles were characterized by Particle size analysis, Zeta potential, BET analysis, FT-IR, DSC, solubility studies and drug release

Results and discussions: Particle size and zeta potential were found to be in range of 308 ± 12 nm,18 ± 1.87 mV for uncalcined MSN and for calcined and drug loaded was found to be in range of 342 ± 07 nm, - 28 ± 2.38 mV and 378 ± 05 nm, - 43 ± 0.96 mV respectively. Drug loaded MSN and pure drug showed 0.0176 µg/ mL and 0.0023 µg/ mL solubility in water. Therefore results showed that there is 7 times folds increment in solubility of drug loaded MSN than pure drug. After drug loading, the specific surface area was decreased from 915.35 m^2 /g for MCM48 to 416.48 m^2 /g for drug loaded MSN, showing that drug has been successfully inserted into the MSN mesopores. The BJH–KJS method showed reduction in the pore size and mesopore volume from 0.62 cc/g for MCM48 to 0.41 cc/g for drug loaded MCM48. FT-IR of the drug peaks in drug loaded MSN further confirms the drug remain intact inside MSN.

Conclusions - Hence, we can conclude that these highly ordered 3D mesoporous nanostructures could emerge as smart and innovative nanocarriers for solubility enhancement of poorly soluble drug candidates like azoles and allylamines etc.

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In vitro solubility, drug release and permeability assessment of an Eprosartan Mesylate Nanosuspension

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Background and Rationale: More than 40% of new chemical entities in the last two decades are dropped off on the developmental phase of pharmaceuticals due to their poor solubility and permeability. Consequently, much attention has been focused on formulation designing to improve the solubility and permeability and thus bioavailability of such potential candidates. One such approach is the preparation of nanosuspension (NS). Eprosartan mesylate (EM) is an angiotensin-receptor blocker with a low and variable oral bioavailability of 13-15%, which could be attributed to its poor solubility and permeability. Thus, it was decided to prepare a nanosuspension of EM to enhance both of these parameters.

Methods: A) Preparation and lyophilization of the EM nanosuspension: The NS was prepared by the sonication-assisted precipitation technique using Soluplus® as the stabilizer. The optimized NS was converted into a dry, re-dispersible powder by lyophilization using mannitol as the cryoprotectant. **B)** Saturation solubility and dissolution study: Saturation solubility studies were performed to assess the effect of different pH and the impact of fed and fasted conditions on the solubility of the drug in the NS. The dissolution test was carried out in 900 ml of Milli-Q® water, 0.1 N HCl (pH 1.2), acetate buffer (pH 4.5), and phosphate buffer (pH 6.8) containing 0.1% sodium dodecyl sulfate to maintain sink condition employing a USP 24 type II apparatus. **C)** Parallel artificial membrane permeability assay (PAMPA): PAMPA studies were carried out to investigate the possible increase in permeation. The BD Gentest® (Corning Inc., MA) containing a pre-coated lipid membrane sandwich between donor and acceptor chamber in 96-well format was used for determining permeability. **D)** *Ex-vivo* Permeability studies using the everted gut sac model: The everted gut sac model as reported by Wilson and Wiseman is used to investigate the transport of the drug across intestinal epithelium. Sacs of small intestines of rats were prepared and loaded with the pure drug and EM NS. Permeation flux and apparent permeability coefficient were determined. **E)** Caco-2 permeability assay: The transport of re-dispersed EM NS across the Caco-2 monolayer was determined and compared with pure EM. Transport experiments were performed in both absorptive (A-B) and secretary direction (B-A).

Results and Discussion: The saturation solubility of EM in water was 0.104 ± 0.006 mg/mL. Solubility studies revealed an increase in the rate and degree of solubilization from EM NS in all media. It was observed that the time required for 50% dissolution of EM through dry NS formulation in water is less than 15 min, which is significantly different from pure EM in which cases only 10 % release was seen at the same time. All the transport studies concurred by showing a significant increase in the drug in NS instead of the plain drug. Good association between PAMPA and everted gut sac permeation results reveals EM permeability predominantly occurs through passive diffusion mechanism.

Conclusion: The absolute bioavailability of EM was 7.1% and improved to 39.9% for EM NS, suggesting that NS had overcome solubility and permeability limited bioavailability associated with pure EM.

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MESOPOROUS SILICA NANOPARTICLE: DEVELOPMENT, *IN-VITRO* AND *IN-VIVO* EVALUATION IN THE MANAGEMENT OF ATOPIC DERMATITIS

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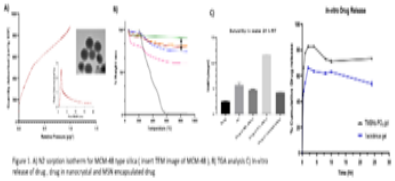
Background and Objective: Atopic dermatitis (AD) is a repetitive inflammatory skin disease characterized by xerosis, eczematous lesions, pruritus, and high serum immunoglobulin (IgE) levels resulting in itching and scratching which causes mechanical skin injury, dermal thickening. Most of the drugs used to treat AD belong to BCS class II. Recently, mesoporous silica nanoparticles (MSNs) have attracted a lot of attention as multifunctional nanocarriers for many BCS class II and IV drugs due to their unique properties such as ordered porous structure, tunable size, high surface area, biocompatibility and amenability to surface functionalization. The objective of the work was to develop a stable, robust and scalable formulation of Tacrolimus loaded MSN for topical delivery by optimization of various process and formulation parameters .

Methodology: MSNs were synthesized using modified sol-gel process with ammonia as catalyst and tetraethyl orthosilicate (TEOS) as the silicon source. Ratio of surfactant, reaction time, stirring speed and stirring time were optimized. Surface functionalization was done using amino and phosphate groups and solubility studies were carried out. Prepared particles were evaluated for particle size, zeta potential, FTIR, TEM, TGA, XRD and BET. Optimized MSN were loaded with the model immunosuppressant drug. Cytotoxicity studies and *in –vivo* efficacy studies were also performed for the optimized drug loaded MSNs. Particles were finally loaded into Carbopol gel and characterized for pH, viscosity, extrudability, spreadability, assay and i*n-vitro* drug release.

Result and Discussion: MSN with particle size in range of 250-300 nm were synthesized using CTAB: F127 in 1:2 ratio at 1000 rpm for 1 min stirring time. Optimized MSNs were surface functionalized with positively charged group ($-NH2^{+}$) and negatively charged group ($-PO_3^{-}$) with aim to improve their physical and chemical properties like solubility and drug release. Approximately 20% drug loading was achieved. XRD analysis showed the conversion of drug into amorphous form, which is also responsible for improvement of the solubility. Solubility was increased by 7.45 folds with phosphate functionalized MSNs. *In-vitro* drug release shows ~18% rise. Results of cytotoxicity studies on HaCaT cells suggest that it is non-toxic at the intended concentration. In-vivo studies also showed better efficacy due to improved solubility.



Conclusion: The study indicated that the solubility of Tacrolimus was improved with MSNs as compared to pure drug and nanocrystals of Tacrolimus. Technique used for preparation of MSNs is easily scalable and gives quite stable formulation. *In-vitro* drug release revealed that converting drug in to nanonized form not only improves solubility, it also improves the drug diffusion from semi solid dosage form. Improved solubility leads to better efficacy, however, it also improves risk of cytotoxicity. In our study, despite improvement in the solubility, cytotoxicity was not observed up to the concentration of 25 µg/ml which is nearly 25 times higher dose than the recommended dose. These data were supported by *in-vivo* studies using AD animal model. As an outcome of research project, better patient compliance and adherence to more effective therapy can be achieved.

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Nano engineered Inclusion complexes of Rivaroxaban with β-CD for solubility and dissolution enhancement

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Background and Rationale: Rivaroxaban (RVN) is an oral anticoagulant, which is practically insoluble in water or buffer systems (pH 3-9) [1]. Poor aqueous solubility of drugs show rate limited absorption, which affects the drug bioavailability and its therapeutic outcome. Hence, solubility enhancement is important in drug development and formulation development processes. Cyclodextrins (CDs) form inclusion complexes with poorly soluble drugs altering their physicochemical and biological properties usually increasing their aqueous solubility and thereby dissolution rate in aqueous fluids [2]. The present study aims in increasing aqueous solubility of drug RVN by using particle size engineering in combination with spray drying inclusion complexation technique by using β-CD. Further the developed drug-CD inclusion complexes were assessed by *in vitro* characterization and solubility/ dissolution behaviour of RVN were observed.

Methods: A) Preparation of inclusion complexes and nanocomposites of RVN: The inclusion complexes and nanocomposites of RVN were prepared in 1:1 molar ratios of RVN and β-CD by physical mixing (PM), kneading Method (KM), Spray-drying (SD) and high-pressure homogenization and spray-drying (HH-SD).

B) Characterization of inclusion complexes and nanocomposites of RVN: These studies included Solubility estimation in water and acetate buffer pH 4.5 using shake flask method, In vitro dissolution studies using USP type-I basket type apparatus at 75rpm with acetate buffer of pH 4.5 as dissolution medium and aliquots were withdrawn at 10, 20, 30, 45, 60 and 90 min, Particle size and zeta potential, Thermal analysis, Spectroscopic studies, Powder X- ray diffractometry (PXRD) and Scanning electron microscopy (SEM) of the RVN and RVN- β-CD inclusion complexes were performed.

Results and Discussion: Increase in solubility of RVN complexes and nanocomposites in distilled water prepared by PM, KN, SD and HH-SD methods was 2.35, 3.37, 4.04 and 42.60 folds in water, whereas 1.77, 1.90, 3.69 and 26.51 folds increase was seen in acetate buffer (pH 4.5). Nanocomposites of RVN prepared by HH-SD method showed a maximum of 99.2% drug release at 90 min in acetate buffer pH 4.5. Maximum drug release by PM, KN, and SD methods was found to be 41.30%, 58%, and 60.90, respectively at 90 min. However, only 20.6% release was obtained at the same time internally from pure RVN. The particle size and zeta potential of the nanocomposite of RVN prepared by HH-SD method was found to be 441 nm and −28.7 mV, respectively. Sufficiently high negative zeta potential value indicated desired stability of the nanonized system of RVN-β-CD. DSC, PXRD, and SEM revealed noticeable changes in characteristics of RVN indicating formation of a new solid system. The NMR and FTIR studies revealed interaction of RVN with β-CD cavity.

Conclusion: The spray-dried cyclodextrin-based nanocomposites of RVN showed remarkable improvement in solubility and dissolution compared to pure RVN. Characterization studies revealed noticeable changes in characteristic of RVN indicating formation of a new solid system and interaction of RVN with β-CD cavity. Hence, spray- dried cyclodextrin-based nanocomposites can be used as a novel approach for solubility and dissolution enhancement of RVN in formulation development.

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Optimizing Dissolution of Betulin Nanosuspension for Enhanced Anticancer Efficacy in a Resistant Breast Cancer Cell Line

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Background and Rationale: Surfactant/s are commonly incorporated in conventional and nano formulations to enhance the rate and extent of dissolution of drugs exhibiting poor aqueous solubility. The interactions between the drug and excipients significantly influence dissolution rate to impact performance of the formulation. The present study discloses a nanosuspension of betulin, a BCS II molecule by in situ nanotechnology [1]. A specific objective was to evaluate the effect of potential interaction between non-ionic surfactants (lutrol f68, span 80 and tween 80) on the dissolution rate and anticancer efficacy of botulin nanosuspension.

Methodology: Preconcentrates of betulin were prepared by dissolving betulin (10 mg), stabilizers and surfactant/s in Transcutol® HP(1mL) by bath sonication. Pre Concentrates, when diluted with water (upto 5 mL) enabled formation of in situ betulin nanosuspension (BeTNS). *In vitro* release of betulin was evaluated using the USP type II paddle apparatus. Dissolution medium selected was pH 5.5 to mimic intracellular endosomal pH. Betulin was quantified by HPLC. Cytotoxicity was evaluated by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyl tetrazolium bromide) assay on MDA-MB-231 drug resistant cell line. The affinity between betulin and surfactant/s combination were evaluated with the help of thermodynamic parameters, solubility parameter, polarity and mixing enthalpy, wherein lower the values greater the affinity.

Results and Discussion: A direct correlation was observed between drug release from BeTNS and in vitro cytotoxicity in the MDA-MB-231 cell line. Based on the thermodynamic parameters it was seen that the affinity of betulin was in the order span 80> tween 80> lutrol f68. The combination of lutrol f68 and span 80 revealed marked decrease in size (235.68 0.65 nm), nevertheless only ~30% release was observed from BeTNS which was comparable to betulin suspension (BetS) [F2>50]. Further, no advantage of BeTNS was evident as the anticancer efficacy of BeTNS (68.69 µg/mL) and BetS (69.54 µg/mL) was comparable. Tween 80, revealed an increase in dissolution rate (>80% in 10 minutes) however there was enhancement in size (>500 nm). Increasing span 80 led to a significant decrease in size, but did not enhance drug release. Rapid and high release (88.25% in 10 minutes) coupled with nano size (383.74 ± 7.24 nm) was achieved by optimizing the surfactant combination of tween 80/span 80/lutrol f68. We conjecture that span 80 interacted with nanoparticles to cover the surface and reduce the size, while lutrol f68 enabled stabilisation of nanosuspension. However, high affinity of tween 80 and span 80 allowed hydrophilic tween 80 to penetrate through the span 80 layer to reach the nanoparticle surface and enhance dissolution. The high release obtained correlated with superior anti-cancer efficacy (IC50 38.44 µg/mL), suggesting rapid dissolution of the drug from BeTNS as an important contributor to ascertain anticancer efficacy.

Conclusion: Optimizing *in vitro* drug release from BeTNS played a critical role in enhancing anticancer efficacy.

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Synergistic novel triple drug anti-malarial dry syrup of nanosized atovaquone: in vitro dissolution and PK studies

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Background & Rationale: Atovaquone has poor and unpredictable oral bioavailability and high dose and cost. The current research investigated the novel pH-based precipitation method for nanosuspension of atovaquone to reduce its particle size to enhance dissolution and bioavailability. A novel artemisinin combination therapy was also designed with the nanosized drug with reduced dose for the treatment of multi-drug resistant malaria.

Methods: A combination approach of bottom-up followed by top-down was utilized for the preparation of nanosuspension. The in vitro dissolution was carried out in a discriminatory medium (500ml, 2% Cremophor EL medium, USP type II, 50 rpm) rather than OGD dissolution medium (40% IPA in pH 8 phosphate buffer). Pharmacokinetic study was carried out in rats and pharmacodynamic study in a novel triple drug combination was carried out in murine model. This nanosized drug was incorporated in a new triple artemisinin combination dry syrup and this co-formulation was evaluated for *in vitro* dissolution.

Results and Discussion: The pH based nanosuspension showed significantly higher dissolution (freeze dried 63% and adsorbed 46.8%) as compared to a plain drug suspension (8.7%, $p<0.001$), adsorbed micronized suspension (23%), and adsorbed anti-solvent based nanosuspension (28.9%). The *in vivo* pharmacokinetics of nanosuspension showed a 1.9-fold increase in AUC and quicker onset of action as compared to drug suspension ($p<0.0001$). As a triple combination, nanosized atovaquone and proguanil both at $1/80^{th}$ the therapeutic dose and $1/5^{th}$ the therapeutic dose of artesunate resulted in a complete cure.

Conclusions: Novel organic solvent-free, scalable pH-based precipitation method was advantageous over the anti-solvent-based precipitation method and top-down method to increase dissolution and bioavailability of Atovaquone. The potential of the synergistic co-formulation of nanosized atovaquone-proguanil- artesunate in curing malaria infection at reduced doses of all the three drugs can be a solution to the pill burden and multidrug resistance observed with the current therapy.

Keywords: pH-based precipitation; nanosuspension, bioavailability enhancement, novel ACT

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Transepidermal microneedle delivery of second-generation antipsychotic drug

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Introduction: Patient compliance is among the key problems during the treatment raising the requirement of innovative drug delivery systems to exploit clinical results. The delivery of antipsychotics via a transdermal route enhances adhesion and reduces multi-dosing consequently improving patient compliance. Dissolving microneedles (MNs) have been demonstrated for transdermal drug delivery. The dissolution rate of MNs regulates the drug release from MNs that demonstrate drug absorption through the skin. Iloperidone (ILO) has low solubility and high permeability [1]. The complexation of ILO with cyclodextrin may enhance the solubility which enables high drug loading in the polymer matrix of MNs. Moreover, complexing ILO into a polymeric network modulates the dissolution profile. The current research was projected to enhance the solubility and permeability of inclusion complexed iloperidone-loaded dissolving MNs with variable dissolution profiles.

Method and Results: Based on phase solubility studies, an auxiliary agent was optimized, whereas HPβCD was selected as a complexing agent. The ternary inclusion complex was prepared by the kneading method to increase the solubility of the iloperidone. The MNs were prepared by casting the polymeric solution loaded with an inclusion complex of ILO and optimized using a 3^2 factorial design to investigate the effect of polymer and complex concentration on drug loading and release of the drug. The release profile of optimized MNs in phosphate buffer (pH 7.4) with 1% sodium lauryl sulphate (SLS) revealed 20.08±0.46% within 15mins which was enhanced to 94.62±1.61% at the end of 4h (Figure 1a). The inclusion complexed ILO-loaded MNs showed a significantly enhanced dissolution profile of ILO when compared with plain drug ($p<0.05$). Besides the dissolution profile, the optimized batch ATR-FTIR, DSC, SEM, PXRD, NMR, mechanical characterization, and skin insertion. Further dermatokinetics studies were carried out. The optimized microneedle showed an extended-release profile up to 24h with a tunable dissolution profile compared with a plain drug. Significant enhancement in *in-vitro* (Figure 1b) and *ex-vivo* (Figure 1c) permeation of ILO was observed resulting from the enhanced dissolution after the application of MNs. Based on *ex-vivo* and dermatopharmacokinetic studies, microneedles seemed a more viable and feasible alternative to the oral dosage form. Optimized MNs exhibit the highest deposition of drug in the skin which indicates an extended-release profile (Figure 1d).

Conclusion: The development of transepidermal microneedles is a promising approach for the delivery of BSC class II drugs. Our findings suggest that inclusion-complexed ILO- loaded dissolving microneedle can serve as a good platform for transepidermal delivery of the antipsychotic drug.

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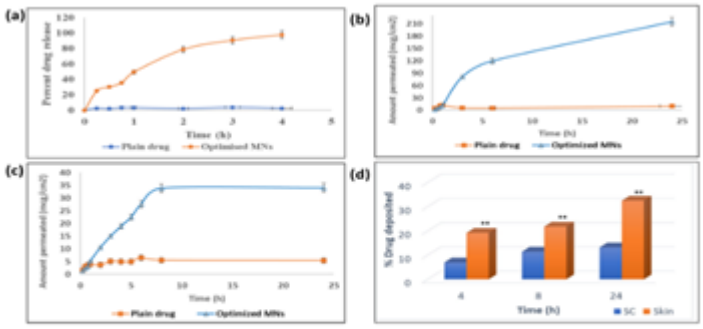

Figure 1 (a) In-vitro release, (b) In-vitro permeation, (c) Ex-vivo permeation of optimized MNs ($p<0.05$) when compared with the plain drug (n=3) respectively, and (d) dermatopharmacokinetic study of optimized MNs ($p<0.001$) when compared with the stratum corneum (n=3)

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Design and Evaluation of Pulsatile device of Flurbiprofen for Colon Specific Drug Delivery

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Background and Rationale: The objective of the present research work was to develop and evaluate Flurbiprofen (FP) loaded microcapsules using pH dependent polymers for chronotherapy of arthritis (1). FP is a non-steroidal anti-inflammatory drug (NSAID) having a short half-life, and hence requires frequent administration. The emerging need for developing sustained release NSAIDs to minimize the dosing frequency was the main concern. Therefore, the possible way by which this can be achieved is by formulating an oral sustained release formulation using a pulsatile device for colon (2).

Methodology: Microcapsules of FP were prepared by emulsion solvent evaporation technique using Eudragit RS/RL-100 as polymers. The basic design of the pulsatile device consisted of an insoluble capsule body, filled with FP microcapsules and sealed with a hydrogel polymer plug. The entire device was enteric coated with 5% cellulose acetate phthalate. The prepared FP microcapsules were evaluated for : drug-polymer compatibility by FTIR, surface morphology by Scanning Electron Microscopy (SEM), particle size and size distribution, DSC, %yield, drug content, entrapment efficiency, *in vitro* dissolution studies, and release kinetics. *In vitro* dissolution profile was determined using USP XXIII rotating basket apparatus (900 ml of pH 1.2, pH 6.8 and pH 7.4 phosphate buffers, 100 rpm, $37^{\circ} \pm 0.5^{\circ}C$). Microcapsules equivalent to 150 mg of FP were loaded into the basket of the dissolution apparatus. 5 ml aliquots were withdrawn at suitable time intervals and replaced with an equal amount of fresh buffer. The absorbances of withdrawn aliquots were determined at a wavelength of 247nm, and the amount of drug in the aliquots was extrapolated from the calibration curve, and cumulative percent of drug released was calculated. Three optimized formulations were selected and further used for fabrication of pulsatile capsule. To examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order (Q v/s t), first order [Log(Q o -Q) v/s t], Higuchi's square root time (Q v/s t1/2) and Korsemeyer Peppas double log plot (log Q v/s log t) respectively, where Q is the cumulative percentage of drug released at time t and (Qo -Q) is the cumulative percentage of drug remaining after time t.

Results and Discussion: The IR Spectra and DSC thermogram revealed that there was no interaction between the polymer and FP. The FP microcapsules were spherical, which was confirmed by SEM. Particle size of the FP microcapsules exhibited normal frequency distribution pattern. A maximum of 89.50% drug entrapment efficiency was obtained in the FP microcapsules. The *in vitro* performance of FP microcapsules showed that sustained release was dependent upon the polymer concentration. The coefficient of determination indicated that the release data was best fitted with zero order kinetics. The Higuchi equation explains the diffusion-controlled release mechanism. The diffusion exponent 'n' values of Korsemeyer-Peppas model were found to be Non-Fickian.

Conclusion: The present study conclusively demonstrated that programmable pulsatile, colon specific release could be achieved from a capsule device over a 24 hr period, consistent with the demands of chronotherapeutic drug delivery.

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Design And Evaluation of Sustained Release Mucoadhesive Microspheres of Ranitidine HCl

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Background and Rationale: Ranitidine HCl, a H_2 receptor antagonist, is used in the treatment of gastric ulcers. It competes with histamine for binding to H_2 receptors on the parietal cells thereby suppressing the gastric acid secretion by predominantly inhibiting the basal acid secretion. The drug has a half-life of 2-3h. The general dosing of Ranitidine HCl is 150mg twice daily, 300mg once daily; and both dose and dosing frequency can be increased in severe conditions of ulcer. One of the approaches for improving the gastric residence is, formulation of the corresponding drug as bioadhesive or mucoadhesive microspheres.

Methodology: Mucoadhesive microsphere formulations, F1-F6 were prepared using emulsion solvent evaporation method. Various trials comprising different ratios of mucoadhesive to rate retarding polymer concentrations were performed and ratios ranging from 1:2-1:5 were prepared in the combinations of chitosan-eudragit RS100 and carbopol-eudragit RS100. Prepared batches were assessed for various parameters like drug entrapment efficiency, swelling index, *in vitro* mucoadhesion, *in vitro* drug release and *in vivo* anti ulcer activity. *In vitro* drug release studies were carried out in USP type I dissolution test apparatus. Microspheres equivalent to 150mg of the drug were used for the dissolution study. Microspheres containing the active ingredient were placed in 900ml of the dissolution medium maintained at 37±0.5°C. Dissolution test was carried out in simulated gastric fluid (0.1N HCl and 2gm of NaCl) for 24h. The speed of the basket was maintained at 50 rpm. Aliquots were withdrawn at predetermined time intervals, diluted as required and analyzed for drug content spectrophotometrically at 313 nm against blank medium. Equal volume of the dissolution medium was replaced in the vessel after each withdrawal to maintain sink conditions. The percentage drug release was calculated and plotted against time to study the pattern of drug release

Results and Discussion: Based on the results, F2 was selected as the best formulation because of its morphological shape, good drug entrapment and *in vitro* mucoadhesion; this batch showed 98.89 ± 2.57% cumulative drug release at the end of 24h with r^2 value of 0.990 for first order kinetics. The release mechanism of the drug from the formulation was found to be erosion. Also the *in vivo* activity at the end of 24 h showed ulcer protection of about 78.71% which was not the case with the conventional dosage forms available in the market. The stability study showed that there were no significant changes at the end of 2 months storage at 30±2°C/65±5% RH.

Conclusion: The developed ranitidine HCl loaded mucoadhesive microspheres were thus, suitable for treatment of peptic ulcer disease conditions with ease of oral administration**.**

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DESIGN AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLET OF FELODIPINE

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Background and Rationale: Felodipine (FP), used in the present study as a model drug, is a di-hydropyridine derivative. The present investigation is concerned with the development of sustained release tablets of FP, using PEG 6000 to improve its dissolution, and different grades of HPMC (K4M, K15M, and K100M), for achieving sustained release of the drug.

Methodology: FP was added and dissolved in molten PEG 6000 (80°C). After cooling to room temperature, the solidified mass was crushed. The crushed mass was passed through sieve No. 12 (1400 mm) and sieve No.42 (355 mm)) to obtain FP-PEG 6000 granules. The release profile of FP from a tablet prepared using macrogol 6000 (PEG) and HPMC was determined. The effect of three different grades of HPMC- K4M, K15M, and K100M, which were used in three different ratios (drug: polymer :: 1:1, 1:2, 1:3) to retard the drug release from the matrices was studied.. The *in–vitro* dissolution studies were carried out using USP Type II Apparatus [Electrolab (ETC-11L) Tablet Dissolution Tester] at 50 rpm and at 37°C ±5°C. The study was carried out in 900 ml of 0.1N HCl for the first 2 h, and then in 900 ml of phosphate buffer (pH 7.4) from the 3rd h to the 24th h. At different time intervals, 10ml samples were withdrawn and the amount of drug release was analyzed spectrophotometrically at 361 nm. Cumulative percent release of the drug was calculated.

Results and Discussion: The formulation F-9 released the drug with slower rate of 86.45 % in 24 h among formulations F-7 to F-9. The release data of the most satisfactory formulation was treated by Korsemayar, Higuchi, zero order and first order equations. The R^2 values of formulation F-8 were found to be 0.9728, 0.9778, 0.9869, 0.9931 respectively and showed the linear relationship with R^2 value close to 1.

Conclusion: We conclude that solid dispersions of felodipine with PEG 6000 increased the solubility of the drug. The release retarding material, HPMC, is cheap, readily available, biodegradable, safe and easy to handle. **References:**

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Development of compression-coated tablet using almond gum as natural polysaccharide for improved drug delivery to the lower intestinal tract

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Background & Rationale: Conventional colon targeted drug delivery systems are not able to maintain the therapeutic drug concentration at the site of action (1). Rectal dosage forms, such as suppositories and enemas are not always effective, since they are highly irritable. Oral route has limitations such as degradation of active ingredients in the upper gastrointestinal tract (2). Hence in the present study, almond gum, a plant polysaccharide, obtained from *Prunus amygdalus* was used to develop controlled release tablets of 5-aminosalicylic acid (5-ASA). The aim of the work reported here is to develop a compression coated colon specific formulation for oral administration. The polymer used in this study gets degraded in the colon and allows the drug to be released in a sustained manner.

Methods: A) Preparation of core tablet: 5-ASA and MCC tablets were prepared by direct compression method.

Preparation of compression coated tablets: Compression coated granules (Almond gum and MCC were mixed and distilled water was added. The wet mass was passed through a sieve and was dried. Magnesium stearate was added) were placed in the die of a press. The core tablet was placed over the granules and covered by compression coated granules and compressed; the compression coated tablet was further coated with ethyl cellulose.

B) *In vitro* drug release study: *In vitro* drug release was determined using USP type II apparatus, carried out in simulated gastric fluid (SGF), pH 1.2 (for the first 2 h), phosphate buffer, pH 6.8 (for the next 3 h) and pH 7.4 (for the next 19 h) in the dissolution medium (900 mL) at temperature 37±0.5°C. The paddle of the vessel was rotated at 50 rpm. Aliquots were withdrawn at predetermined time intervals for 24 h. The samples were suitably diluted and analysed using double beam UV-Visible spectrophotometer at 331nm.

Results & Discussion: No drug was released in the acidic medium at pH 1.2. After 8 h, less than 30% of the drug was released from tablets containing 90 to 240 mg of almond gum. Tablets containing 270 mg of almond gum exhibited the highest drug release rate than the formulation containing 90 mg of almond gum due to the more swelling of tablets at higher polymer concentration and erosion of tablet surface. The formulation with 180 mg of almond gum released 97% of the drug over a period of 24 h and was selected as the best formulation.

Conclusion: A compression coated tablet based on almond gum as polysaccharide was developed, which is expected to degrade in the colon and deliver the drug at a sustained rate. The compression coated tablets were coated with ethyl cellulose as a hydrophobic polymer.

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DISSOLUTION RATE ENHANCEMENT OF POORLY SOLUBLE DRUG BY SOLID DISPERSION SYSTEM.

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ABSTRACT: Solubility is the property of a solid, liquid, or gaseous chemical substance called solute to dissolve in a solid, liquid, or gaseous solvent to form a homogeneous solution. In the last few decades, solid dispersion (SD) technology has been studied as an approach to produce an amorphous carrier to enhance the solubility, dissolution rate, and bioavailability of poorly water-soluble drugs, and much attention has been paid towards the use of novel carriers and methodologies in exploring novel types of SDs to enhance therapeutic efficacy and bioavailability.

METHODS - Preparation of Solid Dispersions (SD) and Physical Mixtures of Dolutegravir by fusion method: Appropriate amounts of polymer (PEG 6000,PVP K 30) were melted at a temperature of 80±2°C. Dolutegravir was dissolved in the molten polymer by constant stirring for 15 min. This mixture was kept in a refrigerator at 4°C for 3 days to solidify to form the solid dispersion. The resulting solid dispersions were scraped, pulverized in a mortar and sieved through 45# sieve. Solid dispersions were stored in amber glass vials and kept in a desiccator at 20±1° for further analysis.

Evaluation of Solid Dispersions of Dolutegravir : The solid dispersions were evaluated for parameters like flow properties, solubility, drug content uniformity, and i*n vitro* dissolution. *In vitro* dissolution studies were performed for pure drug, physical mixture, and the solid dispersion. A paddle type dissolution apparatus was used. It was kept at a temp of 37±0.5°C. The dissolution medium was 900 ml of pH 6.8 phosphate buffer. The paddle was rotated at a speed of 50 rpm. 5 ml samples were collected at a predetermined time intervals, i.e., 5,10,15,20,30,45,60,90 min, and the sample was replaced by fresh medium after each withdrawal, in order to maintain sink conditions.. Absorbances of the suitably diluted samples were taken at a wavelength of 225 nm by the use of a UV spectrophotometer.

RESULTS : Comparative study of the pure drug, the physical mixtures, and the solid dispersions:

The drug content in the SD was found to be 96 – 100 %. The flow properties like angle of repose values ranged from 26 – 45°, Carr's index values ranged from 13 – 38.37 and Hausner's ratio ranged from 1.16 –1.62. *In vitro* dissolution studies were performed for all the formulations in pH 6.8 phosphate buffer. The formulation SDPEG15 containing drug and polymer in the ratio of 1:15, of PEG solid dispersion system exhibited a faster dissolution compared to the pure drug and the physical mixture, and complete dissolution took place within 45 min.

CONCLUSION : The present study was aimed at improving the aqueous solubility of poorly soluble drug dolutegravir, by employing the technique of soluble dispersions, using hydrophilic carriers like PEG 8000. It can be concluded from the results that solid dispersion systems prepared using polymers can aid in improving the dissolution properties of poorly water soluble drugs.

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Enhancement of Dissolution of Carvedilol by Lipid based Solid Dispersions

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Background: Carvedilol is a non-selective beta blocker used in the treatment of mild to moderate congestive heart failure. It has poor aqueous solubility and low oral bioavailability of about 25 - 35% with absorption occurring majorly via the intestinal lymphatic route. Use of long chain triglycerides is reported to enhance lymphatic uptake of highly lipophilic drugs. The present work was aimed at improving the dissolution of the drug through lipid-based approaches such as self micro emulsifying drug delivery systems (SMEDDS), solid dispersions (SDs) and lipid based solid dispersions (LBSD).

Methods: A. Solubility of carvedilol in various oils, surfactants and co-surfactants was determined by the shake flask method followed by emulsification studies to choose the components for the SMEDDS formulation. Pseudo ternary phase diagram was constructed by using the water titration method with the help of TRIPLOT V14 (4.1.0.2) software.

B. SDs in inert carrier Gelucire 50/13 were prepared by the solvent evaporation method.

C. Finally, LBSDs were prepared as combination products of SDs and SMEDDS. The SMEDDS containing carvedilol were added to the SDs, mixed well with spatula on water bath, cooled and finally stored at 8˚C. The product was also subjected to XRD studies.

D. *In vitro* dissolution studies of carvedilol from the formulations were carried out at 37 ± 0.5˚C, using a USP type II apparatus (paddle), at 50 rpm, in 900 ml of 0.1N HCl, in the case of the SMEDDS and in 900ml of pH 6.8 phosphate buffer, in the case of SDs and LSBDs. Aliquots of the dissolution medium were withdrawn at predetermined intervals and were analysed spectrophotometrically at 240 nm.

Results and Discussion: Based on the solubility studies, oleic acid, Tween 80 and Caproyl 90 were selected as oil, surfactant and co-surfactant respectively, for the formulation of SMEDDS. *In vitro* dissolution studies of SMEDDS of carvedilol in the surfactant: co-surfactant ratio of 1:3 ratio exhibited drug release of 83.98% in 1hr and 87.53% in 1hr from SDs of carvedilol in Gelucire 50/13. The release was further enhanced to 92.97% in 1hr when evaluated as the LBSD. On comparing the diffractograms in XRD of LBSD and carvedilol, no obvious peaks representing crystals of carvedilol were seen in LBSDs, indicating that the increase in solubility could be attributed to the amorphous state of the drug.

Conclusions: The formulation of lipid based solid dispersions combines the benefits of SMEDDS approach, where a portion of the drug is solubilized within the lipid excipients, and solid dispersions approach, where the remaining portion of the drug is dispersed within the lipidic inert carrier phase, to enhance its dissolution characteristics. The blend of lipids and surfactants within LBSD has the potential to increase the absorption of carvedilol by increasing its lymphatic uptake.

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Ethyl cellulose film coating optimization of sustained release aspirin spherules using DOE for the application to reduce cardiac complications in COVID-19

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Background & Rationale: This study aims to address one of the pressing difficulties associated with the design and development of sustained-release (SR) aspirin (ASP) spherules for oral administration in COVID-19. This is achieved by Design of Experiments (DOE) followed by formulation optimization and detailed mechanistic characterisation exploring scanning electron microscopy (SEM), powder x-ray diffraction (PXRD) and differential scanning calorimetry (DSC) apart from drug release and kinetic model analysis.

Methods:(a) Experimental design and response surface methodology (RSM): *In silico* modeling and evaluation was performed and interpreted by Design Expert®12 Software (Stat-Ease, Inc.). The design selected here was the central composite design (CCD).

(b) Preparation of polymer-coated spherules by Bed coating during rolling process (BCDR): The granules, spherules and rate control membrane-coated spherules were prepared by coating the granules produced by wet granulation with starch to spherules. These units were later coated by ethyl cellulose (EC) rate control membranes with varying structure.

(c) *In vitro* release study and kinetic modeling of prepared aspirin spherules: Drug release studies of aspirin spheruleswere carried out using USP type I basket apparatus.. Phosphate buffer (6.8) (900ml), was taken and 1.5g of spherules were added to it, basket rotation was set at 75 rpm, and temperature at 37± 0.5^0C. The kinetics and mechanism of drug release from spherules were determined by fitting the *in vitro* drug release data into zero order, first order, Higuchi, and Korsmeyer-Peppas models. The best-fitted model was confirmed using R^2 and n values.

Results and Discussion: EC coated spherules have a 10% lower burst release (BR) than uncoated spherules, which have a release of 80-91% initially. The spherules were then sequentially coated until the desired release profile was obtained. Design of space by DOE showed a coating efficiency-70.14% and cumulative percentage coating -200% and drug release -61.54%. The results of DOE to experimentally validated results were within 20% deviation.

Conclusions: This study aimed to prepare an SR spherule-based oral formulation for ASP, from granules by modifying them using coating with an SR polymer (EC), to treat COVID-19, which was successfully achieved by DOE and experimental validation. The proposed method can be adopted for rapid formulation optimization.

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Evaluation of Ionotropic Cross-linked Chitosan/Gelatin B Microspheres of Trimetazidine Hydrochloride

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Background and Rationale: Controlled drug delivery systems received tremendous attention and the significant research interest in the long-term maintenance of drug levels coincides with the increased medical and public acceptance of such systems. Encapsulated slow-release microspheres can be prepared by the process of microencapsulation. Natural polysaccharides as polymers offer certain advantages over synthetic one in respect to toxicity, availability and cost. In this present study microspheres of Trimetazidine Hydrochloride (TMZ) for oral delivery were developed with the aim to improve patient compliance and to obtain improved therapeutic efficacy in the treatment of angina pectoris.[1,2]

Methods: Microspheres were prepared by complex coacervation and simple coacervation methods without the use of chemical cross–linking agent (glutaraldehyde) to avoid the toxic reactions and other undesirable effects of the chemical cross-linking agents. Alternatively, ionotropic gelation was employed by using sodium-tripolyphosphate (Na-TPP) as cross-linking agent. Chitosan and Gelatin B were used as polymer and copolymer respectively. All the prepared microspheres were subjected to various physico-chemical characterization. *In-vitro* drug release characteristics and release kinetics were carried out as per the following procedure:

***In-Vitro* release Study:** Microspheres equivalent to 50 mg Trimetazidine Hydrochloride were subjected to in vitro drug release studies to assess their ability in providing the desired controlled drug delivery. Drug release studies were carried out using USP XXIII basket dissolution rate test apparatus (100 rpm, 37 ± 1^0C). To avoid the floating of microspheres on the surface of the dissolution and make them available into the dissolution media the basket type dissolution test apparatus was used. 900 ml of 1.2 pH buffer was used as dissolution media for 2 h followed by 7.4 pH phosphate buffer up to 12 h. At different time intervals, 5 ml of the sample was withdrawn and replaced with same quantity of fresh media. The sample was analysed for Trimetazidine Hydrochloride spectrophotometrically at 269 nm using a UV/VIS spectrophotometer against a reagent blank. All the experiments were carried out in triplicate. To examine the drug release kinetics and mechanism, the cumulative release data of the Trimetazidine Hydrochloride microspheres were fitted to various release kinetics models.

Results and Discussions: TLC and FTIR studies indicated no drug-polymer incompatibility. The drug release kinetics study indicated that the release data was best fitted with zero order kinetics. All the microspheres showed sustained release of drug by a Fickian diffusion mechanism. From the results obtained in the *in vitro* release studies it was observed that the TMZ microspheres prepared by complex coacervation method showed better release pattern compared to microspheres prepared by simple coacervation method. DSC and XRD analysis indicated that the TMZ trapped in the microspheres existed in an amorphous or disordered-crystalline status in the polymer matrix.

Conclusions: The micro particulate drug delivery system proposed in this work based on chitosan and Gelatin B seems to hold promise for oral administration of TMZ and found to be simple and reproducible. From the study, it may be concluded that it is possible to design a sustained drug delivery system for the prolonged release of TMZ, improving therapy by possible reduction of time intervals between administrations, improve patient compliance and to obtain improved therapeutic efficacy in the treatment of angina pectoris.

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FORMULATION AND EVALUATION OF ALBUTEROL PULSIN CAP FOR PULSATILE DRUG DELIVERY

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Background and rationale: In the current research work albuterol was taken as a model drug. It is a beta 2 adrenergic receptor agonist, used in the treatment of asthma. The formulation is contained within the cap, the plug prevents the release of the drug into the gastric fluid. On reaching the small intestine the plug swells and delays the drug release. The system releases the drug after a predetermined lag time of 8 hours and thus the dosage form can be taken at bedtime so that contents will be released in the morning hours when the symptoms are more prominent. Albuterol with superdisintegrants like crospovidone, sodium starch glycolate, cross carmellose F4 were selected based on drug release within a given period. Based on these evaluation parameters, it was optimized as a promising approach for albuterol pulsatile drug delivery system.

Methods: PREPARATION OF ALBUTEROL GRANULES AND PULSIN CAP: Albuterol granules were prepared by the wet granulation method. Preparation of modified pulsin cap or pulsatile drug delivery was by following steps: Granules equivalent to 150 mg of the drug were filled in the capsule bodies and were plugged with hydrogel plugs. The treated body and the untreated cap of the capsules were sealed with a small amount of 5% ethanolic solution of ethyl cellulose.

IN VITRO DISSOLUTION STUDY OF ALBUTEROL PULSIN CAP: *In vitro* dissolution studies of the Pulsin caps of albuterol were carried out by the USP II paddle method at 50 rpm, and 37±0.5°C, using 0.1N HCl as dissolution medium for 2 hours. The dissolution fluid was replaced at the end of 2 hours with a 6.8 phosphate buffer. Five ml aliquots were pipetted out at predetermined time intervals and this was replaced with 5ml of fresh 0.1N HCl to maintain the volume of the buffer. The samples were analyzed at 269 nm using a spectrophotometer. The lag time and percentage release were determined for each formulation.

Results and discussion: Drug release data of Pulsin cap final dosage form cannot be explained by zero-order nor by first-order equation, as the plots showed the linearity r^2=0.06338 and r^2=0.478, respectively. The drug release followed Peppa's model (r^2=0.8206) and the slope value was n=2.06. It is more than 0.89, so it shows super case II, which means the drug release is by polymeric chain erosion.

Conclusion: As an overall conclusion, Pulsincap batch - H5F4 showed a consistent release of the drug after the predetermined lag time, which was considered as optimized, and was taken as a promising approach for the pulsatile release of albuterol.

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------ ☺ ------

FORMULATION AND EVALUATION OF FAMOTIDINE NANO EMULSION

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Background and Rationale: Famotidine is a potent H_2 receptor antagonist.. Nano emulsion is an approach to improve water solubility and bioavailability of lipophilic drugs. In the present investigation, an attempt was made to maximize the therapeutic efficacy of famotidine by developing a nano emulsion.

Method: Phase diagrams were constructed, the different concentrations of oil were selected at a difference of 6.45%, 6.90%, 7.40% and 8% from the nano emulsion region. Percentage of oil was selected, the formula that used the minimum concentration of Smix for its nano emulsion formation was selected from the phase diagram. The release profiles of famotidine crude drug powder and nano emulsion were compared. *In vitro* drug release was performed using a dialysis membrane. Five milliliters of NE, placed in dialysis bag (HIMEDIA dialysis membrane), was subjected to release study in 200 ml of dialyzing medium (pH 4.5 phosphate buffer), maintained at a temperature of 37°C, stirred at a speed of 50 rpm. Aliquots of 1 ml were withdrawn at regular time intervals (5, 15, 30, 45, 60, 90, 120 and 180min) from the dialyzing medium and diluted to 10ml with phosphate buffer. The volumes withdrawn were replaced with fresh medium each time. The samples were analyzed at 265.5nm and, percent cumulative drug release was calculated.

Ex vivo studies were carried out as follows: the nano emulsion sample (1ml containing 4mg) was injected into the isolated rat stomach using syringe and the two sides of the stomach were tightly closed. The tissue was then placed in a beaker /receiver compartment filled with 200ml of tyrode solution (pH 7.17-7.35); continuous aeration and a constant temperature of 37°C and magnetic stirring were maintained. 1ml samples were withdrawn periodically from the receiver compartment at time intervals of 5, 15, 30, 45, 60, 90, 120, 150 & 180 min and diluted to 10ml with tyrode solution and replaced with an equal volume of fresh tyrode solution. The absorbance was measured using a UV-VIS spectrophotometer at a wavelength of 265.5nm, keeping the respective tyrode solution as blank.

Results and Discussion: The prepared nano emulsions were characterized for their clarity, viscosity, drug release, particle size, drug content as well as for *in vitro* stomach and intestinal permeability studies and in vivo study for best formulation. The *in vivo* studies revealed a significant increase in anti-ulcer activity as compared with standard marketed tablets of famotidine. The drug release after 3h for all formulations varied from 70.27% to 83.58% as compared with 51.61% for pure drug. The drug release from the nano emulsion was found to be significantly higher as compared to the pure drug. It could be suggested that the nano emulsion formulation resulted in a spontaneous formation of a nano emulsion with a small droplet size, which permitted a faster rate of drug release into the aqueous phase, much faster than the pure drug. Oral administration of aspirin suspension produced haemorrhagic damage along the long axis of the stomach. For these studies, doses of famotidine 10 mg/kg that inhibit gastric acid secretion to a similar degree in rats were used, while the aspirin induced gastric lesions required 500 mg/kg were used to induce gastric ulceration. The formulation F2 has decreased the intensity of gastric mucosal damage induced by aspirin has shown a protection index of 88.65% when compared to control, whereas standard marketed tablets of famotidine have shown 45% of protection induced by aspirin compared to control. In control groups the ulcer incidence was 100%. Thus the nano emulsion formulation F2 was more effective to reduce ulcer incidence rather than standard marketed tablets of famotidine.

Conclusion: Thermodynamically stable, famotidine loaded nano emulsion, improved the therapeutic efficacy of famotidine, by improving its solubility, permeability and oral bioavailability.

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Formulation and Evaluation of Ketorolac Tromethamine Loaded Transferosomal Gel Using Box Behnken Design

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Background and rationale : The major objective behind this formulation is enhancing the topical delivery of hydrophilic drug (Ketorolac tromethamine) by formulating ketorolac tromethamine loaded transferosomal gel using Box-Behnken design.

Methods: A) Incorporation of optimized transferosomal formulation in gel: Transferosomes were prepared with various types of phospholipids & surfactants at different concentrations by ether injection method. The optimized formulation was incorporated in a gel base composed of Carbopol 934P and was evaluated.

B) *In Vitro* Release kinetics: Studies were performed using two side open ended boiling tube as a donor compartment and a beaker (250 ml) as receptor compartment. The dialysis membrane was placed between the donor and the receptor compartments. Transferosomal suspension was added to the donor compartment tube with membrane clamped to it. The receptor compartment was filled with pH 7.4 phosphate buffered saline and maintained by continuous stirring at 50 rpm with a magnetic bead and maintained at 37^0C. At predetermined time intervals, 5 ml samples were withdrawn and replaced by an equal volume of buffer. The samples were analyzed after appropriate dilution at a λmax of 324, using a spectrophotometer. The release rate was calculated by plotting the amount of drug permeated versus square root of time. The slope is the release rate(µg/cm²/hr½).

Results and Discussion: All the formulations with Tween 80 and soya lecithin have shown good vesicle formation. The concentration of cholesterol was optimized; the optimized concentration of 30 mg has shown good vesicles with 60% entrapment efficiency and drug release of 40% at the end of 6 hours. The concentration of lipid, edge activator and surfactant were optimized by using Box-Benken design. Based on the responses obtained, F18 was found to be optimized formulation with entrapment efficiency of 86.7% and drug release of 78.2% at the end of 8 hours, which was close to the value predicted by the design.This optimized formulation was incorporated in a gel base made of Carbopol 934P, and was evaluated. The spreadability of the gel was found to be 6.62, the pH of the gel was found to be 6.68, the drug content was 91.8 and the drug release was found to be 60% by the end of 8 hours, and followed zero order kinetics with Higuchi release mechanism.

Conclusion: Ketorolac tromethamine was successfully formulated as a transferosomal gel, with good permeation.

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Formulation and Evaluation of Liposomal Repaglinide by Glycerolphosphate Chitosan Complexation for Antidiabetic Activity

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Background and Rationale : Repaglinide is mainly used as an antihyperglycemic drug. The present work focussed on the formulation of repaglinide loaded liposomes, by the hand shake method, using a phospholipid, and chitosan and glycerolphosphate as complexing agents.

Method: Repaglinide liposomes were prepared by the hand shaking method (thin film hydration technique). The drug, phospholipid and stearic acid were taken in a round bottom flask, as per the required quantity of each formulation (F1-F9) along with glass beads and 10 ml of chloroform. It was then manually shaken until the chloroform evaporated, leaving behind a thin film. After this, 20ml of phosphate buffer (pH 6.8) was added to the round bottom flask and shaken to get the liposomal dispersion. The obtained liposomes were subjected to sonication at 51ºC for 2mins [1]. The *in vitro* drug release studies were conducted for repaglinide liposomes in pH 1.2 Hydrochloric acid buffer for 2 hours and in pH 6.8 phosphate buffer for 10 hours in dialysis membrane. Required amounts of the liposomes were added to a dialysis membrane and immersed into the diffusion medium, temperature was maintained at 37°C ±1°C and the medium was agitated at 50 rpm. 5ml of diffusion media was withdrawn every one hour and replaced with an equal quantity of the medium to maintain a constant volume.

Results : The *in-vitro* release profiles of the formulations, that is formulations F1-F9 were studied. It was clearly evident that the diffusion behaviour of formulations F6 & F9 was increased by almost 71.06±0.027 & 85.21±0.002, as they were complexed with glycerophosphate and chitosan, in comparison to the other formulations. Different models were adopted for fitting the data in kinetic modelling and results showed that the *in vitro* drug release followed zero order kinetics. The '*n*' value of Korsmeyer Peppa's model showed a non-Fickian mechanism of release for the best formulation.

Conclusion : Thus, the prepared liposome of repaglinide proved to be a potential candidate as a liposomal drug delivery system for diabetes.

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Formulation of felodipine *in situ* gelling depot injection and *in vitro* release studies

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Objective: Felodipine is a long-acting 1,4-dihydropyridine calcium channel blocker. However, poor aqueous solubility and extensive first pass metabolism contribute to a low oral bioavailability of about 15%. The present study focuses on the formulation and evaluation of an injectable thermo-reversible *in situ* gelling system as a depot for sustained release of felodipine.

Methods: Thermoreversible *in situ* gels of felodipine were prepared by using various ratios of Poloxamer 407 (P407) and Poloxamer 188 (P 188), using the cold method. DMSO was used as a solvent and benzalkonium chloride as a preservative. Evaluation of the gel included determination of gelation temperature, gelation time, syringeability and *in vitro* drug release studies. The *in vitro* drug release studies were performed over a period of 120 hours, using modified diffusion apparatus with pH 7.4 buffer as a diffusion medium. A cellophane membrane (previously soaked overnight in the buffer) was tied to one end of a specially designed glass cylinder (open at both ends) having an inner diameter of 3.4 cm. 2 ml of the formulation was placed into the glass cylinder known as the donor compartment. The cylinder was suspended in a beaker (receptor compartment) containing 200 ml of phosphate buffer pH 7.4 as diffusion medium with the membrane just touching the surface of the medium. Receptor medium was maintained at a temperature of 37±2°C with a stirring rate of 50 rpm using a magnetic stirrer. About 3 ml of sample was withdrawn at designated time intervals and was replaced with an equal volume of fresh diffusion medium. The aliquots were suitably diluted and analysed at 363 nm using a UV spectrophotometer. The ability of the formulation to gel was determined *ex vivo* by injection into a chick muscle which was followed by dissection and examination of the tissue.

Results and Discussion: Thermoreversible *in situ* gels of felodipine were formulated using P 407 (20%), P188 (5%), felodipine (35mg), benzalkonium chloride (0.02%) and DMSO (0.5ml). Selection was based on exhibition of gelation temperature close to the body temperature even upon incorporation of drug. All formulations showed an initial burst effect as a result of the immediate drug release from the sol form of the preparation before conversion to gel. The best selected formulation could sustain drug release for 120 hrs. The *in vitro* release profiles of the drug from all the formulations appeared to follow Korsmeyer-Peppas model. The drug was released from *in situ* gels by Fickian diffusion through the extra micellar aqueous channels of the gel matrix. The optimized formulation was found to form a compact gel in the chick muscle which confirmed the ability of the formulation to gel to a depot in the muscle tissue.

Conclusions: The developed injectable product is a simple formulation with potential to reduce the frequency of drug administration, improve patient compliance, improve drug bioavailability and therapeutic outcome.

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In vitro drug release studies of an ethosomal bee propolis extract based hair growth promoting gel

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Background & Rationale: Hair growth products of natural and synthetic origin are available, with more market share for synthetic products. The reported side effects have declined the popularity of synthetic products with more acceptance for products from natural origin. The modern formulation technologies adapted into natural products have increased their potential. The presence of polyphenolic compounds like caffeic acid, chlorogenic acid, kaempferol present in the ethanolic extract of the bee propolis has potential hair growth promoting activity. The vesicular delivery systems such as liposomes, niosomes, ethosomes etc can be utilized to improve the activity as well as the stability of these extracts. Aim of the present investigation was to develop a novel ethosomal hair growth promoting gel containing ethanolic extract of bee propolis and evaluate its efficacy.

Methods: A) Preparation of ethosomal gel containing ethanolic extract of bee propolis: Ethanolic extract of bee propolis was encapsulated into ethosomes by the hot method, with necessary modifications. The ethosomes with 40% ethanol were loaded into carbopol 934 gel base to prepare formulations ETF1, ETF2, ETF3 with gel base concentration of 0.5% w/v, 0.75% w/v and 1% w/v. The gels were subjected to evaluation studies, including *in vitro* drug release studies.

B) *In vitro* release study of developed hair gel formulations:

In vitro release was carried out using a Franz diffusion cell containing 25 ml of pH 7.4 phosphate buffer solution as receptor medium. The temperature was maintained at 37±2^{o}C and the medium was stirred at 50 rpm, using a magnetic bead. The ethosomal gel was spread uniformly on the surface of the cellulose acetate membrane. The samples were withdrawn at fixed time intervals and sink conditions were maintained throughout the study. The Folin- Ciocalteu method was used to measure the total phenolic content of the samples.

Results and Discussion: The release profile varied with difference in concentration of gel base. There was an initial burst release of 8.7±0.04 % and 8.2±0.12 %, from formulations ETF1 and ETF2 after the completion of one hour. This was comparatively superior to the release of drug observed from ETF3. After the completion of 24 hours, maximum % drug release of 91.06±0.18 was reported from ETF1. The data clearly suggested the significance of gel base concentration in drug release, as the higher concentrations may retard the drug release from drug loaded ethosomes. The developed ETF1 with ethosome at 40% v/v and carbopol gel base at 0.5% w/v was superior in terms of selected quality parameters and kinetics was applied to the release profile. The data was fitted to various models like zero order, first order, Higuchi model and Korsmeyer-Peppas model to determine the mechanism. The data obtained suggested that the formulation of the ETF1 followed zero order diffusion-controlled drug release mechanism.

Conclusion: The combination of ethosomes and optimized gel base could improve the hair growth potential of bee propolis extract. The developed gel may be an effective as well as safer replacement for the existing synthetic hair growth gels.

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In vitro drug release study of Medicated Chewing Gum Containing Indomethacin IP (MCGI)

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Background & Rationale: Medicated chewing gum (MCG) is a novel drug delivery system containing a masticatory gum base with a pharmacologically active ingredient. During the chewing of the gum, the drug contained in the gum base is released into saliva to either get absorbed through oral mucosa or it may reach the stomach for GI absorption. The drugs causing side effects such as GI disturbances and irritation may be formulated as a medicated chewing gum. Indomethacin IP is a potential NSAID and is reported with excess stomach secretion, stomach cramp, diarrhea, water retention and even rupture in the wall of stomach or intestine. MCG may be one of the better alternatives to minimize the drawbacks and maximize the availability of Indomethacin IP.

Methods:A)Formulation of medicated chewing gum of Indomethacin IP (MCGI): The powdered drug was sifted through sieve no.40 and was accurately weighed. The gum taken in a china dish was heated in a water bath until it melted, i.e., at 70^0 C. Glycerol and soya lecithin were added to the melted gum. The drug dissolved in ethanol was added to the melted gum base and was stirred thoroughly until it became uniform. The flavor and coloring agent were added at the last stage. The resultant mixture was cooled, rolled, and cut into pieces to produce sticks of chewing gum.

B) *In vitro* drug release studies of the formulated medicated chewing gum sticks of Indomethacin IP: An *in vitro* drug release study for MCGI was performed using specially designed hand operated equipment which may mimic the normal mastication process of humans. It consists of movable piston and a fixed base plate which is kept in a transparent cylinder containing medium (Phosphate buffer solution, pH 6.8). MCGI was placed in between the movable piston and a fixed base plate. During the up and down motion of the piston at 30 cycles/min, the drug in the MCGI can be released into the medium. From the medium, 1 ml of the sample was withdrawn at 5 min intervals for a duration of 60 min. The sink condition was maintained for the entire duration of the study. The samples withdrawn were diluted, using phosphate buffer solution of pH 6.8, and their absorbances were measured using a UV-Visible spectrophotometer, at a wavelength of 317 nm. The experiment was repeated for 40, 50, and 60 cycles/min chewing frequency.

Results and Discussion: The effect of chewing frequency on drug release from the MCGI was considered as a major parameter to be assessed. The maximum percent drug released after a period of 30 min was 73.18±0.003, 78.40±0.19, 82.52±0.03 and 89.77±0.04 at 30 cyc/min, 40 cyc/min, 50 cyc/min and 60 cyc/min respectively. The percent drug released from conventional capsules of Indomethacin IP, after a duration of 30 min was 61.15±0.15. The percent drug released from the MCGI was influenced by the frequency of chewing. As the chewing frequency was increased, percent drug release from the MCGI also increased. The overall data suggested the faster onset of drug release and superior release profile of MCGI over the conventional capsules of Indomethacin IP, at all investigated chewing frequencies.

Conclusions: The MCGI of Indomethacin IP may provide a local and systemic delivery of drug with a faster onset of action than the existing oral formulation of the drug. Further, the MCGI was able to release maximum amount of drug incorporated.

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In vitro static dissolution studies of periodontal strips containing complexes of β cyclodextrin (β CD) with Ciprofloxacin

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Background and Rationale: Dental diseases are a major public health problem throughout the world. These diseases may be chronic and long term treatment is often necessary. Antibiotic treatment of periodontitis shows good results in controlling the pathogens. Vehicles for local delivery of therapeutic agents include dentifices, mouth washes, gels, irrigation solutions and slow release devices of antibiotics. Controlled release delivery maintains drug concentration for prolonged periods of time at the site, and this can be achieved by systemic or local application. There are two types of controlled release local delivery devices, the reservoir devices and the monolithic devices. The objective of the present investigation was to develop polymeric strips of chitosan containing antibacterial agent- β CD complex for local controlled drug delivery into periodontal pocket, to maintain therapeutic concentration in the gingival fluid for a long duration.

Methods: A) Development of chitosan films containing drug-βCD complex: Ciprofloxacin- βCD complex was prepared by the kneading method at 1:1 molar ratio. Chitosan 2%, was soaked in 1% acetic acid solution for 24 hours, to get a clear solution. The solution was filtered through a muslin cloth. Required amount of CIPRO-βCD complex was added into the polymeric solution, vortexed and was kept aside for 30 minutes. The films were prepared by casting method in a glass mould, and allowed to dry at room temperature for 24 hours. After drying, films were cut into suitable size strips.

B) *In vitro* release study of developed films: A set of six test strips, all of them having a known weight of the drug, were placed separately into small test tubes containing 1ml of phosphate buffer pH 6.6. The tubes were sealed and kept at 37^{o}C for 24 hours. At periodic intervals, the buffer was collected, and replaced with fresh 1ml medium. The CIPRO concentration in withdrawn aliquots was measured using UV/Visible spectrophotometer at 274 nm.

Results and Discussion: The release of CIPRO from the chitosan strip for first day was 25.2 µg followed by 18.49 µg and 14.27 µg on 2nd and 3rd days, respectively. The release after the 6th day was reduced to less than 10 µg and was found to be uniform over a period of 24 days. Initially, high release was observed due to the soluble βCD complexation. It was observed that there was marked reduction in the release from day 7 to day 24. Incorporation of βCD with drug in the chitosan, though, showed an initial burst release and the release was extended up to 24 days. Around 75.14% of CIPRO was released at the end of 24 days. The plot of cumulative amount of drug release per unit surface area against square of time, confirmed Higuchi's diffusional model.

Conclusion: The present study has achieved controlled release delivery of ciprofloxacin, directly into the periodontal pocket, which can prove to be highly beneficial in periodontal disease.

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In vitro release studies of Amphotericin B loaded ethosomal cream for the management of Pulmonary Aspergilloma

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Background and Rationale: Pulmonary Aspergilloma is a clinical syndrome of worldwide presence caused by the fungus *Aspergillus*. Aspergilloma, most commonly associated with pulmonary TB, represents the growth of *Aspergillus* within a pre-existing lung cavity. Current treatment strategies to eradicate Aspergillosis is surgery, systemic and IV use of antifungals like Amphotericin B (AMB), which are associated with many drawbacks like poor penetration and drug retention in the aspergillus cavity, risk of pneumothorax, relapse of infection and high mortality rate. The potential of ethosomes as a vesicular drug delivery system can be explored to improve the penetration and prolong the retention of AMB. Aim of this study was to develop AMB loaded ethosomal cream for pulmonary aspergillosis associated with TB.

Methods: A) Formulation of AMB loaded ethosomal cream: AMB loaded ethosomes were developed by hot method with necessary modifications using 20,30,40 v/v concentrations of ethanol, propylene glycol, cholesterol, soya lecithin, DMSO and distilled water. Ethosomal formulation with 40% v/v ethanol was then incorporated into Carbopol 934 cream base in 3 different concentrations (0.25, 0.5, 0.75%w/v). Ethosomal creams (ETC1, ETC2,ETC3) were subjected to various evaluation studies including *in vitro* drug release studies.

B) *In vitro* study of developed ethosomal creams: *In vitro* release study was carried out using modified Franz diffusion cell apparatus at a temperature of 37±0.5°C using phosphate buffer solution pH 7.4. Ethosomal creams were uniformly spread on a cellophane membrane and placed in the diffusion cell apparatus. Samples were withdrawn at fixed time intervals of 0,1, 2, 3, 4, 5, 6, 24 and 48 hours by maintaining sink conditions. Withdrawn samples were analysed using Shimadzu HPLC LC20AD at 406 nm using SPD-20A detector.

Results and discussion: It was observed that ETC1 with 0.25% w/v Carbopol 934 had an initial burst release of AMB with 6.94±1.85% release in 1 hour, which then doubled in the next 3 hours. 59.10±1.08% of AMB was released after 24 hours from ETC1. Drug release from ETC2 and ETC3 was unexpectedly retarded and half of the entrapped drug was not released even after 48 hours. The % AMB released after 48 hours from ETC1, ETC2, ETC3 were 93.24±0.63, 50.40±0.78 and 41.37±1.71 respectively. At the end of 48 hours, % drug unreleased from ETC2 and ETC3 were found to be 49.60 and 58.63 respectively. The possible relation between polymer concentration in cream bases and drug release profile was spotted in this investigation with faster drug release at early stages from the cream base prepared with 0.25%w/v Carbopol 934. ETC1 with better drug release profile was subjected to drug release kinetics and was confirmed that ETC1 was following first order diffusion-controlled release profile.

Conclusions: Developed formulation may be beneficial to increase the therapeutic outcome by sustaining the release of AMB at the target site for 48 hours, help in drug retention and reduce the procedure related complications that exist in the present approaches.

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MICROWAVE ASSISTED SYNTHESIS OF BETA CYCLODEXTRIN NANOSPONGES FOR TOPICAL CO-DELIVERY OF QUERCETIN & CURCUMIN.

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Background & Rationale : Inflammation is a protective response to localized injury, due to physical causes such as trauma, chemical, corrosive substances, biological stress, infections, disease conditions or even exposure to UV radiation, or autoimmune disease such as psoriasis. Curcumin and quercetin are a group of naturally occurring polyphenolic compounds that exert potent inflammatory, antioxidant and anti-carcinogenic activity. Their usage is limited due to their poor solubility characteristics. Accordingly, the current study was designed to investigate the beneficial anti-inflammatory activity of both flavonoids as a combination by formulating as topical gel. The purpose of this study was to enhance the solubility, dissolution rate, topical permeability of poorly water-soluble, drugs quercetin and curcumin by complexation with cyclodextrin-based nanosponges.

Materials & Methods: A) **Formulation Development** : Microwave synthesizer was used to mediate the poly-condensation reaction between β-cyclodextrin and crosslinker diphenyl carbonate with selected parameters such as polymer to cross-linker ratio, watt power, reaction time and solvent volume. Drug loading was done by solvent evaporation method and evaluated for *in vitro* studies, entrapment efficiency, percentage drug content and antioxidant activity. The prepared nanosponges were characterized for particle size, FTIR, DSC, SEM, PXRD, & Raman spectroscopy. Nanosponges were dispersed in 1 % Carbopol 934 hydrogel and the nanosponge loaded gel was evaluated for viscosity, pH, spreadability, diffusion studies and anti-inflammatory activity by carrageenan induced paw oedema model in albino wistar rats.

B) ***In vitro* release studies (in brief):** The *in vitro* release study of quercetin hydrate and curcumin from the nanosponge equivalent to 10mg was determined using Orbital shaker apparatus method. Rotation speed was kept at 50rpm and appropriate temperature was maintained. Release study was carried out in 100mL of phosphate buffer pH 6.8 (pH of normal skin) as dissolution medium. 5mL of sample was withdrawn at predetermined intervals and replaced by its equivalent volume of fresh dissolution medium to maintain the sink condition. Samples were analyzed and the concentration of drugs was determined using UV spectroscopy. Cumulative percentage drug release from nanosponges was calculated and compared with that of pure drug. Percentage cumulative drug determination was carried out in triplicate.

Results and Discussion: The SEM analysis of nanosponges showed that they were spherical in shape and spongy, with particle size in the range of 312 ±10.4 nm. Entrapment efficiency was found to be 82.75%. Release studies showed 68.5 ± 72 % drug release at 6 hrs. The results were found to be satisfactory.

Conclusion: The study showed that nanosponge-based gel formulation can be a possible alternative to conventional formulations of quercetin and curcumin with enhanced bioavailability and skin retention characteristics for topical application.

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Preparation and Evaluation of Controlled Release Gastric Floating Drug Delivery System of Rabeprazole Sodium

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Background and Rationale: Gastric ulcers are induced due to many factors like excessive intake of alcohol, chronic smoking, irregular dietary habits, influence of external and internal stress factors, other factors like bacterial infection caused due to *Helicobacter pylor*i[1], Rabeprazole is a Proton-pump inhibitor (PPI) which prevents the production of acid in the stomach. It is used to treat gastroesophageal reflux disease (GERD), certain ulcers, inflammation of the oesophagus, and Zollinger-Ellison syndrome. It is poorly absorbed from the lower GIT and has a short elimination half-life (3 h)[2]. The purpose of this research was to prepare and evaluate a floating drug delivery system of Rabeprazole sodium.

Methods: The core tablets (effervescent type) were prepared by direct compression using microcrystalline cellulose, sodium bicarbonate, citric acid, magnesium stearate and HPMC K100 and HPMC K15. The physicochemical parameters like precompression and post compression evaluations were performed as per Pharmacopoeia standard and the compatibility study was performed by FTIR and DSC methods. ***In vitro* drug release studies:** USP dissolution apparatus type II was employed to study the *in vitro* drug release from various formulations prepared. The dissolution medium used was 900 ml of acidic buffer of pH1.2 for 2 h and phosphate buffer of pH 6.8 for 10 h. The tablet was placed in the basket. The temperature was maintained at $37^0C \pm 0.5^0C$ and the stirring rate was 200 rpm. Samples were withdrawn at regular time intervals and the same volume was replaced with fresh dissolution medium. The samples were measured by UV-visible spectrophotometer at 276 nm (pH 1.2) and at 284 nm (pH 6.8) against a blank. The release studies were conducted in triplicate and the mean values were plotted versus time. ***In vitro* buoyancy studies:** The *in vitro* buoyancy was determined by floating lag time method. The tablets were placed in a 250 ml beaker containing 0.1 N HCl. The time required for the tablets to rise to the surface and float was determined as floating lag time. The time between introduction of dosage form and its buoyancy in 0.1 N HCl and the time during which the dosage form remains buoyant were measured. The release data were subjected to different models in order to evaluate their release kinetics and mechanisms.

Results and Discussion: The compatibility study of the prepared Rabeprazole sodium tablets implies the information about no interaction between drug and polymer. The drug release kinetics was observed by non-Fickian diffusion mechanisms. HPMC K100 shows better release properties than HPMC K15. The floating lag time was found to be significantly increased with the increasing concentration of the gas generating agent. After the dissolution study of the prepared Rabeprazole sodium floating tablet, it was concluded that the formulations with HPMC K100 showed better controlled release effects than HPMC K15. The release kinetics data implies that the release mechanism of the all formulation was Non-Fickian.

Conclusions: The developed floating tablets of Rabeprazole sodium could achieve prolonged drug release for at least 12h, which may be expected to improve bioavailability and patient compliance

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RELEASE CHARACTERIZATION OF BENZOCAINE FROM MUCOADHESIVE BUCCAL FILMS

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Background & Rationale: Mouth ulcer is very common in recent years, which occurs due to the damage of epithelial tissue and/or lamina propria that finally leads to tissue necrosis. Benzocaine has been used to treat mouth ulcers due to its excellent local anaesthetic effect that leads to relief of the pain of the mouth ulcer, due to its rapid onset of action (20 sec – 1 min), and intermediate duration of efficacy (5-30 min). Buccal films of benzocaine is a novel approach to treat mouth ulcers and could serve as an alternative to the conventional dosage forms like gels, ointments, mouth washes, syrups and injectables. Hence an attempt was made to develop the buccal films of benzocaine to treat mouth ulcers with an aim of prolonging the drug release and improving the patient convenience.

Methods: **A). Fabrication of Buccal Films of Benzocaine:** The buccal films of benzocaine were fabricated using a mucoadhesive polymer blend of chitosan and HPMC by solvent casting method. Polysorbate 80 and propylene glycol were incorporated as plasticizers.

B). Drug Release and Permeation Studies: *In vitro* release study was carried out using USP Dissolution Test Apparatus (Paddle type) in 500ml simulated saliva at 37 ± 0.5ºC and 50 rpm for a period of 6h. The *ex vivo* permeation study was carried out using Keshary - Chien diffusion cell with buccal mucosa of goat as the model surface in 30ml simulated saliva at 37 ± 1ºC for a period of 6h.

Results: All fabricated film formulations prepared were smooth and translucent, with good flexibility. The weight and thickness of all the formulations were found to be uniform. Drug content in the films ranged from 97 – 99%, indicating favorable drug loading and uniformity. The inclusion of HPMC, a hydrophilic polymer, significantly reduced the bioadhesive strength and *in vitro* mucoadhesion time of the films, although the degree of swelling increased. *In vitro* drug release and permeation studies in simulated saliva showed a prolonged release for a period of 6h for all formulations. Kinetic analysis of the release data indicated that the film shows Higuchi model drug release by diffusion and swelling based mechanism simultaneously.

Conclusion: The formulation with Chitosan: HPMC ratio 1:1, 5% w/w Polysorbate 80 and 5% w/w propylene glycol as plasticizers showed the best results which exhibited the cumulative percentage of drug release of 87.9 and the cumulative amount of drug permeation across goat buccal mucosa of 7.62mg/cm^2 in 6 h. This can be selected for the night time application for the treatment of mouth ulcer which can successfully release benzocaine over a period of 6h.

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Solid state investigation of loratadine physicochemical properties

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Background and rationale: The low aqueous solubility of drugs is a major challenge to the design of oral dosage forms. Various methods have been attempted for solubility enhancement of API, such as salt formation, emulsification, and solid dispersions. Crystal engineering approach offers an alternative and potential method for improving the solubility, dissolution rate and subsequent bioavailability of poorly soluble crystalline drugs. Loratidine is a weakly basic drug belonging to BCS Class II (40% oral bioavailability). The solubility of loratadine decreases exponentially with increasing pH, which results in high variability in pharmacokinetic parameters. In the present study cocrystals of loratadine were prepared to enhance physicochemical properties such as solubility and dissolution pattern.

Methods: Loratadine cocrystals were prepared with coformers (hippuric acid, hydroquinone, adipic acid, L-tartaric acid and succinic acid) using solvent drop grinding method. The formation of a new cocrystals was confirmed by FTIR, PXRD and DSC.

In vitro dissolution studies of the prepared cocrystals and pure drugs, filled in hard gelatin empty capsules were carried out in 900 ml of pH 6.8 phosphate buffer, temperature was maintained at 37 ± 0.5 ºC and, stirring speed of 50 rpm was used. Aliquots were withdrawn at regular time intervals for a period of 120 min and analyzed spectrophotometrically.

Results and discussion: Cocrystals have improved the dissolution rate of loratadine significantly compared to pure drugs. The order of the dissolution of the cocrystals was found to be loratadine-hippuric acid >loratadine-hydroquinone >loratadine-adipic acid > L-loratadine-L-tartaric acid >loratadine-succinic acid >loratadine . Around 54.15 % drug dissolution was observed for loratadine-hippuric acid cocrystal in 120 min, while the pure drug showed only 13.94% dissolution.

Conclusion: The significant improvement in the dissolution rate was observed in case of cocrystals compared to pure drug. Hence, co-crystals can be incorporated in tablet dosage form to enhance *in vitro* and *in vivo* performance**.**

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Solubility and Dissolution Enhancement of Aripiprazole by Self-Emulsifying Approach

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Background and rationale: Poor water solubility and dissolution rate leading to low bioavailability are the most debated challenges of a pharmaceutical entity. Biopharmaceutics classification system (BCS) II and IV drugs are the candidates which encounter the above-mentioned problems. Self-emulsifying drug delivery systems (SEDDS), are one of the methods used to enhance the solubility of poorly soluble drugs. The objective of the present work was to develop a SEDDS, in order to improve the solubility and dissolution rate of the BCS class IV drug, Aripiprazole.

Method: Preliminary solubility trials of the drug in suitable oils, surfactants, and co-surfactants were carried out to screen these agents for the preparation of self-emulsifying delivery systems. Based on superior solubility profiles, isopropyl myristate, Tween 60, and isopropyl alcohol were selected as oil, surfactant, and co-surfactant respectively. From the phase diagrams, self-emulsifying regions were identified and utilizing the data, the SEDDS formulations were optimized. The optimized liquid formulations were converted to solid SEDDS using the adsorbent Neusilin®. Both liquid SEDDS and solid SEDDS were filled into hard gelatin capsules. The *in vitro* drug release from liquid SEDDS and solid SEDDS were performed using USP dissolution apparatus type II at a paddle speed of 50 rpm, in 900 ml of 0.1 N HCl, maintained at 37±0.5°C. From each vessel, 5 ml aliquots were collected at predetermined time intervals, filtered and analyzed for drug content by UV spectroscopy.

Results and Discussion: The *in vitro* drug release profiles of both liquid and solid SEDDS in 0.1N HCl were superior. In a one-hour drug release study, the drug release from all the formulations ranged between 90.10± 0.67% to 99.12±1.09%. Moreover, the dissolution profiles of SEDDS were found to be 2-fold higher in comparison to the dissolution profile of the marketed formulation (Arip 5mg), and 8-fold to that of pure aripiprazole (5mg).

Conclusion: The results of the study suggested that a self-emulsifying drug delivery system of Aripiprazole would be suitable to overcome the solubility and dissolution concerns. Consequently, the bioavailability and therapeutic potential could be enhanced with a considerably lower dose of the drug.

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Solubility Enhancement of BCS class-2 drug by using hydrophilic polymers

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Background: The purpose of this research was to enhance the solubility of poorly soluble drugs [BCS Class-II]. Nebivolol hydrochloride is the racemate of the enantiomers, l-nebivolol hydrochloride and d-nebivolol hydrochloride. It is a competitive and highly selective beta receptor antagonist with mild vasodilating properties, possibly due to an interaction with the L-arginine\nitric oxide pathway.

Methods- Preparation of nebivolol fast dissolving tablets; Nebivolol fast dissolving tablets were prepared by direct compression method. Six formulations of nebivolol (250mg) were formulated by direct compression technique using different hydrophilic polymers, such as PEG-400, HPMC K4M in different concentrations, along with other excipients - microcrystalline cellulose, sodium starch glycolate, mannitol, talc and magnesium stearate. Before compression, the granules were evaluated for pre-compression properties. Then the above mixture was compressed into tablets by using a rotary tablet press, with a punch size of 8mm. The obtained tablets were evaluated with different post-compression studies, like hardness, friability, thickness, weight variation, *in vitro* disintegration and *in vitro* dissolution studies.

***In vitro* Dissolution studies of Nebivolol fast dissolving tablets;** *in vitro* dissolution studies were performed by using USP type-II apparatus [paddle type-LabINDIA, Model DS-8000.Mumbai] at 75 rpm. 900ml of 0.1N HCl was used as the dissolution medium, which was maintained at 37±0.5° C. Aliquots of dissolution medium [5ml] were withdrawn at specific time intervals and were filtered with micro filters. The amount of drug dissolved was determined by UV-Spectrophotometry, at 282 nm. All six formulations were prepared by using different concentrations of polymers.

Results and Discussion: All six formulations were prepared by using different concentrations of polymers like PEG-400 and HPMC K4M. Formulations F1, F2 & F3, containing PEG-400 released the drug as follows: F1 -98.23% in 40 mins; F2 - 60.25% in 50 mins, and F3 - 72.21% in 60mins. Formulations, F4, F5 and F6 containing HPMC K4M, released the drug as follows: F4 - 85.38% in 60 mins; F5 - 79.53% in 60 mins and F6- 82.58% in 60mins. F1 was selected as an optimized formulation because it gave best results in terms of *in vitro* drug release - rapid release manner and best fitted to first order with r value of 0.999.

Conclusions: Thus, in the present investigation, fast dissolving tablets of Nebivolol were successfully designed by direct compression method and evaluated. It can be concluded that PEG-400 can be used as an effective excipient to achieve rapid release characteristic to the fast dissolving tablets of nebivolol.

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Solubility Enhancement of Lawsone by Complexation with Beta Cyclodextrin

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Background and Rationale: Lawsone, also known as hennotannic acid is the active constituent, obtained as a red orange dye present in the leaves of the *Lawsonia inermis* (henna plant) as well as in the flower of *Eichhornia crassipes* (water hyacinth). Lawsone has been found to have various activities such as antibacterial, antifungal and antiviral. Lawsone has poor solubility in aqueous media resulting in low bioavailability and poor permeability.[1] Many approaches are available and reported in literature to enhance the solubility of poorly water-soluble drugs, and thereby increase their bioavailability. Cyclodextrins (CDs), a group of oligosaccharides formed by glucose units bound together in a ring, show promising ability to form complexes with drug molecules and improve their physicochemical properties without molecular modifications. Lawsone was complexed with cyclodextrin to form inclusion complexes. The inclusion complex increases its solubility by incorporating Lawsone in its hydrophobic inner surface of cyclodextrin. The present study deals with the complexation of Lawsone with beta cyclodextrin for its improved action.

Methods: A) Preparation of Inclusion complex of Lawsone: Kneading and co-precipitation methods were carried out for the preparation of the inclusion complexes. The molar ratio between lawsone and beta cyclodextrin was selected as 1:1 from phase solubility studies. Further, the inclusion complexes were prepared by kneading and co- precipitation methods, using water and methanol mixture (1:1). [2]

B) Dissolution rate studies: The prepared complexes were tested for *in vitro* dissolution profiles of the drug using USP dissolution test type 2 apparatus. Inclusion complexes equivalent to 50 mg of Lawsone/ 50 mg of pure drug were placed in the dissolution vessel containing 900 ml of pH 7.4 phosphate buffer, maintained at 37°C, and stirred at 50 rpm. Aliquots were withdrawn at fixed time intervals and equal volume of fresh medium was replaced. Samples were filtered and absorbance was read at 453.2 nm against blank.

Results and Discussion: The inclusion complexes of Lawsone with beta cyclodextrin resulted in considerable enhancement in the solubility of Lawsone. Time to release 80% of Lawsone was 1 hour for pure drug, and only 5 minutes for the complexes prepared by co-precipitation and kneading methods. Complexes prepared by co- precipitation method showed 90% drug release within 30 minutes, and for complexes prepared by kneading method showed t_{90} value for Lawsone at 45 minutes. So it is evident from the results that the improvement in the dissolution rate depends upon the complexation process. The complexes could achieve improvement in wettability of Lawsone and hence improved aqueous solubility.

Conclusions: Complexes prepared by co- precipitation method showed improved lawsone solubility, in comparison to those prepared by kneading method.

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The release study of peanut protein from sublingual immunotherapy tablet for peanut induced allergic asthma

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Background and Rationale: The increasing prevalence of peanut induced allergy and the subsequent life-threatening anaphylactic reactions has sparse treatment options. The current management of peanut allergy includes strict peanut avoidance and use of epinephrine injection as an emergency therapy for anaphylactic reactions. Peanut contains an array of allergens (Ara h1 to Ara h17 proteins) inducing IgE mediated allergy. Allergen immunotherapy is a novel approach for the effective treatment of IgE mediated food allergy. Sublingual immunotherapy is an accepted form of allergen immunotherapy and has favorable safety profile and particularly low risk of anaphylaxis and paucity of GI adverse events. The sublingual tablet undergoes rapid disintegration with better dissolution in the saliva. The aim of the study was to develop sublingual immunotherapy tablets for peanut induced allergic asthma and to assess the *in vitro* release of allergens from the sublingual dosage form.

Methods: A) Formulation of fast disintegrating sublingual tablet: The peanut allergens were extracted from crude peanut, standardized and formulated into fast disintegrating sublingual tablet using super disintegrants by direct compression method.

B) *In vitro* release study of allergens: The study was performed in 500ml simulated saliva using USP type II paddle apparatus at 30 rpm by maintaining a temperature of 37±0.5°C. 5 ml samples were collected at regular intervals and were analyzed spectrophotometrically.

Results and discussion: The dissolution profile of allergens from the fast-disintegrating tablets indicated that more than 80% of the allergen was released within 15 mins due to the super disintegrant action suggesting an efficient delivery of allergens for immunotherapy.

Conclusion: The fast-disintegrating sublingual tablets are suitable for immunotherapy due to the efficient delivery of allergens and hence a promising approach for the treatment of allergen induced asthma.

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Dissolution Profile matching of Venlafaxine extended release capsules using MUPS Technology

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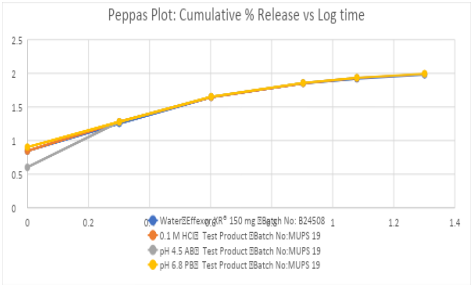
Background & Rationale: Immediate release dosage forms are easy to develop and manufacture. One of the major disadvantages of immediate release dosage forms is dose dumping and peak-valley blood drug levels. Hence extended release dosage forms are developed. Venlafaxine extended release (ER) capsules were developed by pellet technology. These capsules were compared with the Innovator product. Aim of this study was to compare the dissolution profiles of the developed product with Innovator, establish similarity and its mechanism of release.

Methods: A. Formulation of Extended release capsules Inert sugar spheres were drug loaded using Wurster technology. These drug loaded pellets were coated with an ER polymer to retard the drug release. HPMC was used as a binder and pore former. Ethyl cellulose was used as an ER polymer. ER pellets were lubricated with talc and filled in hard gelatin shells**. B.** ***In vitro*** **Dissolution studies:** Formulated extended release capsules were subjected to dissolution testing in pH 1.2, pH 4.5 Acetate buffer and pH 6.8 phosphate buffer. Dissolution was performed using basket apparatus, in 900ml media maintained at 37^{o}C, stirring rate set at 100 rpm, and samples were collected at 1,2,4,8,12 and 20hrs and subjected to HPLC analysis.

Results & Discussion: Formulated venlafaxine ER capsules developed by Wurster technology showed a dissolution profile similar to innovator formulation in all the three media evaluated. F1 and F2 values were also calculated. F2 values were above 50% in all the three media. For determination of mechanism of release, the dissolution data was fit into Peppas model. Peppas plots for the developed MUPs were found to be linear, as indicated by the correlation coefficient values. The Peppas plots had slope values above 0.5 and below 1, except in pH 4.5, indicating diffusion with swelling. In pH 4.5, the release at the end of 1 hour was less than that in other buffers. This might be the reason for its slope above 1. Drug release by diffusion is a common phenomenon with ethyl cellulose, which was used in the present study as release retarding polymer.



Conclusion: The formulated venlafaxine extended release capsules by MUPS technology is a suitable alternative and more reproducible considering the technology used.

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Drug-Silica-Cellulose Ternary Matrix for the Oral Delivery of Cyclosporine A

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Background and Rationale: Cyclosporine A (CsA) is a high molecular weight drug known for its immunosuppressive activity. Owing to its high lipophilicity, potency, and negligible water solubility, the oral pharmacokinetics of CsA is highly irregular, thus warranting a suitable delivery system to increase its dissolution.[1] Supersaturated formulations are widely explored to improve the oral bioavailability of water-insoluble drugs. Among them, mesoporous silica (MS) has been explored to achieve a higher degree of supersaturation via adsorption of the drug. However, merely using MS to improve the dissolution of CsA can cause precipitation of the drug in the gastric media, necessitating the use of precipitation inhibitors (PI) such as cellulose derivatives.[2] Thus, the study aimed to formulate CsA, MS and cellulose as a ternary matrix (TerMat) and evaluate its effect on the physiological dissolution of CsA.

Methods: (A) Formulation of CsA/MS/Cellulose/TerMat: TerMat was prepared by solvent impregnation-rotary evaporation technique, yielding the CsA/MS/Cellulose/TerMat in dried powder form. The matrix was characterized by FESEM, FTIR, PXRD, DSC, and HPLC to analyze the loading of CsA. Additionally, binary matrices (BinMat) of CsA/MS and CsA/Cellulose were also prepared for comparison.

(B) *In vitro* biorelevant dissolution of CsA: The physiological dissolution of CsA from the BinMat and TerMat was determined in non-sink mini fasted state simulated intestinal fluid (FaSSIF) media, and biorelevant dissolution transfer study wherein the BinMat and TerMat were initially suspended in a simulated gastric fluid (SGF), pH 1.2 for 1 h, followed by transfer into the simulated intestinal fluid (SIF), pH 6.8 for additional 6 h. The dissolution media were stirred at 300 rpm and maintained at 37±2°C. Samples were withdrawn at regular intervals, and the amount of CsA dissolved was measured using HPLC. The data were analyzed and modeled using the DD Solver package to obtain various parameters and predict drug release mechanisms.

Results and Discussion: The FTIR spectra confirmed formation of hydrogen bonds between CsA, PI and MS. The XRD graphs and DSC thermograms suggested the conversion of crystalline CsA into an amorphous form. The FESEM images exhibited drastic change in surface morphology of the samples and showed complete embedment of CsA-loaded silica particles in the HPMC matrix. In the non-sink mini FaSSIF medium, the dissolution of CsA/MS was higher than the bulk CsA at the beginning of the dissolution cycle but dropped significantly as the study progressed due to the recrystallization and precipitation usually seen with MS. On the other hand, though CsA/Cellulose increased the solubility, the dissolution rate was significantly higher (2-fold) for TerMat. In the biorelevant transfer method, the dissolution profiles of BinMat improved slightly, whereas TerMat showed a 3.37-fold improvement compared to the mini FaSSIF dissolution study. Based on the model acceptance criteria, the dissolution behavior of TerMat was seen to follow Korsmeyer and Peppas-Sahlin models indicating the dissolution of CsA to be a function of fickian diffusion and the swelling property of cellulose.

Conclusions: CsA-Silica-Cellulose ternary matrix enhanced the dissolution of CsA in simulated gastric and intestinal media. Thus, the current strategy can be an attractive technique for improving the solubility and dissolution of lipophilic and high molecular weight drugs for oral delivery.

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In vitro release study of developed Aspirin-PLGA Microspheres for dental stem cell stimulation

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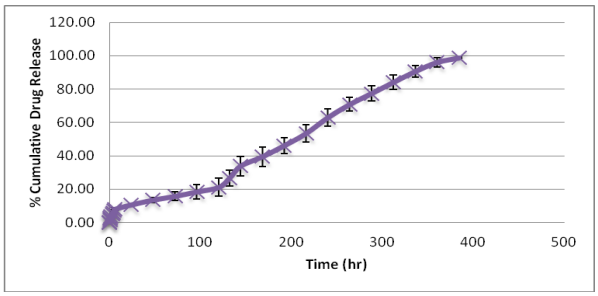
Background & Rationale: According to WHO, dental caries and periodontal diseases are the most prevalent oral diseases; the progression of these diseases leads to tooth loss. The main aim of clinical management of mentioned diseases is to focus on the severity and extent of the disease. Recently, it has been reported that aspirin can reverse the effects of tooth decay by stimulating existing stem cells in the tooth. But, it is necessary to figure out a suitable formulation, which can retain at the tooth site and release the drug for a long period. The objective of the present study was to investigate the *in vitro* release behavior of aspirin from the PLGA microspheres.

Methods: Aspirin-loaded PLGA microspheres were formulated by double emulsion technique. The optimized formulations were characterized for particle size, encapsulation efficiency, *in vitro* drug release, release kinetics. ***In vitro* release study**: The drug release behavior from microspheres was studied in 10 ml of simulated salivary fluid (pH 6.8) at 37±2°C. The whole assembly was maintained at 37 °C at 50 rpm. Aliquots were withdrawn at specific time intervals,and analyzed for drug release 265 nm by UV spectrophotometry.

Results: Aspirin-loaded PLGA microspheres were found to have 87.31±1.52% as the encapsulation efficiency and 7.52 µm as the particle size. Further, the *in vitro* drug release study in simulated salivary fluid was performed. The study confirmed that the microspheres released aspirin in a lesser amount (~10.57±0.32%) in the initial 24 h, with the remaining 98.76±0.49% drug being released within 16 days. From the Figure, it is clear that triphasic release was observed, with an initial slow burst phase (0-1d), a lag phase (1-5d), and an accelerated release phase (5d ~ 16d). This confirms that release is due to polymer erosion, swelling, and degradation. The release kinetics confirmed zero-order release with non-Fickian transport. Hence the study confirms that release occurs as a result of polymer erosion, swelling, and degradation.



Conclusion: Developed formulation demonstrated its suitability to release the drug at the site for a long duration of time and hence it can potentiate the stimulation of the stem cells and thereby facilitate the regeneration of dental tissues.

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Maraviroc Oral Disintegration Tablet: Analytical Design of Experiments (DoE) for Assessment and Comparison of *in vitro* Dissolution Profiles

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Background and Rationale : The bioavailability of a drug in a solid oral dose depends on its release from the drug product and its balance in dissolution. Compared with a reference drug, the newly developed formulation needs to establish bioequivalence by comparing the dissolution profile. The objective of present study was to compare dissolution profiles of a newly developed maraviroc oral disintegration tablet and the reference Axentri® tablet; the current research was designed to establish and validate an integral analytical consistency by Quality by Design (QbD) approach to quantify maraviroc from dissolution samples using the RP-HPLC method.

Methods : Maraviroc was formulated into an orally disintegrating tablet using direct compression technique at different concentrations of sodium starch glycolate as super disintegrant and talc and magnesium stearate as glidants. The dissolution test in 0.1N HCl was performed according to standard procedures to predict bioequivalence. The results of dissolution tests were analyzed using the QbD Box Behnken Design multivariate RP-HPLC method.

Results and Discussion : The optimized formulation (F2) was selected as it showed 90% drug release in 5 min and a disintegration time of 22 sec, with dissolution profiles to the marketed reference to meet the FDA requirements of *f2* similarity factor statistics. The integrated analytical QbD method was statistically analyzed by ANOVA, counter-plot, and 3D response surface plots, which demonstrated that the model is statistically significant. The developed method was validated as per ICH guidelines Q2 (R1).

Conclusion: In conclusion, maraviroc oral disintegrating tablets have been well prepared, and exhibited superior and consistent release patterns, established by the implementation of the QbD analytical method for orally disintegrating tablet excellence and adoption.

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NANOPARTICULATE ORODISPERSIBLE TABLET FORMULATION OF AMLODIPINE BESYLATE AND PREPARATION METHOD

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Background and Rationale: The present study relates to an Amlodipine besylate orodispersible nanoparticulate tablet dosage form, its preparation method and lyophilization. The present study describes the process for the preparation of amlodipine nanoparticles with significant improvement of solubility and dissolution characteristics. Nanoparticulate orodispersible tablet form of amlodipine besylate was prepared by direct compression method with enhanced bioavailability and improved rate of absorption.

Methods: A) Preparation of Amlodipine nanoparticles and orodispersible tablets: Amlodipine nanoparticles were prepared by using anti-solvent evaporation method, wherein Amlodipine besylate, dissolved in methanol, was added dropwise to diluted surfactant solution, at RT under stirring, to form the nanoparticles. This was then heated and maintained at 50^{o}C under stirring (250-300 rpm) for 1-2 hours to evaporate methanol; further the mixture was centrifuged at 20,000 rpm for 20 to 30 minutes. The pellet obtained was freeze dried at a controlled temperature of -44^{0} C, pressure of 2.5×10 Pa for 48-72 hours. The lyophilized powder was blended with suitable polymers and superdisintegrants, and orodispersible tablets were prepared by direct compression.

B) *In vitro* selective release studies: *In vitro* dissolution profile of the six developed formulations was studied in 0.1N HCl and phosphate buffer (pH6.8).

Results and Discussion: Of the various formulations, F8 containing Poloxamer 188 and PVA, as stabilizers revealed maximum drug release - 99.1±0.24% in 0.1N HCl and 99.5±0.42% in pH 6.8 buffer.

Conclusions: Amlodipine nanoparticles prepared by this method showed significant improvement in aqueous solubility as well as dissolution characteristics which may significantly improve its oral bioavailability.

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Taguchi design for optimization and development of bovine serum albumin nanoparticles of methotrexate by desolvation technique.

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Background & Aim: - Albumin nanoparticles have been presupposed as an effective way for passive targeting of anti-rheumatic drugs to the inflamed joints via the enhanced permeability & retention (EPR) effect, and insufficiency of protein at the affected region. The application of Taguchi design will lead to systematic strategy for the preparation of nanoparticles with desired size and polydispersity index taking all the significant variables into consideration. Hence the aim of this study was to fabricate size controlled methotrexate-loaded bovine serum albumin (BSA) nanoparticles.

Methods: - The nanoparticles were prepared by desolvation technique. Orthogonal array of L_{16} type was used as an experimental design to detect the optimum conditions for preparation of size controlled BSA nanoparticles. The effects of four experimental parameters viz., albumin concentration, pH, ratio of desolvating agent and rate of addition of desolvating agent were optimised to produce size controlled nanoparticles. The prepared nanoparticles were characterized for particle size, PDI, entrapment efficiency and *in vitro* drug release.

The *in vitro* release studies were performed in Franz diffusion cells separating the receptor fluid and the nanoparticle dispersion with a dialysis membrane (molecular weight cut off 12000-14000 Da). Phosphate-buffered saline (PBS) (pH 7.4) maintained at 37±0.5 ºC was used as a receptor fluid. Nanoparticulate dispersion equivalent to 5mg of the drug was applied to the donor compartment. Aliquots were withdrawn at periodic time intervals and after suitable dilution, were analysed spectrophotometrically at 307 nm for drug content.

Results and Discussion: - From Taguchi design analysis, pH and albumin concentration were the most influencing parameters affecting particle size and PDI. The best results (size less than 200 nm of MTX NPs with polydispersity index less than 0.5) were obtained at pH 8.5, drug: albumin ratio of 1:6, ratio of desolvating agent / BSA solution 1:4, and rate of addition of desolvating agent 0.5 $ml.min^{-1.}$ The optimised formulations were found to have particle size of 116.3nm, PDI of 0.242, entrapment efficiency of about 74.92 %. The optimized nanoparticles exhibited good sustained release for up to 7 days.

Conclusion:-The use of Taguchi design for the preparation of size controlled methotrexate loaded albumin nanoparticles has provided development of the formulation with optimum properties , with less experimental procedures. Further this presents an important model for predicting the release properties of methotrexate from albumin nanoparticles.

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FORMULATION AND EVALUATION OF CONTROLLED RELEASE GASTRORETENTIVE DOSAGE FORM FOR CHLORDIAZEPOXIDE

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Background and Rationale: Chlordiazepoxide is a long-acting benzodiazepine with anxiolytic, sedative, hypnotic activity and also used in symptomatic treatment of alcohol withdrawal. It increases inhibitory effect of GABA by binding to benzodiazepine sites at the GABA receptor-chloride ionophore complex in the central nervous system. But, its multiple dose therapy leads to accumulation of the parent compound and active metabolites, causing excessive sedation, respiratory depression and muscle weakness. Gastro-retentive drug delivery system (GRDDS) may be used to increase gastric retention time coupled with drug release for extended time to reduce the dosing frequency, and thereby reduce the plasma peak fluctuations. Chlordiazepoxide, as GRDDS will reduce drug accumulation and side effects by maintaining plasma blood levels. The aim of the present work was to develop a controlled release Gastroretentive floating tablet of Chlordiazepoxide and investigate effects of hydrophilic and hydrophobic retardants on *in vitro* release.

Method: **A)**: **Formulation of Floating Tablet**: Formulations were prepared by direct compression using HPMC (hydrophilic polymer) and ethyl cellulose (hydrophobic polymer) as rate controlling polymers, and they were evaluated for thickness, diameter, weight variation, hardness, and friability along with buoyancy studies and *in vitro* drug release.

B): ***In vitro* release study**: *In vitro* drug release studies were carried in USP type II apparatus at 50 rpm maintained at 37 ± 5°C. Tablets were placed into the dissolution medium of 900 ml 0.1 N HCl. Ten ml aliquots were withdrawn at specific time intervals and replaced with equivalent volume of fresh medium; aliquots were filtered and analyzed using UV spectrophotometry after suitable dilutions, if required.

Results and Discussion: The precompression & post compression parameters were within acceptable limits. Floating lag time was 3 min. *In vitro* dissolution studies of formulations showed controlled release of the drug over a period of 12 hrs. Among the twelve formulations, F12 was selected as the best formulation which had the maximum retardant effect (67.1% in 12 hours), and floating lag time of 50 sec. A decrease in release of the drug was observed with increasing polymer ratio.

Combination of ethyl cellulose and HPMC K15M polymers which restrict the penetration of dissolution medium inside the tablet also restricts the formation of gel layer around the tablet. So, the combination of both hydrophobic and hydrophilic retardant minimized the burst release of drug from the tablet and achieved a desired drug release which is practically difficult using a single type of polymer.

Conclusion: A floating drug delivery system, using a suitable composition of HPMC K15M and ethyl cellulose could give the desired dissolution profile for formulating the controlled release tablets of Chlordiazepoxide.

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Formulation and Evaluation of Venlafaxine HCl Chewing gum for Management of Depression

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Background and Rationale: Drug release of a formulation is considered as a major quality profile. *In vitro* release studies of medicated chewing gum is critical because of complexity of drug release apparatus and data correlation. As per the American Medical Association chewing of gum enhances mental alertness, and mastication or chewing process can also help to elevate mood and is useful in management of depression, where medication is to be taken for prolonged duration. Medicated Chewing gum loaded with antidepressant agents can be a better alternative to conventional dosage form. Venlafaxine HCl (Effexor) is a SSRI antidepressant approved by USFDA in 1993 and marketed as tablets and capsules. Mastication of medicated chewing gum enhances the patient compliance; also drug absorption through oral mucosal route may increase the bioavailability of drug.

Methods: **A) Formulation of Venlafaxine HCl containing chewing gum**: Ingredients - gum base as elastomer, liquid glucose and glycerin as plasticizers, talc as an anti-adherent, sucrose as a sweetening agent and peppermint oil as flavoring agent were used. By conventional rolling method optimization of four different compositions were prepared, from which one composition (MCG-II) was taken up due to better organoleptic properties compared to the other three. MCG –II composition was further considered for *in vitro* dissolution and stability studies. For the stability studies, MCG-II composition was wrapped in aluminum foil and study conducted at 40°C stability chamber for 3 months

B) Drug release test of Medicated Chewing gum: Dissolution was performed using 40 ml pH 6.8 phosphate buffer in non-compendial drug release apparatus, set at 30-40 mastications per minute for 30 minutes at 37°C±0.5°C temperature. At 5 min intervals, 5 ml aliquots were collected and replaced with fresh 5 ml preheated buffer. Each time interval sample was analyzed by UV spectroscopy at 224 nm.

Results and Discussion: MCG-II, containing 60 percent gum base and 15 percent sucrose showed 98 percent drug release in 30 minutes. The mastication strokes per minute was found to influence the drug release pattern. Drug release from medicated chewing gum can be modified using different types of gum base and different percentages of plasticizer. During stability studies, the texture and hardness of the formulation was not affected.

Conclusion: Medicated chewing gum enhances the drug release profile which can enhance overall patient compliance and maximum drug release can be achieved in a shorter time, which can further improve drug absorption and bioavailability of drug.

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In vitro and *ex vivo* drug release study from ocular thermosensitive *in situ* gels

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Background and Rationale: Conventional ophthalmic eye drops suffer from several limitations - short retention time on the eye surface, rapid precorneal drug loss and only a small fraction of drug administered is absorbed. *In situ* gel systems represent a good strategy to overcome these problems; when instilled as a drop into the conjunctival sac , they undergo reversible solution to gel phase transition in response to physiological stimuli and thereby achieve increased residence time. Aim of this study was to formulate an *in situ* gelling formulation of Ofloxacin Hydrochloride, which undergoes gelation within the eye at physiologic temperature, and characterize its rheological and permeation properties.

Methods: **A) Preparation of sterile ophthalmic *in situ* gelling ophthalmic formulation**: A solution of Poloxamer-407 (11-15% w/v) in acetate buffer (pH) at 0-2°C was mixed with a dispersion of Methocel E50LV (0.5%w/v) and a solution of Ofloxacin hydrochloride (0.3% w/v), mannitol and BKC; the solution was sterilized by membrane filtration and packed in previously sterilized containers, in an aseptic environment.

B) Characterization: Formulations were evaluated for gelling ability, rheological behavior by Brookfield viscometer (LVDV-II) with T-bar spindle (S-92). The *in vitro* drug release testing of the formulations was performed using Franz diffusion cells at 37±2°C using synthetic membrane. Three models (zero order, logarithmic and the Higuchi model) were used to study the release kinetics of the formulations. The transcorneal (goat corneas) permeation studies were performed using Franz diffusion cells.

Results and Discussion: The formulations containing Poloxamer exhibited effective phase transition to gel at concentration more than 13%; addition of Methocel imparted a greater mechanical strength to the formed gels. These gels depicted pseudoplastic or shear thinning behavior. The *in vitro* release profiles of formulations showed a better fit using the Higuchi model (R^2 - 0.98). *Ex vivo* permeation of drug release through goat cornea displayed zero order release kinetics.

Conclusion: In conclusion, the thermosensitive in situ gels are a viable alternative to conventional eye drops to achieve sustained drug release and prolonged precorneal residence time and thereby improved ocular bioavailability. These findings suggest that the thermosensitive *in situ* gels developed in this study would be useful ocular drug delivery systems.

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Solubility and Dissolution Enhancement of Gliclazide using Mixed Solvency Approach

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Background and Rationale: The therapeutic efficiency of a drug is based on bioavailability and, eventually, upon the solubility and absorption of drug molecules. Solubility is an essential parameter to achieve the necessary concentration of drug in the systemic circulation and hence to attain biological activity in the body. Gliclazide is an oral hypoglycemic drug which lowers blood glucose level. The major drawback of this drug is its poor aqueous solubility; its oral bioavailability is only 50%. To overcome these difficulties, increase in the aqueous solubility of gliclazide is an important goal.

Methods: Equilibrium solubility of gliclazide in different solvents/with different solubilizers [sodium caprylate (CP), sodium citrate (SC), sodium acetate (SA) and beta cyclodextrin (βCD)] were determined by excess solute method. Different blends were prepared in distilled water and equilibrium solubility was determined for selected solubilizers. Solid dispersions, by new mixed solvency approach, in which organic solvents were excluded from the conventional solvent evaporation method, as well as physical mixtures (PMA) of the drug with different ratios of drug and solubilizers were prepared. Prepared solid dispersions were compared for dissolution studies with pure drug and physical mixtures. The stability studies were conducted as per ICH guidelines.

Results and Discussion: From the result of solubility data, it was evident that aqueous solubility of gliclazide was increased considerably in blend F (30%CP+5%SC+5%SA), which has higher CP concentration; blend Q (10% CP+5% βCD+2.5% SA+2.5% SC), with lower concentration of CP, also showed increase in solubility of drug. Blend Q was selected to be used in solid dispersion (SDA) preparation of gliclazide. *In vitro* drug release studies from pure drug, SDA and PMA were carried out in distilled water. The cumulative drug dissolved in 10 min in case of solid dispersion (SDA) and physical mixture (PMA) were found to be 99.75% and 96.10% respectively. On the other hand, it was found to be only 56.52%, in the case of pure drug. Stability studies indicated that the formulation is stable with respect to the drug content at all temperatures and conditions of storage. It was found that the percent drug content after a period of 3 months for gliclazide was 99.82±0.14% at 4±1 ^{o}C whereas it was 99.68±1.3% at 25±2 ^{o}C / 60±5% RH and 99.36±1.6% at 40±2 ^{o}C/ 75±5% RH.

Conclusion: From all the above studies, it was concluded that the approach of mixed solvency is novel, safer and user friendly. It also eliminates the problem of toxicity associated with the use of organic solvents. This approach can be employed to improve the dissolution pattern of drugs.

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Controlled and prolonged release of an herbal antioxidant (Curcumin) from lipid nanocarrier

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Background and rationale: Antioxidant and anti-inflammatory potency of curcumin is well established from ancient times, and is found useful in many tissue and neuro degenerative disorders. However, the therapeutic efficacy of curcumin is obstructed due to its poor bioavailability, rapid degradation, susceptibility to the physiological environment, hepatic metabolism, rapid clearance and poor stability [1]. Presently, lipid nanocarriers (SLN and NLC) appear to be a promising novel drug delivery approach to overcome the limitations of herbal lipophilic drug moieties. The lipidic base of these nanocarriers makes them biocompatible, increase cell permeation and minimize the irritation or toxic effects. Further, special structural composition provides protective housing to the drug and better control over the release behavior [2]. Thus, this study was designed with an objective to evaluate the drug release profile and stability of curcumin loaded SLN and NLC.

Method: A) Design and optimization: Experimental design for preparation of NLC/SLN was developed by 3^3 Box-Behnken design using Design Expert® (Version 10.0.1, State-Ease Inc., Minneapolis, U.S.A.). **B) Formulation and characterization:** The optimized formulations were prepared as per the optimized formula suggested by the Response Surface Methodology. The curcumin loaded NLC and SLN were prepared by melt-emulsification ultrasonication method. The formulations were then characterized for drug interaction, thermal behaviour, crystalline and surface properties by FTIR, DSC, XRD and SEM analysis, respectively. Further, the formulations were also evaluated for particle size, PDI, zeta potential and drug entrapment efficiency. **C) *In vitro* drug release and release kinetic modelling**: The *in vitro* release studies of Cur-NLC and Cur-SLN were carried out in Franz Diffusion cell using dialysis membrane, in 7.4 pH phosphate buffer, maintained at 37^0C. Samples were analyzed by HPLC (Thermo Fisher Scientific, MA, USA). The final data was statistically analyzed for release kinetic modelling using DDSolver 1.0 (Microsoft Corp., USA).

Results and Discussion: The particle size of NLC (<150 nm) was significantly lower than SLN (near about 250 nm), while entrapment efficiency was considerably higher. The drug release study showed initial burst release followed by sustained release for upto 48 h. Cumulative release was significantly higher with Cur-NLC (>90 %). The release kinetic modelling indicated Weibull kinetic model as best fit based on the R^2, AIC and MSC values, and the diffusional exponent 'n' showed that release of drug takes place by Fickian diffusion with initial surface erosion. Both the formulations were found stable for the defined period of time as per ICH guideline (Q1A).

Conclusion: With lower particle size, higher entrapment efficiency and drug release profile we concluded that NLC offers advantage over SLN for prolonged drug delivery.

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Design and Development of Pulsatile Drug Delivery System for management of Rheumatoid Arthritis

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Background: The aim of present study was to formulate and evaluate a bilayer tablet formulation for effective management of rheumatoid arthritis; the formulation consisted of Leflunomide, as an immediate release layer and Etoricoxib as delayed release layer.

Methods: The immediate release layer was prepared by wet granulation method using sodium starch glycolate, as a disintegrating agent. The delayed release layer was prepared by wet granulation method using mannitol, sodium starch glycolate, talc and magnesium stearate. Cellulose acetate coating was done on the Etoricoxib layer to obtain the desired lag time for pulsatile release pattern. Immediate layers as (IR1 to IR8) and Delayed release layer as (DR1 to DR8) were separately optimized and prepared. The compressed tablets were evaluated for its hardness, weight variation, friability and *in vitro* release study using Veego USP NF dissolution apparatus.

Results and Discussion: The *in vitro* release study of both the layers was separately carried out of all the batches. In Immediate release layer study, IR1 and IR3 could not release the desirable amount of drug; IR2 shows the highest amount of drug release. So IR2 of immediate release and DR2 of delayed release were found to be optimized batches. The immediate release layer showed 78.9% release in 90 mins and delayed release layer showed 95.7% release in 5 hours. Bilayer tablets of the optimized batches (IR2 & DR2) were prepared and in vitro release studied in 0.1N HCl & phosphate buffer upto 300 min. Initially the immediate layer gave complete drug release of leflunomide within 90 min in 0.1N HCl. After 240 min, the coating of cellulose acetate (time dependent polymer). over the core tablet of Etoricoxib, acted as delayed release layer, to give burst release.

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Dissolution enhancement of poorly soluble drug with HPMCAS based polymeric amorphous dispersion films

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Background and Rationale: The oral bioavailability of a drug depends on many factors, the most common being solubility and permeability. Effective delivery of drugs with poor water solubility is quite challenging and various formulation strategies are utilized to increase the solubility of the drug. Many drugs are available as crystalline forms and depict poor aqueous solubility. Converting the drug to its amorphous form increases the aqueous solubility, but this also makes it physically or chemically unstable with a tendency to convert into the more stable form. Formulating an amorphous solid dispersion where the drug is dispersed into an excipient(s) matrix provides stability to the amorphous form of drug, prevents recrystallization, and maintains high solubility. Polymeric amorphous solid dispersions (PASDs) preserve the drug in amorphous form with polymers acting as crystallization inhibitors to provide significant increase in solubility and dissolution rate [1] .

Methods: Itraconazole (ITR) was selected as a model drug with poor solubility and HPMCAS 716G and HPMCAS 912G were the polymer grades selected for evaluation. Drug and polymers were first dissolved in solvents- dichloromethane: methanol in 2:1 ratio. The films were cast by pouring the clear solutions over an acrylic sheet, and solvent was allowed to evaporate. Two drug loading ratios of 10%, and 15% were selected, along with API and physical mixture, used as control. The films were characterized for drug content and *in vitro* release using Paddle apparatus; the impact of different paddle speeds and different media volumes on dissolution of ITR was evaluated .

Results and Discussion: The 10% ITR-912G film was very clear and transparent indicating drug in solubilized (amorphous) state whereas 10% ITR-716G was slightly opaque. 15% ITR films with both polymers were opaque indicating inadequate polymer concentration to prevent recrystallization. For 10%-ITR films, the paddle speed only impacted the rate of dissolution slightly, and the 10% ITR-912G film provided greater than 90% dissolution in 45 min across all paddle speeds, and even with low media volume.The rate of dissolution for the 10%ITR-912G film was the highest amongst all films evaluated at all dissolution conditions. No dissolution was evident in API or physical mixtures of all ratios.

Conclusion: The dissolution study for PASD films of ITR provided a good indication of solubility enhancement achieved. The HPMCAS 912G provided better results than 716G with 10% drug film providing better results. The film with completely solubilized drug had no impact of paddle rpm/media volume on drug dissolution. These parameters impacted the dissolution of film in which drug was insoluble or partially soluble.

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------ ☺ ------

Employing mixed hydrotropic technique for solubility enhancement of BCS class II drugs.

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Background and Rationale: Hydrotrophy is a solubilization technique whereby addition of a large amount of solute results in an increase in aqueous solubility of the other solute. Aim of this study was to investigate the application of a novel method called mixed hydrotropy technique, which includes the use of a combination of two or three hydrotropic agents to enhance the solubility of poorly soluble drugs. The rationale behind the study was to reduce the amount of individual concentration of hydrotropic agents to get synergistic or enhanced solubility of poorly water soluble drugs. For current study urea, sodium benzoate and sodium salicylate were used as hydrotropic agents while celecoxib was used as a model drug.

Method: Hydrotropic solutions were prepared using the hydrotropic agents in distilled water. Firstly, solubility of the drug was identified in the individual hydrotropic agent i.e. sodium benzoate, sodium salicylate and urea. Afterwards, concentrations of hydrotropic agents were increased from 1-40% to identify the solubility of the drug. After identifying the solubility of the drug in individual hydrotropic agents, different blends were prepared either by taking all the three hydrotropic agents in combination or by taking two at a time, in combination.

Results and Discussion: The result showed increase in solubility of the model drug using hydrotropic agents as solubilizers. It was observed that as the concentration of hydrotropic agents increased from 10-40%, the solubility of the drug also increased. The solubility enhancement ratio of drug in 40% concentration of each hydrotropic agent was found to be 73.5; 41.5; 31.8; solubility in water was very low- 0.0012 mg/ml. However, such high concentrations can cause toxicity or cause adverse reactions. In the current mixed hydrotropic technique, we have used optimized ratios of all the hydrotropic agents in combination to enhance the solubility of poorly water soluble drugs.

Conclusion: It can be concluded that with carefully designed experimental techniques, solubility of water-soluble drugs can be improved by “Mixed hydrotropic approach”. It will also help in making various stable oral liquid dosage forms of poorly water soluble drugs.

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Evaluation of Site Selective Release and Cytotoxicity of Vincristine from *in situ* Nanogel

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Background & Rationale: Vincristine (VS) is a natural alkaloidal chemotherapeutic drug, which acts by inhibiting microtubule and arresting cell division in metaphase in different cancer cells. It is available as an injectable; due to poor lipophilicity it shows low tissue permeability when given through any other route. Hence, a formulation strategy that can help to circumvent the above-discussed problem is highly coveted. Injectable *in situ* forming gels possess versatile pharmacokinetic characteristics, simple administration procedure, localized and sustained drug delivery for varying periods, diminished drug- associated adverse effects due to localized delivery to only morbid cells. Therefore, in the present study a thermosensitive *in situ* nanogel of vincristine was prepared which will be acting as a depot in breast cancer cell lines, which can sustain the drug release.

Methods: A) Preparation of Nanoparticle loaded VS in situ gel: The formulation was prepared in two stages. At first VS was entrapped into Eudragit RSPO (positively charged) nanoparticles by solvent evaporation. Then in the second step, *in situ* nanogel was prepared by suspending the freeze-dried nanoparticle mass in 20% Poloxamer 407 solution, containing drug (0.10%, w/v). With different variables, a total of nine formulations were prepared and subjected to characterization tests. **B) *In vitro* drug release study and cytotoxicity assessment**: *In vitro* drug release study was performed in two stages. First, the release of VS from nanoparticle was determined, and in the second phase, release study was performed with nanoparticle loaded *in situ* gel. *In vitro* anticancer efficiency was assessed using MCF- 7 breast cancer cell lines by measuring cellular viability of cancer cells through MTT assay.

Results and Discussion: Very similar drug release profiles were obtained from nanoparticles in both the buffers, may be due to Eudragit RSPO being pH independent. All the nanoparticles showed a sustained release profile with no burst effect. Moreover, all the nanoparticles showed a cumulative release within the range of 80-100% in 90 h. In case of *in situ* nanogel, it displayed a steady-state release of 58.7 % and could control the drug release even beyond 72 h. Finally 95.8 % of VS was released in 360 h (15 days). In MTT assay, a dose dependent controlled cytotoxicity was observed in depot (gel) form as compared to free solution at any concentration.

Conclusions: The delivery system offers less cytotoxicity than free drug; sustained drug release which minimizes frequent drug administration, along with avoidance of repeated painful i.v administration. From these results it can be concluded that a thermo sensitive *in situ* nanogel of VS could be a better option than conventional formulation.

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Formulation and Evaluation of Fast Disintegrating Tablets of Solid Dispersion containing Cefdinir

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Background & Rationale: Cefdinir is an advanced third generation broad spectrum cephalosporin antimicrobial agent, which has low solubility and permeability. Here our aim was to study solid dispersions of the drug with different polymer ratios versus pure drug for increasing the solubility of Cefdinir and formulate them in oral or fast disintegrating tablets.

Methods: **Formulation of Solid Dispersions (SD)**: Solid dispersions were prepared with Cefdinir: polymer and cefdinir: polymer: 10% Sodium lauryl sulfate (SLS) in 1:1 (F1), 1:2 (F2)1:3 (F3), 1:4 (F4), 1:5 (F5), 1:6 (F6) weight ratios by solvent evaporation method. Required amount of drug and carrier were dissolved in sufficient volume of ethanol with continuous stirring and the solvent was then completely evaporated at 40º C to obtain dry mass. **In vitro dissolution studies**: Dissolution rate studies were performed in phosphate buffer (pH 6.8) at 37±0.5º C using USP II rotating paddle apparatus at 50 rpm. Pure Cefdinir and all the batches of SDs were subjected to dissolution studies. At predetermined time intervals, 5 ml of dissolution medium was withdrawn, filtered through Whatman filter paper and drug content in aliquots was estimated by UV spectrophotometry at 286 nm. Each test was performed in triplicate. **Parallel artificial membrane (PAMPA) permeability study**: The PAMPA model is an artificial *in vitro* model suitable for the passive diffusion study (passive permeability) of a compound.

Results and Discussion: Formulation components were selected based on their apparent solubilizing capacity towards the drug. Evaluated physical parameters were found to be satisfactorily. Cefdinir was found to show enhanced solubility and permeability when formulated as solid dispersion. It was evident from the solubility studies that Cefdinir was sparingly soluble in pH 6.8 PBS solution, slightly soluble in 0.1 N HCl, very slightly soluble in water, insoluble in methanol and ethanol. The results of % drug entrapment was found to be 83.18 ± 1.93 in F5 formulation, and *in vitro* drug release of pure drug was 41.80% at the end of 1 hr, while optimized SD (F5) showed 66.17%. The permeability study of F5 formulation was also higher compared to the free drug.

Conclusions: The solubility and the permeability of cefdinir from solid dispersion were found to be significantly higher than the drug alone. Thus the solid dispersion of cefdinir with increased dissolution was successfully developed.

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Formulation Development of Diclofenac Sodium Topical Solution Using Mixed Solvency Concept & Its Evaluations

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Background and Rationale: The concept of mixed solvency is an emerging field which can be applied for solubility enhancement. This concept suggests that all substances, whether solid, liquid or gas, have solubilizing power. The objective of present research was to develop an aqueous based diclofenac sodium lotion and to prove solubilizing power of solid substances.

Methodology: Solubility studies were performed using approximate solubility technique as follows: 5 ml of solvent was taken in a clear glass vial and accurately weighed drug (10 mg) was added to the solvent system, and the vial was shaken to dissolve the drug. When a clear solution was obtained, 10 mg (accurately weighed) drug was again added, and the process was repeated till saturation (nearly). Total weighed quantity of drug dissolved in 5 ml solvent was considered to be approximate solubility. Approximate solubility of diclofenac sodium in DM water at room temperature was 1.2% w/v. An aqueous blend containing two solid additives, namely niacinamide (5 % w/v) and caffeine (5 % w/v) was observed to have approximate solubility of diclofenac sodium 10% w/v at room temperature. Diclofenac Sodium, Niacinamide, Caffeine, Glycerin, Sodium sulfite, were used for preparing topical formulation. Selection of solubilizers was done on the basis of solubility studies in various blends of solubilizers. *In vitro* permeation studies were carried out using Franz diffusion cell.

Results & Discussion: The formulated lotion, developed by mixed solvency concept possessed good consistency and homogeneity. Drug release was found to be more than 80% and stability data was satisfactory.

Conclusion: Mixed solvency concept can be utilized for development of topical lotion of various poorly water soluble drugs.

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Optimization of Sustained-Release Andrographolide loaded Nanostructured Lipid Carriers: Characterization, Stabilization, and *In Vitro* Evaluation

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Background and Rationale: Andrographolide is a naturally occurring diterpenoid derived from the plant *Andrographis paniculata*. It is a key active constituent with a wide range of biological activities [1]. Poor bioavailability of Andrographolide is a roadblock that makes the wonder drug unprofitable. Despite the various medicinal characteristics, Andrographolide remains an unyielding natural compound [2]. The research focused on the formulation, optimization, and *in vitro* evaluation of Andrographolide loaded nanostructured lipid carriers (AND-NLC) using response surface methodology.

Methods: AND-NLC was developed using the melt-emulsification ultrasonication technique. Box Behnken design was used for optimization, with Stat-Ease design expert software. Glycerol Monostearate was used as a solid lipid, Oleic acid, as a liquid lipid, and Poloxamer 407, as a surfactant in the optimal formulation. The *in-vitro* release drug studies were performed for AND-NLC as well as drug solution by USP Type II dissolution test apparatus.

Results and Discussion: The optimized AND-NLC was spherical and non-aggregated in shape, with an average size of 97.8 nm, a polydispersity index of 0.117, and zeta potential of -28.2. The physicochemical characterization included the evaluation of surface morphology, drug entrapment, drug loading, x-ray diffraction studies, and differential scanning calorimetry. *In vitro* drug release tests revealed that AND-NLC could release the drug for up to 24 hours. The differences in the release profiles might be due to the presence of liquid lipid and surfactant in the AND-NLC formulation. The result of release profiles demonstrated that the AND-NLC exhibits a biphasic release pattern with initial rapid release followed by sustained release of the drug. The formulation was found to be stable in the refrigerator, compared to room temperature, as per stability tests.

Conclusions: As a result of these findings, AND-NLC was identified as a possible drug carrier. This provides a framework for further exploration of the developed formulation.

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Selection of an appropriate dissolution medium and release mechanism from lipid based nanoparticles

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Background and Rationale: Selection of an appropriate dissolution medium is essential in nanoformulation characterization. An appropriate dissolution medium can be selected based on the properties of the drug substance, formulation characteristics and interaction between different components. The formulation excipients can interact with the components of the dissolution medium. Temozolomide (TMZ) is an anticancer drug which has pH dependent stability. It is reported to undergo conversion to its metabolites at plasma pH (7.4). The present study provides a rationale for selecting an appropriate dissolution medium for drugs like TMZ and phospholipid based nanoformulations.

Methods: Solubility of TMZ in different solvents and buffers was evaluated. The stability of TMZ at different pH conditions (1.2, 4.5 and 7.4) was evaluated and the degradation rate kinetics were studied respectively. Further, TMZ loaded lipid nanoparticles were formulated. In order to select an appropriate dissolution medium, *in vitro* drug release studies were conducted in three different dissolution media (0.1 N HCl, pH 4.5 acetate buffer, pH 7.4 phosphate buffer). The effect of drug loading on release rate and release mechanism of TMZ from lipid based nanoparticles was studied.

Results and Discussion: Based on the stability studies, TMZ was found to be stable in 0.1 N HCl and pH 4.5 acetate buffer. TMZ was found to undergo conversion to its metabolites in pH 7.4 phosphate buffer. Conversion of TMZ followed first order kinetics with conversion rate of 0.0011, 0.0011 and 0.0453 h^{-1} in pH 1.2, 4.5 and 7.4 respectively. *In vitro* drug release studies revealed that 100 % drug was released in 2 h and remained stable thereafter in 0.1 N HCl, 100 % drug released up to 12 h in acetate buffer and in phosphate buffer the TMZ concentration increased in initial 1 h followed by decrease in concentration. Phospholipids used in the preparation of nanoparticles were sensitive to extreme pH conditions leading to disruption of particles and dissolution of drug in 2 h when 0.1 N HCl was used as the media. TMZ is not stable in pH 7.4. Hence, pH 4.5 was selected as an appropriate dissolution medium for TMZ. Faster drug release rate was observed with higher drug loading.

Conclusion: Based on the solubility and stability, pH 4.5 acetate buffer was found to be an appropriate dissolution media for TMZ. Extreme pH conditions provided by pH 1.2 (0.1 N HCl) were not suitable for nanoparticles formulated using phospholipids. The % drug loading is likely to affect the release rate of the drug from the nanoparticles.

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Skin permeation and dermatokinetic assessment of designed Apremilast loaded lipid nanocarriers

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Background and Rationale: Apremilast is the selective phosphodiesterase 4 (PDE4) inhibitor used for the treatment of moderate to severe psoriasis. Apremilast prevents the degradation of cyclic adenosine monophosphate (cAMP), which thereafter reduces the production of pro-inflammatory cytokines and increases anti-inflammatory mediators [1]. The oral administration of Apremilast exhibits adverse events such as headache, nausea, diarrhoea, upper respiratory tract infection, and nasopharyngitis. The aim of the present work was to prepare Apremilast loaded solid lipid nanocarriers (SLN) for topical delivery to overcome the limitations of oral therapy and increase the efficacy.

Methods: ***Ex vivo* permeation and dermatokinetic assessment studies of SLN dispersion gel**

The *ex vivo* skin permeation study was performed on goat skin using Franz diffusion cells. The skin was mounted between the donor and receptor compartment with the epidermis facing towards the donor. The receptor compartment was filled with 15 mL of phosphate buffered saline (pH 7.4) as release medium at 32 ± 1°C. Aliquots of 1 mL were collected at predetermined time intervals and an equal volume of fresh medium was replaced to maintain sink conditions. Further, dermatokinetic profile was determined in skin layers (epidermis, dermis). The separated layers were subjected to drug extraction using acetonitrile. The API concentrations (µg/cm^2) estimated in the epidermis and dermis were plotted, and dermatokinetic (T_{max}, C_{max}, $AUC_{0-24h,}$ and K_e,) parameters were evaluated.

Results and Discussion: The *ex vivo* studies depicted cumulative amount of drug permeated through the skin after 24 h was 3.97 ± 0.40% (n=3) from SLN based gel formulation, whereas 2.00 ± 0.06% from the free drug-loaded gel. The SLN formulation flux (0.293 µg/h/cm^2) was 1.72-fold higher in comparison to free drug formulation (0.169 µg/h/cm^2). The permeability coefficient of SLN formulation and the free drug-loaded gel was 0.97×10^{-3} and 0.56×10^{-3}. The drug retention with SLN formulation was 2-fold higher in the epidermis and 5-fold higher in the dermis than free drug-loaded gel (***p<0.0001). The $C_{maxSkin}$ of the SLN loaded gel and free drug-loaded gel were 96.812 ± 2.121 µg/cm^2 (epidermis), 64.686 ± 5.657 µg/cm^2 (dermis) and 39.988 ± 2.518 µg/cm^2 (epidermis), 15.244 ± 3.107 µg/cm^2 (dermis), respectively. The T_{max} of SLN loaded gel and plain gel were found to be similar - 6.00 h in the epidermis and 8.00 h in the dermis. The AUC_{0-24} of the SLN loaded gel and free drug-loaded gel were 1025.813 ± 80.610 µg/cm^2.h (epidermis), 977.365 ± 137.553 µg/cm^2.h (dermis) and 331.083 ± 8.828 µg/cm^2.h (epidermis), 210.340 ± 8.482 µg/cm^2.h (dermis), respectively.

Conclusion: The study assured improved permeation and retention of SLN loaded gel, which was expected due to the occlusive nature of SLN preparation. The nanosize and lipid constituents used in SLN interact with skin to enhance permeation. The higher concentration in the epidermis is expected due to the embedding of SLN in stratum corneum layers. The drug is expected to embed in the stratum corneum (epidermis) and diffuse into deeper layers (dermis), which was depicted by the increase in the T_{max} in dermis layers.

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Solubility Enhancement of Abiraterone Acetate: HPMCAS- Stabilized Solid Dispersion Prepared By Solvent Evaporation Method

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Background and Rationale: Abiraterone acetate (AA) is used as a first-line treatment drug for metastatic castration resistant prostate cancer. One of the major problems with AA is low oral bioavailability (10%) because of its poor oral solubility [1]. On considering this issue, one of the most promising approaches is the implementation of solid dispersion (SD) to improve water solubility and enhance the oral bioavailability of this drug. The present study was conducted to improve the solubility of AA (BCS class IV), by converting it into an amorphous SD applying the solvent evaporation method. The dispersion comprising the different ratios of AA and Hydroxypropyl methylcellulose acetate succinate (HPMCAS) [2] was attempted, in which the drug is molecularly dispersed in the polymeric matrix, to improve the solubility of the poorly soluble drug.

Methods: A) Preparation of solid dispersion using Solvent Evaporation method: The SD of the AA and HPMCAS were formulated using various ratios (4:1, 2:1, 1:1 and 1:2) by solvent evaporation method. Acetone was employed as a solvent in the preparation of SD. The different ratios of the physical mixture (PM) of AA and HPMCAS were also formulated for comparison.

B) Saturation Solubility studies: Excess quantity (approximately 10 mg) of pure drug, SD and PM were added to vials containing 2mL of distilled water and pH 6.8 These vials were kept on the orbital shaker at 200 RPM for 24hrs at room temperature. After 24 hrs., the appropriate aliquots samples were withdrawn, filtered, and analyzed using HPLC.

Results and Discussion: From the saturation solubility studies, SD containing AA: HPMCAS (1:2) exhibited highest solubility, among all SD. The solubility of SD in distilled water was observed to be 1.5-fold and 4-fold higher than the solubility of PM and pure drug, respectively. While in the case of pH 6.8 buffer, it was about 2-fold and 5.5-fold higher than the solubility of PM and pure drug. This may be attributed to the reduction in particle size, increase the surface area, increasing the wettability, due to the interaction of the drug with the amphiphilic polymer, and change from crystalline to the amorphous state.

Conclusions: In conclusion, the SD of AA in the presence of HPMCAS polymer was able to enhance the solubility of AA significantly. This approach may offer additional advantages of reducing the dose of the drug, which in turn can help in lowering the cost of the formulation and reduce unwanted side effects.

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Understanding *in vitro* pharmacokinetic characteristics of statistically designed Eudragit/PLGA nanoparticulate delivery system using paclitaxel as model drug

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Background & Rationale: The objective of this study was to investigate the disposition and characterize the pharmacokinetic (PK) profile of an anticancer drug from the polymeric nanoparticles. Polymeric nanoparticles are the most commonly used nanocarriers to improve PK parameters. In this study, paclitaxel (PTX) has been taken as a model drug to evaluate the role of the nanoparticulate delivery system to impact the PK profile of the drug. Characteristically, PTX displays a bi-exponential pharmacokinetic profile [1].

Methods: Three PTX loaded polymeric nanoparticle formulations with different ratios of polymers (EudragitRSPO, EudragitRLPO, and Polylactic glycolic acid 50:50) were characterized for *in vitro* drug release by dialysis bag diffusion technique. I*n vitro* release data of all nanoparticle formulations were fitted to relevant kinetic models to determine the mechanism of drug release from the particles. Further, *in vivo* PK parameters were determined in male Wistar rats after a single iv dose, using a two-compartment model.

Results and Discussion: The polymeric nanoparticle formulations were statistically designed by using JMP software (SAS Institute Inc.), and were optimized based on particle size (<220nm), release (>70%), and haemolysis (<10%). I*n vitro* release studies showed that the proportion of polymers used significantly impacted the drug release ($p<0.0001$). About 9-20% of drug release was observed in the first two hours and the time required to release more than 65% of the drug from PTX nanoparticles was more than 150 hrs. The results indicated that the particles followed a diffusion-based drug release pattern leading to a sustained release. *In vivo* studies showed that the nanoparticle formulation altered the characteristic bi-exponential PK profile of PTX. Administration of PTX nanoparticles significantly increased the AUC by 5 times and reduced the renal clearance by 75% compared with pure PTX solution alone. $T_{1/2}$ increased 2.8 times. Overall, nanoparticle carriers not only significantly improved pharmacokinetics but also altered the disposition pattern of PTX.

Conclusions: The nanoparticulate carrier influenced the disposition of PTX after the drug was released from the formulation. Overall, nanoparticle carriers significantly improved the PK of PTX and a good correlation can be traced between the *in vitro* and *in vivo* studies. The results also prove that PK of paclitaxel nanoparticles is complex and requires more effort to understand the role of nanoparticle composition in altering the PK and developing more effective anticancer formulations.

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In vitro Release Studies of Timolol Maleate from Ocular Inserts developed using Plantago ovata mucilage and HPMC

ABSTRACT

Background: For the effective treatment of chronic ocular diseases, controlled release ocular inserts are most popular formulations that enhance precorneal residence time, corneal penetration and reduce the drug loss due to nasolacrimal drainage [1]. Natural polymers are gaining importance due to their lower cost and abundant availability, but very few reports of their use in ocular delivery systems can be found.

Objectives: The objective was to develop sustained release ocular inserts of timolol maleate using combination of mucilage from Plantago ovata and HPMC and to study the in vitro release profile as well as mechanism of drug release to find out the suitability for ocular delivery.

Methodology: The mucilage was isolated from epidermal layer of P. ovata seeds following a reported method [2]. The pH of 1% w/v solution of mucilage was measured. The ocular inserts were prepared by solvent casting technique using different combinations of P. ovata mucilage and HPMC by a reported method [3]. The dried films were cut into circular discs (ocular inserts) of diameter 0.8 cm and heat-sealed in polyethylene bags. The ocular inserts were evaluated for surface pH using a digital pH meter, thickness, weight uniformity, folding endurance, drug content and in vitro release profile [3].

To assess in vitro drug release from ocular inserts, an in-house method was developed. The insert from each batch was placed in a 15 ml vial containing 10 ml of phosphate buffer saline solution (pH 7.4) and placed in an oscillating water bath at 32 ± 0.5°C with 25 oscillations per minute. One ml of medium from each vial was withdrawn at every hour till the 9 h. Equal volume of fresh pre-warmed buffer was added immediately after each sampling. The samples were filtered through 0.45 µm membrane and analyzed at 294 nm spectrophotometrically. To determine the drug release kinetics, the drug release data was fitted according to zero-order equation. Further, to determine the release mechanism, the dissolution data was plotted according to Korsmeyer-Peppas' equations.

Results: The pH of isolated mucilage was found to be 6.8, indicating its non-irritant nature. The developed ocular inserts had good physical properties, weight and thickness uniformity and folding endurance values between 55-60. The surface pH of inserts was near to 7, indicating non-irritant nature. The drug content was found to be nearly 100%. The developed formulations showed in vitro release between 92.77 and 97.31% after 9 h of dissolution study. Based on the release profiles, Batch N7 (1:1 ration of polymers) was considered as optimized batch. The kinetic treatment of diffusion data of selected batch showed that the formulation followed zero order kinetics. Korsemeyer-Peppas' plots were straight lines indicating diffusion controlled release.

Conclusion: From the physicochemical properties and in vitro release, it can be concluded that the ocular inserts follow diffusion controlled zero order release and hence can be used for controlled delivery of timolol maleate. This may overcome the problem of nasolacrimal drainage and enhance the corneal residence time of the drug. Natural polymers, being cheaper alternatives to synthetic ones, have the commercial viability also.

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Inhalable Lipid Nanovesicles Encapsulating Voriconazole with Modulated Drug Release and Improved Lung Pharmacokinetics

INTRODUCTION:

Pulmonary delivery of antifungals has been gaining enormous interest in the management of fungal lung infections as it allows higher drug concentrations to be achieved at the infection site with lower systemic exposures. In this context, the current study was embarked on systematic development and characterization of lipid nanovesicles (LNVs) of an antifungal triazole viz., voriconazole (VRC) to improve the release profile and prolong drug retention in lungs.

METHODS:

LNVs were prepared by thin film hydration method employing dipalmitoylphosphatidylcholine (DPPC), hydrogenated phosphophatidylcholine (HSPC) and cholesterol[1]. Factor screening studies was performed using fractional factorial design, followed by optimization of the NLs by Box-Behnken design. The LNVs were optimized taking particle size, entrapment efficiency and drug release studies in PBS 7.4 as the pivotal CQAs. In vitro drug release studies of VRC and LNVs were conducted using dialysis sac method. LNVs were placed in the dialysis membrane (12 kDa), tethered at both the ends and suspended in 20 mL of the dissolution medium, i.e., phosphate buffer saline (PBS 7.4) containing 0.1% Tween 80, in order to maintain the sink conditions at 37 ± 0.5 °C at 100 rpm. Lung and plasma pharmacokinetic studies were carried out in Balb/c mice by nebulization of 20 minutes using a lab-scale nose-only inhalation chamber [2].

RESULTS:

The optimized batch have a particle size in range of 130-160 nm, and entrapment efficiency of 68-72%. LNVs were nebulized employing in-house nose only inhalation chamber for the generation of LNVs-embedded into microdroplets. The generated microdroplets have a mass median aerodynamic diameter and volume mean diameter of less than 4 μm, thereby corroborating the potential of the developed nanosystem to target the lungs effectively. Drug release studies showed negative influence of cholesterol, and positive influence of both the lipids in controlling the release rate of VRC. More than 95% of VRC was released in 6 h while developed LNVs sustained the drug release, when observed for 48 h (57.24 ± 2.61%) with an initial burst release for 2 h (36.52 ± 2.95 %). Drug release showed best fit into the Korsmeyer-Peppas model (R=0.932) with the value of diffusional release exponent, being less than 0.45, indicating drug release to be primarily governed by Fickian mechanism. Pharmacokinetic studies revealed marked improvement in the lung retention profiles vis-a-vis marketed VRC formulation upon nebulization.

CONCLUSION:

Overall, the study describes the potential of LNVs for sustaining the drug release of VRC and improving its retention profile in lungs.

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Discriminating Dissolution Rates of Anti Tubercular Drug Microparticles in Biorelevant Lung Media using USP I, USP II & USP IV Apparatus

Background & Rationale: Tuberculosis, mainly a lung disease, fundamentally necessitates multidrug therapy. Particulate DDS provide improved targeting potential with the possibility of improved efficacy and dose reduction. However, there exists a quest to discriminate the release performance of drug-loaded particulate carriers in different biorelevant media, through an appropriate dissolution method. Currently, there is no official dissolution testing method for nano and micro systems. Flow-through cell dissolution apparatus (USP Type IV) has used for release testing of such particulate carriers [1,2]. We have evaluated and compared the release of our anti-tubercular drug polymeric microparticles in two biorelevant lung fluids using three dissolution apparatuses, Float-A-Lyzer® in USP IV (SOTAX) dissolution apparatus, and Dialysis membrane sac method in USP type I (basket) and USP type II (paddle) apparatus.

Methods: The polymeric microparticles of first-line anti-TB drugs Rifampicin, Isoniazid, Ethambutol and Pyrazinamide were prepared separately by simple one-step precipitation method. The particles were characterized for physicochemical properties and evaluated for in vitro release in two different biorelevant lung media namely Simulated Lung Fluid (SLF) pH 7.4 and Artificial Lysosomal Fluid (ALF) pH 4.5, over 24h. The release was conducted using three different methods 1. Flow-through cell USP IV dissolution apparatus (CE7 SOTAX, AG) in a closed-loop system, with a Float-A-Lyzer® (MW cut-off 17-20kD) at three different flow rates (8mL/min, 16mL/min and 24mL/min), 2. USP Type I Basket apparatus (Veego instruments, India) at 100rpm, and 3. USP Type II paddle apparatus (Veego instruments) at 50rpm, with a Dialysis Sac membrane (HiMedia MW Cut off 17-20kD). The Rifampicin, Isoniazid and Pyrazinamide were analyzed by UV spectrophotometric method at λmax of 475 nm, 263 nm and 269 nm respectively. Whereas, Ethambutol was analyzed by Colorimetric method using Acetylacetone Reagent at λmax 412 nm.

Results & Discussion: The polymeric microparticles showed an average particle size of 2.0-3.0 µm and 12-14% drug loading, with % entrapment efficiency of >40% for all four drugs. The differential release rate was observed for all the drugs based on their solubility, physicochemical properties, and pH of the release media. The release rate for all drugs was rapid in ALF pH 4.5 compared to SLF pH 7.4. Lower release in SLF could allow particles to efficiently phagocytosed by alveolar macrophages. In contrast, rapid release in ALF pH 4.5 proposes their efficient intracellular release delivery at the site of action and hence efficacy. USP IV demonstrated slower release and better discrimination compared to USP type I & II methods in both the biorelevant media.

Conclusion: The USP IV, Flow-Through Cell Apparatus with Float-A-Lyzer®, is an optimum and discriminatory method for in vitro release studies from nano and micro systems compared to conventional USP type I and II apparatus with dialysis sac method.

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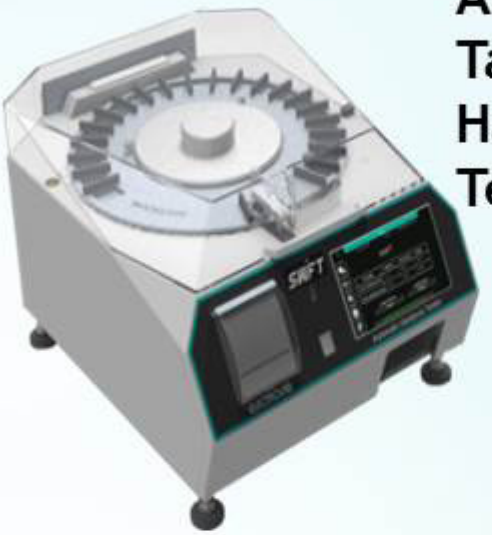

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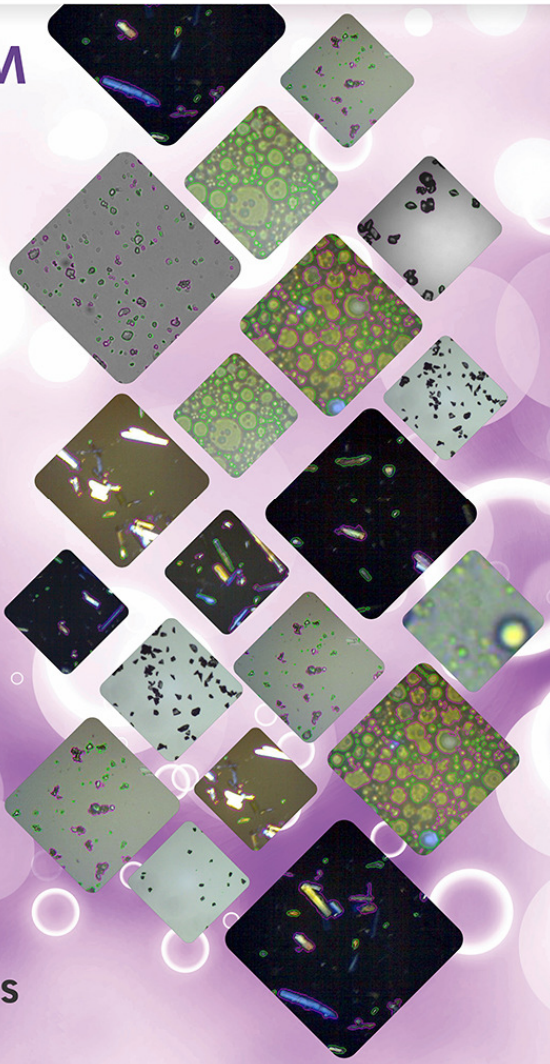

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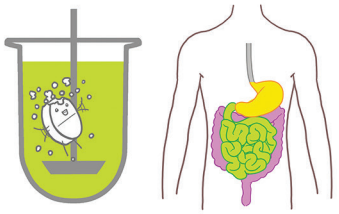

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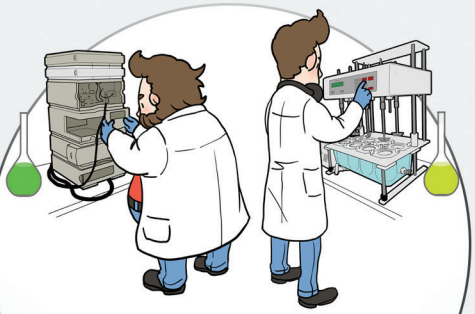

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You can buy Biorelevant Media, and learn how to use them, from us

www.biorelevant.com

www.biorelevant.com

In the early 2000's we ran a CRO (Contract Research Organization) in Switzerland that was focussed on improving the solubility of oral drugs. We soon discovered how helpful it was to test poorly soluble compounds in dissolution media simulating gastrointestinal fluids and developed a unique product that produced these fluids in an instant. It proved so successful that we decided to concentrate our efforts on supplying customers all over the globe with these biorelevant media. Since 2007 we have been supplying our range of patented Biorelevant media to numerous pharma companies, Universities & Institutions. The 25 biggest Pharmaceutical companies in the world all now buy from us.

From our laboratory in Central London, we test numerous different drugs and devise the most effective experiments for you to run. State-of-the-art equipment in our factory in East London, combined with a 'Just in Time' approach to manufacturing, ensures we maintain good, fresh stock of our lines. All input materials are analysed by an independent GMP-certified laboratory before production and finished products are subject to rigorous analysis before release. Biorelevant fulfilment operation has been built alongside our production facilities which enables us to dispatch your orders incredibly fast.

We collaborate closely with Professor Dr. Jennifer Dressman at Goethe University, Frankfurt. We are working hard to introduce an exciting raft of new biorelevant dissolution media with amazing predictive power that will transform the way oral drugs are developed. We've run our own laboratories for many years so understand exactly what customers require to be successful in this industry. Put simply our products improve your chances of success.

Given below are the details of local channel partner for the Biorelevant media.

Tejas Dabhole:

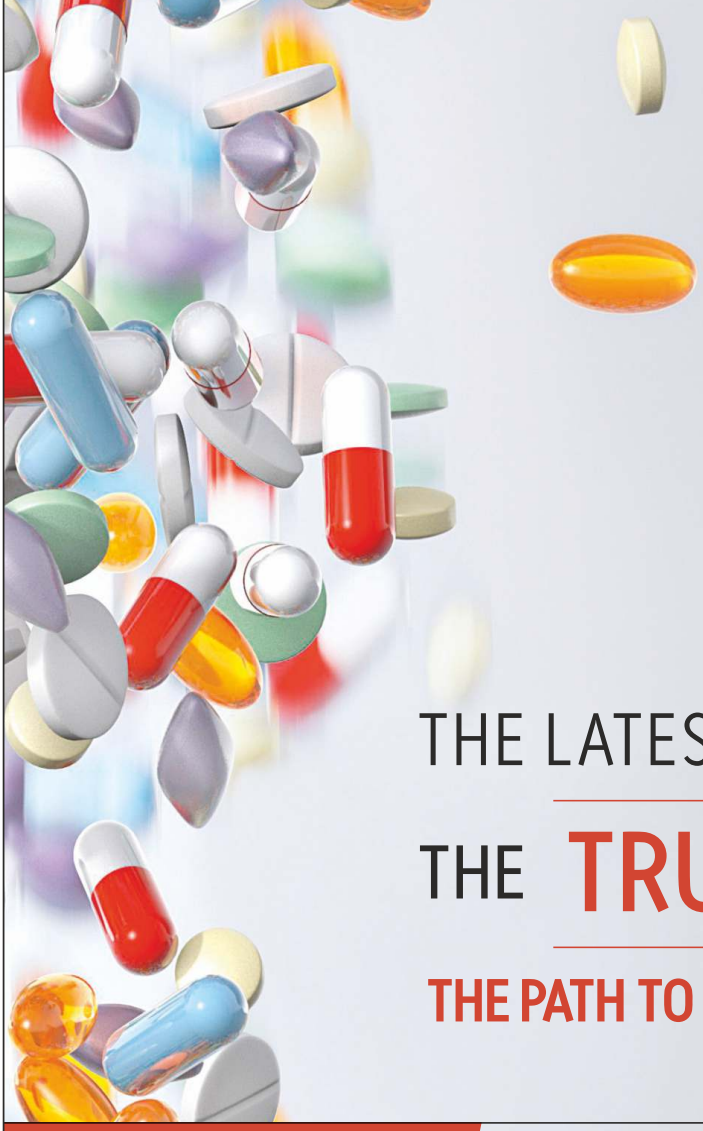
✆ +91 9004779906

✉ tejas.dabhole@invenilife.com

Ashish Singh:

✆ +91 9892919053

✉ ashish.singh@inveniolife.com



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METHOD DEVELOPMENT

Many of the worlds most ground-breaking pharmaceuticals are made with the help of methods developed using Waters Chromatographic Solutions. More proof that world-class drug development demands world-class method development. So if you want to get there first, partner with Waters at waters.com/methods

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Fax: 080-49292204, E-mail: Waters_India@waters.com

Mumbai : Tel : 022-25170127, Fax : 022-25170616, E-mail : Office_Mumbai@waters.com
New Delhi : Tel : 011 - 40194100 - 4149, Fax : 011 - 40194115, E-mail: Office_Newdelhi@waters.com
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From the everyday consumer to scientists in the laboratory, we all rely on accurate information to make critical decisions. Waters Corporation is the world's leading specialty measurement company focused on improving human health and well-being through the application of high-value analytical technologies and industry leading scientific expertise.

Our decisions and actions are guided by two simple words – Deliver Benefit. Our founder, Jim Waters, coined these words to encapsulate the idea that we should positively impact our customers, employees, shareholders and society at every opportunity.

Driven by that ethos for over sixty years, Waters has continually pioneered chromatography, mass spectrometry and thermal analysis innovations. Whether it's discovering new pharmaceuticals, assuring the safety of the world's food and water supplies, or ensuring the integrity of a chemical entity in production, we are constantly working with our thousands of customers to change the world.

With a global workforce of more than 7,400 employees, Waters operates in 35 countries, including 14 manufacturing facilities and with products available in more than 100 countries. Our diverse organization is well-positioned to Deliver Benefit through innovations that enhance human health and well-being.

SPOOKFISH
INNOVATIONS PVT LTD

Scale-up Production and Ensure Quality with Visual Intelligence. Interested ?

Marlin – Online Tablet/capsule Inspection
Snipe – Induction Seal Inspection System

Applying the latest computer vision technology and machine learning techniques, Spookfish offers cutting edge solutions for the Pharmaceutical Industry. Designed to provide improved visual inspection of tablets and capsules, and to ensure seal integrity, these online inspection systems provide a competitive edge with their speed and accuracy.

MARLIN
ONLINE TABLET/CAPSULE INSPECTION

Marlin is a family of visual inspection systems for orals, including tablets, hard-gel capsules and soft-gel capsules (including transparent capsules). Marlin's innovative design makes the inspection stations retro-fittable onto existing machines to enable seamless inspection of products without any reduction in production throughput.

Marlin X: Visual inspection of orals on bulk counting lines

Marlin Blue: Visual inspection of orals on blister packaging lines

Marlin Flip: Visual inspection of orals on conveyor belts

SNIPE
INDUCTION SEAL INSPECTION SYSTEM

Snipe is an online induction seal inspection system which retrofits onto existing bottle packaging lines.

Poor induction seal quality remains a serious concern in the pharmaceutical industry. Sub standard seals can lead to contamination and reduced potency when exposed to harsh environments.

Using the latest high resolution thermal technology, Snipe accurately detects any areas of potential leakage on a seal, verifying the integrity of the bottle and rejecting any defective products via a pneumatic rejection mechanism.

Configurable for bottle variants of any height, the system has also been designed with a high level of versatility.

Get in touch for fast, accurate and safe production

Mob: +91 9108 993 345 | Email: innovate@spookfish.co.uk

VISION INTO PERSPECTIVE

www.spookfish.vision

Spookfish Innovations Pvt Ltd, founded by a team of scientists, is on a quest to offer a fresh approach to solving problems using computer vision. The company builds technology by applying the latest computer vision and machine learning techniques to help manufacturing companies with high speed automated quality inspection of products. Spookfish's systems have inspected and verified millions of day to day products used by consumers on a regular basis such as tablets/capsules, food products and metals such as currency coins and paper to name just a few.

More recently, Spookfish is contributing to the containment of Covid-19 with HARLEQUIN, a quick, effective and non-contact fever detection system for mass-screening in multiple settings.

SNIPE, one of the latest innovations from Spookfish, provides an effortless and efficient way to ensure quality of a packaged bottle seal. Poor quality of induction seals leads to exposure of the products such as tablets, to harsh environments and results in severe contamination and reduced potency.

SNIPE is an online inspection system and retrofits onto packaging lines to verify the integrity of bottle seals following the sealing process using a non-destructive approach. SNIPE stands out due to both the high precision of leakage detection and cost-effectiveness of technology, coupled with simple, intuitive software.

FOUNDERS:

Dr. Anupriya Balikai

Dr. Sudeep Sundaram

Contact Details:

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Email - innovate@spookfish.in

Website - https://www.spookfish.co.uk/

Treasured memories from the past SPDS events

Treasured Memories

Delegate Registering for
Disso India - Hyderabad 2018
at Hotel Avassa

Lighting of the lamp
during the Inauguration
Disso India - Hyderabad 2018

Delegates interacting
with the partners

Attentive delegates
during
Disso India - Hyderabad 2018

Treasured Memories

The Organising Committee
of Disso India - Hyderabad 2018

Dr. Sandip Tiwari
during his talk
at Disso India - Hyderabad 2018

Vijay Kshirsagar, Dr. B. M. Rao,
Dr. Uday Bhaskar, Dr. Raghuram Rao,
Prof. Padma Devarajan,
Dr. Ramaswamy releasing
the Scientific Abstract Book
of Disso India - Hyderabad 2018

Dr. Ramaswamy, Dr. Alka Mukne,
Vijay Kshirsagar, Dr. Vinod Shah,
Prof. Padma Devarajan,
releasingthe Pharma Times
Dissolution Special issue
joint project of IPA & SPDS

Treasured Memories

Panel discussion during
Disso India - Hyderabad 2018

Dr. Vinod Shah answering the questions at the Panel discussion during Disso India - Hyderabad 2018

Dr. Roger William
during his talk
Disso India - Hyderabad 2018

Chairperson Dr. Rajeev Raghuvanshi presenting a momento to Dr. Jennifer Dressman

Dr. Arvind Bansal
presenting a momento
to Speaker Dr. Grove Geoffrey

Dr. Dange Veerpaneni
during his talk

Dr. Raghuram Rao
addressing the delegates
during the inauguration
at Disso India - Hyderabad 2018

Dr. Umesh Banakar
during his talk
at Disso India - Hyderabad 2018

Treasured Memories

The poster session
at Disso India - Hyderabad 2018

Delegates interacting
with the Poster presenters

Delegates interacting
with the Partners

Delegates interacting
with the Partners

Treasured Memories

Mr. Amit Lokhande from ICT, Mumbai
receiving 1st Prize
for his poster presented
at Disso India - Hyderabad 2018

Mr. Pankaj Sontakke
from BCP, Mumbai
receiving 2nd Prize
for his poster presented
at Disso India - Hyderabad 2018

Mr. Rijo John from ICT, Mumbai
receiving 3rd Prize
for his poster presented
at Disso India - Hyderabad 2018

The ACG Team
at the stall

The SOTAX India Team
at their Booth

The Lab India Team
at their stall

The Shimadzu & Electrolab
Teams
at their stall

The Inveniolife
Team
at their stall

DRPI 2022

First Announcement

We are happy to inform you that **DRPI 2022** is already being planned.

DRPI 2022 activities will begin in the month of April 2022 with a '**CALL FOR ABSTRACTS**.'

Exact dates and schedule for **DRPI 2022** would be announced online on the website: http://drpi.spds.in

Visit http://drpi.spds.in for the details of the competition and contact details.

Thank You

It may have something to do with home schooling three children, but Lakshmi is suffering more frequently from headaches at the moment, and relies on paracetamol to help her through.

Now, as an integrated pharma supply company, ACG may not actually make the medication Lakshmi uses. But we do provide the capsules her medication is packed into, the blister packs used to protect them, and equipment used to pack and track them – ensuring they always arrive safely in her hands.

The benefits of using an integrated supplier go beyond things simply working better together. It also means having a single source of supply. So, while you help Lakshmi cope with her headaches, you should experience far fewer too.

Contact us to learn more.
www.acg-world.com

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ACG

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