DRPI 2022

drpi.spds.in

Dissolution Research Presentations India

IN ASSOCIATION WITH

aaps® American Association of Pharmaceutical Scientists

Association of Pharmaceutical Teachers of India

SCIENTIFIC ABSTRACT BOOK

All India Finals: 16th July 2022

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 formed in 2012 with an objective of promoting the science and technological developments in the ever-evolving area of dissolution. The Society has National and International stalwarts and experts from academia, industry and regulatory as its members. Its purpose is to disseminate knowledge about this technical field, and to familiarize the advances in dissolution science among all types of pharmaceutical professionals.

SPDS is the only professional body dedicated to dissolution science and its applications..

:: 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

DRPI 2022

Dissolution Research Presentations India

IN ASSOCIATION WITH

aaps® American Association of Pharmaceutical Scientists

Association of Pharmaceutical Teachers of India

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

For the details about organising committee, past winners and earlier abstract books visit:

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 led 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 cosponsored by the American Association of Pharmaceutical Scientists (AAPS).

As 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 was held among various regions of India (North, South, East 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 awards were sponsored by SOTAX, ACG and BASF.

Now, once again the 3rd DRPI event- DRPI 2022-Online has been conducted; the collaboration with APTI & AAPS continuing. For the third time there has been renewed interest all over amongst the research students and faculty all over the country. A lot of learnings from previous DRPI events have been taken into consideration to improve the systems; evaluation procedures, being decentralized now with more faculty from zonal committees have taken up this task. This time too, the awards being sponsored ACG, BASF & Sotax.

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

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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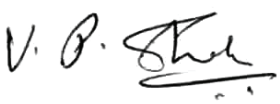
VPS Consulting, LLC

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

Padma Devarajan

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

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.

Society for Pharmaceutical Dissolution Science

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TEL : 91 22 26851903

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

Dear Delegates,

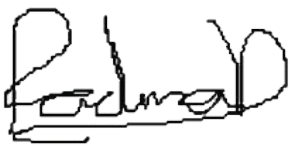
DRPI an innovative platform for young scientists to showcase their research and their talent is growing in strength from year to year. The huge success of DRPI 2020, and DRPI 2021 stands testimony to the importance of this event. DRPI is a one of a kind symposium that extends outreach across the country.

The uniqueness of DRPI is the format. Spread across zones which covers the entire nation this event is special for more than one reason. First, DRPI is a focused conference wherein presentations revolve around the theme of dissolution. Importantly it has created a 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 Indian Pharmacopeial commission has also acknowledged importance of dissolution testing. The second special feature is the video presentation mode which plays a critical role in development of students. The third is the mentoring and tutorial session provided to make the video, refine the abstract and fine tune the presentation.

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 ones research capability. DRPI serves as a forum for spreading knowledge in a niche and focus area that SPDS wishes to promote, while also serving as a self-development platform for young scientists from academia and the industry. Heartfelt thanks to our collaborating partners AAPS and APTI, 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 fervor.

DRPI is a winning platform not only for the winners but all participants as each one would 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
Scientific Chair, SPDS

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".

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

राष्ट्रीय औषधीय शिक्षा एवं अनुसंधान संस्थान
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14 July 2022

DRPI has acquired a position of leadership in the scientific events conducted for students of Indian pharmacy institutions. This has become possible due to strong scientific content, fair assessment and unique learning experience offered in DRPI. Dissolution as a science is undergoing rapid advancements and it becomes imperative that young students get exposed to evolving concepts. Participation in DRPI provides students a deep insight into their research project, through the rigorous evaluation by subject matter experts. As the next step SPDS hopes to internationalise DRPI and enhance healthy competition amongst students.

In near future, SPDS shall enhance engagement with Indian academia through collaborative research, hands-on trainings and mentorship. This will provide students and young faculty members, opportunity to sharpen their domain knowledge and improve professional skills. This is bound to have positive impact on pharmaceutical eco-system in the country.

I am confident that all the participants of DRPI shall be immensely benefited by this unique event and help them grow in their professional endeavours. I thank the pivotal role played by organizing committee, judges and experts, in making DRPI the most 'sought after' event in Indian academia and industry.

Arvind K Bansal, PhD, FAAPS
Scientific Chair - SPDS

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

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

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Dear Colleagues,

It is indeed a pleasure and privilege for me to be the General Secretary of SPDS and an integral part of DRPI 2022. This is the third 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 2022 Online Research Presenters shall find their time spent at the competition enriching and enlightening. My sincere thanks to all the Teachers & Guides who have motivated a good number of young Research Students and their teachers who have given their approval for their participation in this event. 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 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 2022

Dr. L. Ramaswamy
General Secretary

Saranjit Singh

Ex-Prof. & Head of Dept of Pharm Analysis, NIPER SAS Nagar
Scientific Chair, DRPI 2022

Biosketch

Dr Saranjit Singh is Ex-Acting Director, Ex-Dean and Ex-Professor and Head of the Department of Pharmaceutical Analysis of the National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab. He is gold medallist from University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, from where he studied for B. Pharm., M. Pharm., and Ph.D. degrees.

Dr Singh has experience of >40 years in education and research. He has published >250 research papers, general articles, reviews and book chapters. He has one patent and one edited book on drug stability to his credit. Before his superannuation from NIPER, his team executed >100 industry sponsored projects. He is regularly invited to hold full-day training sessions for pharmaceutical industry in India and abroad. He has delivered >550 invited lectures, and has spoken at the forums of AAPS, USP, DIA, IPA, IDMA, SSX, etc. He guided 147 Master's and 15 Ph.D. students.

He is a member of Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations and has been a Temporary Advisor to the World Health Organisation in the Expert Committee on Specifications for Pharmaceutical Preparations. He also has been a member of Scientific Committee of Indian Pharmacopoeial Commission.

He is Contributory Editor of Trends in Analytical Chemistry (TrAC) and Editorial Board member of several leading journals, including Journal of Pharmaceutical and Biomedical 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.

Dr Saranjit Singh,
2817, Phase 7, SAS Nagar (Mohali) 160062 Punjab
All India Scientific Chair, DRPI Online 2022

DRPI is in its 3rd edition this year. I was asked by Executive Committee of SPDS to continue as All India Scientific Chair this year also. Unlike last year, wherein the abstract book was published much later after completion of the event, this time it was decided to try an all-out effort to release it on the day of Finals itself.

With experience at hand on holding the event online for two years in 2020 and 2021, and with all systems and IT backbone structure in place, it was comparatively easier and smooth conduct of DRPI this time. In previous editions, the core committee had to work hard on submitted abstracts, as multiple language and grammatical errors, and style variations were observed. A number of abstracts had to be returned to the authors for resubmitting them with suggested changes. The very purpose of the exercise was to give young researchers a learning of how to express their, otherwise high quality research, in the form of an abstract. In all cases, the research mentors, who were involved along with students in abstract revision, could understand the quality expectation of very senior professionals involved in DRPI core committee. So this year, the abstracts at submission stage were much better organized and the committee had to make much lesser effort.

Another change observed this year has been remarkable improvement, specifically in the quality of research submitted and presented, though the number of submitted abstracts was lower. This time, abstracts were also given marks during the selection process at Zonal level. A very close competition was observed. The submissions happened from all over the country, and all five Zones were represented. Yes, there was shortfall in expected numbers from some Zones. Unfortunately, one abstract was submitted in Industry category, which was not followed by submission of the presentation. So this category had to be dropped from this year competition. This foretells us for the need to have better outreach among young researchers to secure good quality presentations in good number in each category (M. Pharm., Ph.D. and Industry) during future events.

Any event of All-India scale requires team effort and I am very happy that a large number of faculty colleagues from all over the country eagerly offered their services during the abstract evaluation process at the Zonal level. In subsequent semi-Finals and Finals, we had judges from both India and abroad from Industry, who evaluate the presentations and help us choose the best for cash awards. My personal thanks to everyone involved. I have special regards for Dr Vinod P Shah, a legend in Dissolution Science, and Patron, SPDS, who takes keen interest in our event and honours us with his gracious presence at all stages of competition, even at odd hours, as he joins online all the way from US.

As envisioned from inception itself, and which has been my promise, DRPI online 2022 also has been conducted in most fair and transparent manner. Hope the readers will enjoy the science presented in the abstracts in subsequent pages. It is matter of pride that the standard of research is no less than International events, for which both young researchers and their mentors deserve appreciation. Congratulations to the winners of competition. Many thanks to our very efficient expert IT team for timely compilation of the abstract book.

Best wishes to all.

Prof. Saranjit Singh

Mala Menon

Adjunct Professor-Pharmaceutics at Bombay College of Pharmacy, Mumbai
Scientific Vice-chair, DRPI 2022

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.

MESSAGE

Bombay COLLEGE OF PHARMACY Estd 1957 Autonomous

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

Date: July 14, 2022

It is a great pleasure to be a part of the DRPI Scientific committee!

DRPI Online is an excellent platform for Young researchers in the last three years. Since 2020, the DRPI 2020, DRPI 2021 and now DRPI 2022, have generated a lot of enthusiasm in both research students & Faculty of Pharmacy colleges all over India. In spite of the pandemic and problems, an overwhelming number of abstracts have been received. It was a great pleasure and learning while working as part of the Core Scientific Committee for this event and interacting with the scientific committee from different zones.

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

Wishing the DRPI 2022 event a great success! All the Best Wishes to the Young Researcher Participants!

Dr Mala Menon
Vice Chair, All India Core Scientific Committee,
DRPI 2022-Online

Krishnapriya Mohanraj
Professor of Pharmaceutical Analysis, Bombay College of Pharmacy, Mumbai
Scientific Core Committee member, DRPI 2022

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
(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

Greetings!

Best wishes for the online Disso Research Presentations India 2022- DRPI 2022

It is wonderful to be associated as a member of DRPI Scientific core committee for selecting the awardees for the Young Researcher Award from various academic institutions across all over the country.

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. In 2020, 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 an 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 bloomed into DRPI 2021- with AAPS and APTI support and now we are conducting DRPI 2022

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

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 young researcher in the Dissolution related arena.

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, the judges - for their acumen to evaluate, and the audience- for their encouraging participation.

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

Saluting the spirit of DRPI-2022 to bring to the fore research on dissolution related sciences and providing a golden opportunity for industry-academia interactions.

Awaiting the growth of DRPI into an international event

Prof. Krishnapriya Mohanraj
Professor of Pharmaceutical Analysis
Bombay College of Pharmacy

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:

Varsha Pradhan

Partner – Regulatory Affairs, Roche Products (India) Pvt. Ltd
Scientific Core Committee member, DRPI 2022

Biosketch

Dr. Varsha Pradhan has a professional career spanning 28 years which includes life cycle management of drugs coupled with an understanding of global Pharma education. She has completed her MS in Regulatory Sciences from the University of Maryland Baltimore USA . Prior to that she has completed her B.Pharm from KMK college of Pharmacy Mumbai, M Pharm from ICT Mumbai & a PhD from School of Pharmacy & Technology Management, NMIMS Mumbai. She was the recipient of UNIDO fellowship for Post graduate training in Pharmaceutical Technology at the University of Ghent, Belgium in 1992.

Her industrial experience includes Production areas of GSK in Sterile Process department, Formulation development in Cipla & Sandoz for generics solid oral dosage forms, semisolids & injectables. She has done consulting roles related to Regulatory intelligence and Pharmacovigilance in various organizations like Sidvim Life Sciences, APCER Life Sciences and Asia Actual India Pvt. Ltd.

In academia she has been a Faculty at MET's Institute of Pharmacy & NMIMS Mumbai. She contributed to bridge the gap between industry and academia & bagged the "Best Faculty Award 'in 2010 at NMIMS Mumbai. She holds an Indian Patent for her PhD formulation 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 a Guest Faculty for the Executive MPharm Drug Regulatory Affairs Course at Delhi Pharmaceutical Sciences & Research University, which has working professionals from industry, State FDA & CDSCO. She is also General Secretary for Society for Paediatric Medicines & Healthcare Initiative and is working on several collaborative projects with European Paediatric Formulation Initiative.

Dr. Varsha is also an active member in SPDS since its inception and is now a member of the Core Scientific committee for DRPI 2022.

SOCIETY FOR PAEDIATRIC MEDICINES AND HEALTHCARE INITIATIVE

MESSAGE

13 July 2022

Greetings! A warm welcome to all participants of DRPI 2022.

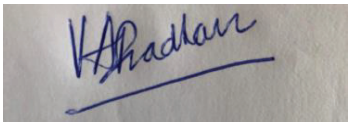
It is indeed a privilege and pleasure for me to get associated with DRPI from its inception. I am happy to be a part of the Scientific Central core committee & truly appreciate the efforts of teachers across the country to encourage students to participate in the competition.

Covid pandemic and the emerging health threats has brought in regulatory flexibility and agility in the global accessibility to medicines. Dissolution is critical quality attribute of a pharmaceutical product. One can see innovations in the last 3 years in tools, standards, and approaches to assess the safety, quality and efficacy of a Pharmaceutical Product. I am happy to note that DRPI 2022 has also brought forward research work from students across the country which exemplifies the changing regulatory environment.

It is my humble request to industry to support educational institutes for research funding which will further encourage the student community to pursue their research activities.

I also take this opportunity to thank AAPS & APTI for their support and would eagerly wait for DPRI 2023 to be a global event .

My best wishes to all the participants in this event!



Dr. Varsha Pradhan

General Secretary
Society for Paediatric Medicines and Healthcare Initiative
&
Partner- Regulatory Affairs
Roche Products (India) Pvt. Ltd.

Society for Paediatric Medicines and Healthcare Initiative (PMHI)
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Nathalal Parekh Marg, Matunga, Mumbai 400019, Maharashtra, India.
Email:info@pmhiindia.org

Hema Nair
Associate Professor, Sri Venkateshwara College of Pharmacy, Hyderabad
Scientific Core Committee member, DRPI 2022

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)

MESSAGE

Heartiest Congratulations on the ongoing DRPI 2022. It is a matter of great pride and joy to organize, witness and participate in the Third Edition of Disso Research Presentations India, DRPI 2022. With the backing of AAPS and APTI, this unique venture by The Society for Pharmaceutical Dissolution Sciences (SPDS) is slowly becoming an event to look forward to by faculty and students alike.

The online nature of this platform and the nominal registration charges has successfully overcome the earlier barriers faced by students while presenting their work at a scientific forum. All students from pharma institutes spread across the length and breadth of this country have been and are participating with a great deal of enthusiasm. The unbiased opportunity to win lucrative cash awards and to make a name for themselves by showcasing their research work are added bonuses. The platform has also allowed their mentors, especially the professors who are part of the evaluation team to network and team work with their contemporaries from across the country.

DRPI has resulted in a spotlight on dissolution related research work and thus a furthering of the objective of SPDS. With every passing edition, I am certain this platform will scale greater heights and become a global event in the immediate future.

On my personal front, I am thankful to SPDS for this opportunity to contribute and grow by working as a core committee member for DRPI. It has been a greatly enriching experience. I wish all success for DRPI 2022 and all its forthcoming editions.

Dr. Hema A. Nair

Core Committee Member

Arti Thakkar
Associate Professor, Amity Institute of Pharmacy, Amity University, Noida
Co-ordinator North Zone, DRPI 2022

Biosketch

Dr. Arti R. Thakkar is alumnus of Pharmacy Department, The M. S. University of Baroda, India. She was a visiting scholar at King's College of London, UK (during Ph. D.) and post-doctoral fellow at UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, USA.

Dr. Thakkar has more than 17 years of National & International (India, UK, USA) experience in the Pharmaceutical Sciences (DMPK, QA and DRA). She started her career as a QC Chemist at Elysium Pharmaceuticals Ltd. Baroda. She has worked as a faculty in few academic organizations: Parul University, Baroda; ISF College of Pharmacy, Moga; Baddi University and Delhi Pharmaceutical Sci. and Research University (DPSRU), New Delhi. At present she is Associate Professor, Amity University, Noida. In the past she has developed and established a government (CDSCO & NABL) approved commercialized drug testing laboratory named as ISF Analytical Laboratory (ISFAL), Moga.

Dr. Thakkar has 55 publications in the peer reviewed journals; 73 Presentations in International (USA, UK, China) and National Conferences; 5 Indian Patent and 1 International Book Chapter, 7 Books (D. Pharm., B. Pharm., and M. Pharm.), 5 Research Projects (AICTE, India; INMAS, India; DST, India; NIH, USA and J&J, USA) worth Rs. 1 crore from Indian and International funding agencies, and 11 National & International awards (including IPGA FELLOWSHIP AWARD-2019, BEST RESEARCH GUIDE-2012 award from Troika Pharmaceuticals & LM College of Pharmacy, Ahmedabad and FAST TRACK YOUNG SCIENTIST AWARD from DST, New Delhi, two times Best Poster Presentation award, DMPK Symposium, NIPER, Mohali and BEST RESEARCH PAPER AWARD from PD Sethi Memorial Award) to her credit. She is the first certified trainer of the Quality Assurance Chemist job role, by LSSSDC, New Delhi. She has guided more than 38 M. Pharmacy Students (Pharm. Analysis, QA, DRA & Pharmaceutics) and currently guiding 5 Ph. D. Students. Her core research areas are Formulations Development; DMPK, Method Development & Validation; Current Drug Regulatory Affairs.

She is a life member of IPGA, IHPA, APTI, SPER, MSU Pharmacy Alumni Association (MPA). She is member of AAPS and ISSX. She is executive council member in Society for Study of Xenobiotics (SSX), India, IPGA and MPA. She is co-convener, IPGA Women Forum and Secretary, Delhi Pharmaceutical Council, Women's Indian Chamber of Commerce & Industry since 2020.

Dr. Thakkar has organized National and International conferences (IPGA-2009; IHPA-2010; APTI–2011; Indo-Taiwan International Workshop-2011; INSPIRE Camp – 2012; National Seminar of CRS Indian Chapter-2016; 70th IPC-2018; 3rd & 4th Annual Conference of SSX-India-2018 & 2019, AP-ISSX, 2022) as LOC member and Scientific Services Committee Member 71st IPC-2019. She is Scientific Committee Member of Disso Research Presentation India – 2020 and 2021 and North Zone coordinator 2022, organized by Soc. for Pharmaceutical Dissolution Science.

AMITY UNIVERSITY
UTTAR PRADESH

AMITY INSTITUTE OF PHARMACY

Greetings!

Society for Pharmaceutical Dissolution Science (SPDS) has started Online Disso Research Presentations India for the first time in year 2020 with a unique concept, transparent and unbiased competition during the very depressing time of Covid-19 pandemic. DRPI – 2020 really filled a great positive energy to the researchers working in the Dissolution Science field during the pandemic.

DRPI has evolved in the last two years in an incredibly positive and strong manner. In DRPI – 2020, Association of Pharmaceutical Teachers India (APTI) was collaborating partner and consequently in the second year – 2021, American Association of Pharmaceutical Scientists (AAPS) along with APTI associated with DRPI – 2021. AAPS and APTI continued to be partner for DRPI 2022. And I am sure with this approach of senior leadership of SPDS, it is not far that one day, Disso Research Presentation India would be as a Disso Research Presentation International.

It gives me immense pleasure to be associated with DRPI – 2022 as a North Zone Coordinator. It is really a fantastic opportunity to reach out to the researchers from across India specifically working in the field of Dissolutions Sciences. The strategies, brain storming discussions and initiative-taking attitude to make this event best of the best is the key approach of the DRPI scientific core committee members and senior leaderships. This approach and work commitment makes me feel honour to be part of this committee as a North Zone Coordinator.

Further, I would urge to all the academicians and researchers to encourage the students and fellow colleagues to participate in the future DRPI events. It is an extra-ordinary opportunity to show-case their research at National and International level. So, mark the probable dates in your calendars and accordingly guide your students to work on the research project which can be presented in DRPI – 2023.

I am grateful to the Chair, Co-Chairs and Scientific Committee members of the North Zone for their commitment and contribution for the DRPI – 2022.

I compliment all the participants who got an opportunity to contribute in DRPI 2022. I wish DRPI 2022 a grand success!

Dr. Arti R. Thakkar
Associate Professor,
Amity Institute of Pharmacy

Amity University Campus, A-Block, Ground Floor, District Gautam Budhha Nagar, Sector – 125, Noida (U.P.) India
Tel: +91-120-4392498, 43922445

Sarath Chandran
Assistant Professor, College of Pharmaceutical Sciences, Pariyaram, Kerala
Co-ordinator South Zone, DRPI 2022

Biosketch

Dr. Sarath Chandran C, a life member of APTI (KE/LM-088) is working as an Assistant Professor at the College of Pharmaceutical Sciences, Govt. Medical College Kannur, Pariyaram. An academician specializing in Pharmaceutics with more than 18 years of experience, is involved in regular academic activities for both UG and PG programs. He is an approved research guide for Ph. D in Pharmaceutical Sciences at Kannur University and other reputed research centers. Dr. Sarath Chandran C is involved in collaborative projects, especially in the area of herbal formulation development and he has guided 2 research projects under the MD Ayurvedha program at Kerala University of Health Sciences. He has made 49 oral and poster presentations held at both national and international destinations. He and the research team could publish 30 research papers in peer-reviewed journals and chapters in textbooks with the international editorial team. Dr. Sarath Chandran C has filed a patent under IPR (awaited for a final grant) and associated as a mentor as well as co-ordinator for the KDISC-YIP program for the last 3 years. He is actively associated with Kerala State Pharmacy Council as a Trainer's Trainer and resource person for the CPE programs. He is also associated with professional bodies such as IPA (life member), SPDS, DRPI, KPPA, KPTF, etc. He was recently elected as the Vice President, APTI- Kerala state branch for 2022-2027. Dr. Sarath Chandran C received a prestigious FIP-Pharmabridge fellowship and undergone training at the University of Southern California, Los Angeles, USA. For his service to academia, he was awarded as the Best Teacher in 2014 by Alumni Association and in 2021 by the Kerala University of Health Sciences.

https://www.linkedin.com/in/scshenoy/

https://www.facebook.com/scshenoy77

MESSAGE

Dr. Sarath chandran C, Ph.D.
Assistant Professor
College of Pharmaceutical Sciences
Govt Medical College Kannur
Pariyaram, Kerala- 670 503. India.

Email ID: scshenoy@gmail.com
Mobile No: +91 9895442288

Date:05/07/2022

Dear Madam and Sir,

It was indeed a great privilege to be associated with DRPI2022, which is a fabulous platform for research scholars to exhibit their inventions in the pharmaceutical sciences, with a special focus on dissolution science, solubility, permeation studies, kinetic modeling, etc. Apart from that this platform allows the faculties across the country to assemble under one umbrella of DRPI to discuss science, and technology and listen to the stalwarts of the profession. Undoubtedly a platform that will provide every opportunity to enhance our knowledge and understanding of the latest happening in the industry. I hope that DRPI will progress and soon be recognized as a global event.

I wish all the great success for DRPI-2022

Thanking You.

With Regards & Wishes

05/07/2022

Dr. Sarath chandran C
Coordinator- Scientific Committee
South Zone, DRPI-2022

Residential address: *S/o Dr.S.C.Shenoy, "Vinay", Govt hospital road, Payyanur- 670 307, Kannur, Kerala.*

Swarnalata Saraf
Professor & Director, University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur, CG
Chair Central Zone, DRPI 2022

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.

Prof. Swarnlata Saraf
M.Pharm.,Ph.D.
APTI Vice President (2016-2022)

Director, University Institute of Pharmacy,
Pt. Ravishankar Shukla University, 492010, Raipur
swarnlatasaraf@icloud.com, swarnlatasaraf@gmail.com
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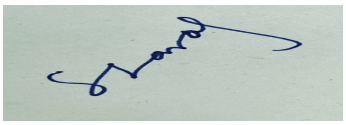
Message

With great pleasure, we are organizing the event in collaboration with AAPS and APTI in dissolution science, a more recent field of pharmaceutical research.

Pharmaceutical dosage forms are developed and approved using dissolution science and technology. Dissolution technology facilitates regulatory decision-making. It is imperative to conduct dissolution research in order to reduce the regulatory burden and unnecessary human studies in new drug development.

The DRPI gives researchers from academia and industry the chance to demonstrate their innovations and research in the fast-moving dissolution science sector, develop scale-up skills, and gain recognition worldwide.

Wishing DRPI 2022 great success.



Biswajit Mukherjee
Professor, Jadavpur University, Kolkata
Chair East Zone, DRPI 2022

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)
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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14/07/2022

Message

I am extremely happy to share that it is the time for DRPI 2022 final. Under the able-leadership of Dr. Ramaswamy, Prof. Saranjit, Prof. Menon, Dr. Vinod Shah ji and others, it is the time to bloom and spread the fragments of the flower of DRPI 2022 that has begun few months back. I have been pleased to be associated with it and wish a grand success of its final.

I particularly congratulate all of my East zone team members whose tireless effort is also a part of it.

All good wishes to the finalists.

Best regards,

14/07/2022

Professor Biswajit Mukherjee
Chairperson
East zone, DPRI 2022

Nayanabhiram Udupa
Research Director, Shri Dharmasthala Manjunatheshwara University (SDMU), Dharwad, Karnataka
Chair South Zone, DRPI 2022

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"

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Message by Dr. N Udupa

Chairman, Scientific Services, South Zone, DRPI 2022

We are happy to know that **DRPI 2022** in collaboration with various Organizations will be organized which will help Pharmacy Students, Researchers, Faculty and Industry Professionals to make their visionary steps as Manufacturing Pharmacists, QA and QC and Regulatory Administrator, Hospital and Clinical Pharmacists, Pharmacy Teacher, Healthcare Centre, Pharmaceutical Marketing Executive, research Scientist and Chemical Analyst specially equip all the professionals to acquire skill and knowledge in the area of Dissolution Science and Technology.

Pharmaceutical and Biotechnological Research helps to discover and develop new drug therapies to save and improve the quality of life. With this event Industry Institute Interaction, Collaboration and Innovations will be motivated. The participants will acquire rich knowledge about latest developments and trends in Pharmaceutical Sciences and in Dissolution Science and Technology. The Participants will also learn Ethical Practice and develop special skills and improve analytical thinking and be able to face problem solving.

I wish great success for DRPI 2022.

Thank you,

Dr. N. UDUPA
RESEARCH DIRECTOR
Shri Dharmasthala Manjunatheshwara University

Vijaya Ratna Jayanti
Honorary Professor, AU College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, AP
Member South Zone, DRPI 2022

Biosketch

- Presently occupied as Honorary Professor, AU College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, Andhra Pradesh, India- 530 003
- Teaching and Research Experience: 38 years
- Publications in peer reviewed journals: 108
- Research projects completed: 5
- Research guidance: 38 Ph.D. students and 100 M.Pharm students
- Patents: 3 in the field of pharmaceutical technology
- Award: A.P. Best Teacher award 2018
- Life Membership of professional Associations: IPA, IHPA, APTi, IGPA, POWER
- Member of Ethics Committee of King George Hospital, Visakhapatnam and member of Ethics Committee of Andhra University, Visakhapatnam
- Administrative positions held: Chairman, Faculty of Pharmaceutical Sciences, Andhra University and Chairman, Board of Studies, Andhra University and Co- Ordinator for Pharm D
- Significantly involved in conducting medical camps in villages, programmes and competitions for women pharmacists
- Won several prizes at national level in academics

Prof. J.Vijaya Ratna

8-1-63/30/7, Flat No.203, Anasuya Apartments, Peda Waltair, Visakhapatnam 530017

I am extremely happy to be associated with SPDS and DRPI. DRPI is a wonderful initiative started by dynamic pharmacy professionals, in the field of dissolution and is aimed at encouraging young pharmacy scholars to understand better and achieve better in the fields of dissolution science and pharmaceutical research. I will feel honored to continue to contribute, in any small way that I can to the conduct of DRPI or any other competition, meant to energize pharmacy students or scholars.

J.Vijaya Ratna

Co-ordinators : DRPI 2022

Pintu De

Associate Professor, Dept. of Pharmaceutical Technology, JIS University, Kolkata
Co-ordinator East Zone, DRPI 2022

Biosketch

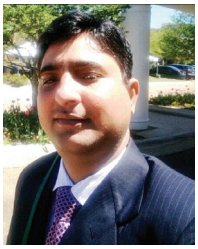
Dr. Pintu Kumar De has joined JIS UNIVERSITY in the Department of Pharmaceutical Technology as an Associate Professor in the year 2017. He is an alumni of Jadavpur University from where he obtained his Graduation (B. Pharm), Post-Graduation (M. Pharm in Pharmaceutics) and Doctoral (PhD in Pharmacy) degree. 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
Co-ordinator West Zone, DRPI 2022

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

Assistant Professor, Pt. Ravishankar Shukla University, Raipur, Chhattisgarh
Co-ordinator Central Zone, DRPI 2022

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

Meenakshi Kanwar Chauhan

Professor, DIPSAR, Delhi Pharmaceutical Sciences & Research University, New Delhi, Delhi

Biosketch

Dr. Meenakshi Kanwar Chauhan graduated and received her Ph.D. from University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India. She has a total of 22 years of experience in teaching and research. Dr Chauhan got selected through UPSC and joined DIPSAR (now under DPSR-University), Govt of NCT of Delhi in 2004. She has produced 50 Post graduates and 7 Ph.D. students. She has been granted one Indian patent and has received funding to the tune of 80 lakh INR from Government agencies. She has executed various research projects funded by national funding agencies like AICTE, DST, ICMR, INMAS, DRDO, etc.). She has been CSIR Research Fellow as SRF and CSIR-Research Associate. She wrote numerous chapters in edited books, contributed more than 100 scientific publications in high impact journals, and her group has received 13 Best Paper awards at National and International Conferences. She served as expert for award of grant for research projects and member screening committee, reviewer of research journals and books.

Dr. Meenakshi has been conferred with numerous awards like the 'Women Researcher Award'-2019 and the 'Most Dedicated Training Placement Officer Award'-2020, 'Outstanding Performance and Research Promotion during 2019-21', 'Research Innovation Award-2022', 'Notable Research Award'-2022, and 'Outstanding contribution to DPSRU in Research Promotion'-2022.

Dr Chauhan's research interests are: the development of intelligent and nano-based non-invasive drug delivery systems for targeting various ocular disorders and novel drug delivery approaches for neurological disorders such as Parkinson's disease, Alzheimer's disease, and dementia. Development of oral protein & Peptide drug delivery, etc.

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Web of Science ResearcherID AAV-2562-2020

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 has served in various Administrative and Academic positions for more than 35 years at Jamia Hamdard. He has supervised 86 Ph.D,. 200 M.Pharm. theses and published more than 400 research papers in International & National journals with cumulative impact points of more than 450; H index of 65, citation of 19731 and i.10 index of 181. Dr. Khar is inventor of two US & ten Indian patents. He has published eleven text books, including the, 4th revised edition (2013) of Lachman/lieberman's Text Book of Industrial Pharmacy.

Presently Prof. Khar is currently Director of B. S. Anangpuria Educational Institutes, Faridabad. He has been the member of "Unani Pharmacopoeia Committee" (2008-2011 and is currently a EXPERT Member of various Research and Academic Institutions and Regulatory bodies

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 an acknowledged leader with over twenty-two years of professional experience in drug research, development and compliance, in pharmaceutical organization, CRO setup 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.

Currently, he 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 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 is a Member, Scientific Programming Committee, 2022 Land O' Lakes Pharmaceutical Analysis; has 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-APA India. 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 23 publications, a book chapter and many scientific presentations to his credit.

Co-chairs : DRPI 2021 - South Zone

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.

Co-chairs : DRPI 2021 - Central Zone

Chanchal Deep Kaur

Professor & Principal, Rungta College of Pharmaceutical Sciences and Research, Raipur, CG

Biosketch

PROF. CHANCHAL DEEP KAUR, one of the eminent known Pharmacist is currently working as Professor and Principal in Rungta College of Pharmaceutical Sciences and Research, Raipur, Chhattisgarh affiliated to Chhattisgarh Swami Vivekananda Technical University, Bhilai, C.G. She did her Ph.D. in year the 2012 from University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur (C.G.) under the guidance of Prof. Dr. (Mrs.) Swarnlata Saraf. She has qualified GATE in the year 2001 with 98.35 Percentile, has done B. Pharm and M. Pharm in Pharmaceutics from Dept. of Pharmaceutical Sciences, Dr. Hari Singh Gour Vishwavidyalaya, Sagar (M. P.) and MBA in HR and Production and Management.

AWARDS: She is recipient of IDMA GP Nair Award for Gold Medal in B.Pharmacy in 2001, Got "Pragatisheel Ratna Award" for best teacher in 2008, "Award of Diligence 2014- 2015" for progressive Principal, "Sushikshit Sikh Mahila Award 2015" by Ambikapur Gurudwara for highly qualified Sikh girl of Ambikapur till 2015, "CG Gaurav Samman 2019", By Ramesh Chandra Foundation, "Best Performer Award 2018-19" and "Best Academician Award 2020" at Pharma Meet 2020 organized by Chhattisgarh Society of Pharmaceutical Sciences and Indian Pharmaceutical Association. Also Received Best Paper Award in International Convention for Oral Research Paper Presentation in year 2016, for poster presentation in the year 2014 and 2011 and For Oral Research Paper Presentation at First National Conclave "Vanoushadhi-2018" Chhattisgarh on 3 rd – 4 th February 2018

RESEARCH ACCOLADES: With 18 years of teaching and research Experience she has completed TEQIP project in Collaboration with Bioinformatics department of CSVTU and three MRP received from CGCOST, Raipur. She has successfully guided 1 DST SERB, New Delhi, National Post Doctoral Fellow, 70 M. Pharm students and 6 Ph.D. scholars and have 7 PhD students registered under her. She has received travel grant from CGCOST and INSA for presenting research work in national and international seminars and conferences. Successfully organized national seminars and conferences as convener and organizing secretary sponsored by CGCOST, ICMR.

PROFESSIONAL CREDENTIALS: She is a life member of CG State Pharmacy Council, APTI, IPA and Shakti Mahila Vigyan Bharti CG Unit and Society for Pharmaceutical Dissolution Science. She was the member of Board of Studies of CSVTU, Bhilai, CG, is Approved PCI and CSVTU Inspector, Member and nominee of IAEC, CPCSEA, Reviewer of various reputed Journals, Worked as Content writer and Presenter in developing E Content for NME-ICT Project of UGC, EMR.

She has delivered 29 invited talks as keynote/eminent speakers in national/international seminar and conferences. She has been chairperson and evaluator of various functions. She has authored 4 books, 5 book chapters and has to her credit 103 publications in national and international journal of repute. She has 10 patents under process. Her key areas of Research includes Targeting approaches, NDDS for plant actives, skin cancer, ovarian cancer, breast cancer and lymphatic disorders.

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.

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Assessment of *in vitro* Drug Release Behaviour of Herbal Drug Exhibiting pH Dependent Solubility

Shikha Jha (shikhajha.niperguwahati@gmail.com)[1], Amit Alexander (amit@niperguwahati.in)[1], Prabakaran A[1]

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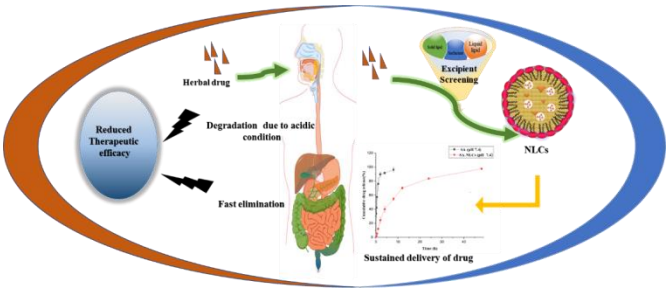
Background & Rationale: Herbal drug (SA) having natural origins comprises of polyphenolic acids and possesses antiproliferative and antioxidant properties. However, SA exhibits low solubility, and fast elimination which limit its clinical application. Therefore, encapsulating in a nanostructured lipid carrier enhances its solubility, and the matrix system offers a sustained release of the drug to the target site. The current aim of the study is to formulate and optimize SA-loaded nanostructured lipid carriers (SA-NLCs) using a quality by design (QbD) approach and thereby assess their release mechanism in different release mediums mimicking the condition of transit of NLCs across GIT to reach a target.



Research Methodology: Optimization and formulation of SA-NLCs were carried out using a systematic approach of preliminary screening of components, optimizing process parameters using the QbD approach, and formulating a stable SA-NLCs with prolonged released behaviour. Components of nanostructured lipid carriers include solid lipid, liquid lipid, and surfactant. Theoretical and experimental lipid screening for solid lipid were performed. Liquid lipid and surfactant were selected based on the solubility of SA in oils. Hot melt emulsification technique was adopted for the formulation of SA-NLCs. Further, SA-NLCs were characterized by their particle size, polydispersity index, and zeta potential, reflecting homogeneity and stability. The process variables selected was studied, and its effect on drug release behaviour was assessed. *In vitro* drug release was carried out using the dialysis bag technique, where a dialysis bag having MWCO of 12-14 kDa was soaked in respective dissolution media for 12 h. The experimental condition was maintained at 37 ^{0}C at 100 rpm. SA and SA-NLCs of equivalent amounts are added in dialysis bag and tied at both ends. One ml of a sample was withdrawn at a predetermined time interval and simultaneously replaced with an equal volume of dissolution medium to maintain sink condition. *In vitro* drug release behaviour of SA in different pH of 1.2, 6.8, and 7.4, reflecting gastric, intestinal, and plasma pH, were assessed and fitted into various kinetic models to study their mechanism of release from the matrix system.

Results and Discussion: Preliminary screening data suggested precirol and oleic acid as a lipid for NLCs. Tween 80 and PEG 200 were selected as emulsifiers in a ratio of 3:1 due to their higher emulsification property. Further, the systematic approach of QbD allowed exploring the parameters and their interaction that affect the response variables. Box Behnken design was adopted to optimize SA-NLCs. Lipid concentration, surfactant concentration, and sonication time were independent variables selected for the study. Lipid concentration had a direct effect on particle size and encapsulation efficiency. Additionally, the amount of lipid also affects the release of drugs from the lipid matrix. Surfactant concentration had an indirect effect on particle size. This parameter also has a moderate effect on drug release behaviour. Thus, optimized SA-NLC exhibits particle size well below the range of 170 nm with a zeta potential value of less than -16mV due to the non-ionic nature of tween 80. *In vitro* drug release from the nanoparticulate system was performed using the dialysis bag in different pH media. As SA exhibits pH-dependent solubility, its release is also dependent on the solubility of SA at different pH. The slower release of the drug in pH 1.2 protects the drug from degradation as it is susceptible to it. Further sustained behaviour was performed for 24 h. This parameter was fitted into the different kinetic models; the Weibull model was found to best fit as per R^2 values. This explains the release mechanism of SA from the matrix system, which includes burst release followed by sustained release of a SA. This would be attributed to the presence of SA in surfactants and well in the lipidic matrix system.

Conclusion: The advent of nanotechnology in drug delivery offers delivery of drugs to the target site minimizing associated side effects of drugs. The inherent property of SA restricts is therapeutic efficacy. Hence encapsulating it proves prolonged time for a drug to maintain above therapeutic level. With proper approach and experimental design, SA-NLCs were optimized and characterized.

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2. Costa, C.P., et al., Quality by design (QbD) optimization of diazepam-loaded nanostructured lipid carriers (NLC) for nose-to-brain delivery: Toxicological effect of surface charge on human neuronal cells. International Journal of Pharmaceutics, 2021. **607**: p. 120933.

Acknowledgement: I would like to acknowledge the facilities provided by National Institute of Pharmaceutical Education and Research, Guwahati for carrying out this project.

Comparative *In Vitro* Drug Release and *Ex Vivo* Permeation Studies of Sinapic Acid Loaded Vesicular Nanocarriers and their Topical Gel Formulations


Ms Nidhi Malviya (nidhimalviya0812@gmail.com)[1], Dr Amit Alexander (amit@niperguwahati.in)[1], Mr Prabakaran A[1]

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Background and Rationale: Sinapic acid (SA) is a polyphenolic compound from plants exhibiting anti-inflammatory and antioxidant properties. However, its poor water solubility hinders its therapeutic activity. Thus, the loading of sinapic acid-into liposomes, ethosomes, and transfersomes could overcome the poor water solubility problem. In addition, preparing nanocarriers-based topical gel could enhance the permeation and retention towards better anti-inflammatory activity.

Research Methodology: The three vesicular formulations, such as liposomes, ethosomes (ethanol), and transfersomes (Tween 80), were prepared using the thin-film hydration method. The prepared vesicular formulations were assessed for particle size, zeta potential, entrapment efficiency, and morphology. In addition, the drug interaction studies with the excipients used in the formulations were performed via DSC, FTIR, and XRD techniques. Moreover, the *in vitro* drug release study was performed using the dialysis bag (12-14 KDa) method in pH 7.4 phosphate buffer saline (PBS) at 37±0.5°C. The sample was withdrawn at a specific time of 24 h and analyzed in UV-Vis spectroscopy. The release mechanism of sinapic acid from three vesicular foemulation were determined using various mathematical models. Further, the sinapic acid-loaded vesicular formulations were loaded into carbopol gel and assessed for *ex vivo* permeation behavior on rat skin. The permeation study of three different nanovesicular-based carbopol gel was performed on the Franz diffusion cell apparatus, and the sample was withdrawn and analyzed for 8h using UV-Vis spectroscopy.

Results and Discussion: The prepared vesicular formulations exhibited vesicle sizes between 67.14 and 146.5 nm with a PDI value less than 0.3. Moreover, the entrapment efficiency of three vesicular formulations was 65.23–85.45%. Further, the morphological examination revealed spherical shapes with no agglomeration. The *in vitro* drug release of vesicular formulations exhibited sustained and prolonged drug release in pH 7.4 PBS. The prepared vesicular formulations followed the Weibull model with the Fickian drug release mechanism. Further, the sinapic acid-loaded vesicular carriers were loaded into carbopol (hydrogel) for ease of topical application. The *ex vivo* studies revealed that ethosomes showed more permeation with the flux value of 8.53. The decreasing order of permeation studies of sinapic acid from the topical vesicular gel was ethosomes, transferosomes, and liposomes. The prepared gel was stable and did not exhibit any change in physical appearance for at least 3 months.

Conclusion: The stable sinapic acid-loaded vesicular formulations were prepared using the thin-film hydration method and exhibited sustained drug release. In addition, ethosomes-based gel showed more permeation than transferosomes and liposomes. Further, *in vivo* studies are required to confirm the therapeutic activity of three nanovesicular-based topical gels for anti-inflammatory activity.

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Conjugation of Ketoconazole to Porous Chitosan Microparticles Enhances its Aqueous Solubility at pH 6.8

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Background and Rationale: Ketoconazole is a commonly used topical antifungal agent. It is a BCS II drug. The solubility of ketoconazole is pH-dependent. It is soluble in strong acidic solution (0.1 N HCl solution, pH 1.2). But the solubility decreases with increasing pH. Porous particles have enormous specific surface area. Hence conjugation of drugs to porous microparticles may enhance the solubility. The objective of this project work to develop a novel method for synthesizing porous chitosan microparticles and enhancing the solubility of ketoconazole by conjugating with the porous network.

Method A- Synthesis of ketoconazole conjugated porous chitosan microparticles (KCPCM) and blank porous chitosan microparticles (BPCM): 4 ml 3% chitosan (CS, 95% degree of deacetylation) solution in 1% 10 ml acetic acid, a specific volume of sodium bicarbonate ($NaHCO_3$) solution, and 50 mg ketoconazole in 2 ml 1% acetic acid were mixed together. It was added dropwise in a hot (100 ^{0}C) sodium hydroxide (NaOH) solution in 50 ml water with gentle stirring. After 2 hr incubation at room temperature, the particles were separated by centrifugation at 10000 rpm for 5 minutes. The product was subsequently washed several times until the pH was neutral and dried. In case of BPCM, the drug was not added. All other steps were the same.

Method B- Analyzing and construction of calibration curve and solubility study: Calibration curve developed in 0.1N HCl solution (pH 1.2) at 223 nm, The slope, and R^2 value were 0.0532 and 0.9984. 2 mg drug and an equivalent amount of product were added in 5 ml PBS 6.8. The mixtures were sonicated for 1 hr. It was followed by the separation of the undissolved particles by centrifugation. 0.05 ml HCl was mixed with the supernatant before taking OD at 223 nm.

Method C- Characterization of products: The surface morphology of the product was checked by Scanning Electron Microscopy (SEM) [ZEISS-EVO-18 Scanning Electron Microscopy], and conjugation between chitosan and ketoconazole was studied with Fourier Transform Infrared Spectroscopy (FTIR) [Perkin Elmer UATR two Fourier Transform Infrared Transform], solubility quantitative estimation of ketoconazole was done with UV- visible spectrophotometer [Jasco-V670, Ultraviolet-visible Spectrophotometers].

Results and Discussion: As per the electron microscopic study, BPCM had micropores that were interconnected. The CS powder was nonporous and had a loose texture. The surface of BPCM had numerous pores and was irregular in shape. Ketoconazole was attached to the polymeric matrix via chemical linkage, as confirmed by FTIR. There were reactions between the amino group of chitosan and the carboxylic group of ketoconazole as confirmed by the peaks at 1647 cm^{-1}, 1467-1545 cm^{-1} with a decreasing transmittance and more number of peaks in the product as compared to chitosan . More than 90% of added ketoconazole was conjugated to the chitosan matrix. The product had a drug loading of 890 µg ketoconazole per 5 mg product. Finally, chitosan conjugated porous microparticles enhanced the solubility of ketoconazole twice at 37 ^{0}C temperature in PBS (pH 6.8).

Conclusions: A novel method for the synthesis of porous chitosan microparticles was developed. It had good drug loading capacity. The solubility of ketoconazole was enhanced twice at room temperature in PBS (pH 6.8).

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Development of Sustained-Release Ketoprofen Loaded Microspheres for Possible Intraarticular Injection

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Background & Rationale: Non-steroidal anti-inflammatory drugs are the most valuable drugs to treat various conditions like pain and swelling in osteoarthritis. Ketoprofen is an effective drug for treating osteoarthritis due to its therapeutic potential. However, conventional dosage form, such as oral solid dosage form, has less therapeutic efficacy due to the short half-life of ketoprofen; hence, the drug rapidly clears from systemic circulation. An acute toxicity study reveals that ketoprofen has an irritating gastrointestinal effect. The standard oral dose of ketoprofen is 50 mg, 4 times daily. Thus, the drug must be administered frequently, leading to patient incompliance. This study aims to formulate and investigate the suitability of loading ketoprofen into microspheres for sustained release to minimize dose frequency with enhanced therapeutic effect.

Methods:

A) Preparation of ketoprofen microspheres: The ketoprofen microspheres were formulated using the spray drying technique. The feed was prepared by dissolving the drug in an aqueous glacial acetic acid solution of chitosan and crosslinked with glutaraldehyde. The feed was sprayed through a nozzle of 0.7mm diameter with an aspiration rate of 70% into the drying chamber, and the final product was collected.

B) *In vitro* drug release study from the microspheres: The *in vitro* release study was performed in PBS (pH 7.4) with a temperature of 37±0.5 ºC and 50 RPM using an orbital shaker. The microspheres were dispersed in 200 ml PBS (pH 7.4), and a 2 ml sample was collected at a predetermined time interval using a 0.25µm Syringe filter. The equivalent amount of sample was replaced with PBS (pH 7.4). The sample was centrifuged (7000 RPM), and the supernatant was collected and analysed using UV-visible Spectrophotometer at 260nm.

Results and Discussion: The obtained *in vitro* drug release data was fitted into the different kinetic models like zero order, first order, Higuchi, and Korsmeyer-Peppas model. The correlation coefficient and best fit value for the Higuchi model are obtained with a correlation coefficient of 0.8594, and kH was found to be 0.782, respectively. Hence the release data were also fitted in Korsmeyer -Peppas, showing a good correlation coefficient of 0.969 and n value of 0.2485. Thus, the *in vitro* drug release study of ketoprofen microspheres concludes that drug release depends on the erosion of the polymeric matrix and fickian diffusion of the drug from swelled matrix. The matrix hardness and swelling depending on the crosslinking extent of ketoprofen microspheres. The enhanced crosslinking extent hardens the matrix and retards the matrix erosion, sustaining the ketoprofen release for more than 24 h. Thus, chitosan microspheres are suitable to sustain the drug release from the polymeric matrix and reduce the dosing frequency and patient compliance.

Conclusion: Ketoprofen microspheres are a promising drug delivery system that can sustain the drug release. Also, microspheres reduce the adverse effects of ketoprofen associated with conventional drug delivery.

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Evaluation of the Effect of Sodium Bicarbonate on the *In Vitro* Drug Release Profile of Diclofenac Sodium Loaded Sodium Alginate Beads.


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Background and Rationale: Diclofenac sodium (D-Na) is a commonly prescribed non-steroidal anti-inflammatory drug (NSAID). It helps in relieving pain, inflammation, and joint stiffness in acute or chronic pain. It has potent analgesic and anti-inflammatory activities [1]. It has a half-life of ~ 2h. The 35% administered dose enters into enterohepatic circulation. The sustained-release products of D-Na are on-demand in the market. The objective of this work is to develop D-Na-loaded alginate beads to control the release of drugs and evaluate the effect of the addition of Na-bicarbonate on the release of the drug.

Methods: A) Preparation of beads – In 10 ml 4 % (w/v) sodium alginate solution, 0.0400 gm and 0.0500 gm of sodium bicarbonate were mixed. It was added drop-wise with a 22 gauze disposable syringe in 50 ml 5% w/v calcium chloride solution heated at 60 ºC. The system was agitated gently for 20 minutes. The particles were separated by filtration and subsequently dried at room temperature for 48 h. It was finally dried by heating at 55 ^{0}C for 2 hr. Two similar beads were prepared, one without the addition of $NaHCO_3$, and another one without D-Na.

B) Calibration curve of D-Na in PBS (6.8) – Standard solution of D-Na 5-30 mg/ml was prepared and OD value is taken against 276 nm. The slope we found = 0.276, and r^2 value is = 0.9984

C) Physical characteristics and *In vitro* study- Prepared samples are characterized for particle size distribution, swelling index, functional group analysis using FTIR, drug entrapment efficiency, and dissolution study in PBS buffer (pH=6.8) using UV-VIS spectroscopy[2].

Results and Discussion: The addition of $NaHCO_3$ reduced the particle size of beads from ~1 mm to 0.75 mm. The swelling index was increased from 4.8 to 5.8. This indicates the formation of pores into the beads that can be confirmed by SEM. On the other hand, the presence of $NaHCO_3$ slightly decreased the entrapment efficiency of D-Na from 82.2 % to 73.8 %. $NaHCO_3$ increased the lag time from 90 minutes to 120 minutes and reduced the rate of drug release. There was ~46% drug release after 24 hours, whereas the beads without $NaHCO_3$ released ~75 % drug in 24 h. In both cases, it follows First-order kinetics. From the FTIR data, we found that there is no significant difference in peaks in the without D-Na bicarbonate loaded beads and the D-Na loaded bicarbonate added alginate beads, but there is a decreasing of transmittance in the range 3800-3000 cm^{-1}, 2600- 2000 cm^{-1}, and 1200- 1000 cm^{-1} which represent the binding of diclofenac into the surface of beads.

Conclusion: The swelling index of the microparticles containing sodium bicarbonate and diclofenac sodium was found to be slightly higher than that of the microparticles containing only diclofenac sodium. FTIR data represent the binding of diclofenac sodium into the alginate beads' surface. The drug content, drug release, and entrapment efficiency were found to be higher in the case of only diclofenac sodium microparticles as compared to the sodium bicarbonate-loaded diclofenac sodium microparticles.

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In vitro Dissolution Behaviour and *In Vivo* Anti-hyperglycaemic Activity of Sitagliptin Loaded Microspheres

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Background and Rationale: Nowadays diabetes is a globally increasing disease. Besides insulin injections various oral antihyperglycemic medications are available like sitagliptin that control diabetic condition by increasing insulin production. Sitagliptin has a biological half-life of 8-14 hours and about 38% binds with the plasma protein whereas. A relatively large proportion (79%) of it gets eliminated in unchanged condition by renal excretion. This results multiple high dosing frequency that leads to decrease patient compliance. Keeping this in mind the aim of the study was to formulate a sitagliptin loaded microsphere using the polymers ethyl cellulose and hydroxypropyl methylcellulose to provide better onset of action followed by sustained release.

Methods: A) Microsphere preparation and characterizations: For microsphere preparation emulsion solvent evaporation (ESE) method was used. In this method a homogenous mixture of drug and polymer were made then was added to oil phase with constant stirring following evaporation of organic phase. Microspheres were further characterized on various parameters like surface morphology by Scanning electron microscopy (SEM), dissolution kinetics, FTIR analysis, micromeritics, particle size, % yield, entrapment efficiency (EE), stability study and *in vitro* release study.

B) *In vitro* drug release study: The drug release study was performed in USP type II (paddle assembly) dissolution apparatus at 75rpm and in simulated buffer of pH 6.8 at 37±0.5^{o}C. This study has been conducted for 12 hours (sampling points: 15, 30, 45, 60, 90, 120, 180, 240, 300, 360, 480 and 720 min). 5ml sample was taken and replaced by fresh buffer solution every time that was further analysed in UV-Vis spectrophotometer.

C) *In vivo* study: *In vivo* study has been done on zebrafish (*Danio rario)* hyperglycaemic model. 5 groups were made with 6 fishes in each. Normoglycemic group, without hyperglycaemia receiving only water as placebo treatment, negetive control group, hyperglycaemic fishes receiving water as placebo treatment, positive control group, hyperglycaemic fishes receiving blank microsphere dissolved in water as placebo treatment, standard group, hyperglycaemic fishes receiving standard treatment of anti-hyperglycemic drug STG, and test group with hyperglycaemic fishes receiving anti-hyperglycemic drug STG loaded microspheres. Hyperglycaemia was induced with immersing fishes in 4% glucose solution and dosing was done by oral gavaging and blood glucose level was measured using glucometer. Hyperglycemia was observed after glycose induction and decrease in blood glucose level was observed after STG treatment.

Results and Discussion: The calculated %yield is ranging from 76% to 85% for different formulations. EE is also varying in-between 71.70% to 80.96%. Formulation F2 (drug : polymer 1:3, polymer : copolymer 9:1) showed 35.24% burst release at 15 minutes and 74.30% drug release in 12 hours. After hyperglycaemia induction at 21st day, blood glucose level was found to be 169.33±4.5 mg/dL. After treatment, the blood glucose level was found to be 60.67±2.66, 168.83±2.86, 166.17±10.70, 78.50±3.08, 78.00±3.16 in normoglycemic group, negative control group, positive control group, standard group, and test group respectively which shows the blood glucose level of test group decreased after treatment with STG loaded microspheres.

Conclusions: EE data and %yield data showing ESE method is suitable for making microspheres with minimum loss of raw materials. Dissolution study showing burst release for faster onset of action followed by sustained release of drug. *In vivo* study clearly indicates pharmacological effectiveness of sitagliptin loaded microspheres.

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Optimization of Ketoconazole Loaded Matrix Tablet with Improved Dissolution Properties

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Background & Rationale: Ketoconazole is used in the treatment of fungal infections. It is a BCS Class II drug [1]. The water solubility of ketoconazole is pH-dependent [1]. It is soluble in strong acidic pH (pH 1.2, 0.1 N HCl). Solubility is increasing with decreasing pH [2]. After oral administration, though the drug will be dissolved in the stomach, it will not dissolve in the intestine. The objective of our work is to develop a method for the preparation of matrix tablets with HPMC, Lactose, and PVP K-30 to enhance the dissolution profile of Ketoconazole.

Methods: A 9 Run D-optimal mixture design was done using Design-expert software (Table 1). The amount of HPMC, Lactose, and PVP K-30 were varied while the quantity of other ingredients were kept fixed. The drug was dissolved in a mixture of isopropyl alcohol and HCl (pH 1.2). PVP K-30 was dissolved in it. This was used to prepare the moist mass with HPMC and lactose (previously passed through sieve number 44 and mixed with geometric dilution) and the resultant wet mass was passed through sieve number 8. The wet granules were dried at 55°C and passed through sieve number 44. It was followed by blending with talc and magnesium stearate and compression with 10 stations automatic tablet compression machine. Tablets were also prepared where the drug was directly mixed with HPMC and Lactose. It was considered a control.

Method A (Calibration curve): 0.1 ml HCl was added to 10 ml phosphate buffer (pH 6.8) to prepare the blank for detecting the optical density at 223 nm.

Method B (Characterization): Hardness and dissolution studies were performed in pH 6.8 using the standard protocol. The USP Dissolution apparatus type 2 was used with 900 ml of buffer in the vessel. The fluid (pH 6.8) was maintained at a constant temperature of 37°C. Depending upon our formulation, the rotating speed was 50 rpm. The tablet was introduced in each basket and the dissolution test was started. After 10 minutes, we pipetted out a 10 ml sample from the vessel, and a 10 ml buffer was added to maintain the volume. In this way, the process was repeated for 20, 30, 60, 120, 180, 240, and 320 minutes. In this way, we have performed the dissolution test.

Table 1:

Formulation No	Component 1 HPMC (mg)	Component 2 PVP K-30 (mg)	Component 1 Lactose (mg)	Response 1 Hardness (kg/cm^2)	Response 2 Maximum % Release	Response 3 Time to Maximum % Release (min)
1	287	73	240	5.2	40.68	30
2	274	66	260	4.3	50.94	60
3	285	50	265	4.1	32.32	180
4	250	70	280	4.8	63.63	240
5	300	50	250	4.2	41.52	20
6	300	80	220	4.9	34.50	20
7	250	80	270	5.3	30.21	20
8	250	80	270	5.3	30.21	20
9	270	50	280	4.2	24.17	20

Results and Discussion: Increase in PVP K-30 improved the hardness of the tablet, but it had a dramatic effect on the release of ketoconazole. When ketoconazole was added directly to the tablet, the maximum percentage release was 33% and the time to maximum percentage release was 30 minutes, but when ketoconazole was added with isopropyl alcohol and HCl, the maximum percentage release was 63.63% and the time to maximum percentage release was 240 minutes. So, the percentage release increased.

Conclusion: It is a novel method for the development of a Ketoconazole-loaded matrix tablet. The optimized tablet released 63.63% drug in 240 minutes or 4 hours.

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Physiologically Based Pharmacokinetic Modelling of Atazanavir and Prediction of Pharmacokinetic Parameters after Administration Through the Oral Route and Pulmonary Route in COVID-19 Geriatric Patients having Hypertension as Comorbidity


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Background and Rationale: Coronavirus (COVID-19) disease is also known as severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2). Coronavirus affects different age groups people in different ways. Currently, many clinically approved drugs are used to treat this disease, Atazanavir is one of them. Atazanavir is an antiretroviral drug that inhibits viral protease. Atazanavir is mainly metabolized by the CYP3A enzyme. Many hypertensive geriatrics patients are prone to get affected by COVID-19.[1] Verapamil is a type of calcium channel blocker. It can be prescribed as an antihypertensive drug in combination with atazanavir. Physiologically based pharmacokinetic modeling (PBPK) and simulation is a computer-based approach to predicting the drug concentration in blood plasma and other pharmacokinetic parameters of drugs [2]. The study aimed to predict the pharmacokinetic profile and co-administration of atazanavir (nebulizer) and verapamil (tablet) in COVID-19 geriatric patients having hypertension as comorbidity.

Methods: PK-Sim® software was used for the development of the PBPK model and for prediction of the pharmacokinetic profile of the drugs. The data relating to plasma concentration-time profile after administration of atazanavir through oral route to healthy geriatric patients were collected from the literature [2]. The physicochemical data and ADMET parameters of Atazanavir were also collected from the literature[1]. This data was used to develop the PBPK model of atazanavir. Similarly, the PBPK model of verapamil administered through the oral route was also developed.[2]. Now, in geriatric patients with hypertension as a comorbidity, the physiology (blood flow rate to different organs) has been changed. At first, the individual model was created with atazanavir (400 mg) and verapamil (120 mg) administered individually through the oral route. Then, the population modeling was designed based on individual parameters. Finally, the PBPK modeling after co-administration of atazanavir (nebulizer) and verapamil (tablet) in COVID-19 geriatric patients of age group 60-80 years was done to predict different pharmacokinetic parameters.

Results and Discussion: The pharmacokinetic parameters of the drug, such as AUC, Cmax, Tmax, half-life, and MRT were observed from the plasma concentration with a time profile curve. This study is mainly focused on the prediction of pharmacokinetic parameters after co-administration of atazanavir (nebulizer) and verapamil (tablet) in COVID-19 geriatric patients. In the case of individual modeling of atazanavir (oral) and verapamil (oral), the AUC, Cmax, Tmax, half-life, and MRT were 870.34 µmol*min/l, 2.05 µmol/l, 2.00 h, 8.48 h, 11.44 h, and 192.06 µmol*min/l, 0.60 µmol/l, 169.10 h, 6.34 h, 5.73 h respectively. In the case of the healthy geriatric patient, the AUC, Cmax, Tmax, half-life, and MRT of atazanavir were 660.78 µmol*min/l, 66.32 µmol/l, 0.05 h, 25.99 h, and 12.79 h whereas, in COVID-19 geriatric patient the AUC, Cmax, Tmax, half-life, and MRT of atazanavir (nebulizer) was 4447.63 µmol*min/l, 66.39 µmol/l, 0.05 h, 28.99 h, 17.39 h respectively. In the case of the healthy geriatric patient, the AUC, Cmax, Tmax, half-life, and MRT of verapamil are 250.87 µmol*min/l, 1.72 µmol/l, 0.70h, 10.26 h, 15.41 h whereas, in COVID-19 geriatric patients the AUC, Cmax, Tmax, half-life, and MRT of verapamil are 570.65 µmol*min/l, 17.31 µmol/l, 0.05 h, 15.23 h, and 21.49 h respectively. The AUC, Cmax, half-life and MRT of verapamil along with atazanavir is increased 5 times, 29 times, 2.5 times and 4 times respectively in case of COVID-19 geriatric patients with comorbidity in compared to data obtained from literature. The AUC, Cmax, half-life, and MRT was increased by 2 times respectively in case of atazanavir (tablet) along with verapamil in COVID-19 geriatric patients.

Conclusion: In a comparison of healthy geriatric patients and COVID-19 geriatric patients having hypertension as comorbidity the AUC, Cmax, half-life, and MRT are increased in the case of both atazanavir (nebulizer) and verapamil (tablet). Hence, toxicity occurs due to increased in Cmax value. So the dose adjustment of atazanavir is required. We can conclude from this modelling, that atazanavir can be recommended for prescription through oral route when co-administered with verapamil rather than in nebulizer form.

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Physiologically Based Pharmacokinetic Modelling of Fluvastatin and Prediction of Pharmacokinetic Parameters after Administration Through Oral and Pulmonary Route in Covid-19 Patients having Diabetes as Comorbidity

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Background and Rationale: Fluvastatin is a member of the statin class of drugs [1][2][3]. It is prescribed for the treatment of hypercholesterolemia and prevention of cardiovascular diseases. It is one of the WHO listed essential medicine[1]. Clinical data of patients suffering from COVID-19 indicates that statin therapy has a promising role against different autoimmune disorders like Multiple sclerosis, Rheumatoid arthritis [1][3]. Fluvastatin exhibited good binding affinity to target proteins like RdRp (remdesivir binding site), 3CL-pro (inhibition site) and Helicase (ATP binding site) and the Spike proteins of different mutants of COVID-19 [3]. In this work, our objective is to the prediction of the pharmacokinetic parameters after administration of fluvastatin in elderly COVID 19 patients having diabetes comorbidity.

Methods: The PBPK model has been established by PK-Sim software for the prediction of pharmacokinetic profile of the drugs. The clinical data after administration of 40 mg Fluvastatin through oral route in 24 male healthy European population aged 18-45 years, height 170-180 cm, weight 68 to 75 kg were collected from the literature, chemoinformatic tool like PubMed, PubChem [2]. The ADME data and physicochemical parameters of Fluvastatin were also collected from the literature, [1]. Similarly, the PBPK model of 10 mg Glipizide administered through oral route was also developed [3]. Now in COVID-19 patients with diabetes as comorbidity, the organ volume and blood flow rate to different organs have been changed. At first, the population modeling of 40 mg Fluvastatin in 24 healthy volunteers was designed on the basis of individual parameters. At the same time, population model of 10 mg Glipizide was established in 24 healthy populations. Finally, the PBPK modeling after co-administration of fluvastatin (pulmonary) and glipizide (oral) in the COVID-19 population as well as co-administration of both the drugs through pulmonary route in the same population were done. Thus, the plasma concentration value of the study predicted using the arithmetic mean of the COVID-19 population was observed.

Results and Discussion: In case of healthy population, the AUC, Cmax, Tmax, half-life of 40 mg oral fluvastatin are 44 µM-min/ml, 0.2 µM/l, 5.75 hours, and 3.63 hr respectively. At the same time, in healthy population, the values of AUC, Cmax, Tmax, and half-life of 10 mg oral glipizide which are 27.11 µM-min/ml, 0.12 µM/l, 1.95 hrs, and 10.14 hrs respectively. In case of the co-administration of 10 mg fluvastatin through pulmonary route and 10 mg glipizide in oral route in COVID-19 population, the values obtained of AUC, Cmax, Tmax, and half-life of 10 mg fluvastatin pulmonary and 10 mg glipizide oral form are 63.61 and 27.7 µM-min/ml; 0.27 and 0.11 µM/l; 0.75 and 2 hrs; 2.48 and 9.33 hrs respectively. At the same time, in case of the co-administration of both the drugs through pulmonary route in COVID-19 population, the values obtained of AUC, Cmax, Tmax, and half-life of fluvastatin and glipizide are 55.1 and 117.2 µM-min/ml; 0.17 and 0.05 µM/l; 6.5 and 1 hr; 2.83 and 6.65 hrs respectively. So, if we administer both drugs through pulmonary route then Cmax, T_{max}, and AUC were increased by 10.54, 0.5 and 4.33 times respectively.

Conclusions: It can be concluded that the COVID-19 diabetic patients who take oral glipizide administration of fluvastatin through pulmonary route is safe. But, glipizide should not be administered through pulmonary route together with fluvastatin.

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Physiologically Based Pharmacokinetic Modelling of Hydroxychloroquine and Prediction of Pharmacokinetic Parameters after Administration through Oral and Pulmonary Route in COVID-19 Patients having Diabetes and Congestive Heart Failure Comorbidities

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Background & Rationale: The physiology-based pharmacokinetic modelling combines all the information on ADME and physicochemical properties of the drug molecule with the physiological parameters of a human population to simulate the drug concentration-time profile.[1] Coronavirus disease 2019 or COVID 19 spread all over the world in December 2019 and the WHO declared it a pandemic on 11th March 2020. COVID 19 spreads in humans of all age groups including both males and females and it is more deadly to the patients who are having comorbidities such as diabetes, COPD, cardiac problems, etc. Hydroxychloroquine (HCQ) is clinically used in the treatment of malaria, rheumatoid arthritis, and different intracellular infections for over 70 years. [2] In March 2020, the researchers found some *in vitro* activity of HCQ against COVID 19 in adults. [3] The aim of this study is the prediction of different pharmacokinetic parameters of HCQ after oral and pulmonary administration in covid patients having diabetes and congestive heart failure comorbidities.

Methods: In PK-Sim software the normal European population group of the age range of 20- 50 years, height range of 156- 191 cm, and weight range of 62- 89 kgs were created. Then the European population group of Covid patients of the age range of 40- 75 years, height range of 157- 189 cm, and weight range of 68- 86 kgs were created. Then the hydroxychloroquine (HCQ), Glimepiride, and Metoprolol molecule were generated by gathering all physicochemical and ADME information. Then the different administration protocols were generated for different molecules. At first, all the models were validated by the Normal European population. Then all the pharmacokinetic parameters were examined on the covid population in oral and pulmonary routes by the simulation of the covid population group with all administration protocols.

Results and Discussion: After performing all the simulation by using all the given parameter for the population all pharmacokinetics parameter such as AUC, C_{max}, T_{max}, MRT, half-life was obtained from the software for three molecules. In case of normal population validation with 200 mg oral HCQ dose we get the values of AUC= 191.82 µmol*min/l, C_{max}= 0.14 µmol/l, T_{max}= 3.75 h, MRT= 31.64 h, half-life= 24.60 h. In case of 200 mg pulmonary administration of HCQ in normal population we get the values of AUC= 225.60 µmol*min/l, C_{max}= 0.32 µmol/l, T_{max}= 0.20 h, MRT= 40.34 h, half- life= 35.67 h, and in case of 175 mg pulmonary administration of HCQ in normal population we get the values of AUC= 197.40 µmol*min/l, C_{max}= 0.28 µmol/l, T_{max}= 0.20 h, MRT= 40.34 h, half- life= 35.67 h. In case of normal population validation with 4mg oral Glimepiride dose we get the values of AUC= 10.97 µmol*min/l, C_{max}= 0.06 µmol/l, T_{max}= 1.15 h, MRT= 4.84 h, half-life= 8.49 h. In case of normal population validation with 20 mg oral Metoprolol dose we get the values of AUC= 13.32 µmol*min/l, C_{max}= 0.06 µmol/l, T_{max}= 1.35 h, MRT= 5.35 h, half-life= 4.53 h. In case of population of covid patients after administration of 200 mg oral HCQ tablet, 4 mg Glimepiride tablet and 20 mg Metoprolol tablet simultaneously we get the values of AUC= 150.00 µmol*min/l, C_{max}= 0.10 µmol/l, T_{max}= 4 h, MRT= 26.99 h, half-life= 19.48 h for HCQ, and we get the values of AUC= 11.82 µmol*min/l, C_{max}= 0.05 µmol/l, T_{max}= 1.30 h, MRT= 6.68 h, half-life= 9.72 h for Glimepiride, and we get the values of AUC= 15.17 µmol*min/l, C_{max}= 0.06 µmol/l, T_{max}= 1.45 h, MRT= 6.71 h, half-life= 5.97 h for Metoprolol. And in case of population of covid patients after administration of 175 mg HCQ pulmonary dose, 4 mg Glimepiride tablet and 20 mg Metoprolol tablet simultaneously we get the values of AUC= 152.35 µmol*min/l, C_{max}= 0.27 µmol/l, T_{max}= 0.15 h, MRT= 31.48 h, half-life= 29.20 h for HCQ, and we get the values of AUC= 11.82 µmol*min/l, C_{max}= 0.05 µmol/l, T_{max}= 1.30 h, MRT= 6.68 h, half-life= 9.72 h for Glimepiride, and we get the values of AUC= 15.17 µmol*min/l, C_{max}= 0.06 µmol/l, T_{max}= 1.45 h, MRT= 6.71 h, half-life= 5.97 h for Metoprolol.

Conclusion: From all the simulations we can conclude that there is a marked difference in AUC after administration of 200 mg HCQ through the oral route and pulmonary administration. But, 175 mg HCQ for the pulmonary route was equivalent to 200 mg oral dose. The Concurrent administration of HCQ had no effect on the pharmacokinetics of glimepiride, and metoprolol administered through oral route.

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Understanding the *In Vitro* Drug Release Behaviour of Tamoxifen and Piperine-Loaded Liposomes

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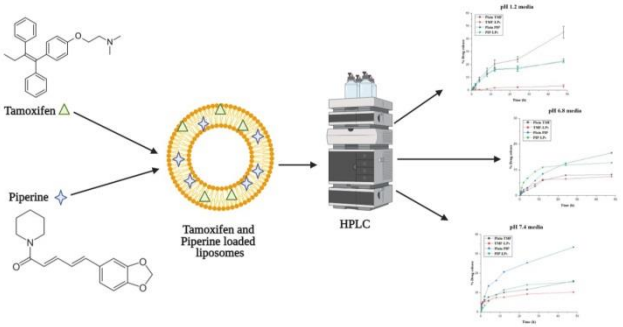
Background & Rationale: Tamoxifen (TMF) is used in the treatment and management of breast cancer. Despite being a promising drug for breast cancer treatment, tamoxifen faces certain biopharmaceutical challenges such as low solubility and poor bioavailability. To overcome these challenges, a combinatorial approach with the herbal bioenhancer drug like piperine would reduce the problems and may potentiate the anticancer activity. However, both drugs exhibit poor aqueous solubility hindering their therapeutic activity. Hence, incorporating these drugs into a lipid-based system like liposomes could enhance the desired therapeutic activity. Thus, the main aim of this study is to prepare tamoxifen and piperine-loaded liposomes (TMF-PIP-LPs). Further, the *in vitro* drug release behavior of TMF and PIP from TMF-PIP-LPs was determined in different pH media using the developed and validated RP-HPLC method.



Methods: A simple RP-HPLC method was developed and validated to simultaneously estimate TMF and PIP as per the ICH Q2 (R1) guidelines. TMF-PIP-LPs were prepared using soybean phosphatidylcholine, cholesterol, and DSPE-PEG_{2000} as lipid components. The prepared TMF-PIP-LPs were further characterized using SEM, FT-IR, DSC, and XRD. The *in vitro* drug release study of TMF and PIP from liposomes were studied in pH 1.2, 6.8, and 7.4 media at 37 ℃ using the dialysis bag method, and its drug release mechanism was determined.

Results and Discussion: The prepared TMF-PIP-LPs exhibited a spherical shape with a particle size of 103.93 ± 1.81 nm, more than 70 % drug entrapment efficiency, and more than 3.9 % drug loading. The *in vitro* drug release study from TMF-PIP-LPs exhibited sustained release behavior for both drugs for up to 48 hours compared with the plain TMF and PIP in pH 1.2, 6.8, and 7.4 media. Moreover, TMF and PIP release from the liposomes followed the Korsmeyer-Peppas release kinetic model with Fickian diffusion.

Conclusion: Tamoxifen and piperine-loaded liposomes were prepared to overcome the solubility issues of both drugs. Further, the *in vitro* drug release of TMF and PIP from liposomal formulation exhibited a sustained release in different pH media. Thus, the sustained release of liposomes may prolong the therapeutic activity.

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Understanding the In Vitro Drug Release Behavior of Etodolac from Mesoporous Silica Nanoparticles in Different pH Dissolution Medium

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Background and Rationale: In recent times, mesoporous silica nanoparticles (MSNs) have been explored as a drug delivery system because of their tunable features, such as controllable pore, high pore volume, and high surface area, which allows for high drug loading. However, drug loading is a critical step in MSNs-based formulations [1]. Hence, we have investigated the effect of various factors (solvent selection, drug MSNs ratio, loading period, and stirring speed) associated with the drug loading process into MSNs using Etodolac (ETD) as a BCS class II model drug. Furthermore, the influence on the aqueous solubility of the drug and the *in vitro* drug release (in various physiological pH conditions) was studied upon loading ETD into the MSNs.

Methods

A) Synthesis of MSNs: MSNs were synthesized by the sol-gel process. Briefly, 0.3 g of CTAB was dissolved in a mixture of 20 mL of ethanol, 45.6 mL of water, and 10.4 mL of ammonia solution with stirring, followed by dropwise addition of 1 mL of TEOS. After two hours of reaction, nanoparticles prepared as white precipitate were separated and washed with ethanol and water. The dried powder was calcinated at 600°C for five hours to obtain blank MSNs.

B) Drug loading: Effects of various parameters on ETD loading were studied using Taguchi DOE. Levels of each factor were selected as solvent (chloroform, ethanol, and methanol), the drug to MSNs ratio (1:1, 1:2, and 1:3), stirring speed (200, 400, and 600 rpm), and loading period (12, 24, and 36 h). Levels with maximum drug loading were selected for further study.

C) *In vitro* drug release: Suspension of 1 mg equivalent of ETD-MSNs was placed in a dialysis bag and kept in 50 mL of release media (with different physiological pH) at 37°C with stirring of 150 rpm. 1 mL of samples were collected at different time intervals and replaced with fresh media. The concentration of the drug in a sample was determined by a UV-Vis spectrophotometer. A similar procedure was followed for the plain drug.

Results and Discussion

The synthesized MSNs exhibited a particle size of less than 250 nm. Furthermore, the nitrogen adsorption study showed a pore size (diameter) of 3.58 nm with a high pore volume (0.65 cm^3/g) and a high surface area (899 m^2/g). Levels of parameters for optimum drug loading were selected based on Taguchi DOE. The prepared ETD-MSNs exhibited more than 15 % of drug loading. FTIR study ensured that there was no interaction between ETD and MSNs. DSC and XRD analysis confirmed the conversion of etodolac from crystalline to amorphous form when loaded into MSNs, which contributed to a more than 3-fold increase in aqueous solubility of the drug [2]. Controlled release of etodolac was observed from MSNs in release media of different pH (1.2, 4, 6.8, 7.4) with a maximum cumulative release (more than 95 %) in PBS pH 7.4 as shown in fig. 1. In addition, the *in vitro* drug release kinetic study followed Korsmeyer-Peppas kinetic model with the Fickian drug release mechanism. Further, the Kopcha model suggested the predominance of diffusion over erosion as a release mechanism. The hemolysis study confirmed the safety of the prepared MSNs (<2 %).

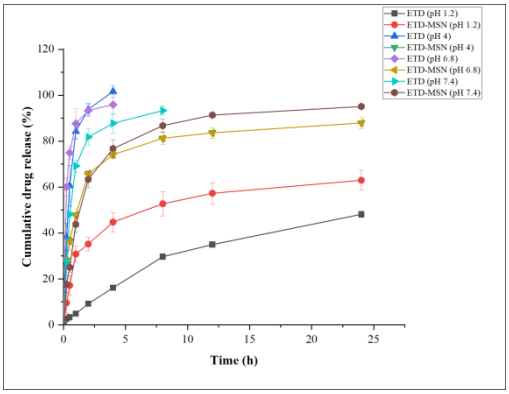

Fig. 1. In-vitro drug (etodolac) release in different pH media (1.2, 4, 6.8, 7.4)

Conclusion

In essence, the optimum ETD loading into MSNs was achieved using the Taguchi design. Drug-loaded MSNs showed enhanced aqueous solubility with controlled *in vitro* drug release behavior. The prepared MSNs were a safe carrier system for delivering the poorly water-soluble drug.

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Cross-linking of Gelatin Capsules and it's Correlation with Dissolution Studies

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Background and Rationale – Gelatin is the key raw material in manufacturing capsule shells. Cross linking phenomena is observed in stressed gelatin capsules; stresses may be humidity or light, and many excipients can trigger the cross-linking, particularly aldehyde compounds like formaldehyde and low molecular weight aldehydes, including sugars. The cross- linking can further result in the formation of a swollen, rubbery, water insoluble membrane (pellicle), which can hinder the disintegration and dissolution of the capsules. Hence, testing of contamination of excipients for formaldehyde and low molecular weight aldehydes is important [1].The present research work focuses on introducing crosslinking in gelatin capsules by exposure to various concentrations of formaldehyde for different time intervals, determining the extent of crosslinking, and correlating the impact of cross-linking on the dissolution rate of the capsules.

Methods – A) Preparation of crosslinked capsules- The capsules were crosslinked by exposing them to vapours of formaldehyde (various concentrations for different time periods). Capsules were then dried at 50°C in an oven to facilitate removal of residual formaldehyde**.**

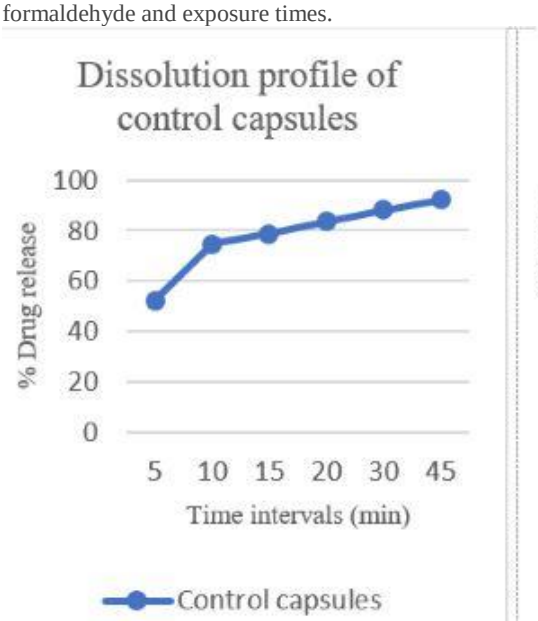
B) 2,4,6-Trinitrobenzene sulfonic acid (TNBS) Assay – The quantification of Ɛ-amino groups for determination of extent of crosslinking was carried out by UV- spectrophotometry based TNBS assay [2].

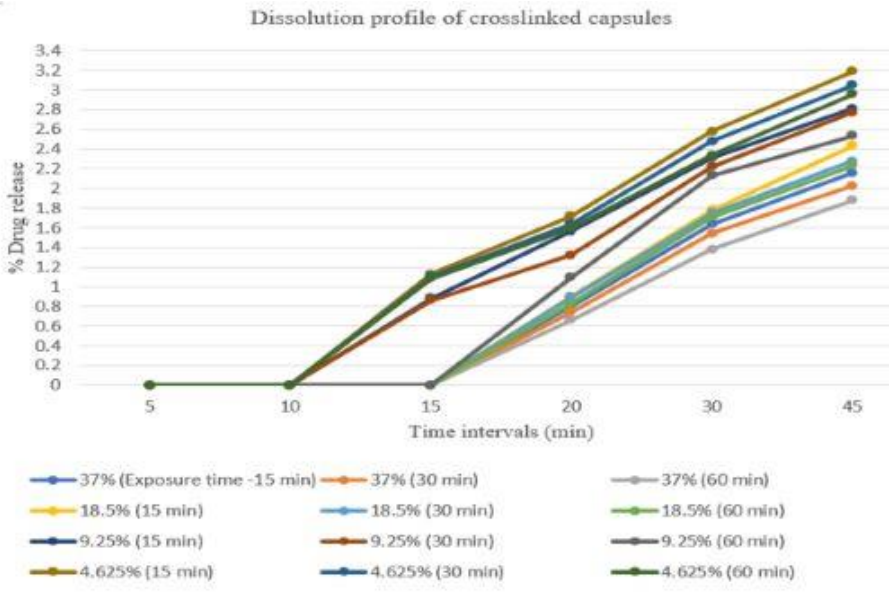
C) Dissolution studies – Dissolution studies were performed for control and crosslinked capsules filled with paracetamol, as a model drug. Paddle type apparatus (Type 1) as per IP was used; phosphate buffer (pH 5.8) was the dissolution medium; temperature was maintained at 37°C; with paddle speed of 50 rpm. At time intervals of 5, 10, 15, 20, 30 and 45 min, 10mL aliquots were withdrawn, and replaced with an equal amount of fresh medium. The paracetamol content in the withdrawn and suitably diluted aliquots was assessed by UV spectrophotometry (λ_{max} 243 nm), using phosphate buffer as blank. From the results, a correlation between extent of cross-linking and dissolution was assessed.

Results – Increase in percent crosslinking of gelatin capsules when exposed to various concentrations of formaldehyde for 15 minutes as compared to control capsules is given in table below:

Concentration of formaldehyde (%) [marketed concentration = 37% =X]	37 (X)	18.5 (X/2)	9.25 (X/4)	4.625 (X/8)
Increase in percent crosslinking	4.13%	2.55%	1.69%	0.85%

The graphs below depict the percent release of paracetamol from control capsules and gelatin capsules crosslinked with various concentrations of formaldehyde and exposure times.





The control capsules released paracetamol rapidly; 52% in the first 5 min, and at the end of 45 min, 92 % of the drug was released. However, a marked decrease in drug release is observed in crosslinked capsules. The percent drug release decreases with increasing concentrations of formaldehyde. There was no drug release observed for first 10 minutes of dissolution study of crosslinked capsules. The percent drug release increased gradually after 10 minutes, but at 30 minutes the percent drug release was very less as compared to control capsules thus indicating that the percent drug release was retarded due to gelatin crosslinking. During dissolution studies, pellicle formation was observed in crosslinked capsules which has led to decreased drug release.

Conclusion -

This study reveals that even low levels of formaldehyde exposure can lead to cross linking with marked decrease in dissolution profile of a drug, which may be attributed to pellicle formation.

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Isolation, Characterization of Banana Starch and its Evaluation as a Disintegrating agent in Dispersible Lornoxicam Tablet

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Objective: The present study was designed to isolate, characterize, and evaluate the disintegration properties of banana starch in dispersible Lornoxicam tablet formulation.

Methods: The alkaline extraction method used sodium hydroxide as a lye solution to isolate starch from unripe banana fruit. Starch was subjected to characterization for physicochemical properties, viscosity and flow properties, Fourier-transform infrared spectroscopy (FTIR) scanning electron, microscopy n(SEM), differential scanning calorimetry (DSC) and X-ray crystallography (XRD) study. The flow properties of starch were determined as per the standard procedure. Tablets were formulated with a wet granulation method using starch as a disintegrant, and the *in vitro* release characteristic of the prepared tablets was analyzed. Different concentrations of isolated starch were studied for disintegrating properties compared to corn starch.

Results: Studies indicate that starch obtained is qualitatively and quantitatively comparable to cornstarch. SEM, FTIR, DSC and XRD data confirmed the polysaccharide nature of the starch. The physicochemical properties of starch passed the prescribed evaluation tests for tablets. These tablets also confirmed the disintegration and dissolution specifications as per Indian Pharmacopoeia.

Conclusion: From the above study, it can be concluded that starch obtained from banana shows qualitatively and quantitatively good disintegration characteristics compared to corn starch. These tablets also confirmed a significant degree of dissolution as per the standards. Evaluations also specified that banana starch possesses acceptable disintegrating characteristics compared to corn starch and can be used as a disintegrant in tablet formulation.

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Amalgamation of Solid Dispersion and Melt Adsorption Techniques for Augmentation of Oral Bioavailability of Novel Anticoagulant Rivaroxaban

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Background & Rationale: A solid dispersion is made up of at least two separate components, often a hydrophilic inert carrier/ matrix and a lipophilic drug. The concept of solid dispersion adsorbate (SDA) was developed to address issues such as difficulties in grinding, solubility issues, insufficient flow, poor compressibility, reduced repeatability of physicochemical properties, instability of the drug and vehicle, and difficulty in scale-up **(1).** The aim of this work was to create SDAs of BCS class II drug- Rivaroxaban (RXN) using a combination of solid dispersion and melt adsorption techniques and evaluate their ability to improve solubility and dissolution. A 2-factor, 3-level experimental design was employed for statistical optimization, wherein the impact of independent variables [amount of PEG 4000 (X1) and amount of Neusilin US2 (X2) on the dependent variables [time required for 85% drug release (Y1) and saturated solubility (Y2) was assessed.

Methods: A) Formulation of SDA in directly compressible tablets: SDA of RXN was prepared by a fusion method **(2)**. In this method, RXN was sifted through sieve number 100. The carrier (PEG 4000) was melted in a porcelain dish and heated till its melting point (**57-63°C**) on a hot plate & then RXN was dispersed into the melted carrier mass with constant stirring to form solid dispersion. Further, the adsorbent (Neusilin US2) was added and stirred until the blend is converted into a free-flowing powder. The SDA was then passed through sieve number 40. Then tablets were prepared by **direct compression** method using 10 mm punch in tablet compression machine with compression force of 10 kN.

B) *In vitro* drug release study: *In vitro* release of pure RXN, marketed tablets (Xarelto®), and directly compressible tablets were carried out using **USP type II** apparatus at **75 rpm** by using acetate buffer (pH 4.5; 900 mL) containing 0.4% sodium dodecyl sulfate as dissolution medium with a temperature setting at **37 ± 0.5°C (3).** Aliquots were withdrawn at a periodic time interval during each exposure and after suitable dilution was assessed for drug release and was analyzed at **248 nm** using UV spectroscopy after filtering through a Millipore filter (0.45 µm).

Results and Discussion: The t_{85} for pure RXN, marketed tablets, and directly compressible tablets were found to be 59.13 min, 20.16 min, and 19.22 min. The highest value of t_{85} for RXN was attributed to its poor aqueous solubility and crystalline nature. t_{85} for directly compressible tablets were ($P < 0.05$) lower than the value for RXN, which could be attributed to improved wetting due to the presence of hydrophilic carrier PEG 4000. t_{85} for a marketed tablet was significantly ($P < 0.05$) lower than the value for pure RXN, which could be attributed to the presence of hypromellose, sodium lauryl sulfate, and croscarmellose sodium. The aqueous solubility of pure **RXN** was found to be **0.012 ± 0.009 mg/mL** whereas the aqueous solubility of **RXN-SDA tablet** was found in the range of **0.032 ± 0.009 mg/mL**. The highest RXN solubility noticed was 0.041 mg/mL, which is 3.4 times higher as compared to the solubility of pure RXN.

Conclusion: This work demonstrated the amalgamation of solid dispersion and melt adsorption technologies in formulating RXN-SDAs, wherein the ternary system comprised of RXN (insoluble drug), PEG 4000 (hydrophilic carrier), and Neusilin US2 (high surface area adsorbent). A DoE approach was employed in the optimization of RXN-SDAs by using 3^2 full factorial designs. RXN-SDA blends exhibited better flow properties and higher solubility as compared to pure drugs. RXN-SDA tablets exhibited a lower t_{85} in comparison to the pure drug, marketed tablets, and directly compressible tablets exhibited improved bioavailability and rapid onset of action in comparison to the pure drug and marketed formulation.

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Combinatorial Topical Liposomal Gel for Treatment of Psoriasis: Formulation Optimization and In Vitro Release Studies.

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Background and Rationale: Psoriasis is an autoimmune disease caused due to dysregulation of autoimmune cells which leads to the formation of hyperproliferation of keratinocytes. Various treatment options are available like topical therapy, phototherapy, biologics, a combination of therapy, oral delivery, and herbal preparations, but due to the side effects, bioavailability issues, first-pass metabolism, comorbidities, and restrictions cause hindrances in taking the treatment. The aim of the study is to formulate, optimize and evaluate the liposomal gel consisting of Apremilast and babchi oil. This formulation is expected to enhance the bioavailability and efficacy of the drug and cause increased penetration through the stratum corneum.

Methods:

A] Pre-formulation Studies: The purity of the drug was determined by FTIR, XRD, and DSC. The solubility of drugs in solvents, lipids, surfactants, and co-surfactants was checked. The melting point of Apremilast and boiling point of babchi oil were determined. The standard curve was plotted in various solvents.

B] Optimization (2^4 Factorial Design): Four factors that were selected included concentration of lipid, concentration of surfactant, concentration of co-surfactant, sonication time, and responses for these factors are particle size and entrapment efficiency.

C] Preparation of Liposomal el: They were prepared by the ethanol injection method in which the organic phase containing both API, lipid, and cholesterol, neem oil in solution, was injected rapidly in the aqueous phase which includes phosphate buffer (pH 6.8), surfactants and co-surfactants. After the formation of liposomes, the solvent was removed using a Rotary evaporator. This solution was injected in 1% Carbopol gel base, with propylene glycol, glycerin, preservatives, and anti-oxidant to get a smooth gel.

D] Characterization of Liposomal Solution and Gel: FTIR, XRD, SEM, and DSC studies were done followed by determination of particle size, zeta potential, and drug content. Diffusion study of liposomal solution in 0.1N HCL, phosphate buffer pH 6.8, pH6.5, pH 7.4 with 0.15% SLS, and buffer pH 5.4 with DMSO was analyzed at 229nm and 265nm, respectively. Texture profile, viscosity, pH, and drug content were carried out. Diffusion of gel was studied in phosphate buffer pH 7.4 and assessed spectrophotometrically at 229nm and 265 nm respectively.

E] Cell Line Study: This study was carried out to check the cytotoxicity, anti-proliferative, and anti-psoriatic activity of formulation on HaCAT.

Results and Discussion: After all pre-formulation studies, optimized formulation F9 showed a particle size of 84.62nm, and entrapment efficiency was found to be 92.53, and 89.24 for Aprimelast and Babchi oil, respectively. Drug release of plain drug Aprimelast and Babchi oil was compared with a liposomal solution in 0.1N HCL, phosphate buffer 7.4 with 0.15% SLS showing the maximum prolonged release for Apremilast and for babchi oil it showed 87.65-92.04% release. Drug release in buffer pH 5.4 with DMSO for Apremilast and babchi oil was found to be 96.82% and 90.04%, respectively. Drug release of liposomal solution in buffer pH 6.8 and 6.5, showed improved percent release as compared to both plain drugs. Gel characteristics like gel strength, firmness, spreadability, and viscosity were compared with 1% Methotrexate marketed gel and all the parameters were found to be in range with the standard. Drug release of both Aprimelast plain gel and babchi oil plain gel when compared with liposomal gel in phosphate buffer 7.4 showed the release for maximum time compared to both plain gels. Cell line studies reported that the formulated liposomal gel is non-cytotoxic and shows anti-proliferative activity. The formulated gel was used on IMQ-induced psoriatic cells and was compared with standard Asiaticoside and showed a similar potency for anti-psoriatic activity.

Conclusion: The formulation was successfully optimized and evaluated. it showed an improvement in efficacy, It is easy to apply, will protect the skin, and reduce the dryness of the skin. This topical liposomal gel may be used to effectively treat mild to moderate psoriasis.

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Design and QbD based Development of Orodispersible Tablet comprising Co-Crystallized Anti-Migraine Ddrug

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Background and Rationale: Migraine is a common headache disorder characterized by recurrent attacks of moderate or severe intensity. Early diagnosis and treatment of migraine improves the quality of life of patient. More than 60% of synthesized drugs and 40% of drugs in development are poorly soluble and exhibits bioavailability issues. Over the last decade, there has been a growing interest in pharmaceutical cocrystal design, which appears to be a promising strategy for improving the bioavailability of drugs with low aqueous solubility. Cocrystallisation of drugs with coformers is a promising method for modifying the solid-state properties of the drugs, such as **solubility** and **dissolution**. Thus, based on the thorough literature review and need we aimed to prepare cocrystals of poorly water-soluble drug and to develop a suitable formulation for the treatment of Acute Migraine.

Methods: Drug selection was justified based on the data obtained through in silico screening using SwissADME, ADMET and Molinspiration. Cocrystals of the selected drug were prepared by Solvent Evaporation method. The solubility and melting point of the crystalline phase was determined. The potential cocrystals was characterized by IR, DSC and XRPD. Other pharmaceutical properties like **solubility** and **dissolution rate** were also evaluated. Orodispersible tablets of the prepared cocrystals were formulated, optimized using QbD approach and evaluated.

Results and Discussion: The cocrystals that were prepared revealed the variation in melting point and solubility. The analysis of IR indicated the shifting of characteristic bands of pure drug. The changes in 2θ values in XRPD was observed. DSC spectra of cocrystals indicated altered endotherms corresponding to the melting point. The proposed technique was found to enhance the drug **solubility by 7 folds**. The cocrystals exhibited a faster dissolution **rate of** about **54%** increase as compared to **pure drug** and **20% increase** as compared to **marketed formulation** as shown in figure 1. The use of Box-Behnken response surface methodology with three factors and two levels helped to found the relationship between factors and responses. Seventeen formulations offered by the Box–Behnken design through Design Expert Software (version 11) were prepared. All the formulations were characterized by parameters such as hardness, thickness, weight variation, friability, dissolution and disintegration time. The final formula was prepared based on predicted and observed values. The prepared batch was compared with dissolution rate of pure drug and marketed formulation as shown in figure 2. The orodispersible tablets of cocrystals were successfully prepared by direct compression method using superdisintegrant with improved disintegration time and dissolution rate.

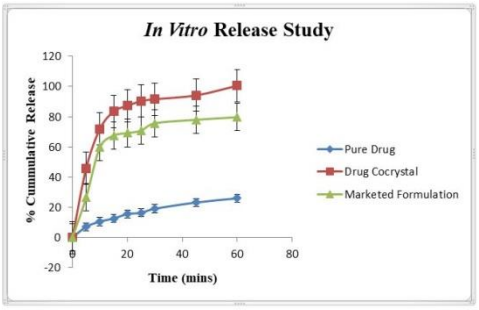

Figure 01: Comparison of *In Vitro* Release Study of Pure Drug, Drug Cocrystal and Marketed Formulation

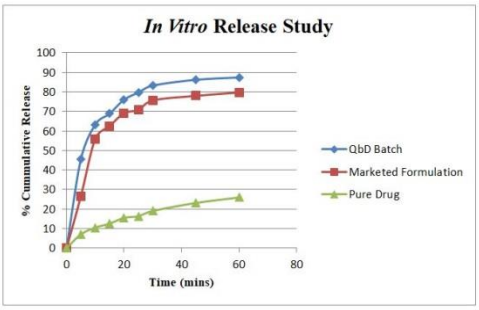

Figure 02: Comparison of *In Vitro* Release Study of QbD batch, Marketed Formulation and Pure Drug

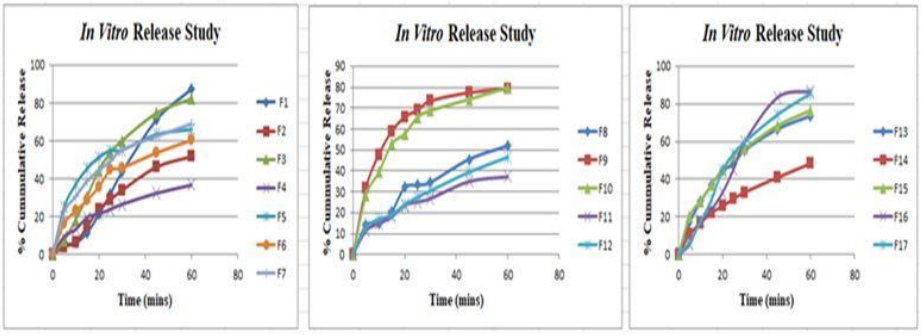

Figure 03: *In Vitro* drug release for formulation F1-F17

Conclusions: The model drug cocrystal with modified properties was prepared with a suitable coformer and formulated as orodispersible tablets having faster disintegration and greater dissolution rate. Thus, it can be concluded that the optimized formulation with desirable parameters can be obtained by Box–Behnken design with the response and variable relation.

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Design, Development and Evaluation of Antifibrinolytic Gel for Dental Purposes

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Background: The objective of present work is to formulate and evaluate Antifibrinolytic gel of Tranexamicacid (TXA) for dental application as to increase the local residence time and to give higher efficacy. Further, it is also aimed to evaluate the gel for ascertaining the required performance, especially in case of hemophiliacs. Tranexamic acid has a proven antifibrinolytic affect and there are no gel formulations currently available in market. As such mouthwashes are used for post procedural bleeding as well as dental and gingival bleeding which have its limitations; so there is requirement to formulate a gel formulation.

Methods: In the present work formulation was developed after screening of various gelling polymers like HPMC, Guar gum, Gellan gum, Sodium CMC, and Carbopol with their different grades. Among these polymers Carbopol was selected as best gelling polymer and further optimized. Dispersion method was used for the preparation of Carbopol gel. Batches T1-T12 and F1-F8 were prepared as preliminary batches and optimized batches respectively. All the batches were evaluated. The dissolution test was carried out using the standard USP apparatus II with some modifications (Marzouk, 1999) by placing a modified paddle over a watch glass and using a pH 6.8 buffer solution. 300 mL phosphate buffer pH 6.8 was used as the dissolving medium. The temperature was kept constant at 37.50°C. The rotational speed was 50 revolutions per minute. 5ml samples were extracted at specified intervals of 5, 10, 15, 20, 25, 30, minutes and replaced with fresh, 37.5°C buffer solution each time. The samples were then derivatized and spectrophotometrically analysed at 567 nm. All experiments were carried out in triplets (n = 3). The amount released was determined using the regression line of a standard curve of the drug created in the same medium. The residence time of optimized formulation was checked with the help of falling film technique.

Results: After evaluating the batches T1-T12 Carbopol 940 and Carbopol 974 were selected for further optimization. Batch F2 which was considered as optimized batch (0.5 % of Carbopol 940 showed satisfactory result % CDR of 86.95±0.83 at 25 minutes and all other parameters such as pH (6.78), Viscosity (25,728), spreadability (5.5), % Extrudability (96%), Bio-adhesive strength (3430 dyne/cm2) and retention time were optimum.

Conclusion: Gel of desired performance was made with help of dispersion method.

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Development and Optimization of API Loaded Polymeric Micelles Using Factorial Design : *In Vitro* Diffusion Study & *Ex Vivo* Permeation Study

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Background and Rationale: Olmesartan medoxomil (OM) is an antihypertensive agent belonging to the class of angiotensin receptor blockers (ARB's). It is a prodrug and belongs to BCS class-II and when administered orally, undergoes ester hydrolysis in the GIT to the active metabolite olmesartan. The drug has low solubility and also suffers from p-gp efflux resulting in low oral bioavailability of 26% [1]. Thus, a dual strategy was implemented to increase the solubility using polymeric micelles as a nanoscaled drug delivery system and use of a p-gp efflux inhibitor such as soluplus in the formulation to improve the bioavailability of OM.

Methods: A. Preparation of Olmesartan menoxodil loaded polymeric micelles (PMs): PMs were prepared using solvent injection method using acetone as a solvent and optimized using 3^2 factorial design. The prepared polymeric micelles were further evaluated for various pharmaco-technical parameters such particle size, entrapment efficiency & zeta potential.

B. *In vitro* drug diffusion study: The diffusion of drug from PMs was determined using the dialysis technique at the physiological pH. The study was carried out at 37±0.5◦C with an agitation speed of 50 rpm initially for 2 hrs in SGF followed by SIF for up to 24 hrs with 250 ml being the volume of the respective release medium. The sample after suitable dilutions were analysed spectrophotometrically at specified wavelength.

C. *Ex vivo* permeation study: Ex-vivo permeability study was carried out using intestinal section of rats. The tissue was placed in an organ bath with continuous aeration at 37◦C. The receptor compartment was filled with 200ml of Krebb's solution. The samples were analysed spectrophotometrically for the content of API.

Results and Discussion: Polymeric micelles of Olmesartan menoxodil comprising soluplus were successfully developed for oral delivery using solvent injection method. Soluplus is polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft copolymer, a non-ionic amphiphilic excipient with solubilizing and p-gp inhibiting activity. The micelles formulation was optimized by 3^2 factorial design considering surfactant and drug concentration as the independent variables and corresponding dependent response variables being particle size and entrapment efficiency. Optimized PM exhibited particle size of 154 ± 3.8 nm, entrapment efficiency of 89.28 ± 4.42 %, & zeta potential of -5.69 ± 0.9 mv. At the end of 4hrs pure drug showed 98±1.1 % drug release as it could freely diffuse in its solution form whereas the optimized formulation showed a 70 ± 1.3% drug release over a period of 24hrs. In in-vivo study, after oral administration, Olmesartan pure suspension showed the Cmax value of 35.63±1.1 µg/mL while polymeric micelles showed Cmax of 52.87±1.3 µg/mL at the end of 4hr. The Tmax of drug reduced by 2hrs due to improved permeability of micelles compared to that of pure drug (6hrs). The hydrophilic carrier system could be attributed to Olmesartan successfully achieving increase in the Cmax and AUC values in comparison to the pure drug i.e. From 119.97±2.3 hr*µg/mL to 225.97±1.8 hr*µg/mL. The apparent permeability of pure drug was found to be 0.0008 while that of formulation was found to be 0.0016 which is twice to that of the pure drug. The permeability studies revealed that the p-gp efflux had been inhibited by soluplus and hence an increased bioavailability was observed.

Conclusion: In the present study the potential of polymeric micelles in oral drug delivery of Olmesartan medoxomil to treat hypertension was investigated for the first time. Conversion into PM resulted in particle size lower than 200nm greatly helped to increase the effective surface area of these particles providing increased dissolution and enhanced absorption of Olmesartan medoxomil in the systemic circulation through the endocytic pathway. The addition of p-gp efflux inhibitor 'soluplus' also contributed to the increased permeation of Olmesartan.

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Enhancement in Rate and Extent of Dissolution of Niclosamide: A Promising Approach for Its Repurposing

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Background & Rationale: Niclosamide (NCL) is an anthelmintic drug belonging to BCS class II. In past few decades, a plethora of pharmacological activities have been discovered for this old molecule. NCL exhibits significant potential in treating cancer, bacterial and viral infections including SARS-CoV-2, metabolic diseases such as Type II diabetes, non-alcoholic steatohepatitis, non-alcoholic fatty liver disease, artery constriction, endometriosis, neuropathic pain, rheumatoid arthritis, sclerodermatous graft-versus-host disease, and systemic sclerosis. Clinical efficacy of NCL is critically limited by its meager aqueous solubility (1.6 µg/ml at 20°C) and hence poor oral bioavailability (10%). The aim of this work was to enhance the rate and extent of dissolution of NCL using commercially scalable approaches such as amorphous solid dispersions (ASD) and inclusion complexes.

Methods: **A) Preparation of ASDs:** The ASDs were prepared using fusion method. Appropriate amounts of NCL and polymer (PEG 1500/4000/6000/8000/Gelucire 44/14) in different weight ratios like 1:2, 1:5 and 1:10 were heated at a temperature of 70±5°C. NCL was dispersed in the molten polymer by constant stirring. The resulting dispersions were cooled rapidly, pulverized and sieved through 40# sieve.

B) Preparation of inclusion complex of NCL: Based on phase solubility studies, the molar ratio of 1:1 was selected for preparation of inclusion complexes between NCL and sulfobutylether-β-cyclodextrin (SBECD). Physical mixing, co- grinding, kneading and co-evaporation methods were employed for the complex preparation.

C) Characterization of ASDs and complexes- The formulations were characterized by FTIR, DSC and PXRD studies.

D) *In vitro* Dissolution studies: The ASDs and complexes were subjected to *in vitro* dissolution studies using USP type- II apparatus. Dissolution medium comprised 900 ml of pH 7.4 phosphate buffer with 1% Tween 80 maintained at 37±5°C by stirring at rpm of 100 rpm. Aliquots were withdrawn at 15, 30, 45, 60, and 90 min and replaced with fresh medium. Aliquots were filtered, diluted suitably and subjected to UV spectroscopic analysis at 370 nm.

E) Tablet formulation development and evaluation: Directly compressible tablet formulation of NCL-SBECD kneaded complex was developed using suitable quantities of Avicel PH102, croscarmellose sodium, talc and magnesium stearate. Resulting formulation was evaluated for average weight, friability, hardness, disintegration time, drug content, and in vitro drug release.

Results and Discussion: Solid state characterization studies of NCL ASDs and complexes indicated partial or complete loss of crystallinity of the drug in its ASD and complex formulations. All the formulations showed better and faster drug dissolution compared to neat drug. SBECD complex prepared by kneading method showed 100% drug release within 15 minutes. Among ASDs, the one prepared with PEG 4000 in 1:10 ratio showed the highest drug release of 57.55±1.23% in 90 min followed by PEG 8000 (1:5) (55.20±1.34%), PEG 6000 (1:5) (51.57±1.81%), and lastly PEG 1500(1:10) (39.77±1.06%). ASD of NCL prepared with Gelucire 44/14 in 1:5 ratio exhibited 52.13±0.57% drug release in 90 min. Extreme hydrophilic nature of SBECD, formation of inclusion complex between NCL and SBECD, and loss of crystallinity of NCL could have attributed to the most significant enhancement in rate and extent of dissolution of NCL from its kneaded complex. Tablet formulation containing the complex showed more than 90% of drug release within 15 min.

Conclusion: The ASDs and inclusion complexes of NCL led to significant improvement in rate and extent of dissolution of NCL. The NCL-SBECD kneaded complex showed the highest rate and extent of drug dissolution and was successfully formulated into tablets. Such a formulation is expected to appreciably improve the oral bioavailability of NCL and hence its repurposing potential.

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Enhancement of Dissolution Rate of Selexipag through Formulation of SMEDDS Dosage Form

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Background and Rationale: The objective of the present investigation was to develop and evaluate self-microemulsifying drug delivery system (SMEDDS) for improving the delivery of a BCS class II drug selexipag. Selexipag is an agonist for the prostacyclin receptor and has low bioavailability of around 49%. There are various methods available to enhance the dissolution rate of BCS Class II drugs like micronization, solid dispersion, salt formation, self-emulsification, spray drying, cyclodextrin complexation, etc. In present work formulation of an oral SMEDDS is done to improve dissolution rate and thereby improve bioavailability of Selexipag. SMEDDS is the mixture of drug, oil, surfactant and cosurfactant, which is thermodynamically stable dosage form. It has many advantages out of which main one is it can be easily scaled up and commercially feasible.

Method: In this present study phase titration method was used for SMEDDS development. From the solubility study of drug in oil, surfactant and cosurfactant; capryol 90, cremophor EL and transcutol HP were selected respectively. Ternary phase diagram was plotted to identify the area of microemulsion existence. A simplex centroid mixture design was used to determine the individual and interaction effect of three independent variables – amount of oil (X1), amount of surfactant (X2) and amount of cosurfactant (X3) on three dependent variables – emulsification time (Y1), % cumulative drug release in 30 minutes (Y2) and globule size (Y3) and 9 different batches (B1 to B9) were prepared for optimization.

Results and Discussion: From all batches, batch B3 formulated using 15% oil, 57.5% surfactant and 27.5% cosurfactant showed emulsification time of 25 sec, % drug release of 92.33% and globule size of 72.84 nm which is desirable and the formulation developed was found to be thermodynamically stable. In-vitro release of prepared SMEDDS was compared with pure API, and it showed higher dissolution rate in comparison to pure API.

Conclusion: Thus, the formulated and optimized SMEDDS enhanced the dissolution rate of drug and thereby enhance the bioavailability of selexipag which will be effective in treatment of Pulmonary Arterial Hypertension.

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Evaluation of Cefdinir Monohydrate Loaded Gel with Solid Lipid Nanoparticle

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Background and Rationale: Cefdinir Monohydrate is a BCS Class IV Drug. The goal of this study was to develop a suitable drug delivery system for it. It is an antibiotic that is used to treat pneumonia, ear infections, strep throat, and cellulitis. It is a less preferred option for pneumonia, otitis media, and strep throat, but it may be used in people who have a severe penicillin allergy. It is taken orally. Cefdinir Monohydrate has an oral bioavailability ranging from 16% to 21%. Thus, using the probe sonicator technique, solid lipid nanoparticles were prepared and then incorporated into the Carbopol gel matrix.

Methods: A) Probe Ultrasonication technique: Tween 20 was added after the GMS had been melted. After that, the drug was dissolved in DMSO and added to the lipid phase above. With constant stirring and heating at around 70°C, an aqueous phase containing various concentrations of Carbopol 934 was created in 20 mL of distilled water, to which the lipid phase was gently added. After 3 minutes of agitation at 2000 rpm, the prepared solution was ultrasonicated with a probe sonicator. For ultrasonication, the frequency was set to 0.5 for 30 minutes at 45 percent amplitude. After sonication, the dispersion was diluted with 80 mL of distilled cold water and stirred continuously for 15 minutes. Cefdinir Monohydrate was suspended ultrasonically in a stable SLN suspension.

B) Solubility Studies (Shake Flask Method): Solubility of Plain drug and optimized formulation were estimated in water. In this excess amount of drug and formulation was added in water.it wad roated at constant speed in an orbital shaker for 24hrs and filtered .and diluted with water, the absorbance was determined at 285nm, solubility was calculated using calibration curve.

C) Preparation of Cefdinir Monohydrate Loaded SLN Gel: Optimal SLN dispersion was successfully incorporated into an aqueous gel base containing Carbopol 934. Carbopol 934 was weighed and dispersed in a small amount of distilled water to create an aqueous dispersion, which was then allowed to hydrate for 4 to 5 hours. To make the aqueous dispersion comparable to 1 percent Cefdinir Monohydrate, glycerol (10% w/w) was added. At a speed of 1200 rpm, an overhead stirrer was used to add triethanolamine to the dispersion. The gel was left to stand overnight to remove any trapped air.

D) *In vitro* SLN Gel release studies: The amount of drug released from each formulation was determined using a modified Franz diffusion cell. For this purpose, a membrane with a pore size of 2.4 nm (cellophane membrane 70 Hi-Media, India) and a surface area of 3.14 was installed on the diffusion assembly. Because this diffusion cell has two compartments, the receptor chamber was filled with 25 ml of a phosphate buffer solution with a pH of 0.05M and stirred with a magnetic stirrer at 70.5°C at 750 rpm, while the donor chamber was filled with SLN gel. After the required interval, a 5-ml sample was taken from the receptor side through the tube, and the same volume of phosphate buffer solution was added. samples were diluted and analysed at 285 nm using a spectrophotometer.

Results and Discussion: The Solid lipid nanoparticles were prepared from 117.9 nm size ranges. The drug entrapment efficacy and zeta potential of prepared SLN were found to be 92.90±0.3 percent and -40.0 to -45.0 mV. The reduced particle size increased the saturation solubility due to the increased surface area of the reduced particles. Saturation solubility of plain drug is 0.087 mg/ml and SLN formulation is 1.051 mg/ml, therefore saturation solubility of SLN Formulation was increased than plain drug due to size reduction of particle and concentration of stabilizer which increases saturation solubility of drug in solid lipid nanoparticle.

In vitro drug release of SLN was 36% in the first hour, compared to 10.5 percent for gel loaded with pure drug, indicating a significant difference. Furthermore, at the end of 24 hours, the drug was released 100 percent in gel loaded with SLN but only 64 percent in gel loaded with pure drug. As a result of the formulation of cefdinir monohydrate into solid lipid nanoparticles, the drug was able to release almost completely from the formulation, demonstrating the superiority of SLN over pure drug.

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Evaluation of *In Vitro* Drug Release and *Ex Vivo* Permeation of Antibiotic from Polymeric Nanoparticles.

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Background and Rationale: Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria change in response to the use of these medicines. These bacteria may infect humans and animals, and the infections they cause are harder to treat than those caused by non-resistant bacteria. Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming difficult, and sometimes impossible, to treat as antibiotics become less effective. A novel method to overcome such resistance is to incorporate the antibiotic in polymeric nanoparticles. There are several polymers available naturally having antibacterial activity themselves. Some of these polymers are chitosan, poly-ε-lysine, quaternary ammonium compounds, polyethylenimine, and polyguanidines. Incorporating the antibiotic in these polymeric Nanoparticles will have a synergistic effect and also a sustained release of drug hence the dose of the drug can also be reduced. Due to this synergistic action bacterial infections can be effectively treated.

Methods: **A) Formulation of Antibiotic Incorporated Polymeric Nanoparticles and incorporation of Nanoparticles into gel:**

Chitosan was dissolved in 1% Acetic Acid. Sodium TriPolyPhosphate (TPP) was dissolved in water. Antibiotic Drug was then added to the TPP Solution. TPP and Antibiotic solution was then added drop-wise to the chitosan solution with constant stirring until nanoparticles were formulated. Nanoparticle incorporated gel were prepared by using Hydroxy Propyl Methyl Cellulose (HPMC) K100M as gelling agent.

B) *In vitro* and *Ex Vivo* release from Polymeric Nanoparticles:

***In Vitro* Studies.** The prepared Polymeric Nanoparticles suspension was evaluated for i*n vitro* release study where 5 ml of nanoparticle suspension was transferred to dialysis bag. The dialysis bag was suspended in a media volume of 200 mL PBS, pH 7.4, at 37°C and rotated at 100 rpm. At scheduled intervals, 2 ml of the medium was collected for the HPLC analysis. The same volume of fresh PBS buffer at the same temperature was added immediately to maintain sink condition.

***Ex vivo* Studies.** Goat skin was used for experimentation. Skin was prepared and mounted on Franz diffusion cells between receptor compartment and donor compartment with stratum corneum facing the donor compartment. The receptor compartment was filled with 20 ml phosphate buffer pH 7.4 continuously stirred at 100rpm and temperature was maintained at 37 ± 0.5 ºC. 2 gram of gel was applied to the skin surface. Sample was withdrawn after every 1 hour and the same amount was replaced to maintain sink condition. The Study was performed for 8 hours.

Results and Discussion: The *in vitro* release study showed that 90% of the drug was released in 8 hours. And *ex vivo* studies showed that 49.72 % of drug was permeated through the skin after 8 hours.

Conclusions: Due to encapsulation of the antibiotic drug in nanoparticles and incorporation of the prepared nanoparticles in gel the release of the drug was sustained for a longer period of time and since the drug is incorporated in polymeric nanoparticles where natural polymers themselves have antibacterial activity there will be a synergistic effect, thereby reducing dose and hence problem of antibiotic resistance can be overcome.

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Formulation and Evaluation of Dosage Form for Management of Kidney Stones

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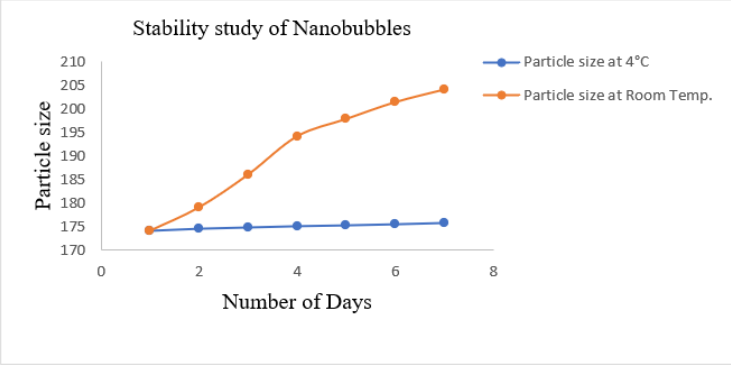
Background and Rationale: The objective of the present research was to develop formulation of dosage form for management of kidney stones. To achieve the objective sodium hexametaphosphate nanobubbles were prepared so as to deliver the drug at the target site. Currently, available treatments for kidney stones takes about 6-12 months to get rid of stones also, other options are surgical procedures. To overcome the drawbacks of surgical procedures and to decrease the treatment duration current research was carried on developing the nanobubbles of drug. Sodium hexametaphosphate is calcium ion chelator which forms complex with Ca2+ ions and dissolves it; as 80-90% kidney stones are calcium based hence, drug is capable of dissolving the stones. Whereas, nanobubbles formulation consists of gas core which gets burst off in contact with ultrasound so, nanobubbles along with the drug gives synergistic effect for treatment of kidney stones.

Method: In this current study thin film hydration was employed for nanobubbles development. After preliminary study based on three factors box-behnken design was used for optimization. A Box Behnken design was employed to determine the individual and combined effect of three independent variables - Concentration of phosphatidylcholine (X1), Concentration of stearic acid (X2) and Sonication time (X3) on three dependent variables – Particle size (Y1), % Drug release (Y2) and % Entrapment efficiency (Y3). All the factors were evaluated in three levels and 13 different batches were prepared for optimization.

Results and Discussion: The best result was found in optimized batch C8. Optimized batch showed particle size 174nm, Drug release 94%, Entrapment efficiency 73.2%. Based on the design space generated using the results of 13 batches for optimization, a check point batch was prepared for validation of design space. The results of checkpoint batches were satisfactory as the predicted values were close to experimental values. Check point batch was prepared by taking X1 (81.65 mg), X2 (5.57 mg), X3 (3min). Results of checkpoint batch were particle size was 223.7nm, % Drug release 93.18 and % Entrapment efficiency 63.4.

Conclusion: Thus, nanobubbles formulation was optimized. Stability of nanobubbles of optimized batch was performed at 4°C and at room temperature for 7 days and particle size was measured daily. Stability issue was not observed at 4°C as variation in size was not more; whereas, at room temperature size was increased with increase in days hence for more stability nanobubbles should be stored at 4°C.Also, even for long term storage final formulation should be lyophilized powder. Optimized batch (C8) was lyophilized and the final product in powder form was obtained which can be reconstituted with water for injection to generate the nanobubbles before administration.



Stability study of nanobubbles

Lyophilized product of optimized batch (C8)

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Formulation of Transdermal Cubosomal Drug Delivery System of Raloxifene to Improve its Solubility and Bioavailability using QbD Approach

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Background and Rationale: Raloxifene HCL (RLX) is a class of selective estrogen receptor modulator (SERM) which is often suggested for osteoporosis and to postmenopausal women at high risk to breast cancer. Limitations of RLX being its low water solubility (0.000512 mg/ml), low oral bioavailability (2%) owing to significant presystemic metabolism.[1] The aim of the work was to formulate RLX-loaded cubosomes, an alternate transdermal delivery of RLX to overcome its limitations. Cubosomes, when given topically provides an optimistic approach for bioavailability enhancement for poorly-water soluble drugs by directly entering in the lymphatic system and avoiding extensive first pass metabolism. Also, cubosomes being cuboidal in shape can encapsulate different drug molecules with hydrophilic, hydrophobic and amphiphilic properties.[2]

Methods: A) Preparation of RLX-loaded cubosomes: The RLX-loaded cubosomes was prepared using ethanol injection technique followed by microfluidization method. The formulation was optimized using QbD-based 2^3 factorial design.

B) *In vitro* drug diffusion study: Diffusion of RLX from cubosome was determined using dialysis bag method. 5ml of cubosomal dispersion was placed in each dialysis bag, sealed at both the ends and tied to the paddles of the dissolution vessels.The study was carried out at 37±0.5◦C with an agitation speed of 50. The sample after suitable dilutions were analyzed spectrophotometrically at specified wavelength.[3]

C) *Ex vivo* permeability study: *Ex vivo* permeability studies were carried out using a vertical Franz cell apparatus. The abdominal skin of excised female Wistar rat was collected and subjected to cleaning. The cleaned skin was mounted in the diffusion cell between the donor and receptor compartment. The prepared cubosomes was placed upon the cleaned and dried skin. The whole setup was fixed over a magnetic stirrer, and the receptor compartment solution was subjected to continuous stirring at 50 rpm by using a magnetic bead. The temperature was maintained at around (37 ± 0.5) °C. Sample was withdrawn and measured for the amount of drug diffused using UV spectrophotometer.[1]

Results and Discussion: Cubosomes of raloxifene comprising of GMO & Pluronic F127 were successfully developed for site specific delivery using microfluidization. The cubosomal formulation was optimized by 2^3 factorial design consisting concentration of RLX, GMO and Pluronic F127 as independent variables and particle size, zeta potential, entrapment efficiency, drug diffusion being dependent response variables. In-vitro release studies were carried out at physiological pH. Pure drug showed 58% drug release whereas optimized formulation showed 98.26% drug release over a period of 24hrs. RLX loaded cubosomes were compared with transdermally administered pure RLX hydro-ethanolic solution and *ex vivo* permeation was found to be increased by 1.22 folds.

CONCLUSION: Cubosomes established itself to be a stable formulation and offered a potential approach for enhancing the bioavailability of a BCS class II drugs. It was obvious that cubosomes containing RLX is also promising technique to deliver the RLX through the skin to overcome the potential side effects associated with its oral administration.

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Investigating Enteric Polymers to Formulate Solid Dispersion using Hot Melt Extrusion Technology for Enhancing Oral Bioavailability: A Case Study using Curcumin as a Model Drug


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Background and Rationale: Aqueous solubility of a drug substance is one of the key properties required for a successful pharmaceutical formulation development. Solubility is closely related to dissolution rate which is a kinetic process. For immediate release drug products, it is essential to have a faster rate of dissolution to produce rapid onset of effect. In addition, faster rate of dissolution is also required to enhance the extent of drug absorption as water content start decreasing in the lumen towards the lower part of gastrointestinal tract (GIT). Therefore, different approaches have been used in various commercial drug products to enhance dissolution rate. Among various approaches, formulating solid dispersion/solution remains most popular in pharmaceutical industries. The popularity of this approach is also due to the adoption of hot melt extrusion (HME) technology from plastic industries to pharmaceutical industries, as it eliminates the use of organic solvents and also remains a very simple unit operation and hence, reduces overall manufacturing cost. Interestingly, it has been observed in few marketed products such as Tolsura^{Ò}, Xtandi^{Ò} that enteric polymers (which were so far used in the dosage form to protect the drug from the harsh acidic environment) when used to prepare solid solution enhances the oral bioavailability significantly in comparison to solid solution of drugs prepared using pH independent hydrophilic polymers and surfactants(1). The objective of the present work was to prepare and optimize enteric polymer based solid dispersion of curcumin using HME technology for enhancing dissolution rate.

Methods: Solid dispersion of curcumin was prepared using HME technology. Various polymers including hydrophilic pH independent polymers as well as enteric polymers were screened based on computational method as well as miscibility study using DSC. To evaluate the role of polymers in enhancing the dissolution rate, discriminative dissolution method was developed. An assay method was developed to analyze drug content in formulated solid dispersions. In addition, prepared solid dispersion was also characterized using DSC and PXRD(2).

Results: Among various enteric polymers such as HPMCAS, HPMC Phthalate, Eudragit L100-55 and Eudragit L100, it was possible to prepare solid dispersion using HPMC Phthalate. This is due to fact that all other enteric polymers need high temperatures at which, significant degradation of curcumin was observed. Importantly, despite milling, the extrudes were able to resist curcumin release in pH 1.2 i.e. <10% release was observed meeting the USP acid dissolution phase. On the other hand, at pH 6.8, >85% curcumin dissolved within 30 mins. Drug content in milled extrudes was found to be between 85% and 115%. In addition, DSC and PXRD studies revealed amorphous nature of curcumin in the milled extrudes.

Conclusion: The study clearly demonstrate that enteric polymer can be used to prepare solid dispersion of curcumin using HME technology. In addition, process parameters in HME technology can be optimized to prevent premature drug release in the acidic environment from the milled enteric polymer based extrudes. Therefore, the developed technology can be used not only to enhance dissolution rate of poorly soluble drug in intestine but also to deliver drugs which are acid labile and currently coated with enteric polymers using organic solvents.

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Synthesis and Evaluation of Choline and API-ionic liquids for Solubility and Permeation Enhancement of Topical Antifungal Drug

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Background and Rationale: Antifungal drugs show dissolution-dependent permeation on topical application. Model drug clotrimazole (CLT) is an OTC topical API for fungal infections. It is a BCS class II drug with poor water solubility (0.49 µg/ml), which hinders bioavailability in the skin. Biocompatible choline-amino acid based ionic liquids (CHO-AA ILs) can act as a solvent, increasing drug solubility and permeation depending on the counterion used. API-IL is a novel concept of utilizing properties of counterion to modify API characteristics. The study aimed to improve the solubility, permeation, and flux using ILs [(1)].

Methods: A) Synthesis of ionic liquids: In **Part I**, biocompatible CHO-AA ILs were synthesized using choline as cation and different amino acids (phenylalanine, serine, aspartic acid, isoleucine, valine) as anions by solvent evaporation method in different molar ratios [CHO: Counterion (1:1,1:2)] [(2)]. In **Part II**, novel CLT-ILs in different molar ratios [API: Counterion (1:1, 1:2.5, 1:5)] were synthesized using a solvent evaporation process in which CLT acts as a cation while alpha hydroxy acids (citric acid, malic acid, tartaric acid) as counterions in common solvents (ethanol, methanol) [(1)].

B) *In-vitro* release and permeation: The release study of API-ILs in Transcutol P® was conducted using 10 ml Franz diffusion cells (n=6) on regenerated cellulose membrane in a receptor medium [Phosphate buffer pH 4.0: Methanol (3:7), pH=5.1-5.25], which mimics skin pH maintaining the sink conditions at 32±1^{0}C, 500 rpm for the duration of 6 hr [(3)]. The concentration was measured by taking 1 ml aliquots after each 1 hr using UV spectrophotometry at 261 nm, where the non-interference of counterion was proved. The CLT-malic acid (1:2.5) IL was formulated into an oleogel, and permeation was evaluated using Strat-M® membrane at 300 rpm using the same media in a 20 ml receptor cell.

Results and Discussion: Part I: The neutralization reaction between choline and counterions resulted in choline-amino acid ILs confirmed by ATR spectroscopy. The CLT exhibited very low solubility in the synthesized CHO-AA ILs hence it failed to act as a solvent. **Part II:** The formation of CLT-ILs were confirmed using DSC, NMR, & ATR spectroscopy. CLT-ILs resulted in several folds higher water solubility as compared to CLT only. CLT- malic acid (1:2.5) IL showed a 2-fold increase in flux and release. The IL oleogel formulation showed 1.71 times more permeation than CLT oleogel.

Conclusion: Ionic liquids are promising for solubility and permeability enhancement of poorly water-soluble drugs. Tunable ILs engineering can allow modification in API properties resulting in higher dissolution and permeation.

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Albumin Nano-Vector Mediated Co-Delivery of Lapatinib and Honokiol for Enhanced Therapy of Triple Negative Breast Cancer

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Background & Rationale: Lapatinib (LPT) is a dual inhibitor of epidermal growth factor receptor (EGFR) and HER2 receptor. It's large oral dose (1250 mg/day), low oral bioavailability (24 %) and dose related toxicities pave a path for further improvement in the delivery system. Accordingly, it is necessary to develop an injectable delivery system that effectively elevates bioavailability of LPT and precisely targets the tumor. Previous reports have shown that Honokiol (HK) (Magnolia species), improved the therapeutic potential and reduced the toxicity associated with LPT.Thus, the present work deals with development of albumin nanoparticles of co-loaded LPT (albumin binding 99%) and HK for improved targeting triple negative breast cancer (TNBC). Similarly, the present work sought to elucidate whether genipin could be exploited as an alternative cross-linker (natural, non-toxic) instead of glutaraldehyde (toxic).

Methodology In this current investigation LPT–HK–BSA–NPs were fabricated by desolvation (antisolvent precipitation) using ethanol as an anti-solvent followed by addition of cross-linker genipin. Further NPs were optimized, characterized for different quality (Particle size, % entrapment efficiency (% EE), % drug loading), *in vitro* release (dialysis bag method using pH 7.4 phosphate buffer and pH 5.5 ammonium acetate buffer), hemolytic toxicity study, qualitative and quantitative cell uptake studies, *in vitro* cytotoxicity studies.

Results and Discussion: LPT–HK–BSA–NPs exhibited appreciable quality attributes (Particle size:129.26 ± 9.84 nm, PDI:0.184 ± 0.05, Zeta potential -28.86±1.55 and entrapment efficiency ~95% for LPT and ~96% for HK). The encapsulated drug showed amorphous nature verified by PXRD. The circular dichroism study displayed least alterations in the structural conformation of BSA–NPs prepared using genipin as a cross-linker. However, BSA–NPs prepared using glutaraldehyde showed significant changes in structural conformation. The transmission electron microscopy revealed the spherical shape of LPT–HK–BSA–NPs. In *in vitro* drug release showed biphasic and sustained release pattern. Moreover, enhanced release was obtained at tumor microenvironment pH 5.5 and nanoparticles were compatible for intravenous administration (No haemolytic potential). In cell culture studies, efficient internalization of Cou-6-loaded BSA–NPs was observed in MDA-MB-231 and 4T1 cell line cells as compared to Cou-6 solution. The quantitative cell uptake study exhibited approximately 2-fold increase in uptake of LPT–HK–BSA–NPs as compared to free drugs in MDA-MB-231 and 4T1 cell line. LPT–HK–BSA–NPs showed approximately 2 and 2.5-fold reduction in the IC_{50} as compared to free drugs in MDA-MB-231 and 4T1 cell line. The apoptotic index (0.98) observed in case of LPT–HK–BSA–NPs was approximately 2-fold higher than the physical mixture of LPT and HK (0.49).

Conclusions: The developed LPT–HK–BSA–NPs displayed promising therapeutic potential in the treatment of TNBC. Also, strategy can be exploited further as a scalable platform technology for difficult to deliver co-deliver drugs

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Apremilast and Thymoquinone Loaded Nanoemulgel for Synergistic Anti-psoriatic Therapy

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Background and Rationale: Psoriasis is an autoimmune, inflammatory skin disease, hence topical therapy is the first choice for its treatment. Apremilast (APT) is approved by US FDA under the brand name of Otezla® for the treatment of severe plaque psoriasis. However, its oral delivery is associated with side effects like nausea, vomiting, arthritis and immunosuppression, which can be overcome by its topical delivery. APT acts by inhibiting phosphodiesterase-4 (PDE4) enzyme and modulate a network of pro-inflammatory and inflammatory mediators. While thymoquinone (TQ) exerts its effect by acting as a free radical scavenger, also preserving the activity of various anti-oxidant enzymes such as catalase, glutathione peroxidase. Hence, the selected combination will maximize the therapeutic response against psoriasis. However, the major challenge in topical drug delivery is meager penetration of drugs through psoriatic skin. To this end, nanoemulsion (NE) have proved to be efficient for the delivery of numerous therapeutic agents through topical route.

Preparation, optimization and characterization of NE, Nanoemulgel (NE-gel): APT and TQ was screened for its saturation solubility in different oils. Different surfactant and co-surfactant were screened to obtain minimum globule size and PDI. Transcutol, Cremophor RH40 and Labrafil 1944 CS was selected as oil, surfactant and co-surfactant respectively. The NE was optimized using Design of expert (DoE). Emulsion was formulated by spontaneous emulsification method, incorporated into different strength of Carbopol gel and characterized for pH, viscosity and spreadability. *In vitro* release study was performed using cellophane membrane by dialysis method. *Ex vivo* permeation was performed on pig ear skin using Franz diffusion cell. Dermal pharmacokinetics was performed by tape stripping method.

Results and Discussion: NE was prepared and optimized using DoE (Globule size 28.82nm and 0.170 PDI). 1% gel showed thixotropic behavior while 0.5 % showed Newtonian and 1.5 % showed ant thixotropic hence 1% gel was selected. NE-gel showed sustained release with no burst effect (24%) in 2h as compared to NE, which showed burst release that is more (45%) in release in first 2h. While free drug loaded in gel showed only 25 % release which could due to precipitation of drug in gel system. The negligible amount of drug was detected in receptor compartment in nanoemulgel which signify low systemic concentration, NE and NE-gel showed 5-fold improvement in permeation across the viable layer of skin compared to free drug dispersed in gel.

Conclusion: The final formulation showcasing sustained release with improved local concentration (up to 5-fold) and minimal systemic exposure. This formulation strategy not only presents a selective option, but also an efficacious and safe option for clinical application in psoriasis.

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Characterization Of Various Geometrical 3D Printed Tablets Using *In Vitro* Dissolution Study

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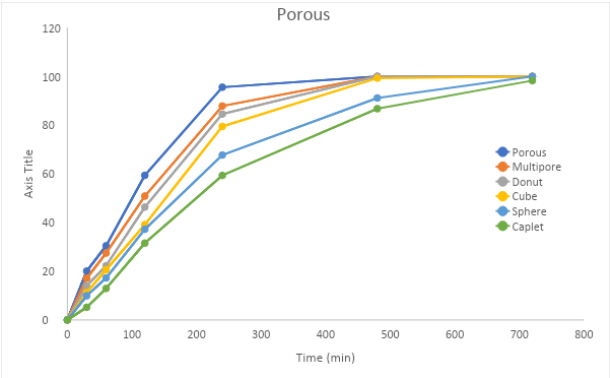
Background and Rationale: It has been reported the shape and size of tablet influence the gastro-intestinal transit rate. Gastro-intestinal transit rate is important for designing of dosage form for bioavailability. *In vitro* studies suggest that flat tablets have greater adherence to the oesophagus than capsule-shaped tablets. Studies in humans have also suggested that oval tablets may be easier to swallow and have faster oesophageal transit times than round tablets of the same weight. Patient compliance with medication regimens may be influenced by the size and shape of a tablet or capsule. Since physical attributes are the deciding factors for the GI transit time, so by studying impact of physical attributes on GI transit time we can design drug in a better manner for better patient care.

Method: *In Vitro* Dissolution Study: Dissolution studies were performed as per USP guideline using eight station dissolution test apparatus (Labindia, DISSO-2000, Mumbai, India) equipped with paddles employing 900 mL of 0.1 N HCl for first 2 hrs and pH 6.8 phosphate buffer for remaining period of time as dissolution medium. The paddles were operated at 100 RPM, temperature 37±1ºC, and throughout the experiment sink condition were maintained. Samples were suitably diluted and PVA content was analysed spectrophotometrically.

Results and Discussion: Dissolution tests confirm that geometry plays an important role in defining drug release profiles. When the weight of the tablets was kept constant, drug release rates were in the following order (fastest first); **porous > multipores > donut > cube > sphere> caplet**. The time to 90% release (t90) varied from under 4 h **(porous)** and nearly 12 hours (caplet).



Conclusion: Geometry helped us to define that different shapes of 3D printed tablets influence the gastrointestinal transit time and hence the bioavailability.

Acknowledgement: I would like to express my sincere gratitude to my supervisor Dr. Gaurav Kumar Jain for continuous support in this research, for his patience, motivation, enthusiasm and immense knowledge. His guidance helped me in all the time of research. I would also like to thank Mr. Gaurav, PhD scholar for his valuable advice, excellent guidance and encouragement.

Deep Eutectic System (DES) of Quercetin for Improvement of Solubility and Oral Bioavailability

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Background and Rationale- Poor solubility and dissolution profile of the new drug candidates is a major reason behind their failure during drug development. DESs are a class of eutectic mixtures that are liquid at room temperature and possess the ability to enhance the solubility of poorly soluble drugs[1]. DES represents an attractive enabling technology with high thermodynamic stability and easy industrial scalability.

Quercetin is a dietary flavonoid and is recognized as a lucrative choice in the field of nutraceuticals due to its ant-oxidant, anti-inflammatory, and anti-carcinogenic property. Poor solubility and dissolution rate limited oral bioavailability of quercetin hinders its nutraceutical application[2]. Hence, the liquid formulation of quercetin using DES was investigated as a strategy to overcome the poor solubility and dissolution rate of quercetin and to improve its oral bioavailability.

Methods- A) Selection of DES for quercetin – A library of DES was generated by heating method and was characterized by FTIR and PLM. Choline chloride: Levulinic acid (1:2) DES was selected based on the maximum solubility of quercetin in it and was carried forward to the further stages.

B) Generation and characterization of DES-based formulation of quercetin- DES based formulation of quercetin was generated by stirring method at 30 mg/ml drug loading and was further characterized by FTIR and PLM.

C) *In vitro* evaluation of DES based formulation of quercetin- Kinetic solubility study was performed in FaSSIF by shake flask method. *In vitro* dissolution study was conducted in 900 ml of aqueous buffers (pH 1.2, 4.5, 6.8) with 2% w/v SLS and biorelevant media (FaSSIF) using USP type II apparatus. Short-term accelerated stability was performed according to ICH Q1A (R2) guidelines.

D) *In Vivo* pharmacokinetic study- *In vivo* oral pharmacokinetic study was performed in adult Sprague Dawley rats. Pharmacokinetic parameters such as *Cmax, Tmax, AUC 0-t* for DES based formulation of quercetin were calculated using PK solver software and was compared with aqueous quercetin suspension.

Results and Discussion- DES based formulation of quercetin showed a 2-fold enhancement in kinetic solubility in comparison to pure quercetin. A higher cumulative percentage release (p value<0.05 at all time points) of quercetin was observed from DES based formulation. (41.66% and 16.49% in pH 1.2, 45.60% and 21.82% in pH 4.5, 43.10% and 18.90% in pH 6.8, 4.03% and 1.05% in FaSSIF for DES based formulation and pure quercetin, respectively) The dissolution parameters (MDT, AUC, % DE) were found to be significantly higher (p value <0.05) for DES in comparison to pure quercetin. The formulation was found to be chemically as well as physically stable for one month. *In vivo* oral pharmacokinetic study revealed 1.3 times enhancement in relative oral bioavailability (p value < 0.05) of DES based formulation of quercetin in comparison to pure drug.

Conclusion- DES based formulation successfully improved the oral bioavailability of quercetin by enhancing solubility and dissolution profile. Enhancement of solubility and dissolution can be attributed to a combination of DES-induced hydrotropy and cosolvancy mechanisms. Overall, DES can be efficiently explored for developing an enabling formulation of 'difficult to deliver' molecules in the field of nutraceuticals.

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Development and Optimization of Lymphocyte Membrane Camouflaged Nanoparticles Comprising Novel Combination Therapy for the Treatment of Triple-negative Breast Cancer.

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Background and Rationale: As per the cancer organization, breast cancer is one of the most prevalent types of cancer. In the United States, the average risk of women developing breast cancer is about 13% which means there are almost 1 in 8 women, who have a probability of developing breast cancer. 81% of the patients are observed with triple-negative breast cancer (TNBC) from the total cases of breast cancer. This high occurrence rate of TNBC makes them the most aggressive. Conventional anticancer drug therapy has the unique disadvantage of allodynia (nerve pain) which is the main reason behind the stoppage of the chemotherapy [1]**.** The combination therapy of Paclitaxel (PTX) and Cannabidiol (CBD) used in this therapy overcomes allodynia produced by conventional anticancer drugs [2]**.** CBD also has a low affinity for the cannabinoid CB1 and CB2 receptors which increases the anticancer activity of the PTX. The coating of WBC over the nanoparticles containing a combination of PTX and CBD prevents the hypersensitivity reactions associated with conventional available nanoparticles (NPs). It also produces targeting of NPs to the cancerous organ. Due to the less biodistribution in the body and the site specificity of the camouflaged NPs, the side effects are reduced [3].

Method: The Lymphocyte membrane camouflaged nanoparticles consisting of PTX and CBD (LMc-PTX-CBD-NPs) were developed by solvent evaporation method and optimized using CCRD by Design Expert 12.0 Software and characterized for their Particle size, Zeta potential, SEM, TEM, and *in vitro* drug release. The *in vitro* release pattern of LMc-PTX-CBD-NPs was recorded under the sink conditions. The optimized formulation was kept in a dialysis bag (molecular weight cut off, 12 KDa) and was subjected to dialysis against phosphate buffer saline pH 7.4 at 100 rpm and 37^{o}C temperature. At specific time intervals, 2 ml aliquot was withdrawn and was replaced with fresh PBS solution to maintain the sink condition. The % release of both the drugs (PTX and CBD) was determined.

Results and Discussion: The particle size of uncoated and coated nanoparticles was observed to be 149 and 171 nm with the zeta potential of -6 and -10.5, respectively. Particle morphology was analyzed by using SEM and TEM showing globular particles with a uniform coating of lymphocyte membrane over the NPs. The *in vitro* release study showed about 92% of PTX release up to 120 h while CBD took 48 h to release 98% of the drug from PLGA nanoparticles which indicates the controlled release behavior of polymeric nanoparticles. Also, several release kinetic models were employed to analyze the release pattern of the optimized formulation. Results showed that both paclitaxel and cannabidiol follow Higuchi release kinetic model. Greater inhibition of cell migration indicated an improved anti-metastatic effect after analyzing optimized formulation against human breast cancer cells (MCF7). Also, a higher proportion of nuclear fragmentation occurred due to which major changes in cell morphology were observed. Furthermore, the *in vivo* studies showed enhanced antitumor efficacy with LMc-PTX-CBD-NPs treatment after IV administration to rat bearing breast cancer. Thus, camouflaging the drug-loaded NPs could be an effective approach for the successful combination of chemotherapy with reduced side effects and hypersensitivity reactions.

Conclusion: The results obtained after performing the *in vitro* characterization, cell line studies, and *in vivo* studies, it was observed that the prepared optimized formulation (LMc-PTX-CBD-NPs) showed enhanced drug release. Also, enhanced breast cancer inhibition, increased tumor targeting as well as reduced hypersensitivity reactions as compared to conventional nanoparticles consisting dual drug-loaded therapy was achieved due to leukocyte membrane coating. The overall obtained results of investigations reveal that prepared formulation could replace conventional chemotherapies.

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Enhanced Solubility and Biopharmaceutical Performance of Brick Dust Molecule via Stabilized Amorphous Nanosuspension using Acid-Base Neutralization Approach

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Background and Rationale: "Brick dust" compounds have high lattice energy and their solubility in both water and oil is limited by the strong intermolecular bonds within the crystal structure. Nilotinib being a brick dust molecule is also a weak base exhibiting pH-dependent poor aqueous solubility i.e., solubility decreases with increasing pH and is practically insoluble above pH 4.5[1]. Also, it shows a positive food effect and a substrate of p-gp efflux which often leads to high *in vivo* variability and bioavailability issues. Aiming to overcome these limitations, the design of amorphous nanosuspension is proposed to assure reliable drug therapy[2]. Objectives of this study were 1) preparation and optimization of amorphous nanosuspension using Design expert software 2) Impact of nanosuspension on solubility, *in vitro* dissolution 3) Impact of nanosuspension on pH dependency, food effect 4) *In vivo* pharmacokinetic evaluation of nanosuspension

Methods: Here we employed the acid-base Neutralisation method to generate amorphous nanosuspension and used a novel combination of Soluplus® and Hypromellose acetate succinate (HPMCAS-MG) polymer for stabilization of the nanosized particle. Systematic optimization was carried out by employing the I-optimal method using Design Expert® software (Version 13, Stat-Ease Inc., Minneapolis, MN). Nanosuspension was spray-dried and characterized for morphology, dissolution, and *in vivo* pharmacokinetic study.

Results and Discussion: The experimental results identified a formulation with 0.3% (w/v) Soluplus®, and 0.415% (w/v) HPMCAS. The resultant nanosuspension (NS) showed a mean particle size of 130±0.22 nm with a polydisperse index value of 0.279±0.01 and zeta potential of −5.21±0.91 mV**.** X-ray powder diffraction of dried NS showed no characteristic peaks of NIL, revealing an amorphous structure that can be attributed to the rapid precipitation process, in which, amorphous NS is "locked" by the use of HPMCAS and Soluplus®. Nanoparticles were spherically wrapped by the stabilizers with a smooth surface as observed by scanning electron microscopy. Solubility study in biorelevant media i.e., in FaSSIF and FeSSIF showed an overall increase of 36.1-fold and 10.33-fold respectively, which can be attributed to the amorphous nature of the drug. The positive food effect was negated as the FeSSIF-to-FaSSIF solubility ratio was equal to 1. *In vitro* dissolution in FaSSIF and FeSSIF media showed an enhancement of 6-fold and 5.7-fold respectively for dried amorphous NS which could be attributed to the synergistic effect of nanonization and amorphization of the drug. pH dependency of the drug was nullified as shown by two-stage dissolution using SGF and SIF. *In-vivo* pharmacokinetic study in SD male rats following oral administration showed that the relative bioavailability of NS was increased by 1.46-fold in comparison with free drug.

Conclusions: Conclusively, the present technique combined with acid-base neutralization and the spray-drying process could be a novel approach to developing pharmaceutical products with enhanced oral bioavailability.

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Evaluation of Minocycline Loaded Nanoemulgel for the Treatment of Difficult to Treat Acne "Acne Rosacea."

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Background and Rationale: Acne rosacea can be termed as a condition characterized by symptoms of facial flushing along with signs and symptoms, including erythema, telangiectasia, coarseness of skin, and an inflammatory papulopustular eruption like in acne

Minocyline is a widely used drug for acne, however, its assessment for acne rosacea is still growing. The present investigation proposes repurposing of minocycline through a nanoappended formulation, nanoemulgel for amelioration of acne rosacea. The *in vitro* and *ex vivo* appraisal for the same has been carried out to further validate the purported nanoemulgel which was optimised by different characterisation parameter.

The first-pass metabolism of minocycline greatly affects an effective delivery of drug at the desired site of action. This particularly necessitates investigation and fabrication of a suitable drug delivery system for improved therapeutic efficacy, sustained release and locoregional application. Further, literary evidence suggests a topical administration of minocycline for the treatment of facial papulopustular rosacea. Nanoemulgel is also considered to increase dermal permeation, and retention of poorly lipophilic drugs with fewer side effects

Method: A) *Formation of nanoemulsion and converting it in nanoemulgel:* Minocycline loaded nanoemulsion was formulated by aqueous titration method. For this, selected formulation components based on a pseudo-ternary phase diagram were vortexed for few minutes to obtain a clear, transparent and stable isotropic system which was then converted into a sustained release nanoemulgel using carbopol 940 (gelling agent) at appropriate concentration.

B) An *in vitro* drug release profile of an optimized minocycline nanoemulsion and minocycline nanoemulgel equivalently was carried out using semi-permeable dialysis bag with semi-permeable membrane of average diameter. The dialysis bags were immersed in a beaker containing 100 mL PBS pH 5.5 kept at a temperature of at 37 ± 0.2 °C for 24 h. For *ex vivo* permeation studies a layer of stratum corneum (1mm thickness) was used on a franz diffusion cell with each of minocycline nanoemulgel and minocycline nanoemulsion by placing separately in donor compartment facing towards the stratum corneum of 1mm thickness and receptor chamber filled with 10 ml of phosphate buffer saline of pH 5.5, maintained at 37 ± 1°C.

Result and Discussion: The various characterization parameter of the formulation indicates that the nanoemulgel was successfully developed and optimized. Drug release and permeation profile suggested that a sustained release action which is necessary for longer and closer drug contact with epithelial surface leads to prolonged penetration.

The in vitro release of an optimized minocycline nanoemulsion was comparatively higher than that from nanoemulgel under the same set of experimental conditions, similarly the cumulative amount of drug permeated after 6 hours from minocycline nanoemulsion and minocycline nanoemulgel were 75% and 58% respectively. This indicates that the nanoemulgel shows sustained release behaviour and will give a better result after a long hour of usage on the skin.

Conclusion: Acne rosacea is considered a general category disease, but if left untreated, it leads to the worst cases, particularly in males, termed as rhinophyma. The above collective results suggested that prepared o/w nano-emulgel of minocycline can provide sustained release topically. Henceforth, the proposed formulation could be further catered as an improved modality for locoregional, and targeted drug delivery for amelioration of acne rosacea.

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Exploring Sorafenib and Venetoclax Loaded Albumin Coated PLGA Nanoparticles for Inducing Apoptosis and Ferroptosis Mediated Cell Death in Managing Cancer

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Background & Rationale: Monotherapy of anti-cancer drugs usually leads to the development of drug resistance. Here, combination therapy with drugs acting on two different cell death pathways (apoptosis and ferroptosis) is attempted. We used Venetoclax (VTX; apoptosis inducer) and Sorafenib (SOR; ferroptosis inducer) as a synergistic combination, at 1:1 w/w ratio. The combination was ratiometrically loaded in PLGA nanoparticles and was coated with polydopamine (PDA) followed by albumin to provide a stealth effect and tumor targeting **[1]**.

Methods: PLGA NPs were prepared via nanoprecipitation method where, organic solvents, PLGA concentration, stabilizers and their concentration and organic to aqueous phase ratio were optimized. Drug loading for SOR and VTX was achieved in a ratiometric manner to ensure synergy. The drug loaded NPs were then optimized for PDA and Alb coating (concentration and time) to form Alb-PD-PLGA(SOR+VTX) NPs. The NPs were characterized for size, PDI, Zeta-potential and morphology (TEM). The conformation of Alb and coating of PDA and Alb were confirmed via CD spectroscopy and Energy dispersive spectroscopy respectively. *In vitro* drug release at pH 7.4 was performed using dialysis bag method. Qualitative and quantitative cell uptake, cell cytotoxicity assay (reversal assay with Ferrostatin-1) and apoptosis assay on MDA-MB-231, A549 and HeLa cells were also performed.

Results and Discussion: SOR and VTX at 1:1 w/w ratio showed synergy (CI value <0.7) in all the mentioned cell lines. Ratiometric drug loading was achieved by keeping % theoretical drug loading at 7.5 and 9.5% for SOR and VTX respectively. PDA and BSA coating were successfully done onto PLGA NPs, and was evident by TEM, EDS (8.65 % N in PDA coated NPs and 2.68% S in albumin coated NPs) and CDS. *In vitro* release of PLGA(SOR+VTX) NPs showed ~75% release for both the drugs by 4 days whereas, Alb-PD-PLGA(SOR+VTX) NPs showed sustained release for SOR and VTX. This indicated that the coating acted as an additional barrier for the drug to release. The qualitative and quantitative cell uptake studies showed significantly higher uptake for Alb-PD-PLGA(SOR+VTX) NPs. The IC_{50} values for developed formulation in MDA-MB-231, A549 and HeLa were 29, 5 and 3-fold lower than the free SOR and 15, 5 and 3 folds lower than free VTX respectively. In presence of ferrostatin-1 (15µM) IC_{50} values were reversed by 1.57, 1.45 and 1.40-fold in MDA-MB-231, A549 and HeLa cells respectively indicating ferroptosis as one of the cell-death inducing pathways **[2]**. Also, Alb coated formulation showed a higher ($P<0.01$) apoptosis index than non-coated and free drug groups in all mentioned cell lines.

Conclusions: Ratiometric loading of SOR and VTX was achieved in Alb-PD-PLGA(SOR+VTX) NPs and rendered sustained release, higher cellular uptake and improved potency (via induction of ferroptosis and apoptosis) in cancer cell lines. Thus, the formulation holds potential for exploring it's *in vivo* anticancer activity.

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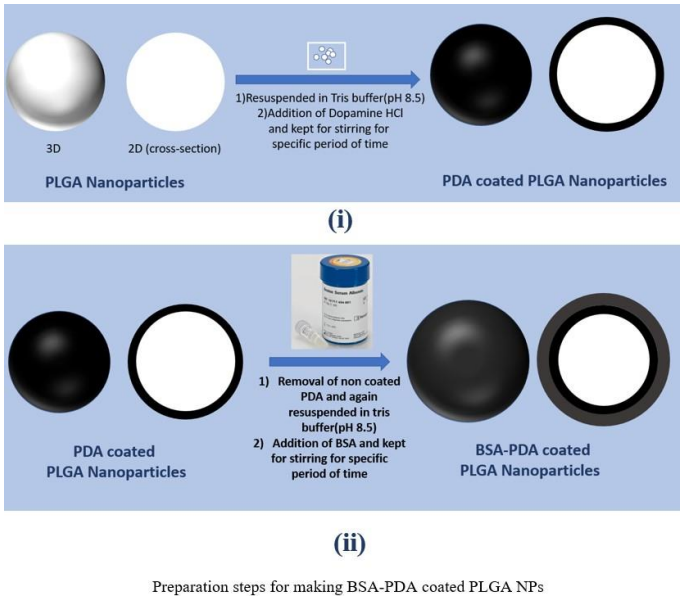

Preparation steps for making BSA-PDA coated PLGA NPs

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In Vitro Release Study of Levobunolol Loaded NLC for the Treatment of Glaucoma

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Background and rationale: Glaucoma is a multifactorial chronic neuro degenerative optic disorder characterized by progressive thinning of the retinal nerve fiber layer (RNFL) and of the neuroretinal rim within the optic nerve head. Levobunolol have therapeutic potential for treating glaucoma. However, the conventional dosage forms show therapeutic effects which are sub optimal due to which drug exhibits poor ocular bioavailability. Therefore, the aim of this study was to enhance the permeation, bioavailability, precorneal residence time and release profile of the drug by formulating Levobunolol loaded nanostructured lipid carrier (NLC) that would result in efficacious treatment of glaucoma.

Material and method:

A. **Formulation and evaluation of NLC**: In this study, Levobunolol loaded NLCs was prepared by Probe sonication technique in which solid-lipid used was Glyceryl monostearate and liquid lipid utilized was Capryol 90. Briefly, both the lipids were melted and mixed at 70°C. As the lipid mixture was melted, during that stage the drug was added. The aqueous surfactant solution of Tween 20 which was already heated, was added into the lipid mixture drop wise using a mechanical stirrer to form the primary emulsion. The primary emulsion was then sonicated using ultrasonic probe sonicator for 15 mins to form a homogenous solution. Lastly, the prepared solution was rapidly cooled using an ice bath for the lipid matrix to solidify and form NLCs. The formulations were evaluated for characteristic properties such as particle size (PS), polydispersity index (PDI), entrapment efficiency (EE), drug loading (DL) and *in vitro* drug release.

Table 1: Box Behnken Design

Factors (Independent variables)	**Levels used**		**Responses (Dependent Variables)**
	-1	**+1**	
Surfactant concentration (%)	1	5	Particle size (nm)
Total lipid concentration (%)	1	2	Poly Dispersibility Index
Sonication time (mins)	10	15	Entrapment efficiency (%)

B. ***In vitro* drug release study**: The *in vitro* release study was performed using Franz diffusion cell system. Each cell has a 10 mL capacity receptor chamber. Then the diffusion cells were mounted with the membranes. The donor compartment was dispensed with 250 mL of NLC while simulated tear fluid (STF) was kept in the receptor compartment and the system was continuously stirred and maintained at 37°C. At predetermined time intervals, 1 mL of sample was withdrawn from the sampling port and refilled with fresh STF. The samples were then analysed by UV within 24 h.

Results and Discussion: The optimized formulation was selected on the basis of Design of experiments (DoE) by Box Behnken Design (BBD) in which the independent variables taken were surfactant concentration (%), total lipid concentration (%) and sonication time (mins) and dependent variable were PS (nm), PDI and EE (%) as given in table 1. The PS and PDI of optimized NLC formulation were found to be 132.9 ±0.47 nm and 0.530 ± 0.01 respectively. The EE of the optimized formulation were found to in the range of 80-90%. *In vitro* drug release studies showed an initial rapid release of drug in the first 5 hrs followed by sustained drug release which lasts until 24 hrs (99.47%). There was an enhancement in the permeation and release pattern of the drug from NLC when compared with the marketed formulation as the marketed formulation showed a drug release of 85% in first 4 hours.

Conclusion: In the present study, Levobunolol loaded NLCs were successfully fabricated using GMS as solid lipid, Capryol 90 as liquid lipid, and tween 20 as a surfactant with minimum concentration via probe sonication method for ocular delivery. The developed formulation showed sustained release of drugs until 24 hours in the eyes when compared with the marketed formulation. The optimized formulation was successfully able to increase the pre corneal residence time.

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In Vivo Assessment of Scalp Retention and Penetration of Minoxidil Solution

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Background and Rationale: Efficacy of minoxidil for the treatment of androgenetic alopecia has been demonstrated through several clinical studies; however, scalp retention and penetration, which is imperative for application frequency, has not been determined till date. [1][2]

Methods: Three radiolabeled formulations of minoxidil (5%) were prepared. Formulation 'A' was prepared by dissolving 5 g of 99mTc-minoxidil in vehicle containing ethanol (40 mL) and water (60 mL). Formulation 'B' contained 5 g of 99mTc-minoxidil dissolved in PG (10 mL), ethanol (30 mL) and water (60 mL). Formulation 'C' was prepared by dissolving 5 g of 99mTc-minoxidil in vehicle containing ethanol (40 mL), water (60 mL) and 10% Hydroxypropyl cellulose (HPC) .

(A) Rheology and texture analysis: The viscosity of the developed formulations was determined using Physica MCR 51 Rheometer (Anton Paar, Austria)**.** The texture profile of the formulations was conducted using a TA-TX2 (Stable Micro Systems Ltd., UK) texture analyzer.

(B) *Ex vivo* retention and permeation using swine ear skin: The *ex vivo* experiments were conducted using SFDC-6 transdermal diffusion cell system (Logan Instruments, USA). Water: ethanol (2:1) was used as a dissolution medium. The dissolution medium was kept at 37±1°C using a circulating water system. At each time point, the unabsorbed formulation was carefully removed from the skin using slightly moist cotton. The radioactive counts in the cotton (amount remained unabsorbed), cleaned intact skin samples (penetrated into skin) and the receptor fluid (permeated into receptor fluid) was measured using gamma counter.

(C) ***In vivo* retention and permeation using human scalp:** The study was a randomized, open-label, three-arm, pilot clinical study conducted at Must and More Diagnostic Center (Rohini, New Delhi). The radiolabeled formulations were filled in spray bottles and were sprayed by actuating twice on the demarcated site. Scalp penetration studies were conducted on the same participants after gap of 72 hours (3days). At the end point, either 1 h or 4 h or 8 h, the application area was thoroughly cleaned with moist cotton to remove all the surface radiolabel and counts were determined using gamma camera to evaluate the scalp penetration.

Results and Discussion: Results showed that formulation C containing 10% HPC demonstrated highest viscosity (0.8 Pa.s) and significantly higher *ex vivo* retention ($p < 0.05$) and permeation (0.75±0.12%, 8h) compared to Formulation A (0.40±0.05%, 8h) and B (0.44±0.05%, 8h). *In vivo* studies using human scalp showed significantly higher ($p < 0.05$) scalp retention in the Formulation C group (57±2.3%) compared to Formulation A (41±1.9%) and Formulation B (44±3.4%) groups. Post 8 h application of formulation, scalp penetration in the Formulation C group was nearly 2.8-fold and 2.2-fold higher than group Formulation A and Formulation B, respectively. Further, absence of minoxidil in systemic circulation during study duration indicates safety.

Conclusion: Increasing the contact time of formulation with scalp by modifying viscosity might result in reduced frequency of application and improved efficacy.

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Influence of Formulation Variables on Lipid Digestion and Drug Supersaturation of Lipid Based Solid Dispersions

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Background and Rationale: The digestion of lipid based solid dispersion (LBSDs) in the gastrointestinal tract (GIT) is critical for drug dissolution and absorption[1]. A better understanding of the fate of LBSD in the GIT is therefore required to engineer efficient LBSDs. In our study we formulated LBSDs of Atazanavir (ATZ), a poorly water soluble weak base molecule using different classes of solid carriers[2]. The objective of this study was to evaluate the impact of formulation variables i.e. drug payload, chain length of lipids and different class of solid carriers on dispersion and digestion behaviour of LBSDs. Furthermore, we also evaluated the supersaturation propensity of ATZ by determining maximum supersaturation ratio.

Method: Preparation of LBSDs: Initially, the influence of the chain length of lipidic excipients and drug payload on lipid digestion was studied by the lipolysis method. Silica-based, clay-based, and polymeric solid carriers were screened by determining their oil adsorption capacity, and LBSDs were prepared by using the adsorption technique. The prepared LBSDs were evaluated for their dispersion and digestion behaviour.

***In vitro* lipolysis method:** Digestion study was performed using a pH-stat lipolysis setup. Digestion was initiated with the addition of pancreatin extract while maintaining a constant pH (6.5±0.5) by 0.6M NaOH titration using a pH-stat apparatus. Samples were withdrawn at predetermined time points and analyzed using the validated HPLC method to determine the amount of drug present in the aqueous phase of digested fatty acid (AP_{digest}). The equilibrium solubility of ATZ in AP_{digest} was determined by shake flask method at room temperature. The Maximum Supersaturation Ratio (SR_M) was calculated for each formulation by dividing the solubilised drug concentration in AP_{digest} by the equilibrium solubility of the drug in $AP_{digest.}$

Results and discussion: The medium chain triglyceride containing formulation showed high drug payload and greater extent of digestion compared to long chain lipid formulation. The higher risk of drug precipitation was observed at increased drug payload. Therefore, 80% of equilibrium oil solubility (65 mg) of drug load was used for further formulation development. The average droplet size of the Neusilin-LBSD and the HPMCAS-LBSD on dispersion were ~150-250nm whereas clay based LBSD showed higher droplet size. The droplet size of each of the formulations showed an increasing trend with the increase in the ratio of solid carrier:liquid preconcentrate. The aqueous phase distribution result showed HPMCAS-LBSD and Neusilin-LBSD maintains supersaturation for physiologically relevant periods of time. In case of Montmorillonite-LBSD, less recovery of ATZ (approx. <50%) was observed in aqueous phase over 60 min. The equilibrium solubility of ATZ in AP_{digest} was found to be 87±0.4 µg/mL. The maximum supersaturation ratio was found to be the highest in the case of HPMCAS-LBSDs (SR_M=2.97±0.10) which represented the higher supersaturation propensity compared to the Neusilin-LBSDs (SR_M=2.45±0.30) and Montmorillonite based LBSDs (SR_M=1.02±0.35).

Conclusion: Formulation variables like chain length of fatty acids, drug load and the choice of solid carrier influence the dispersion and digestion of the LBSDs to a great extent. Neusilin US2 and HPMCAS can be considered to be suitable carriers as compared to Montmorillonite based on the dispersion and digestion studies.

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Intrinsic and Apparent Dissolution of Different Crystal Habits of Fenofibrate using USP Type IV Apparatus

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Background & Rationale: The solid form of an active pharmaceutical ingredient (API) exerts a substantial impact on its physicochemical properties and product performance. Many studies have demonstrated the effect of polymorphism and particle size on the dissolution rate of API. However, the impact of crystal habit remains a relatively unexplored area[1]. The objective of this study was to assess the effect of the crystal habit of fenofibrate, a model BCS class II drug, on the intrinsic and apparent dissolution rate, using USP Type II and USP Type IV apparatus and to correlate the dissolution behavior with the differential surface properties of two different crystal habits.

Methods: A) Generation of crystal habits and solid-state characterization: Rod and plate shape crystal habits were generated by antisolvent crystallization and were further characterized by optical microscopy, SEM, pXRD, FT-IR, and DSC studies.

B) Powder and intrinsic dissolution rate studies in USP Type II apparatus: Discriminatory dissolution method was developed by varying the SLS concentration, paddle speed, and media volume. Powder dissolution studies were performed in 0.9% w/v SLS in water while IDR was determined using Wood's apparatus in 1% w/v SLS in water.

C) Apparent dissolution studies in USP Type IV apparatus: The study was performed using powder cells in 0.9% SLS in water

D) Mechanistic understanding of dissolution behavior: Face indexation studies of crystal habits were done to identify the dominant facets. ESP of fenofibrate molecule was calculated using Guassian16® software to elucidate the electron rich and electron deficient nature of functional groups. This was further correlated to identify the polarity of chemical groups exposed on the dominant facets of both crystal habits using Mercury® software. The underlying mechanism of discrimination at 0.9%w/v SLS in water was studied by assessing the solubilities and micellar diffusivities of both the habits at various surfactant concentrations.

Results and Discussion: The higher discrimination at 0.9%w/v SLS was attributed to the significant difference in the drug-loaded micellar diffusivities of both the habits. Plate shaped crystal habit showed a higher dissolution rate in both USP Type II and Type IV apparatus. Better discrimination was achieved in the USP Type IV apparatus and the percentages of the dissolved drug at all time points were significantly different ($p<0.05$). The IDR of rod and plate shaped crystal habits was found to be 0.0766 mg/min/cm^2 and 0.0833 mg/min/cm^2, respectively. However, the definite crystal habit of rod shaped crystals was lost when subjected to compaction. Differential surface anisotropy of both the crystal habits was correlated with their different dissolution performance.

Conclusions: The two crystal habits of fenofibrate exhibited significantly different dissolution behavior in 0.9%w/v SLS. The nature of the surface chemical groups exposed and their relative contributions to the crystal surface contributed to this dissolution behavior. Overall, USP Type IV apparatus demonstrated more discriminatory power than USP Type II apparatus in identifying differential dissolution from crystal habits.

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Investigation of Biopharmaceutical Performance of Olmesartan Medoxomil by Developing Phospholipid Complex System

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Background & Rationale: Olmesartan (OLM), a drug used for lowering blood pressure in hypertension has limitations in absorption due to poor aqueous solubility, high first-pass metabolism, and high P-glycoprotein (P-gp) efflux which leads to its poor bioavailability.[1] Phospholipid-drug complex has been considered to be a preferred strategy for drug delivery due to its favourable biodegradable and biocompatible properties.[2] Objectives of this study were 1) Preparation and optimization of Olmesartan medoxomil-phospholipid complex (OLM-PLC) using Design of Experiment. 2) To investigate the impact of molecular complexation on solubilization and i*n vitro* dissolution. 3) To understand the influence of complexation on P-gp efflux of OLM. 4) *In vivo* pharmacokinetic evaluation of optimized OLM-PLC. The present study provides insights into molecular complexation between phospholipid and OLM and its impact on biopharmaceutical performance.

Methods: OLM-PLC was prepared using solvent evaporation technique. A central composite design approach was used to optimize the complex. It displayed the combined effect of independent variables including phospholipid-to-drug ratio, reaction temperature, and the reaction time on the dependent variable such as complexation efficiency. Physicochemical characterization was done by FT-IR, 31P NMR, PXRD, and morphological evaluation were done by microscopic techniques. The performance evaluation of OLM-PLC was done for solubility, permeability, and P-gp efflux ratio, which are the determinants of oral bioavailability for OLM. *In vitro* dissolution studies were performed in 900 mL 0.1N HCl buffer (pH 1.2) and phosphate buffer (pH 6.8) using USP type II Paddle dissolution apparatus maintained at 37±0.5 °C for 50 rpm. Permeability study was performed using Caco-2 cell line assay in which the transport of free OLM and OLM-PLC dispersion were assessed in both directions viz. apical to basolateral and basolateral to apical. Pharmacokinetic study was conducted in SD rats to check the bioavailability of OLM and OLM-PLC

Results and Discussion: OLM-PLC with optimal parameters showed 82.5 % complexation efficiency and thus taken into consideration for further study. FT-IR spectra showed that weak physical interactions between OLM and phospholipid occurred during complex formation. The chemical shift for phosphorous in case of NMR spectra also confirmed interactions between OLM and phospholipid. PXRD pattern confirmed the amorphous nature of OLM-PLC. The apparent solubility of OLM in the complex was significantly enhanced by 1.7 fold and 1.5 fold in pH 1.2 and 6.8 respectively. *In vitro* dissolution study revealed that OLM-PLC showed 1.8-fold better release as compared to OLM in the buffer of pH 6.8. As assessed using Caco-2 cells of OLM, the intestinal permeability was increased by 1.35 fold and a significant decrease in the P-gp efflux (2.03 fold) was observed using PLC. 1.25 fold enhancement in relative bioavailability was observed for OLM-PLC in comparison with OLM.

Conclusions: We have prepared OLM-PLC with enhanced *in vitro* and *in vivo* biopharmaceutical performance with a simple and reproducible method. Thus, the presented approach holds a promising potential for increasing the oral bioavailability of OLM. This could have further implications for the therapy such as decreased dose and dose-related side effects.

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Preparation, Optimization, Characterization and In Vitro Lipolysis-permeation of Self-nano Emulsifying Drug Delivery System Containing Linagliptin and Quercetin.

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Background and Rationale: Self-nano emulsifying drug delivery (SNEDDS) is isotropic mixtures of oil, surfactants, and co-surfactants. SNEDDS used for the drug shows low solubility and low permeability. Drug like linagliptin (LGN) shows problem of low permeability due to P-gp efflux. Also, it shows high first pass metabolism. SNEDDS shows lymphatic absorption thereby by passes first pass metabolism. P-gp efflux can be check by P-gp efflux inhibitor like quercetin (QT). This way bioavailability and permeability problem can be overcome. Formulation was subjected to *in vitro* lipolysis for 1 hr in pH-stat auto titrator apparatus (Titrando 902, Metrohm, Switzerland) to know the impact of digestion on lipid-based formulation with subsequent permeation.

Method:

A) Preparation of SNEDDS: Capmul®MCM EP (oil), Cremophor® RH 40 (surfactant), and Labrafil M1944 CS (cosurfactant) were chosen as chief components for preparing liquids SNEDDS (L-SNEDDS) based on solubility and emulsion forming ability of surfactant and cosurfactant. Components were mixed with drug and subjected to stirring (with heating) and kept for 24 hr at 25 °C.

B) Optimization and Characterization: Screening and optimization of formulation was done by Design Expert® software and Optimized formulation was evaluated against various test/parameter for robustness, stability, size, PDI and zeta potential.

C) *In vitro* lipolysis-permeation: Formulation was constituted in digestive media with porcine pancreatin. Due to enzyme action free fatty acid release from lipid which decreases the pH of media, sense by pH electrode, which is compensated by 0.5 N NaOH by instrument to pH 6.5, pH-stat apparatus (Titrando 902, Metrohm, Switzerland). Sample from lipolysis also put for permeation in franz diffusion cell.

Result and Discussion: It was found that Capmul® MCM EP, Cremophor® RH 40, and Labrafil® M1944 CS in the ratio of 568.59:300:131.40 showed optimum particle size (45.759±3.12 nm), PDI (0.239±0.023) and zeta potential -11.4933±2.53). In *in vitro* lipolysis study, samples formed two phases after centrifugation. Approximately 80% of LGN was recover from aqueous phase (which consist of free drug and drug in colloidal structures) which will be available for absorption. For QT 50% was found in pellet phase, but the pellet was in amorphous form (which was in equilibrium with aqueous phase) which was concluded from good permeation of the QT. Sample from lipolysis were subjected to simultaneous *in vitro* permeation and they showed good permeation for both of drugs.

Conclusion

In vitro lipolysis-permeation method was found to be a promising tool for estimating the *in vitro* performance of formulation which can be used to correlate with *in vivo* performance of drug. Both the drugs showed high permeability.

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Vitamin-D Alendronite Microparticles for Buccal Dental Implant

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Background and Rationale: Vitamin D is also known as cholecalciferol an essential vitamin for the reabsorption of calcium in bones. Vitamin D deficiency can often occur from a combination of insufficient exposure to sunlight, and inadequate dietary intake of vitamin D. Such deficiency is known for resulting in conditions like rickets or osteomalacia, all of which reflect inadequate mineralization of bone, enhanced compensatory skeletal demineralization, resultant decreased calcium ion blood concentrations. Whereas Alendronate sodium is a bisphosphonate medication used to treat osteoporosis and Paget's disease of bone. It is taken by mouth. Use is often recommended together with vitamin D. (Bartley, 2010) The use of micro-particles for this formulation is achievable as vitamin-D supplements, IV is available but they are mostly lipid and require patient compliance, and giving it orally will lead to degradation of vitamin D in the GIT. The micro-particles prepared using PLGA do slowly release vitamin D over some time and get absorbed in the buccal cavity itself, making the formulation more patient compliant, effective, and controlled (Ananchenko et al., 2013).

Methods: Preparation of vitamin-D alendronate microparticles and *in vitro* release studies: Vitamin-D and alendronate sodium micro-particles were prepared in the following manner. 5mg alendronate sodium was weighed and then mixed in 5ml distilled water. The mixture was then vortexed. 5mg of Vitamin D was dissolved in 5ml of dichloromethane and then vortexed. 1mg/ml poly D, L-lactic-co-glycolic acid was prepared by weighing 5mg poly D, L-lactic-co-glycolic acid, and 5ml di-chloromethane and then kept aside. The content of alendronate sodium was dispersed in 5ml PLGA solution and then mixed vigorously. A 0.3% w/v aqueous solution of polyvinyl alcohol was prepared. After the polyvinyl alcohol was solubilized uniformly, the mixture of PLGA and alendronate sodium was dispersed with the help of a micropipette, by dispersing small drops until all the solution is dispersed uniformly. The rotations per minute were set from 800-to 1000. (Giteau et al., 2008). Micro-particles of alendronate sodium were prepared using PLGA and dispersed in 0.3% polyvinyl alcohol. The *in vitro* studies were conducted and the dissolution medium was 1% sodium dodecyl sulfate solution. Sodium do-decyl sulfate enhances the release of the slowly releasing drug in the dissolution medium, the time intervals and samples were withdrawn below:

S.NO.	TIME INTERVAL	ALENDRONATE	VITAMIN-D (STABLE)	VITAMIN-D (NORMAL)
1	1hr	0.069	0.083	0.073
2	3hr	0.091	0.186	0.101
3	6hr	0.129	0.225	0.194
4	24hr	0.171	0.298	0.389
5	48hr	0.229	0.541	0.587
6	72hr	0.593	0.782	0.791
7	96hr	0.683	0.891	0.825
8	120hr	0.884	1.143	0.981
9	144hr	0.982		

The amount of actives released was quantified by UV spectroscopy at 472nm for alendronate sodium and 264nm for vitamin D.(Giteau et al., 2008)

Results and Discussion: It was observed that within 1 week or 170 hours the drug was released by almost 90% and this concluded that the drug was sustained release and did not disintegrate over that period, hence proving to be released in the right manner required.

Conclusions: The conclusion that can be hereby observed is that the PLGA microparticles released the drug over 7 days, which was the requirement to procure the formulation as a sustained release formulation. The drug could be easily absorbed in the buccal cavity and can help in calcium reabsorption.

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An Investigation on Microwave Assisted Piroxicam –Ranitidine Hydrochloride Dispersion and its Ddevelopment as Dispersible Tablets

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Background and Rationale: Piroxicam is categorized as Biopharmaceutical classification system (BCS) class II with poor aqueous solubility and hence low dissolution rate and low bioavailiability. The drug is widely used in the treatment of Gout, Rheumatoid arthritis and Oteoarthritis. Aim of the present study was to increase the solubility and dissolution rate of piroxicam by employing microwave assisted drug –drug dispersion where dispersion of poorly soluble drug is prepared with other drug which is hydrophilic in nature. This study investigated the possibility of developing drug- drug dispersion of Piroxicam with Ranitidine HCl and tried to replace usual carriers for making solid dispersion by a therapeutic drug which is hydrophilic so as to utilize its therapeutic efficacy too. Normally in clinical practice the dose of Piroxicam is usually combined with Ranitidine HCl as an anti-ulcer agent against Piroxicam induced gastric irritation. The current study employed the significance of microwave as it could modify the crystalline nature via its effect of heating and electromagnetic field on the drug.

Methods : A) Preparation of Piroxicam – Rantidine HCl dispersion : Piroxicam 20mg and Ranitidine HCl 150mg mixture prepared by kneading method and were taken in a glass beaker and subjected to microwave for 5minutes at the power of 700 W in a domestic microwave oven.

B) Evaluation of developed dispersion: Scanning electron microscopy, Powder x-ray diffraction, Differential scanning calorimetry , Comparative phase solubility study and Drug content were performed.

C) Formulation as Dispersible tablets: Batches of tablets by adding superdisintegrant Crospovidone K25 (2%, 3% and 5%) were formulated and quality control test for tablets were performed.

Results and Discussion: Evaluation studies of drug-drug dispersion showed a dramatic change in the crystalline nature of Piroxicam through the microwave approach and this could be reason for dissolution enhancement in Piroxicam. SEM analysis showed a smooth globular shape in Piroxicam indicates it losses crystallinity. Diffraction peaks reduced its intensity. There was a change in shift of endothermic peak corresponding to the melting point from 201^0C to 170.78^0C. F12 batch of Piroxicam –Ranitidine HCl dispersion showed almost complete release of 94% as piroxicam and 95% as ranitidine HCl at 15 minutes. Rantidine HCL acted as a suitable hydrophilic carrier for piroxicam.

Conclusions: It was concluded that drug drug dispersion using microwave technology improved dissolution rate of Piroxicam. Since there is no interaction between Piroxicam and Ranitidine hydrochloride, the latter drug acta as a suitable hydrophilic carrier for piroxicam and also the effectiveness of the combination therapy could have been improved patient compliance. Addition of crospovidone make the tablet as a successful dispersible formulation. But further scale up and clinical and stability studies should be done to establish the reproducibility in large scale and safe use in humans.

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Development and Evaluation of Orodispersible Tablets of Loratadine Containing an Amorphous Solid Dispersion of the Drug in Soluplus®.

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Background and Rationale: Loratadine is an orally active, second generation, non-sedating anti-histaminic and is used to manage symptoms of allergic rhinitis, urticaria, and other allergic dermatologic conditions (1). Hence a dosage form which enables rapid dissolution and absorption is preferable. However, loratadine is a BCS class-2 drug. The objective of the present work therefore was to prepare an amorphous solid dispersion of loratadine using Soluplus® (2) as a carrier for bringing about rapid dissolution of the active and to formulate the same as an orodispersible tablet.

Methods: Solid dispersions of loratadine with varying ratios of Soluplus® were prepared by solvent (ethanol) evaporation method. The resultant dispersions were subjected to a solubility study in simulated salivary fluid (SSF). The amorphous nature of the drug in the selected dispersion showing highest solubility enhancement was confirmed by XRPD. The dispersion was formulated into an orodispersible tablet by direct compression after addition of suitable excipients. DOE was used to optimize the tablet composition so as to obtain a tablet with good mechanical strength, rapid disintegration and maximal drug dissolution within 5 min in SSF. The optimized tablet was prepared and evaluated for its physicochemical and performance characteristics including dissolution. The *in vitro* dissolution study was carried out in USP dissolution test apparatus, type II after some modification. An inverted petri dish was placed in the dissolution basket and a 500 ml beaker containing 200 ml of SSF which served as the release medium was placed on the petri plate. Water was taken in the basket to allow for maintaining of the temperature of the medium within the inner beaker at 37 ± 0.5^{o}C. One tablet was added to the medium and stirred at 50 rpm. After exactly 5 mins, a sufficient quantity of the dissolution medium was withdrawn, filtered and the dissolved drug was quantified by UV spectrophotometric analysis at 247 nm.

Results and Discussion: A 1: 4 ratio of loratadine: Soluplus® was found to result in a more than 100 fold increase in the solubility of loratadine. XRPD confirmed the amorphous nature of the drug in the solid dispersion. The supersaturation brought about by Soluplus® can be attributed to a combination of increase in solubility due to amorphization of the drug and solubilization into Soluplus® micelles.The optimization exercise using DOE served to arrive at a formula of a tablet with good hardness (4.5 kg/cm^2) and rapid disintegration (38.7 sec) achieved by incorporation of the optimal proportion of crosspovidone as superdisintegrant and PVP as dry binder. The tablets were found to allow dissolution of 93.78% of the drug within 5 mins in SSF.

Conclusion: A patient friendly dosage form containing a highly soluble form of loratadine was prepared and could be of potential benefit in offering quick relief from allergic conditions. Stability study to ensure that the tablet characteristics remain unchanged on aging is warranted.

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Development and *In* Vitro Evaluation of Fast Dissolving Oral Films of Mefenamic Acid

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Background and Rationale: Most patients prefer to take their medicines through oral route in the form of tablets or capsules. But the paediatrics and geriatric populations find it difficult to swallow tablets or capsules. Hence to address this difficulty, oral dispersible films (ODF) are an emerging drug delivery system where the drug can be incorporated into the polymer film base and can be easily administered with accurate dosing and faster action (1). Mefenamic acid (MA) which is used for the treatment of fever in the pediatric population is selected as the model drug for the study. The solubility characteristics of MA were modified by forming inclusion complexes with β-cyclodextrin (βCD) by the kneading method. The study aimed to develop and evaluate fast dissolving oral films of MA-βCD.

Methods: A) Preparation and evaluation of the MA-loaded ODF: The oral dispersible films were formulated by solvent casting method and the MA-βCD complex solution was incorporated into the prepared polymer solution to cast onto a previously designed mould. The developed ODFs were subjected to characterization studies. Drug content estimation followed by *in-vitro* disintegration and drug release was evaluated.

B) *In vitro* drug release study of ODF: The *in vitro* dissolution release from ODF strips was performed in a 50 ml beaker containing 30 ml of PBS of pH 6.8 maintained at $37^{o}C \pm 0.5^{o}C$. 5ml of sample solution was withdrawn at different time intervals for up to 300 sec. The beaker was intermittently shaken using the mechanical beaker shaker (2). The *in vitro* drug release profile of ODF was compared against marketed products using a separate procedure (3).

Results and Discussion: The characterization studies suggested that the properties of developed ODF were within acceptable limits. During static dissolution studies, 97.35% MA was released at the 240^{th} sec. When a comparison study was performed, MA ODF reported a drug release of 97.14% within 3 minutes, which is comparable to the suspension (96.60%) and superior to tablets which had 38.39% MA released after 3 mins.

Conclusion: Based on the investigation, it can be concluded that the MA ODF may be an excellent alternative to existing oral liquid as well as solid dosage forms for the management of fever in the pediatric population. The selection of appropriate excipients may be the critical factor to enhance the drug release from the developed ODF.

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Development of Novel Emulgel Loaded with Andrographis Extract for the Management of Melanoma : *In vitro* and *Ex vivo* Evaluation.

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Background and Rationale: Multiple modes of treatments are available for melanoma, but they are costly and unsafe. Surgery is sometimes contraindicated, and the available nonsurgical treatments have critical side effects like local pain, swelling, and erythema, flulike symptoms. Topical creams like imiquimod and fluorouracil usage is been limited due to high rates of adverse effects, lower clearance rates. Though topical phytotherapy has great potential for dermal carcinoma, is not yet addressed. Promising results for A*ndrographis* extract were observed against various types of cancers. Hence it is felt worthwhile to design an emulgel formulation with *Andrographis* extract. This novelistic approach can make the patients more compliance and comfort. Hence, this present work deals with the formulation of *Andrographis* extract in the form of Emulgel for utmost anti-cancer potential by minimising the side effects.

Methods:

Methanolic extract of *Andrographis* leaves was done by soxhlet extraction process (1). Phytochemical analysis of the extract for various compounds was done. The analysed extract was found to contain 10% of Andrographolide. The obtained Andrographis extract is used for the formulation of herbal emulgel with reference to the Standard method from the literature (2) The obtained formulations were optimised by using appropriate amount of triethanolamine, ensuring better skin penetration, activity towards melanoma cells. All the formulated emulgels were subjected to various physico-chemical studies, such as drug-polymer compatibility by Thin Layer Chromatography (TLC) and Fourier Transform Infra-Red Spectroscopy (FTIR), surface morphology by Scanning Electron Microscopy (SEM), *in vitro* and *ex vivo* drug release characteristics and release kinetics. The optimised and stable emulgels were screened for anticancer activity in the skin cancer cell lines such as A-431.

Results and Discussions:

TLC and FTIR studies indicated no extract-polymer incompatibility. Drug release pattern for different formulations were studied vigorously and checked with various kinetic models. When the R^2 values of regression plots for first order and zero order were considered, R^2 values of zero order plots were found to be higher than first order plots. All the emulgels showed sustained release of drug by a Fickian diffusion mechanism. Based on the release parameters, 3 best formulations were selected and screened in A-431 cell lines, have exhibited promisable cytotoxic results. Thus, this investigation confirms the use of carbapol emulgels containing *Andrographis* leaf extract as a anti cancer emulgel preparation confirmed by *in vitro* and *ex vivo* studies.

Conclusion:

The unique drug release pattern of formulated emulgels proposed in this work with *Andrographis* extract seems to be promising for topical administration against skin cancer and found to be simple and reproducible. From the study, it may be concluded that this attempt will be made to deliver the active anti-tumour agent via Emulgel formulations. It is highly recommended to go further for the in vivo studies of the formulation against melanoma studies. However, this approach of delivering phyto actives to the dermal carcinoma is a unique method with patentability. It offers a significant benefit to the patients, as this approach is non-invasive in nature. Hence physicians can recommend or prescribe this line of therapy to their patients for their better compliance.

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Dissolution Enhancement of Aceclofenac using Co-precipitation Method

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Background and Rationale: The poor solubility and low dissolution rate of poorly water-soluble drugs in the aqueous gastro-intestinal fluids often cause insufficient bioavailability. The enhancement of oral bioavailability of poorly water-soluble drug remains one of the most challenging aspects of drug development. Several formulation approaches can be taken to improve the solubility and dissolution of poorly water-soluble compounds, such as formulating the API in an amorphous form, crystal engineering, decreasing particles size, such as micronization or nanosizing as well as using prodrugs, salt formation, cyclodextrins, solid dispersions or lipid-based formulations. In the present study, dissolution enhancement of Aceclofenac has been done by co-precipitation method, which may in turn, increase the bioavailability of the drug.

Method: Co-precipitation method: Aceclofenac was mixed with powdered excipients (Aerosil, urea and PVP K30) using a mortar and pestle and the mixture was transferred in a china dish. Then acetone was added to the mixture of each ratio of drug and excipient in the china dish. The mixture was stirred constantly and heated to a temperature of 40-45^{0}C (by using a water bath) with constant stirring. The acetone was removed by evaporation and dried mass was collected and stored in a glass desiccator at room temperature for 24 hours. The resultant dried mass was crushed into particles and passed through sieve no. 60 for regular particle size of the mixture. The best excipient for dissolution enhancement was selected on the basis of percentage yield, drug content and drug release in phosphate buffer of pH 6.8 within 60 min.

Results and Discussion: The percentage yield of all formulations is in the range of 92.2 – 98.18%. The percent drug content of all formulations ranges from 97 to 105 %. The value of angle of repose for all the batches ranged between 16° and 20°. The *in-vitro* dissolution studies showed the maximum drug release by the formulation B_1 (4:1.5 drug: aerosil ratio and 25 ml acetone) because more and more –OH groups were present on the micro particle surface, Aerosil can form a great number of hydrogen bonds with the dissolution medium, absorbing water on the particle surface. This dissolution ability was probably being greater as the specific surface area and the amount of Aerosil increase, the drug can easily diffuse out of the dispersion of aerosil and drug. Also, the drug will stick on the Aerosil which enhanced the drug release. The formulation B_1 showed 75.32±1.81% after 60 min which is greater than other formulations which are in the range of 64.81±0.72 to 70.89±0.51%. Thus, the use of aerosil enhanced the dissolution of Aceclofenac.

Conclusion: On the basis of the evaluation results of the nine formulations, batch B_1 was selected as optimized formulation. The percent cumulative drug release was more in formulation B_1 when compared to percent cumulative of pure drug. Thus, formulation B_1 enhances the dissolution of Aceclofenac by co-precipitation method, which in turn, increase the bioavailability of the drug.

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Evaluation of *In Vitro* Release Studies of 3 in one Formulation of SLN

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Background & Rationale: The present approach was to develop Tenofovir disoproxil fumarate, lamivudine and efavirenz loaded solid lipid nanoparticle (TDF-LM-EFZ-SLN) system to improve the oral bioavailability and intestinal lymphatic targeting potential. One of the major issues associated with conventional dosage form is the rapid dissolution of drug and reduced lymphatic targeting potential. As we know that almost nearly 99% of all viral replication occurs in activated and productively infected $CD4^+$ T-cells of the blood and lymphoid tissues. From research data it was clear that HIV patients on current oral antiretroviral therapy (ART) had lower intracellular drug concentrations in lymph nodes than in blood. For instance, in the same patient, multiple lymph node drug concentrations were as much as 99 % lower than in blood and the insufficient drug level has been linked to viral persistence. We propose that one means to improve these disease outcomes is through the orally administered SLN formulation of anti-HIV drugs which sustains the drugs release in the dueodenal pH.

Methods: The freeze dried SLN formulation equivalent to 5g of Tenofovir disoproxil fumarate, lamivudine, Efavirenz should be weighed accurately. The *In vitro* drug release studies were performed in 0.1 N HCl pH for 2 hrs and phosphate-buffer solution (PBS) pH 6.8 for 12 hrs at 37 ± 2 °C using the dialysis bag diffusion technique. The dialysis membrane should be previously soaked in dissolution medium for 12hrs prior to use. The SLN dispersion was placed in the dialysis bag (Spectra/Por®, molecular weight cut off 100K Da) and sealed at both ends. The dialysis bag was immersed in dialysis medium (250ml 0.1 N HCl followed by PBS) at 37 ± 2 °C and magnetically stirred at 100rpm. After each sampling the dissolution media were completely replaced with 250 ml of fresh media, to maintain sink conditions, defined as the volume of medium being at least three times higher than that necessary to obtain a saturated solution of drugs. The content of TDF, LM, EFZ in the samples was determined by simultaneous UV spectrophotometric method.

Results and Discussion: The cumulative amount of TDF, LM, EFZ release in 0.1 N HCl at the end of 2 hr was found to be 1.79%, 2.2% and 1.5% respectively. This reduced release was attributed to the high stability of the lipid in acidic pH. *In vitro* release for to be TDF, LM, EFZ sustained in phosphate buffer 6.8 and nearly 21.4%, 17.3% and 11.1% over a period of 12 hours denotes a good stability of compritol based SLN in the release media. The initial in vitro burst release of drugs was probably caused by the drugs adsorbed on the nanoparticle surface.

Conclusion: *In vitro* studies demonstrated that SLN provided metabolic protection of TDF, LM, EFZ and were transported to lymphatic system by endocytosis and due to small particle size the bioavailability of drug also increased.

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Formulation and Evaluation of Floating Microspheres of Cefpodoxime Proxetil using Simple Lattice Design.

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Background and Rationale: Floating drug delivery system is a novel delivery system having bulk density less than gastric fluids thus it remains buoyant in the stomach for prolonged period without influencing the gastric emptying rate. GRDDS significantly increases gastric residence of drugs, enhances oral bioavailability and solubility of less soluble drugs at high pH resulting in reduced drug wastage. Cefpodoxime proxetil, a third-generation cephalosporin was chosen since it has oral bioavailability of 50% and is completely absorbed solely from upper GIT. Thus, the usage of floating system enables prolonged retention of drug within the gastric region improving therapeutic effect and substantial benefits for patients. Cefpodoxime proxetil half-life is 2.2hrs; owing to its short half-life, it must be administered frequently. The present work aims to formulate Cefpodoxime proxetil floating microspheres which offer a suitable, practical approach for achieving prolonged therapeutic effect by continuously releasing medication over extended period, it also beneficially decreases dosing frequency leading to increased patient compliance.

Method: Cefpodoxime proxetil loaded floating microspheres were successfully formulated by the "*Solvent evaporation method*" using HPMC K4M and EC. This method was selected because of its effective and convenient characteristics. Simple lattice design was utilized for optimization of formulation and prepared floating microspheres were further evaluated for percentage yield, micromeritic properties, FTIR spectroscopy, *in vitro* buoyancy, particle size, drug entrapment, scanning electron microscopy, *in vitro* drug release studies and *ex vivo* studies.

Results: Cefpodoxime proxetil release from polymer-coated microspheres was slow, extended over 12 hrs and dependent on core: coat ratio, wall thickness and microspheres size. The percentage yield significantly increased with increased amount of polymer. With an increased concentration of EC entrapment efficiency increased. The micromeritic properties were found to be good and surface morphology affirmed structure with a smooth surface. FTIR analysis confirmed no chemical interactions. Formulation CPM2 exhibited good percentage yield, micromeritic properties, in-vitro buoyancy(70%), entrapment efficiency(65%) and drug release(73 %) for 7hrs. The pattern of drug release from optimized formulation best fitted with zero-order kinetics. From 'n' value of Korsmeyer-Peppas model transport mechanism was found as anamolous transport. Polymer coated Cefpodoxime proxetil microspheres exhibited good prolonged-release characteristics and was found suitable for once-a-day oral controlled release products.

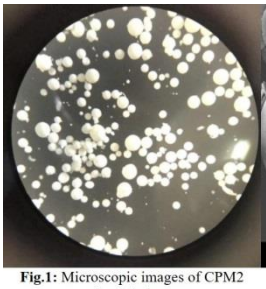

Fig.1: Microscopic images of CPM2 formulation.

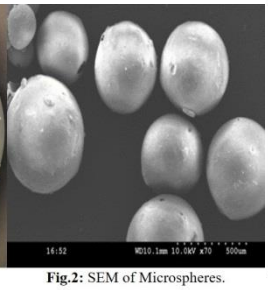

Fig.2: SEM of Microspheres.

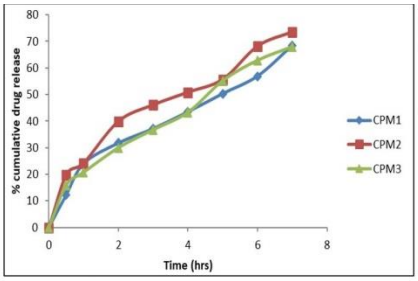

Fig.3: Dissolution profiles of optimized formulations.

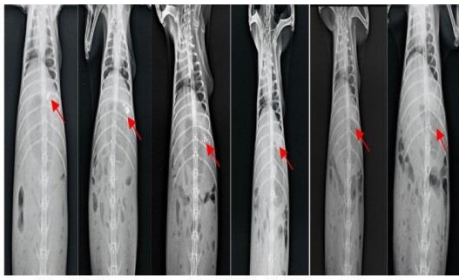

Fig.4: X-Ray photographs of GIT of rabbits at different time intervals after administration of floating microspheres.

Conclusion: The *in vitro* buoyancy after 7hrs was >70% indicating satisfactory performance of optimized formulations. CPM2 formulation showing best appropriate balance between drug release rate and buoyancy is considered as best fit for Cefpodoxime proxitel floating microspheres. The CPM2 formulation floats in stomach and prolongs the gastric residence time (GRT). Consequently, it provides sustained action. Hence, it can be concluded that Cefpodoxime proxitel floating microspheres are potential candidate for safe and effective controlled drug delivery for extended period with reduced dosing frequency.

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Formulation and Evaluation of Flurbiprofen Loaded Albumin Microspheres for Sustained Drug Delivery

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Background and Rationale: A well-designed modified drug delivery system can overcome many of the problems of conventional dosage forms and enhance the therapeutic efficacy of the administered drug. The purpose of present work is to develop sustained release microspheres of water insoluble drug, flurbiprofen, using Bovine Serum Albumin by solvent evaporation method. On the basis of studies, the expected outcome is that albumin enhances the solubility of flurbiprofen from microspheres, hence presenting a suitable method for preparing the sustained-release albumin microspheres for poorly water- soluble drug Flurbiprofen for effective management of chronic pain without side effects associated with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).

Methods: Bovine serum albumin (BSA) microspheres containing Flurbiprofen were prepared by solvent evaporation method. Different concentrations like 10-60% solutions of BSA were made to which Flurbiprofen drug was added and used as the aqueous phase. Physico-chemical characterization of microspheres such as drug-polymer interactions by FT-IR spectroscopy, Surface morphology by using JEOL JSM T-330A Scanning Electron Microscope, mean particle size and size distribution, drug loading and incorporation efficiency.

***In vitro* release and release kinetics studies**: The drug- release studies of the microspheres were carried out for 12 h at 100 rpm by using USP Dissolution testing apparatus II – paddle method. The temperature of the dissolution medium was controlled at 37 ± 0.1°C. A quantity of microspheres equivalent to 100 mg of drug was weighed. The dissolution medium was 900 ml of phosphate buffer (pH 7.2±0.2). Five millilitres of the dissolution fluid was withdrawn at regular time interval and was replaced with fresh quantity of medium. The samples were filtered, and the filtrate was assayed spectrophotometrically to determine the dissolved drug concentration using a spectrophotometer (Model 1601 Shimadzu, Japan). To examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order, first order, Higuchi's square root of time and Korsemeyer Peppas double log plot respectively.

Results and Discussion: The results of FTIR spectral showed that there was no significant interaction between the drug and polymer. Albumin microspheres showing smooth surface were confirmed by Scanning Electron Microscopic (SEM) study. The mean particle size and entrapment efficiency were found to be varied by changing various formulation parameters. The *in vitro* release profile could be altered significantly by changing various formulation parameters to give a sustained drug release from the microspheres. The release kinetics studies were found to fit into zero order and Non Fickian diffusion-controlled mechanism was observed. The drug was released continuously for a period of 12 hours.

Conclusion: From the preliminary trials it was concluded that it is possible to formulate sustained release Flurbiprofen loaded albumin microspheres for effective management of chronic pain without side effects associated with NSAIDs.

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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 study is enhancing the topical delivery of hydrophillic drug ketorolac tromethamine by formulating transferosomal gel using Box-Behnken design [1].

Method: The influence of the type and concentration of the lipid, surfactant, cholesterol and edge activators on the vesicle formation were investigated and optimized using Box-Behnken design. The prepared transferosomes formulation was evaluated for vesicle formation, entrapment efficiency, drug content and drug diffusion studies. The optimized formulation was incorporated in the gel prepared by Carbopol 934 and evaluated for physical appearance, homogeniety, pH, viscosity and spreadability[2]. *In vitro* diffusion studies were performed using Franz diffusion cell at 50 rpm, 37^0C temperature in pH 7.4 phosphate buffer saline media for determination of drug release of optimized transferosomal suspension.

Results and Discussion: All the formulations with Tween 80 and soya lecithin has shown good vesicle formation. The concentration of cholesterol was optimized based on vesicle formation, entrapment efficiency and *in vitro* drug diffusion studies. Cholesterol at a concentration of 30 mg has shown good vesicles with drug release of 40% at the end of 6 hours. Concentration of lipid, surfactant and edge activator was optimized using Box-Behnken design. Based on responses obtained F18 was considered as 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 predicted value by the design. The pH of the gel was found to be 6.68, spreadability 6.62, drug content 91.8% and drug release was found to be 60% at the end of 8hours.

Conclusion: It can be concluded that the formulation was stable, observed to follow zero order kinetics with Higuchi release mechanism.

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Formulation and Evaluation of Lipid Based Drug Delivery System of Candesartan Cilexetil

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Rationale and Background: The objective of our investigation was to develop Lipid Based Drug Delivery Systems of Candesartan Cilexetil. LBDDS are an emerging technology designed to address challenges like Solubility and bioavailability of poor water-soluble drugs. These enhance the drug solubility within the gastrointestinal tract thereby enhancing the oral bioavailability of the highly lipophilic compounds. Candesartan Cilexetil is an esterified prodrug of Candesartan, a nonpeptide angiotensin ll type l receptor antagonist used in the treatment of hypertension. The bioavailability of CC is dissolution rate limited following oral administration. To improve the solubility, dissolution and hence oral bioavailability, CC was formulated as LBDDS.

Methods: The solubility of Candesartan Cilexetil (CC) in different lipids was determined at 25°C by shake flask method and those showing maximum solubility were selected for the formulation of LBDDS. Lipids were accurately weighed and placed into a round bottom flask, heated at 80°C with constant stirring until all lipids were melted, measured amount of CC was added into molten mixture at 70°C with stirring to form a homogeneous mixture. Aerosil was then added to the molten mixture until it forms free flowing powder. The powder thus obtained was filled into capsule and subjected for further studies. *In vitro* dissolution studies were carried out in different media in pH 6.8 phosphate buffer, pH 6.8 phosphate buffer with 1% SLS and pH 6.8 phosphate buffer with tween 20, 0.1N HCl with 1% SLS using Dissolution apparatus USP type-ll paddle type maintaining temperature at 37 0.5°C at 50 rpm. Surface morphology of LBDDS was studied with SEM and crystallinity of drug and the formulation were studied using XRD.

Results: CC showed maximum solubility in Transcutol and Labrasol, hence were selected as lipids for formulation of LBDDS. Drug release was high in 0.1N HCl with 1% SLS and hence was selected as a dissolution medium. The dissolution profile for formulation F5 containing drug with transcutol and Labrasol showed highest drug release among all formulation i.e., 94.09%. The SEM of F5 formulation showed that drug was completely embedded into lipid matrix and the particles were spherical and porous with a size around 25µ. XRD of formulation F5 indicated absence of crystallinity in LBDDS. This could explain the enhancement of dissolution of CC in LBDDS.

Conclusion: It was concluded that LBDDS formulation containing CC significantly increases the solubility and dissolution.

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Formulation and Evaluation of Modified Pulsincap Drug Delivery System of Ketoprofen for Chronotherapy of Arthritis

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Background and Rationale: Pulsatile system is gaining a lot of interest as it increases patient compliance by means of providing time and site-specific drug delivery system. The objective of the present research work was to develop and evaluate Ketoprofen (KP) loaded microcapsules using pH dependent polymers for chronotherapy of Arthritis. KP is a Non-Steroidal Anti-inflammatory agent having 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 overcome is by formulating an oral sustained release formulation using a pulsatile device for colon.

Methodology: Microcapsules of KP were prepared by emulsion solvent evaporation techniques by using Eudragit RS/RL-100 as polymers. The basic design of pulsatile device consists of an insoluble capsule body, filled with KP microcapsules and sealed with hydrogel polymer plug. The entire device was enteric coated with 5% Cellulose Acetate Phthalate (CAP) solution. The prepared KP microcapsules were subjected to drug-polymer compatibility by Fourier Transform Infra-Red Spectroscopy (FTIR), surface morphology by Scanning Electron Microscopy (SEM), particle size and size distribution, the physical state of drug in the microcapsules was determined by Differential Scanning Calorimetry (DSC), %yield, drug content, entrapment efficiency, *in vitro* dissolution studies, and release kinetics.

***In vitro* dissolution studies:** *In vitro* dissolution profile of each formulation was determined by employing USP XXIII rotating basket method (900 ml pH 1.2, pH 6.8 and pH 7.4 phosphate buffer, 100 rpm, $37^{o}\pm0.5^{o}C$). Microcapsules equivalent to 100 mg of KP was loaded into the basket of the dissolution apparatus. 5ml of the sample was withdrawn from the dissolution media at suitable time intervals and the same amount was replaced with fresh buffer. The absorbance of the filtrate was determined at wavelength of 258nm against pH 7.4 blank. The amount of drug present in the filtrate was then determined from the calibration curve and cumulative percent of drug release was calculated. Three optimized formulations were selected and further used into 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(Q0-Q) v/s t], Higuchi's square root of time (Q v/s $t_{1/2}$) 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 (Q0-Q) is the cumulative percentage of drug remaining after time t. The stability study was carried out for selected formulation as per ICH guidelines.

Results and Discussion: The IR Spectra and DSC thermo gram revealed that, there was no interaction between the polymer and KP. The KP microcapsules were spherical in nature, which was confirmed by SEM. KP microcapsules with normal frequency distribution were obtained. A maximum of 94.50 % drug entrapment efficiency was obtained in the KP microcapsules. The *in vitro* performance of KP microcapsules showed that sustained release was dependent upon the polymer concentration. The co-efficient of determination indicated that the release data was best fitted with zero order kinetics. Higuchi equation explains the diffusion-controlled release mechanism. The diffusion exponent 'n' values of Korsemeyer-Peppas model were found to be non-Fickian. From the stability studies, it was observed that there were no significant changes in the physical properties and drug content of the capsules and therefore the formulations are quite stable.

Conclusion: Pulsatile drug release over a period of 2-24 hours, consistent with the requirements for chrono pharmaceutical drug delivery was achieved from insoluble gelatin capsules, in which microencapsulated KP was sealed by means of a suitable hydrogel plug. Thus, pulsatile drug delivery system can be considered as one of the promising formulation techniques for preparing colon specific drug delivery systems and hence in chronotherapeutic management of Arthritis.

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Formulation and Evaluation of Nano Co-crystals based Oral Film of Brexpiprazole

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Background and Rationale: Antipsychotic drugs treat conditions ranging from anxiety to schizophrenia. The primary concern of oral antipsychotic drug delivery is patient compliance. Brexpiprazole (BPZ) is a BCS class II, a new antipsychotic drug with lower solubility and bioavailability profiles. Nano co-crystals can significantly increase the surface area and enhance dissolution rate, alongside bioavailability. Thus, when presented into orally disintegrating films (ODFs), the rapid hydration by saliva induces faster disintegration and dissolution and improves medicament release. The study objective is to overcome solubility issues, reduce the dose-related side effects associated with oral therapy, and improve patient compliance for psychotic patients via a nano co-crystal based ODF.

Methods: A) Preparation of nano co-crystals of Brexpiprazole: The nano cocrystals were prepared via the antisolvent addition method using the coformer nicotinamide. The formulations were optimized using a custom design approach. The amount of coformer, antisolvent volume, and stirring time were taken as variables of the responses solubility and dissolution rate. The optimum nano co-crystal formulation was further incorporated into the film formulation.

B) Preparation of oral disintegrating films of brexpiprazole nano co-crystals: An aqueous solution of hydroxypropyl methylcellulose (HPMC), plasticizer, saliva stimulating agent, super disintegrant, and sweetening agents were stirred under magnetic stirring. The optimized nano co-crystal formulation was incorporated into the above polymer solution to obtain a patch area of 6.2 cm^2 containing 4 mg of Brexpiprazole and kept for solvent casting.

C) *In vitro* dissolution study: The *in vitro* dissolution study was carried out using USP dissolution apparatus type II with 900 ml of phosphate buffer pH 6.8 (0.1% SLS) as the dissolution media at 37±0.5°C with the RPM of 100. A 4 mg drug equivalent to co-crystal based ODFs and Pure BPZ-ODFs were introduced for dissolution studies. At 10, 15, 30, 45, 60, 90, and 120-minutes, samples were obtained and replaced with an equivalent volume of blank solution. The samples were subsequently filtered and analyzed spectroscopically, and the percentage (%) of drug dissolved or released was calculated.

Results and Discussion: The co-crystals prepared were evaluated for solubility and *in vitro* drug release. Brexpiprazole solubility is found to be 0.0073±0.00027 mg/ml, whereas the co-crystal formulations exhibited a solubility ranging 0.23 to 0.087 mg/ml. The differential scanning calorimetry and X-ray pattern supported the solubility enhancement profiles. The dissolution rate of co-crystals formulation was found to be 64.1±0.10 - 71.23±0. The comparative *in vitro* dissolution studies between BPZ-nano cocrystal film and pure BPZ-oral film were performed. The coformer formulation showed a maximum % drug release of 78.4±0.48% at 120 minutes against 3.568±0.125 from pure drug film.

Conclusion: Oral disintegrating films of Brexpiprazole nano cocrystals are practically approachable with a faster release, improved solubility, and dissolution rate of the drug in a short time. Both coformer nicotinamide and antisolvent methods assured the formation of co-crystals with superior solubility and dissolution profile. So, in conclusion, oral disintegrating films containing nano co-crystal of Brexpiprazole give assurance in improving solubility and overcoming the patient compliance issue associated with antipsychotic drugs.

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Formulation and Evaluation of Nano Sponges based Topical Drug Delivery System for Rheumatoid Arthritis

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Background & Rationale: Rheumatoid arthritis (RA) is a chronic, symmetrical, inflammatory autoimmune disease that initially affects small joints, progressing to larger joints, and eventually the skin, eyes, heart, kidneys, lungs. Often, the bone or cartilage of joints are destroyed, and tendons, ligaments are weakened [1].The main goal of the first-line treatment is to decrease inflammation, relieve pain and the medications to be considered are fast-acting non-steroidal anti-inflammatory drugs. Piroxicam, a main member of non-steroidal anti-inflammatory drugs (NSAIDs), is mainly used for the treatment of rheumatoid arthritis, which causes gastrointestinal irritation when administered orally. It also has systemic effects when administered intramuscularly [2]. A nanosponge is an emerging technology which can overcome gastrointestinal irritation and precisely control the release rates of drug. Due to their porous structure and small size; they can easily bind to drugs which are poorly-soluble leading to better bioavailability and solubility of such drugs [3]. An attempt was made to formulate piroxicam nanosponges which were then incorporated into gel prepared by using Carbopol 934 P where the solubility of the drug is enhanced and sustained release formulation was prepared.

Methods: Nanosponges were prepared by emulsion solvent diffusion method by changing the drug polymer ratio and process parameters were optimized by factorial design. Characterization of piroxicam nanosponges were done by FTIR spectroscopy, differential scanning calorimetry, X-ray diffractometer and scanning electron microscopy.

Results and Discussion: The presence of all characteristic peaks of piroxicam in physical mixture in FTIR spectra reveals that the drug is intact and there is no interaction between drug and excipients. *In vitro* studies for pure drug and formulation was carried out. The dissolution data of the formulation was fitted to zero order, Higuchi matrix and Korsemeyer-Peppas to ascertain the kinetic modelling of drug release. From the *In-vitro* studies, % drug release was found to be 86.7% at 24 hour, implies that the formulation showed sustained release.

Conclusion: It was concluded that the piroxicam can be developed into nanosponge gel that can release the drug upto 24 hours with increased solubility and sustained release. Therefore, topical piroxicam nanosponges are promising drug delivery for topical application as being more useful than conventional formulation therapy.

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Formulation and Optimization of Self Micro Emulsifying Drug Delivery System of Clopidogrel Bisulphate Using Mixture Design

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Background and Rationale: Self-emulsifying, micro emulsifying and nano emulsifying drug delivery systems (SEDDS/SMEDDS/SNEDDS) are highly effective in enhancing the aqueous solubility, dissolution and bioavailability of poorly-water soluble drugs. The present investigation is aimed to develop self-micro emulsifying drug delivery system (SMEDDS) to improve the *in vitro* dissolution of a BCS Class II anti-platelet agent, clopidogrel bisulphate.

Methods: A) Formulation development: Phase titration method was used for preparation of SMEDDS. D-optimal mixture experimental design was applied to optimize liquid SMEDDS using three independent variables; the oil phase X1 (Oleic acid), the surfactant X2 (Tween 80) and the co-surfactant X3 (PEG 600). R1: Self emulsification time (sec), R2: Percentage drug release within 90min were selected as two dependent variables.

B) *In vitro* dissolution: *In vitro* drug release behavior of drug from pure clopidogrel bisulphate and L-SMEDDS dispersion was determined using modified dialysis method in USP type II dissolution apparatus. On oral administration, L-SMEDDS form o/w emulsion when they come in contact with gastric media. At this stage, the drug exhibits several different complex states such as molecular state, micellar solution, and entrapment in emulsion globules. Hence, this method was used. Dialysis membrane was soaked in freshly prepared 0.1N HCl medium for 12h at room temperature. L-SMEDDS formulation and pure drug equivalent to one dose was filled inside the dialysis bag and both the ends of dialysis bag were sealed tightly without any leaks, tied to end of paddle. 900 ml of 0.1N HCl as dissolution media was maintained at 37°C and paddle was rotated at 50 rpm. Samples (5ml) were withdrawn at time intervals of 5, 10, 15, 30, 45, 60 and 90mins. Replacement with fresh media was done and the samples were filtered. The concentration of drug was determined by UV-spectrophotometer at 219 nm.

Results and Discussion: FTIR studies confirmed that the drug and excipients were compatible. The liquid SMEDDS were evaluated for thermodynamic stability studies, visual observation, robustness to dilution, drug content, self -emulsification time, dispersibility test and drug release. Contour plots and Response surface plots indicated that with the increase in oil ratio (X1) there is increase in self-emulsification time and decrease % drug release. For these formulations predicted vs. actual responses showed correlation of 0.963 for self -emulsification time, 0.9177 for % drug release in 90 minutes. Optimized formulation (OPF1) Oil (20.25ml), surfactant (39.74ml) and co-surfactant (40ml) obtained from the design (with criteria < 40 sec for Self emulsification time, >85% release in 90 min) shown self-emulsification time of33.87seconds, 101.41 ±0.21%of drug release in 90min, particle size of 528.6nm and PDI of 0.560, from which it can inferred that micro range emulsion has been formulated and the particle size possess large interfacial surface area for drug absorption. The surface morphology of Optimized formulation (OPF1) was examined by SEM analysis was found to be smooth. Zeta potential is useful in knowing the surface charge of the particle which can determine its stability. Zeta potential can be either positive or negative, stable formulations may possess +30 to -30 mV charge. The formulation OPF1 has shown a Zeta potential of -15.9 mV. The optimized formulation (OPF1) showed best results in terms of self -emulsification time (<40 seconds) and drug release (>85% in 45 min) and was stable for 1 month.

Conclusion: The results demonstrate the potential of SMEDDS as a means of improving solubility, dissolution and hence the bioavailability.

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Formulation of Novel Cocrystal of Nevirapine and its Dissolution Enhancement by Co-grinding Crystallization Method


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Background & Rationale: Nevirapine is an antiretroviral drug which is mainly used in the treatment of HIV/AIDS. The drug belongs to BCS class II and thus shows high permeability, low solubility. Many different approaches of increment in dissolution of poorly soluble drugs have been implied to enhance the dissolution characteristics of this drug. The aim of the present study was to enhance the solubility and dissolution profile of a poorly aqueous soluble drug nevirapine by forming pharmaceutical cocrystal.

Methods: The nevirapine cocrystal was formed by three different methods such as co-grinding method, solvent drop crystallization method, and solvent evaporation method in a 1:1 and 1:3 stochiometric ratio of drug:coformer by screening various coformers. The prepared nevirapine cocrystal was analyzed for its melting point and solubility study. The prepared cocrystal was confirmed by Infrared Spectroscopy (IR) and further it was subjected to *in vitro* drug release study and development of formulation.

Results and Discussion: The cocrystal of nevirapine with gallic acid coformer prepared by co-grinding method, solvent drop crystallization method, and solvent evaporation method in a 1:1 and 1:3 stochiometric ratio and among all the formulations the formulations containing 1:3 ratio of Nevirapine:gallic acid showed highest percentage drug release i.e., 87.36% in 0.1N HCl by co-grinding crystallization method at 120 minutes of the dissolution studies.

Conclusion: A significant increase in the solubility and dissolution of nevirapine was obtained from the cocrystal with the gallic acid as a conformer. The cocrystal is formed by using gallic acid as a conformer and by co-grinding crystallization method which will warrant for the future direction in the development of dosage forms.

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In vitro and *In vivo* Characterization of Solid Lipid Nanoparticles of Andrographis Echioides with Special Emphasis on Anti-diabetic Activity

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Background and Rational: Medicinal plants with known therapeutic properties and no side effects have now occupied lead positions in the pharmacopoeia. However, the delivery of plant/herbal therapeutic molecules as drugs is problematic due to poor solubility, poor permeability, low bioavailability, instability in biological milieu, etc. These limitations of herbal drugs can be overcome by attaching or encapsulating them with suitable nanomaterials which can significantly enhance the pharmacokinetics and greatly improve their performance. In this study, we hypothesized that loading plant extract into nanoparticles to improve its oral bioavailability and hence the effectiveness of the extract in anti-diabetic activity.

Methods: *Andrographis echioides* extract loaded solid lipid nanoparticles (ASLNs) were prepared by High-speed homogenization and Ultrasonication method using Solid lipid (Acconon C-44 EP/NF). Scanning electron microscopy (SEM) is utilized to exemplify the surface morphology of the ASLNs. The average particle size of ASLNS was determined by dynamic light scattering (DLS) at scattering angle 90^{o} and temperature of sample holders is about 25^{0}C by using (Nanopartica SZ-100 HORIBA Scientific, Japan). Stability of nanoparticles depends on zeta potential; zeta potential was determined by using a Zetasizer (Nanopartica SZ-100 HORIBA Scientific, Japan). To determine drug entrapment efficiency, the freeze dried ASLNs were dissolved in methanol and phosphate buffer saline Ph 7.4 (PBS) under water bath at 65ºC for 30 min and then cooled to room temperature to preferentially precipitate the lipid. Drug content in the supernatant after centrifugation (6500 rpm for 15 min) was measured against the blank by UV-VIS spectrophotometer (Shimadzu 1700).

***In vitro* release and release kinetics studies**: *In vitro* dissolution studies were carried out using (Electro lab – TDT 08L) at 50 rpm in 900ml. of 0.1N HCL for 60 mins and phosphate buffer (pH 7.4) for 120 mins as dissolution media, maintained at 37+ 0.5^{0}C. 5ml aliquots were withdrawn at the specified time intervals and analysed spectrophotometrically against blank in 0.1N HCl and in phosphate buffer (pH 7.4) UV spectrophotometer. An equal volume of fresh medium, which was prewarmed at 37^{0}C, is replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies were performed in triplicate. The results of the experiments are given as a mean sample ± standard deviation (SD) and were analysed according to t-test and one-way analysis of variance (ANOVA).

The ASLNs were tested for physical stability to show that there was no effect of drug loading on the stability of SLNs. The optimized ASLNs were tested for anti-diabetic activity in male Swiss albino rats.

Results and Discussion: In the present study, *Andrographis echioides* extract loaded Solid lipid nanoparticles was successfully prepared by High-speed Homogenization followed by Ultrasonication method. The study revealed that most of the ASLNs was fairly spherical in shape, the surface of the particle showed a characteristic smoothness, and the particle size was in the non-metric range, as depicted by SEM. All formulations had values of polydispersity, which indicates the uniformity of particles in the formulations. having appreciable zeta potential which indicates that all formulations stable. Maximum of 97.4% of drug content and 73.2 % Encapsulation efficiency was obtained. The highest drug release from optimized formulation was found to be (96.34%) at and after 30 min. From the stability study data, it shows that there was no drastic change in evaluation data of optimized formulation during manufacturing and after storage at stress condition at 4˚± 2˚ C. In this study, administration of ASLNs to STZ-induced hyperglycaemic rats incontestable distinguished reduction in blood glucose level, standardization of serum biochemical profiles including lipid contents, comparing to STZ control rats. Therefore, it can be concluded that the ASLNs is remarkably effective against STZ-induced diabetes in Wistar rats thereby validating its ethno medicinal usage

Conclusion: In this Present study *Andrographis echioides* extract loaded Solid lipid nanoparticles was successfully prepared by High-speed Homogenization followed by Ultrasonication method and evaluated for Particle size, Poly dispersive index, zeta potential, shape and surface morphology (SEM), % Drug entrapment efficiency, drug content and In vitro drug release study. Thus, from enhancing the dissolution rate, study confirmed that the ASLNs formulation may improve the dissolution rate of *Andrographis echioides*. Thus, by decreasing the particle size of herbal ASLNs it was confirmed that the ASLNs formulations may improve the permeability rate of *Andrographis echioides* which may lead to enhanced bioavailability and thus Anti-diabetic activity. From the ascertained oral hypoglycemic activity of ASLNs in STZ-induced diabetic rats, it can be further inferred that ASLNs will function a motivating candidate in complementary and alternative medicine for the effective management of diabetes.

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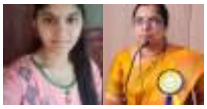
InVitro Diffusion Studies of Nanolipidcarriers of Rutin for Brain Targeting Through Nose - Application of Box-Behken design



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Background and Rationale: Nanolipid carriers get easily penetrated into small capillaries due to their tiny size which can be taken up within cells allowing an efficient accumulation at the target site. Administration of drug through the nasal route avoids first-pass metabolism and the high permeability at the vascular site surpasses the blood-brain barrier. The larger surface area of nasal mucosa affords rapid absorption and gives fast onset of action. The selected drug is Rutin, a flavonoid proved to possess anti Parkinsons activity with a need to improve its bioavailability. The main aim of the present study is to fabricate Rutin-loaded nano lipid carriers for efficient delivery to the brain through nasal route for the treatment of Parkinsons disease.

Method: Nanolipid carriers of Rutin were prepared by melt emulsification followed by probe sonication method. Heating of both lipid phase (in lipid phase drug was added) and aqueous phase to 70°C then aqueous phase is added to lipid phase under magnetic stirring and then sonication for 40 minutes and then obtained Nanolipid carriers were freeze-dried. A total of 17 formulations were (RNL1-RNL17) prepared according to Box Behenken Design by taking lipid concentration (X1), surfactant concentration (X2), stirring speed (X3) at three levels. Then all were evaluated for *in vitro* release studies.

***In vitro* drug release studies:** Studies were performed using Franz diffusion cell by taking pH 6.4 phosphate buffer in the receptor compartment and Rutin Nanolipid carriers in the donor compartment. The studies were performed for 24 hours. Aliquots were withdrawn at periodic time intervals and after suitable dilutions, aliquots were analyzed by UV spectrophotometry for calculation of percentage of drug release.

DoE software version 10 was applied on these results to study the influence of three (X1, X2, X3) variables on drug release by polynomial equation, response surface and contour plots. Finally, the optimum concentrations of three variables were obtained to get maximum drug release and entrapment efficiency within desired size range for brain targeting.

Results and Discussion: The results of *in vitro* release studies of all 17 formulations were obtained. As per the polynomial equation obtained for drug release by Box, Behnken design demonstrated that concentration of lipid and surfactant have shown negative effect whereas stirring time has shown a positive effect on drug release which was also confirmed by response surface and contour plots. The optimum concentrations of lipid (0.29), surfactant (0.51), and stirring time (40) with maximum percentage drug release (45%) were obtained from overlay plot. Hence, the present work revealed the optimized formulation for maximum percentage drug release with desired particle size for crossing BBB.

Conclusion: The present work successfully designed and developed an optimized Nanolipid carrier for increasing the bioavailability of Rutin for brain targeting through nose to treat Parkinsons disease.

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Lyophilized ODT: A New Approach in the Delivery of Antireteroviral Drug for Paediatric Patients

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Background and Rationale: AIDS stands for acquired immunodeficiency syndrome; a pattern of devastating infections caused by the human immunodeficiency virus [(1)]. Among the antiretroviral drugs, Dolutegravir is a new-generation HIV integrase inhibitor with many different advantages compared with other antiretroviral agents available. It belongs to BCS class II drug that has low solubility and high permeability. Orally disintegrating tablets (ODTs) are solid dosage forms that disintegrate in the mouth in less than 60s, and are thus swallowed without the need for water [(2)]. Rapid disintegration of tablet cause quick dissolution and thus fast onset of action. ODTs are the suitable dosage forms for special populations like paediatrics, geriatrics, psychotic, dysphagic, bedridden patients. Considering the above clinical manifestation, a fast-dissolving drug delivery of the proposed drug can prove to be beneficial in treating such conditions effectively. It can be prepared by techniques like spray drying, sublimation, freeze drying, moulding, direct compression etc [(3)].

Methods: The current study utilises the method of lyophilisation for the preparation of the ODTs. To check the effect of freezing technique on the formation of ODTs it is done by two different methods one by 24hrs refrigeration at -19˚ C and another by using Liquid nitrogen - 196˚ C, 350 psig. The formulations were then subjected to lyophilization. The ODT obtained were optimized by Factorial design using design expert software.

Results: The tablets were evaluated for different tests like friability, disintegration time and dissolution time results obtained from disintegration test showed that lyophilized ODTs disintegrated within 2.01 seconds showed % friability of 0.66%. The optimized formulation was further evaluated for dissolution profile. It was studied that F7 showed drug release of 90.24% compared to plain DTG powder of 24.12% at 16th min. The different kinetic models such as Zero order, First order, Higuchi model and Korsemeyer Peppas model were analysed for the optimized formulation.

Conclusion: Lyophilization has been considered as the most successful, since the resultant tablets have a highly porous structure, which permits rapid disintegration and thereby considering dissolution profile of the optimized formulation it is concluded that the process of preparation of ODTs by lyophilization improved the solubility of the drug.

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Mirtazapine Oral Disintegrating Film: A Novel Approach for Effective Management of Depression

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Background & Rationale: Depression is a common mental disorder, characterized by sadness, low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration. Mirtazapine is an antidepressant drug belonging to BCS class II used for the treatment of moderate to severe depression. It is the only tetra cyclic anti-depressant drug that has been approved by USFDA to treat depression. However, the drug suffers from low bioavailability due to poor solubility and first pass hepatic metabolism. Thus, the present study aimed at increasing the solubility of mirtazapine by complexation technique and then incorporating it into an oral dispersible film to enhance bioavailability and patient compliance.

Methods: Complexes of Mirtazapine with 2-hydroxypropyl β-cyclodextrin (2HPβ-CD) in different ratios (1:1, 1:2, 1:3 and 1:4) were prepared by kneading technique. The polymers and plasticizers for the film formulation were selected after initial screening studies where hydroxypropyl methylcellulose (HPMC), polyvinylpyrrolidone (PVP K 30) and propylene glycol, polyethylene glycol (PEG 400) and glycerin were investigated. Optimization studies were carried out using 3^2 full factorial design where concentration of plasticizer (X_1) and concentration of polymers (X_2) were taken as independent variables. The dependent variables selected were folding endurance (Y_1), disintegration time (Y_2) and % drug release. (Y_3). Further, the optimized formulations were evaluated for the parameters like thickness, weight variation, surface pH, disintegration time, %drug content, %drug release, *in vitro* permeation, percentage moisture loss, percent elongation, folding endurance, different kinetic models of drug release and stability studies.

Results and Discussion: Solubility studies showed that mirtazapine – 2HPβ-CD complex in a ratio of 1:2 had the maximum solubility; this complex was further used in the formulation of oral dispersible films (ODFs) of mirtazapine. The ODF formulation with Mirtazapine – 2HPβ-CD complex in a ratio of 1:2, HPMC K 15 at a concentration of 2.5% and propylene glycol at 2% showed thickness of 0.29±0.04mm, weight variation 112.00±3.09mg, surface pH 6.81±0.05, disintegration time 27.11 sec, drug content 93.3±1.88%, percentage moisture loss 1.61±0.54, percent elongation 28.03±2.08 and folding endurance 226±0.01, cumulative drug release of 98.40 ±0.09% at the end of 5 min. Whereas, films made with pure drug showed only 43 ± 0.23% of drug release in 5 min. *In vitro* permeation studies of optimized formulation exhibited 80.21% of drug permeation in 30 min compared to films containing pure drug which showed only 46.4%±0.06 of permeation in 30 min. The films were found to be stable over a period of 1 month at room temperature.

Conclusion: Mirtazapine solubility was effectively enhanced using hydroxypropyl β- cyclodextrin as complexing agent. The ODF prepared provide a safe and effective route of drug delivery for geriatric, pediatric and non-cooperative patients and offer a new and innovative drug delivery system for treating depression.

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Niosomal Formulation for Dermal Delivery of Capsaicin

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Background and Rationale: Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder of joints, characterized by joint pain, stiffness, redness, swelling and decreased movement of the affected joints. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first line therapy for the treatment of RA. Though these drugs provide the relief of pain and inflammation, their long-term use results in untoward effects such as cardiovascular complications, renal morbidity and gastrointestinal ulcers. Hence the focus is shifted toward use of natural agents such as capsaicin because of their documented safety and efficacy. However the patient compliance to the drug is reported to be poor owing to multiple skin problems like irritation, burning sensation, erythma and even low percutaneous penetration because of the barrier function of the stratum corneum. Recently niosomes are gaining popularity in the field of dermal drug delivery because of its special characteristic features like increasing penetration of drugs, acting as local depot to provide sustained release and serving as a solubilizing matrix for both hydrophilic and lipophilic drugs. Hence the aim of the study is to formulate niosomes of capsaicin to increase permeability and provide local action when applied topically.

Methods: The capsaicin loaded niosomes were prepared by ether injection method. 3^2 factorial design was used to study the effect of independent variables such as cholesterol concentration (A) and concentration of surfactant (B) on the dependent variables viz., particle size (Y_1),% entrapment efficiency (Y_2) and PDI (Y_3). *In-vitro* release study of niosomal suspension was carried out by dialysis bag method. The vesicle suspension was placed in the dialysis bag dispersed into a beaker containing 500mL of PBS pH 7.4 maintained at $37^oC \pm 0.5^oC$. Samples were withdrawn at predetermined time intervals and analyzed for drug content by using UV-visible spectrophotometer at 279nm. Finally, topical gels enriched with optimized niosomes of capsaicin were prepared using carbopol 934 as base and evaluated for various technological parameters. *In vitro* diffusion studies of prepared gel was carried out and data was fitted in different kinetic models.

Results and Discussion: The niosomes were statistically optimized using 3^2full factorial design and the optimized formulation displayed acceptable particle size (640.1 nm), PDI (0.010), entrapment efficiency (95.2%), along with sustained release up to 24 hours. Thus, F5 formulation was selected further for SEM studies and Gel formulation. The prepared topical gel (F5NG) incorporated with optimized niosomal formulation (F5) showed spherical particles with pH of 6.74 ± 0.04, satisfactory homogeneity, spreadability and viscosity. *In-vitro* diffusion profile of capsaicin from niosomal dispersion (40.765%) and niosomal gel (31.775%) showed sustained drug release in comparison with drug solution (85.855%) and plain drug gel (63.213%) within 8 hours. Further, release order kinetics from prepared niosomal gel confirmed zero order controlled release of drug.

Conclusions: Thus, it can be concluded that niosomal gel represents a promising particulate carrier system having controlled release of capsaicin for rheumatoid arthritis.

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Size Optimized Bromelain Nanoparticles to Intensify EPR Effect in Anticancer Therapy Developed by Nanoprecipitation Technique

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Background and Rationale: Bromelain is an extensively investigated natural product, which has got antimetastatic property. Tumour heterogeneity is found to be an alarming hindrance in the treatment of cancer and hence personalization of medicine emerged as an important consideration. Size reduced passive targeting therapy of nanomedicine could overcome difficulties like lack of tissue selectivity, in addition the dose limiting toxicity. Bromelain, being an enhanced apoptotic agent can be used as an effective treatment in mammary cancer, a complex heterogenous disease which is a leading cause of deaths worldwide. Size reduction could lower the surface area, along with reduction in diffusion layer thickness and thereby exhibits an enhanced dissolution at the release site. Nanoparticles bridle the constraints for free therapeutics, in addition could navigate biological barriers that are heterogeneous across patient populations and diseases.

Methods: A) Development of size optimized Bromelain loaded nanocarriers by Nanoprecipitation technique: Tween 80, surfactant has been selected to aid in size reduction. PLGA dissolved in acetone and surfactant constitutes one phase, which is mixed together with the second phase which constitutes Bromelain dissolved in water, and nanoprecipitation is carried out in magnetic stirrer for continuous 4 hours and recovery of the precipitated particles done in high speed refrigerated ultracentrifuge. Optimizing the particle size and encapsulation efficiency can be regarded as an innovative strategy in maximizing the accumulation of drug carriers and maximum drug release *in situ*, this has done by Box Behnken design developed through Design Expert software.

B) *In vitro* drug release study and release kinetics: Drug release was studied in simulated conditions with the help of rotary shaker, 10 mg of weighed formulation transferred to 100 ml glass beaker containing 50 ml phosphate buffer pH 7.4, and then kept in rotary shaker. And the kinetics of study has been tested for zero order equation, first order equation, Higuchi model and Korsmeyer-Peppas model.

Results and Discussion: Size is optimized to less than 100 nm which confirms the ability to pass through leaky tumour vasculature, by which the size reduction could lower the surface area, along with reduction in diffusion layer thickness and thereby exhibit an enhanced dissolution at the release site. Increasing amount of surfactant exhibits a drastic reduction in particle size, while the amount of drug augment the encapsulation efficiency. The optimized formula exhibits an encapsulation efficiency of 88.71% with a particle size of 78.64±2.14 nm. *In vitro* drug release data shows an initial burst release of 17.59% drug within 1 hour and 89.14% at 24th hour, in addition an active release by Supercase-II transport through diffusion and polymer relaxation is evident from the kinetic data

Conclusion: The study broadcast the significance of optimizing size and encapsulation efficiency of Bromelain loaded nanocarriers for overcoming the heterogeneity in mammary cancer, as Bromelain being an agroeconomic product, having potential antimetastatic property.

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Studies to Demonstrate Sustained Release and Water Resistance Under 'In Use' Conditions from a Long-acting Antimicrobial Spray

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Background and Rationale: The Covid pandemic has resulted in the routine use of masks and sanitation measures. In this context, a novel versatile antimicrobial spray was developed, intended for use on inanimate surfaces e.g. to fortify masks, on doorknobs etc.; as also for use on hands or even in the mouth. Silver nanoparticles (AgNPs) and chlorhexidine digluconate (CG), both potent antimicrobial agents with activity against bacteria and viruses were the actives used (1,2). The objective of the present work was to demonstrate long-acting and water-resistant nature of the product when sprayed on a surface and allowed to dry, mimicking the 'In Use' condition.

Methods: AgNPs were generated by reduction of silver nitrate by trisodium citrate in presence of polyvinyl pyrrolidone as a stabilizer and imaged via SEM. Required amount of a solution of CG was added. The resultant dispersion was further mixed with an ethanolic solution of eucalyptus oil and ethyl cellulose to prepare the spray. The long acting and water-resistant properties were demonstrated using a cotton fabric as base which was sprayed with the product (2ml/16sq.cm), allowed to dry and subjected to the following studies:

1). *In vitro* release: A Franz diffusion cell was used to study the ability of the dried spray to release the actives in a controlled manner under ambient conditions (25 – 30 C). The treated fabric was cut into 4 sq.cm piece, placed between the two chambers and locked in place. The receptor chamber was completely filled with distilled water continuously stirred with a magnetic needle; which served as the acceptor medium. Aliquotes of 4 ml were collected over an 8hr period and replaced with an identical volume of water. The amount of CG released was quantified by UV spectrophotometry at 255 nm and the results represented graphically.

2). Measurement of Zone of inhibition: Small circular pieces of cloth cut from the fabric 24 and 48 h after spraying and also after gentle washing were placed on agar plate seeded with *Staphylococcus aureus* for measuring zone of inhibition.

Results and Discussion: A sustained release of chlorhexidine was observed with 32.6% active unreleased at the end of 8hrs, although the fabric was in intimate contact with the release medium. The fabric with dried spray when placed on a seeded agar plate, showed a zone of inhibition which was only slightly reduced even when the spray was 48 h old or even when the cloth was rinsed in water prior to placement onto the agar surface. The PVP-EC film formed on drying of the spray, thus effectively trapped the actives and held them in place on the fabric even when washed or otherwise placed in contact with water. The results clearly demonstrate the long acting and water-resistant nature of the developed spray, both of which are key for its intended performance.

Conclusion: Thus, the spray, while being instantaneously active due to the ethanol; after drying on a surface, e.g. on a mask or a door knob, would resist washing off and loss due to sweat etc. and would continue to release the actives for a sustained duration, thus offering prolonged protection. Nevertheless, further studies on long term stability and actual duration of action of the spray are necessary.

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The PEGylation: Apigenin Encapsulated Stealth Nanoliposome Promotes Superior Drug Release and Pharmacokinetics Profile Ensuring Robust Promise in Hepatocellular Carcinoma.

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Background and Rationale: Hepatocellular carcinoma (HCC) is currently positioned at the sixth rank in cancer related death worldwide and the reasons behind chemotherapeutic unresponsiveness are drug resistance, recurrences, therapy related side effects along with unpredictable drug accumulation in target tumor. Over the development of nanotechnology, lipid nano carriers showed enormous promise for delivering chemotherapeutics in cancer therapy, yet challenges were there for metered dose accumulation vs clearance rate. At this point, PEGylated nanoliposomes could expand the circulation time as well as precise and controlled drug release in tumor site. Bioflavonoids such as apigenin, quercetin, curcumin etc. are already gained interest in cancer therapy and different nanotechnological approaches were attempted in cancer drug delivery. Here, unexplored areas like **novel apigenin encapsulated PEGylated stealth nanoliposome (Api-PEG-NL)** were developed and characterized while comparing with plain apigenin nanoliposomes (Api-NL). Finally, cytotoxic and apoptotic potentiality of optimized PEGylated nanoliposomes were evaluated against HCC based on drug deposition at neoplastic site.

Methods: Apigenin nanostructured PEGylated stealth liposomes have been developed by thin film hydration method after confirming the physical and chemical compatibility among the components through FTIR-process. Different nanoformulations (Api-NL/ Api-PEG-NL) from different batches were studied and optimized depending on observed drug loading, particle size estimation (through DLS, FESEM, AFM), zeta potential along with *in vitro* drug release (using two different release media, 1% of beta cyclodextrin and 50% serum). Drug release data were plotted using different kinetic models. Further, *in-vivo* pharmacokinetic study was performed with free drug or different test nanoliposomes (Api-NL/ Api-PEG-NL) to check plasma and hepatic drug concentrations. Finally, cell cytotoxicity was determined through MTT assay and flow cytometric (FACS) estimations showed the apoptotic potentiality of test nanoliposomes in liver cell lines.

Results and Discussion: Drug loading of prepared test nanoliposomes was 3.8% with drug entrapment efficiency more than 80%. DLS, FESEM, AFM studies revealed the test nanoliposomes were within the range of 150 nm. Superior extended drug release pattern was observed in case of Api-NL compared to Api-NL. Plotted kinetic equations and corresponding correlation coefficient (R^2) value obtained from *In vitro* drug release data showed the drug release kinetics best suits with Higuchi kinetics model and analyzed Korsmeyer-Peppa's kinetic model indicating n value (0.45<n< 0.89)

Conclusion: The study established the superiority of novel apigenin encapsulated PEGylated stealth nanoliposome (Api-PEG-NL) for better drug diffusion and deposition towards neoplastic liver cells over conventional nanoliposomes.

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In vitro Permeation Study of Transdermal Patch Containing Analgesic Drug Combating Pain in Mensurating Females

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Background and Rationale: Meftal 500 mg wase the most commonly prescribed drug for females who have stomach pain and spasm during menstruation. In order to overcome drawbacks of oral delivery, there is a need to develop a new drug delivery system The transdermal drug delivery system containing API Mefenamic Acid with combination of EC: PVP with permeation enhancers like eucalyptus oil and PEG-400 shows optimum activity. 3^2 Factorial designs were used where 3 levels Low, medium and high and 2 independent factors quantity of polymers and quantity of permeation enhancers and see the effects against moisture content and % *in vitro* drug release. The patch was prepared by solvent evaporation method. The *in-vitro* study and moisture content were done on all nine formulations namely MF1 to MF9. MF6 had less moisture content and after 24 hours obtained percentage cumulative drug releases were 49.30±1.17, 61.56±1.32, 42.47±0.87, 50.93±0.59, 29.25±0.22, **82.16±0.96**, 54.72±2.09, 34.92±0.57, 32.50±0.52. The MF6 showed highest release and R^2 value were **0.993** in future TDDS patch containing Mefenamic acid with permeation enhancers helpful in combating pain in mensurating females.

Methods: For optimization 3^2 factorial designs were most suited using design expert software. There are 3 levels and 2 factors. The optimization was done on the basis of moisture content and *in-vitro* permeation study. Total 9 formulations namely MF1 to MF9 were prepared. MF6 was Smooth, thin, and flexible film obtained at the ratio (1:4) of ethyl cellulose (EC) and polyvinyl alcohol (PVA) with permeation enhancer eucalyptus oil (EU) and PEG-400 (1:1) by a solvent evaporation method.

Characterization: A) Moisture content: The film was weighted individually and kept at desiccator containing activated silica at room temperature for 24 hours. Individual film was weighed repeatedly until they show the constant weight. Calculate moisture content.

B) *In-vitro Permeation study*: The *in-vitro* permeation study of fabricated transdermal patches of the analgesic drug was carried out by using a cellophane membrane and Franz diffusion cell. The membrane was sandwiched between donor and receptor compartments of the diffusion cell. A 2.2 cm diameter patch was placed in intimate contact with the membrane; the backside was covered with aluminum foil that acts as a backing membrane was placed in the receptor compartment filled with 17mL of phosphate buffer pH 6.5. The cell contents were stirred with a magnetic stirrer and a temperature of 37 ± 5°C was maintained during the experiment. Through the sampling port 1 mL of the sample was withdrawn at different time intervals for a period of 24 hr, simultaneously replacing an equal volume of phosphate buffer pH 6.5 to maintain sink condition. The samples were analyzed spectrophotometrically at 284 nm.

C) Release kinetics Studies: In order to examine the release mechanism of drug sample from the prepared transdermal patch of the optimized formulation (MF6), the results of the percent cumulative drug release were examined in accordance with the kinetic models such as Zero-order, First-order, Higuchi equation, Korsemeyer–Pappas equation, and Hixson-Crowell equation. The R^2 value nearer to 1 indicated the model fitting of the release mechanism.

Result and Discussion: The *in-vitro* study was done on all nine formulations namely MF1 to MF9, after 24 hours obtained percentage cumulative drug releases of different formulations were 49.30±1.17, 61.56±1.32, 42.47±0.87, 50.93±0.59, 29.25±0.22, **82.16±0.96**, 54.72±2.09, 34.92±0.57, 32.50±0.52. The various flux were calculated. The optimized MF6 preparation various release model studied like Zero order, First order, Higuchi equation, Korsemeyer–Pappas equation and Hixon-Crowell equation. The obtained graph in zero-order, the plot of cumulative percentage drug released versus time, in the first order, log cumulative percentage drug remained versus time, in Higuchi model, a plot of cumulative percentage drug released versus square root of time, Hixon Crowell model the cube root of cumulative percent drug retained versus time and the Korsemeyer–Pappas model, a plot of log cumulative percent drug released versus log time were linear. The regression coefficient R^2 values were 0.986, 0.877, 0.826, 0.923, **0.993** respectively.

Conclusion: All TDDs patch made up of solvent evaporation method. In permeation study, highest percentage of drug release seen in MF6 was **82.16±0.96 %** and various the regression coefficient R^2 values were calculated 0.986, 0.877,0.826,0.923,**0.993** respectively. The best-suited model was Korsemeyer–Pappas model due to the highest R^2 value i.e., **0.993** with less moisture content. It showed that in the future a new milestone for the development of a transdermal patch of analgesic drug which could reduce the pain in menstruation period in females with fewer and minimum side effects. Once the patch is removed therapy may terminate and have no extra side effects this is the speciality of the Transdermal drug delivery system.

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Solution-mediated Phase Transformation Study of Various Hydrochlorothiazide Cocrystals to Achieve Improved Intrinsic Dissolution Rate.

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Background and Rationale: Cocrystals have got a lot of attraction as a new solid form due to their capacity to alter drug molecules' poor physicochemical qualities but very few cocrystal based products are commercially available. The parameters associated with the cocrystal formulation were choosing of cocrystal, preformulation experiments, solution-mediated phase transformation, intrinsic dissolution rate, solubility, permeability, etc.[1] Among them, solution-mediated phase transformation is a crucial parameter. There are so many reported cocrystals of hydrochlorothiazide but none is commercially available. The present work explores the hurdles involved in the translational development of hydrochlorothiazide cocrystals formulation. For the present work, API selected was hydrochlorothiazide (HCT) and coformer used were picolinamide (PCM), nicotinamide (NCT), and 4-aminobenzoic acid (PABA). HCT is a diuretic, which works by preventing the kidneys from retaining water. However, this active pharmaceutical ingredient is a Biopharmaceutics Classification System IV drug having low solubility and permeability which leads to poor absorption and therefore, results in low bioavailability.

Methods: HCT-PCM, HCT-NCT, and HCT-PABA cocrystals were reproduced and recharacterized by DSC, TGA, and PXRD.[2,3] Solution-mediated phase transformation study of HCT-PCM, HCT-NCT, and HCT-PABA cocrystal were performed by shake flask method. Intrinsic dissolution rates of HCT and HCT-PABA cocrystal were performed using a rotating disc method in 900 mL of distilled water.

Results and Discussion: HCT-PCM and HCT-NCT cocrystal show phase transformation within 30 min (Figures 1 & 2), indicating that the cocrystal phase is not stable. As a result, HCT-PCM and HCT-NCT cocrystal was not selected for product development. The equilibrium solubility of HCT-PABA cocrystal in distilled water was higher than that of HCT, resulting in better bioavailability (Figure 4). Further, the PXRD analysis of solid residue left after solubility experiments revealed no phase change up to 4 h (Figure 3), suggesting that the cocrystal phase is stable. The dissolution profiles of HCT and HCT-PABA in distilled water show that the IDR of HCT from HCT-PABA is comparatively higher than pure HCT (Figure 5), which corroborates the higher solubility of HCT-PABA. Improved solubility vis-à-vis dissolution rates will improve the bioavailability.

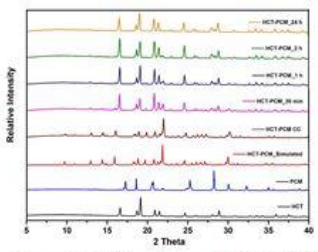

Figure 1: PXRD patterns of HCT, PCM, HCT-PCM cocrystal, and solid residues.

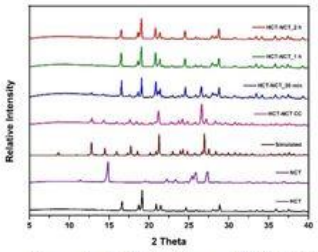

Figure 2: PXRD patterns of HCT, NCT, HCT-NCT cocrystal, and solid residues.

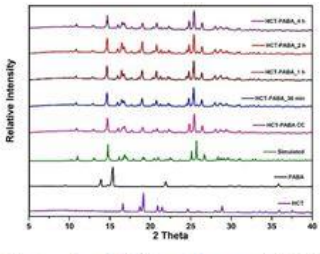

Figure 3: PXRD patterns of HCT, PABA, HCT-PABA cocrystal, and solid

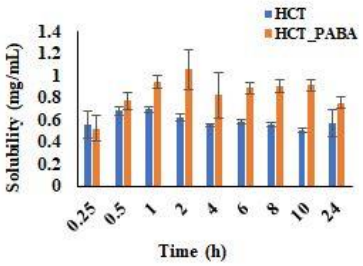

Figure 4: Solubility profile of HCT and HCT-PABA cocrystal in distilled water.

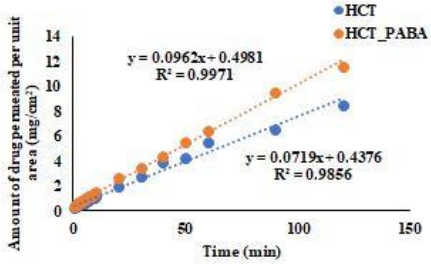

Figure 5: Intrinsic dissolution profiles of HCT and HCT-PABA in distilled

Conclusions: HCT-PCM and HCT-NCT cocrystal was not selected for product development as both the cocrystal shows phase transformation within 30 min. The higher solubility, good phase stability, and higher IDR of HCT-PABA cocrystal than that of pure HCT in aqueous media make HCT-PABA cocrystal a possible candidate for tablet dosage form development.

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Citric Acid Esterified Waxy Rice Starch Enhances Disintegration and Dissolution Efficiency

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Background and Rationale: Bio-based materials from natural sources such as starch remain one of the most important biopolymers owing to its unique physicochemical and functional properties. Polymorphic changes in the starch skeleton consequent upon water adsorption also have the potential to influence the biopharmaceutical and pharmacokinetic properties of the drug within the dosage form [1,2]. Chemical modification of native starch is often carried out by introducing functional groups into the starch skeleton to improve the functional properties of the starch and overcome the limitations of the native starches [3]. As a result of modification of the native starch, improved functional properties like gelatinization, pasting behavior, increased water solubility, disintegration and susceptibility to enzyme attacks have been observed which could promote drug loading and controlled release behavior of a pharmaceutical dosage form [4,5]. Therefore, the current work was designed to study the physicochemical attributes, tablet disintegration, dissolution efficiency and fit factors (dissolution profile comparison) of the starch and its derivatives obtained from Assam waxy rice.

Methods: Starch was isolated by simple protein denaturation method and derivative of the starch was prepared through citric acid modification. WRS (waxy rice starch) and citrated waxy rice starch (c-WRS) were characterized through FTIR, CHN, DSC, XRD, SEM and TEM. The rate of consolidation, consolidation index, angle of internal friction, micromeritics properties, packing rearrangement and cohesive properties were determined. Active pharmaceutical ingredients (API) i.e., paracetamol tablets (500 mg) were prepared by using WRS, c-WRS and corn starch as disintegrating agent. By using disintegrants from 1-5 %, three different tablet formulations were prepared with code W_1-W_5, CW_1-CW_5 and S_1-S_5 for waxy rice starch, citrated waxy rice starch and standard corn starch respectively. USP dissolution rate test apparatus, Type-I used to study dissolution profile of tablet compact. Quality control test were performed along with tensile strength, disintegration test, disintegration efficiency ratio (DER), dimensionless disintegration quantity (DERc), dissolution efficiency (DE), mean dissolution time (MDT), fit factors f_1 and f_2 were investigated for prepared paracetamol tablet compacts.

Results and Discussion: The average particle size obtained was 2.45 µm and 3.02 µm for WRS and c-WRS respectively. Immediate release of API from tablet compact was observed when the concentration of the starch increased from 1 to 5% indicating facilitation of the tablet compact disintegration. The reduced time for disintegration of tablet indicates better dissolution of API which facilitates increased bioavailability and maximum pharmacological response. At the starch concentration of 1 to 5 %, the DE were increased from 71% to 83% for both WRS and c-WRS and MDT was also improved from 8.06 minutes in W_1 to about 5.93 minutes in CW_5. Fit factors f_1 and f_2 were also calculated and found f_1 in between 0-15 and f_2 in between 50-100. All the results were statistically significant at $p<0.05$, $p<0.01$ and $p<0.001$. From DE and DER studies revealed that both WRS and c-WRS produced better results in drug release pattern of API compared to standard corn starch.

Conclusions: Therefore, the results from the current investigation imply that WRS and its derivatives have a potential as tablet disintegrant resulting in enhanced dissolution of the API to improve its bioavailability

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Effect of Printing Process Parameters on the Physico-Technical Behaviour of the Selective Laser Sintering (SLS)-Mediated 3D Printed Printlets


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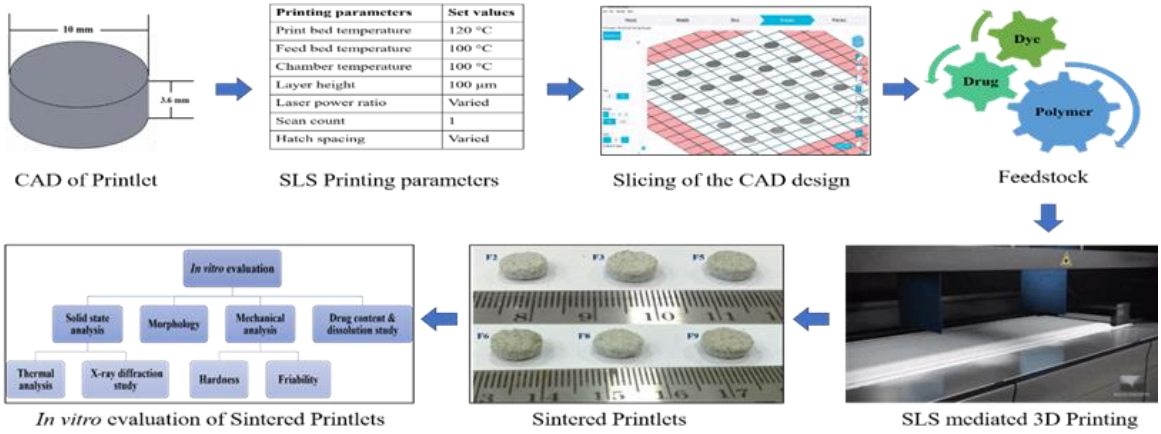
Background and rationale: Selective laser sintering (SLS) is a powder-based 3D printing technology in which a laser beam is used to selectively bind powder particles together to create 3D objects in a layered manner. The SLS technique has recently been used to fabricate various dosage forms, with different shapes and release aspects ranging from orally-disintegrating tablets to immediate and modified dosage forms. The objective of this work to study the influence of printing process parameters on both printability and the physicochemical, mechanical properties of the printlets including crystalline nature of drug. For this work, Dapsone, Poly (1-vinylpyrrolidone-co-vinyl Acetate) were used as model drug and polymer carrier, respectively, along with a near-infrared absorbing dye.

Methods: The theoretical drug-polymer miscibility and interaction parameter was calculated. The flow properties of the individual drug and polymer along with the mix was carried out. A cylindrical circular shaped printlet was designed with 10 mm diameter and 3.6 mm thickness. For the sintering of the powder mixture, a fixed concentration (weight percentage) of drug: polymer: dye (5: 93.75: 1.25) was used. Different batches of the printlets were printed with two printing variables i.e., laser power ratio (LPR) and hatch spacing (HS) at three levels (a total of 9 batches). After printing, the printlets were characterized for morphology, hardness, friability, thermal analysis, diffraction analysis, drug content and dissolution study. For the dissolution study of the printlets, USP type-II dissolution apparatus (paddle type) was used, where 0.1N HCl of pH 1.2 was used as the dissolution medium, and the study was conducted for 2h (maximum gastric emptying time). Printlet was added to 250 ml of dissolution medium which was maintained at a temperature of 37±0.5°C and stirred at 50 rpm. At specific time intervals, aliquots of 5 ml were removed and replaced with the same volume of fresh dissolution medium to maintain sink condition. The collected aliquotes were filtered through 0.22 µm syringe filter and analyzed spectrophotometrically aat 290 nm.

Results and Discussion: The difference in solubility parameter and the interaction parameter between drug and polymer was found to be 2.74 $MPa^{1/2}$ and 0.50 respectively, which favours the miscibility. Both drug and polymer along with the physical mixture showed passable flow properties which showed the suitability of these materials for sintering process. Batches with LPR of 1 was not able to sinter and no printlets formed. All the sintered printlets were cylindrical in shape and showed equivalent dimension to the designed 3D model. Printlets made with higher LPR and lower HS were heavier (dense) than those printed with lower LPR and HS. The hardness values of the printlets were between 04 N to 32 N. Printlet with lower LPR and increased HS showed the highest percentage friability. Both thermal analysis and diffraction analysis confirmed the loss of crystallinity of drug in the printlets. Drug entrapment efficiency was found to be more than 90 % in all the sintered printlets. From the dissolution study, all the printlets showed complete drug release within 45 to 60 minutes in the dissolution medium. The effect of printing parameters on the dissolution profile of the printlets was primarily observed at initial time points, i.e., 2 minutes and 5 minutes, followed by complete dissolution of the printlets over time as the polymer is soluble at acidic pH. By increasing the LPR, the mechanical strength of the printlets increased as a result initial dissolution of printlet slightly decreased in compared to lower LPR. This effect is observed with all the printlets at constant HS. By reducing the HS, the distance between two consecutive laser beams decreased as a result powder particles get more laser energy and sintered effectively and vice versa. Hence, with reducing the HS, the initial dissolution of the printlets decreased as compared to increased HS. The effect of HS is observed with all the printlets at constant LPR. Overall, printlet with lower LPR and higher HS showed faster dissolution as compared to the rest batches.

Conclusion: The drug loaded printlets were successfully fabricated using SLS 3D Printing technique. The effect of two variables can be seen on the physicochemical behaviour of the printlets. No thermal degradation of drug was found during printing process which showed the suitability of this printing technique to prepare solid dosage form. Loss of crystallinity of drug in the sintered printlets showed the ability of SLS technique to prepare amorphous solid dispersion in a single-step process.



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Engineering a Nanoparticle Mediated Buccal Gel for Site-Specific Co-delivery of Berberine and 5-Fluorouracil for Oral Cancer

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Background and Rationale: Oral Cancer (OC) is an aggressive cancer associated with high rates of morbidity and mortality owing to recurrence and metastasis. Therapy outcomes for OC have not improved for several years and the quest for novel and improved drug delivery systems is ongoing. Phytoconstituents have shown promising results when administered alongside conventional drugs in the treatment of cancers.[1] In this work we attempt to explore the potential of berberine (BBR); the major constituent from *Berberis arisata*, when co-delivered with 5 fluorouracil (5FU) the first line drug used in OC treatment.

We also attempted site specific (local buccal) drug delivery which is expected to have reduced side effects and improved efficacy when compared with conventional systemic drug delivery. BBR belongs to BCS class IV and 5 FU to class III, making local drug delivery a challenging task, since the system had to be developed such that it aids the solubility of both drugs and at the same time aids permeability and retention in the buccal mucosa. We designed an oil in water nanoemulsion (NE; which would provide an excellent blend of hydrophilic as well as lipophilic environments to aid solubility and permeability of two drugs with different physicochemical characteristics simultaneously) followed by its incorporation in a gel for mucoadhesion.

Methods: The NE was formulated using the classical method of pseudo ternary phase diagrams. Miglyol® 812N, Tween 80 and polyethylene glycol 400 (PEG 400) were selected as oil phase, surfactant and co surfactant respectively. Based on the pseudo ternary phase diagrams three NEs with varying oil content were selected for further evaluation. The optimized NE was incorporated into 0.8 % gellan gum gel. The gel was evaluated for physico chemical properties, *ex vivo* permeability in porcine buccal mucosa using Franz diffusion cell apparatus, *in vitro* apoptosis on AW13516 OC cell line using MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) assay and mucosal irritation in rabbits.

Results and Data Analysis: The optimized NE contained 3 % oil and 40 % surfactant mixture, with particle size 37.7 nm, polydispersity index 0.126 and zeta potential - 0.7. The entrapment efficiency was 94.67 and 93.25 % for 5 FU and BBR respectively. The optimized gel had viscosity 13500 cps, pH 7.1, spreadability 10 cm/s, and mucoadhesive strength 490 dynes/cm^2 ± 5.3. Drug content was 0.55 % w/w for each drug. BBR and 5 FU crossed porcine buccal mucosa and were retained therein for up to 6 h (40 % and 33% cumulative, respectively). Cytotoxic activity of both drugs increased in a dose dependent manner individually as well as in equimolar combinations. Biocompatibility studies revealed no significant buccal irritation in rabbit mucosae after 7 days of gel application.

Conclusions: A dual drug loaded NE incorporated in a mucoadhesive gel base was successfully developed. The formulation aided permeation and retention of both drugs in porcine mucosa; which were important for local action. The formulation exhibited synergistic apoptotic activity on OC cells and was biocompatible.

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Evaluation of *In Vitro* Dissolution of Ibuprofen Minitablets for Sustained Release Potential

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Background and Rationale: The chronic pain associated with musculoskeletal conditions progresses with age. Ibuprofen is a high dose analgesic (dose ranging from 200-1200 mg) used majorly in treatment of rheumatoid arthritis, which warrants for a sustained release formulation to provide a day long pain relief. Owing to combination of high dose drug and sustained release excipients, such formulations end up having a bulky dosage form. Such dosage forms pose issues of dysphagia and choking in the geriatric population. This issue needs to be catered with a formulation that would provide ease of swallowing along with sustained release profile. The present mini tablet is a patient compliant formulation designed to carry maximum possible drug loading with minimal quantity of a single functional excipient to provide sustained *in vitro* release of the active.

Methods: Ibuprofen and the polymer (Carbomer 974 P/Compritol 888 ATO) were added to rapid mixer granulator (RMG) in weighed ratio and allowed to melt completely over a temperature range of 70-80°C. The molten mass was extensively mixed by the RMG blades. The temperature was slowly reduced to allow cooling with chopper being applied intermittently to cut the solidifying mass to avoid massive lump formation. The resultant brittle mass was removed through the discharge chute and subjected to milling. The milled mass was passed through # 40, suitably lubricated and subjected to tabletting to obtain the minitablets. The minitablets containing 600 mg of ibuprofen were subjected to *in vitro* release study in USP Type I (Basket apparatus) in 900 mL media at 100 RPM at a differential pH over time (pH 1.2 for the first hour, pH 4.5 till the second hour, & pH 6.8 from third hour onwards).

Results and Discussion: Batch with Carbomer 974P could provide the in vitro release of ibuprofen over a period of 24 hrs with 80% drug loading & 20% polymer whereas compritol 888 ATO could provide 24 hour sustained release at 70% drug loading & 30% polymer. These results are comparable and even better than a single sustained release tablet (Indian Patent Application 202221015336) containing the same drug and excipient combination in spite of the multi-fold higher surface area offered by minitablets. The reason behind this *in vitro* release behaviour offered by minitablets is the gelling tendency of the polymer, carbomer 974 P. As it comes in contact with the medium, it absorbs water, swells and forms a gel network, which creates a barrier to dissolution of the drug. The barrier hinders the drug release in the external media thereby sustaining the release of the active over longer duration of time. Compritol 888 ATO is a lipidic excipient. It does not form a gel network. The *in vitro* release is regulated by the matrix formed between ibuprofen and compritol. $T_{50\%}$ for the optimised batch was observed between 10-12 hrs & $T_{80\%,}$ at 20 hrs for carbomer 974 P whereas the same for the batch with compritol 888ATO was observed at the end of 12 hrs & 20 hrs respectively. Non-Fickian super case 2 transport release mechanism was observed in case of both the polymers. The intricate mixing offered by RMG leads to formation of a well spun matrix which can sustain the release of the active in spite of the increase in the surface area of the dosage form.

Conclusions: A patient compliant formulation with desired *in vitro* dissolution behaviour was achieved by ibuprofen minitablets. Ease of swallowing could be offered without compromising on its ability to sustain the in vitro release of ibuprofen.

Formulation Development and Evaluation of Poloxamer based In Situ Ocular Gel by Validated RP-HPLC Method

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Background and Rationale: The Poloxamer based in situ gel system by using the single drug or with two drugs in combination is been prepared by using different grades of the poloxamers in literature which is employed to treat various ocular disorders like bacterial infections, conjunctivitis, allergic reactions etc. Individual formulations; patient has to administer to treat the bacterial infection and to reduce the allergic conjunctivitis. So, to reduce the frequency of the formulation administration; only one medication by preparing two drugs antibiotic and antihistaminic in combination to achieve the two effects simultaneously, in-situ gelling system was prepared by using two drugs Ciprofloxacin Hydrochloride and Olopatadine Hydrochloride to enhance drug corneal permeability, patient compliance and cost effectiveness.

Methods: A) Formulation and Analytical Method Development: The nine different formulations (F1-F9) were prepared by using 3^2 factorial designs. The APIs (ciprofloxacin hydrochloride and olopatadine hydrochloride) with preservative (benzalkonium chloride) and buffering agent (sodium chloride) were mixed and added in polymeric solution containing Pluronic 407 (Viscolizer) and Pluronic 108 (wetting agent).

B) *In vitro* drug release studies: The *in vitro* release of ciprofloxacin hydrochloride and olopatadine from the prepared optimized formulations was studied using a Franz diffusion testing apparatus. About 2 ml of aliquot was withdrawn at a time interval of 30, 60, 90, 120, 240, 300 upto 480 minutes and replaced with an equal volume of fresh diffusion medium. The aliquots were diluted with the diluent and analyzed using HPLC.

All the prepared formulations were evaluated for clarity, viscosity of sol and gel, gelling time, pH and Assay. The excipients compatibility study, drug content, % drug release and stability study were analysed by the developed and validated RP-HPLC method as per ICH Q2R1guidelines.

Results and Discussion: The optimized conditions were Mobile phase A: 0.1% TFA (60%) and Acetonitrile (40%), C18 column Agilent Zorbex SB-Aq (250*4.6mm,5µ), 30°C column temperature, 10µl/min injection volume, 1ml/min flow rate and 17minutes run time selected. All the formulations were found to be compatible with the excipients. The optimized formulations were found to be opaque, and viscosity of sol and gel were in between 72-92cps and 691-913 cps respectively. The gelling time and pH were 33-39 minutes and 7±0.2 respectively. The drug content and % drug release of final optimized batch were 98-101% and 94.67% in 120minutes and follows Korsmeyer Peppas Release Kinetics. The formulation was stable at accelerated stability condition for the period of three months.

Conclusion: The prepared formulation was cost effective and showing antibacterial, antihistaminic activity simultaneously.

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In Vitro Release, Comparison and Correlation with Microstructure of a Non-Aqueous Hydroxypropyl Cellulose (HPC) Gel Prepared by Conventional and Hot-Melt Extrusion Process

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Background and Rationale: Microstructure properties of the semisolid dosage form are greatly affected by the critical processing parameters (CPPs) [1]. *In vitro* testing is one of the critical quality attributes that reflects the microstructural differences in the semisolid formulations [2]. Developing a non-aqueous HPC gel formulation from a conventional approach consumes a very long time. Herein, the mechanism of gel formulation involves dispersion and hydration of each polymer molecule which generally takes approximately 24-48 hrs for complete hydration and attaining the gel structure. Manufacturing such gel on large scale becomes tedious and time-consuming. Thus, the hot-melt extrusion process proves to be an alternative manufacturing method due to its ability to melt the polymer in a solvent and provide the gel in a continuous process with less air entrapment. Therefore, the current research focuses on evaluating the microstructural differences in the gel developed by both processes and their impact on the release profiles.

Methods: Chlorhexidine gluconate was used as the model drug. Three different polymeric concentrations (3%w/w, 5%w/w, and 7%w/w) of non-aqueous HPC gels were prepared by a conventional and hot-melt extrusion process in propylene glycol. The prepared gels were evaluated by rheology, texture analysis, and SANS to determine their microstructural differences. *In vitro* release of these gels was carried out using Franz diffusion cells at 37°C and 500 rpm with acetonitrile : water (50:50) as the receptor medium. The release profiles were compared using the Mann-Whitney U test to check the similarity as per the SUPAC-SS guidelines. The release profiles were fitted to different models to understand the release mechanism.

Results and Discussion: The non-aqueous HPC gels prepared by two processes were found to have similar physicochemical properties. The release profiles of the gels prepared with different polymer concentrations by both the process followed a similar trend i.e., the lower polymer concentration gel gave the maximum release and vice versa. The results of rheology, texture analysis, and SANS study were approximately similar for the gels prepared by two processes. Microstructural results from the rheological, textural, and SANS study were found to correlate well with the release profiles. According to the Mann-Whitney U test, the release rates of the gels prepared by the two processes were found to be similar. The release profiles of the gels followed a zero-order drug release pattern.

Conclusions: The similarities in the microstructure of the gels prepared by two processes suggested the hot-melt extrusion process to be an alternative method of manufacturing non-aqueous HPC gel on a large scale.

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Lipomer as a Functionalized Nanoplatform to Overcome Mucus and Epithelial Barriers for Promising Oral Delivery

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Background and Rationale: Orally administered nanocarriers must diffuse through the mucus layer and also permeate through the GI epithelium to enable systemic absorption. Mucopenetration is facilitated when nanocarriers exhibit hydrophilicity which favours interaction with mucus without hampering diffusion towards the epithelium. On the other hand, crossing the epithelial barrier particularly passage through the Peyer's patches entails hydrophobicity. We report an innovative approach to balance and present Lipomer (lipid-polymer hybrid nanocarriers) loaded with Curcumin as model drug (Cur-Lipo) for oral delivery. The objective of this study was to evaluate the mucoadhesion, mucopenetration, ex-vivo permeation of Cur-Lipo and also track passage of intact Cur-Lipo across chick ileum, to assess the potential for efficient oral delivery. Cur-SLN (Solid Lipid nanoparticles) served as the reference.

Methods: Cur-Lipo and Cur-SLN were prepared by a facile i*n situ* nanotechnology approach. A preconcentrate of Curcumin was prepared by dissolving Curcumin (70 mg), lipid (Stearic Acid), Cur-SLN was prepared similarly, without addition of Gantrez AN 119 (Mucoadhesive Polymer) in Transcutol® HP (0.75 mL) by bath sonication. Preconcentrate was diluted with water (upto 5 mL) to instantaneously form Ready-to-Use Cur-Lipo/Cur-SLN (14mg/ml). Particle Size, polydispersity index and Entrapment Efficiency were evaluated. Mucoadhesion was measured on Texture analyzer. Mucopenetration using porcine mucin as substrate was monitored by the agarose gel and Transwell plate methods. Permeation through chicken ileum was evaluated using the Franz Diffusion cell & monitored by UV spectroscopy. The acceptor medium was also evaluated for presence of intact nanoparticles by DLS and SEM.

Results and Discussion: Cur-Lipo and Cur SLN of average size 310 nm and 377.91nm, entrapment efficiency > 90%, and PDI < 0.3 ready for administration were obtained reproducibly (n=3). Higher mucoadhesive force of Cur-Lipo (9.34 g) compared to Cur-SLN (1.69 g) is attributed to electrostatic interactions with carboxylic acid groups in Gantrez. Diffusion through mucin in the agar gel was comparable, however Cur-Lipo showed burst transport at 3 hour and high flux of 12.46 µg/cm^2/h with 78.64% detection in the transwell plate compared to Cur-SLN which showed 8.49 µg/cm^2/h flux with 51.70% detection at the end of 6 h. The superior mucin penetration ability of Cur-Lipo proposes the possibility of high lymph mediated uptake through the intestinal Peyer's patches. Nevertheless, the *ex vivo* permeation study revealed marginally higher permeation with 1.91 folds enhanced flux value for Cur-Lipo compared with Cur-SLN and is attributed to higher permeation through Peyer's patches in the chicken ileum.

Conclusion: Cur-Lipo by overcoming both diffusion and absorption barriers presents great promise as an efficient platform oral delivery system with the added advantage of entrapping both hydrophilic and hydrophobic drugs.

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pH- Triggered Nanoparticle loaded Gel for Prevention of Vaginal Transmission of HIV

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Background and Rationale: Acquired Immunodeficiency Syndrome (HIV/AIDS) and other sexually transmitted infections (STIs) have become escalating health problems that have affected the entire world. AIDS has caused the mortality of more than 36 million people since it was first recognized in 1981 and has become one of the most destructive pandemics in history [1]. Heterosexual transmission of HIV accounts for major causes of adult infections worldwide. According to a current report published by NACO (National AIDS Control Organization)in the year 2020, HIV affected people (people living with HIV – PLHIV) are estimated at 23.48 lakhs with daily infection rate of 190[2]. Current reports suggest that among total population affected, women are at very high-risk levels as 53% of infected people comprise of females and 50% of all newly infected population in 2020. In the present project, Atazanavir sulphate, a protease inhibitor, is formulated as a Nanoparticular system. The nanocarrier based gel is delivered in the vaginal cavity which provides ease in administration and prolonged drug release. The vaginal delivery of the formulation ensures that the microbicidal effect of the formulations is localized [3].

The novel vaginal gel containing anti-retroviral drug Atazanavir sulphate encapsulated in Eudragit S-100 as the polymer for nanoparticles helps in localizing the microbicidal effect of the drug in the vaginal cavity since the drugs will be loaded in pH-sensitive nanoparticles form a semen-triggered delivery system for sustained release vaginal delivery. The semen pH (~ pH 7.4) is higher than the vaginal pH hence the presence of semen in the vaginal cavity increases the pH which leads to the release of the drugs from the polymeric nanoparticles. The nanoparticles were loaded in a carrageenan based gel, where carrageenan acts as an HIV entry inhibitor in addition to the antiviral activity of Atazanavir sulphate. The objective of the present research project is to formulate Atazanavir sulphate as a vaginal gel formulation for prophylactic activity against HIV.

Methods: Drug was standardized and evaluated for physicochemical properties. A suitable analytical method using High-performance liquid chromatography (HPLC) for the estimation of the drug was developed. Preformulation studies and evaluation by DSC and FTIR confirmed the compatibility of drug and excipients. The nanoparticulate system was formulated by nanoprecipitation method in which the type of organic solvent, the type and concentration of surfactant and the stirring speed were optimized. The vaginal gel was prepared using carrageenan as the gelling polymer. The developed nanoparticular gel was evaluated for appearance, pH, drug content, gelling capacity and drug release studies. The in-vitro drug release study was carried out in simulated vaginal fluid and simulated seminal fluid. The anti-HIV activity of the formulation was evaluated using TZM-bL cell line using b-galactosidase assay.

Results and Discussions: The Eudragit S100 nanoparticles were found to be stable with an average particle size of 396.7 nm (PDI 0.41) and the in-vitro drug release showed drug release of 7.202% in Simulated vaginal fluid (pH 4.2) in comparison to 99.801% in Simulated seminal fluid (pH 7.7) at end of 8 hours.

Conclusion: Studies indicated that Atazanavir sulphate nanoparticles loaded vaginal gel could be considered as a candidate for further clinical studies as a new efficient HIV prophylactic treatment.

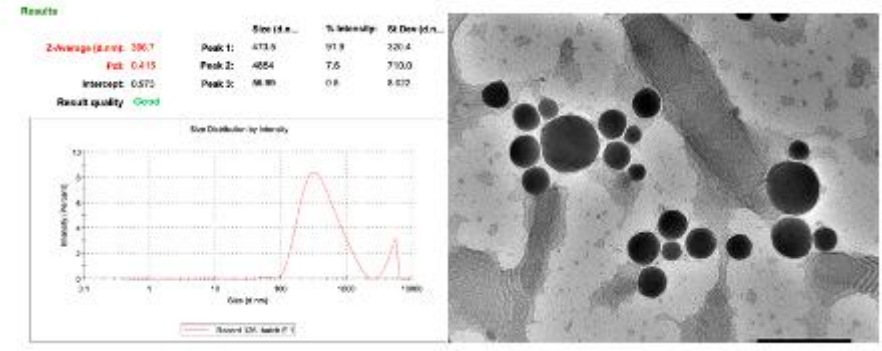

Figure: A. The Results of particle size for selected batch B: TEM image of Atazanavir loaded Eudragit S100 nanoparticles

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Preparation and Characterization of Electrospun Fluocinolone Acetonide Nanofibres for Treatment of Posterior Uveitis

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Background and Rationale: Posterior uveitis is the rare ocular inflammatory disorder that affects posterior part of eye (choroid) which may lead to progressive loss of vision. At present, there are ocular inserts such as retisert available in the market requiring invasive procedures such as surgery to put the insert into the posterior segment of the eye. Nanofibers are small thin paper like fibrous material which consist of polymer matrix along with the drug. They have high resemblance to the ECM hence, providing high biocompatibility. Fluocinolone acetonide (FA) is a corticosteroid which is used for the management of uveitis. Thus, we propose that, Nanofibers loaded with Fluocinolone acetonide will help in reducing inflammation in the ocular tissues along with helping to reduce the spread of inflammation in the eye and provide sustained release of the drug helping in achieving better ocular concentration. To understand the release profile, drug loaded nanofibers were subjected to invitro and exvivo release using artificial PVDF membrane and goat eye cornea respectively. The amount of drug released, kinetics of drug release and scleral penetration values were obtained from this study.

Methods: 1) Formulation development- FA was loaded on novel ocular nanofiber insert produced using electrospinning technique 2) Characterization and drug release- The optimised nanofibers were evaluated for morphology, drug entrapment, degree of swelling, isotonicity, bio adhesiveness, folding endurance, biocompatibility, irritation, sterility and stability. For *in vitro* release, nanofibers were subjected to diffusion study to quantify the amount of drug release through membrane using PVDF membrane. Study was conducted for 24 hours on a Franz diffusion cell using 22 ml of receptor compartment filled with simulated tear fluid. For *ex vivo* permeation and release studies, the above procedure was repeated using excised goat cornea. Whole Eye Model was also used for scleral penetration study

Results and Discussion: Fluocinolone acetonide 0.05% was formulated as nanofibers using 1.5% Chitosan along with 10% Polyvinyl alcohol in a ratio of 1:6. The mean diameter of the Nanofiber was found to be 128.75 nm, tensile strength 0.2882 N/mm2, swelling index 45.2, drug entrapment 95%, and thickness of 0.16 mm. The *in vitro* drug release was 84.59% after 24 hours. *Ex vivo* drug release showed a prolonged release of 65.33% from goat cornea. Tonicity studies showed that the formulation was isotonic with blood cells. Conclusion: Based on the all the evaluation parameters and in-vitro, ex-vivo studies it can be concluded that Fluocinolone acetonide Nanofibers could be a potential candidate for further studies as a new efficient treatment in patients with Chronic Uveitis.

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Development and In Vitro Evaluation of Intranasal Thymoquinone Drug Delivery System for Migraine Management


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Background and Rationale: Migraine is a neglected neurological inflammatory disorder and more than 30% of the young adult population with a headache problem are suffering from migraine. Thymoquinone (TQ), a phytoconstituent rich in anti-inflammatory and anti-oxidant properties, is a safe and promising candidate. To improve TQ's bioavailability in the brain, it was encapsulated inside the nano lipid carriers. For the on-field applicability and to provide immediate relief, intranasal route of drug administration was explored. Aim of this study was to design, develop and evaluate nano lipid carriers (NLC) of thymoquinone for intranasal delivery to manage migraine.

Methods: TQ-NLCs were prepared using melt emulsification method using transcutol and PEG 300 as surfactants. Quality by Design (QbD) approach using Box-Behnkem Statistical Design Expert for development of TQ-NLC formulation was applied for optimizing formulation parameters. To determine *in vitro* drug release profiles of Thymoquinone from the formulation, 10 mg NLC-TQ was dispersed in 2 ml buffer pH 7.4 which was placed in dialysis membrane bag at 37 ±0.5ºC with constant stirring. 3ml samples were removed at specific time intervals maintaining the sink conditions and analysed for the amount released.

Results and Discussion: Optimized formula for the formulation of TQ-NLC 10 mg NLX was found to be 40 mg lipid, 2.75% of surfactant and having 8.5 min of sonication time. The average particle size, entrapment efficiency and drug loading of optimized formulation were found to be 208nm, 95.323 ± 0.4 % and 19.06 ± 0.09 % respectively. A 70% release of TQ from TQ-NLC was achieved at the end of 6 h and maximum drug release from the particles within 3 hours.

Conclusion: An effective formulation of Thymoquinone loaded nano lipid carriers for nasal injestion which provide direct delivery of Thymoquinone to brain via olfactory region of nose was presented. The administration of TQ-NLC reduces systemic exposure, side effects and also assures patient compliance. Nasal drug delivery bypasses the blood brain barrier and directly delivers drug into CNS where the lipidic carrier effectively delivers the drug and also act as a better alternative to parenteral and oral administration of drug.

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Evaluation of Drug Release from Rivastigmine and Resveratrol Loaded Transferrin Functionalized Lipidic Nanocarriers for Alzheimer's Disease

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Background and Rationale: The multiple underlying causes of Alzheimer's Disease (AD) necessitates combination drug therapy, targeting multiple mechanisms of disease pathogenesis. Here, we have employed an acetylcholinesterase inhibitor Rivastigmine hydrogen tartrate (RHT) and a polyphenol Resveratrol (RSV) proven to have beneficial effects in AD. Nanostructured lipid carriers (NLCs) was chosen as drug delivery system due to the lipophilic nature of the blood brain barrier (BBB). Targeted drug delivery via transferrin (Tf) receptor was explored here, since they are known to be overexpressed on the brain. Hence, the objective was to formulate and characterize Tf functionalized NLCs (Tf-NLCs) of RHT and RSV for brain targeting.

Methods: 1) Preparation of NLCs and functionalization with Tf: The NLCs were synthesized by w/o/w double emulsion method. The conjugation of NLCs with Tf was achieved by incubation of Tf with NLCs in the presence of crosslinker 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) [1].

2) *In vitro* drug release from NLCs and Tf-NLCs: It was determined by dialysis membrane technique under sink condition. NLCs and Tf-NLCs were filled inside a dialysis bag and immersed in a beaker with 50 ml phosphate buffer saline (PBS) (pH 7.4) containing 1% tween 80. The beaker was kept on stirring at 100 rpm and 37℃ [2]. Samples were withdrawn at predefined time intervals and analyzed by developed HPLC method for simultaneous estimation of RHT and RSV at 217 and 306 nm, respectively. The nanoparticles were also characterized for its particle size, zeta potential and entrapment efficiency (EE) of drugs.

Results and Discussion: Particle size of <100 nm and EE of 99.6±0.1% and 40.3±5.2% was achieved for RHT and RSV, respectively in Tf-NLCs. For RHT, burst release was observed in the initial 2 hours followed by sustained release for 24 hours. RSV showed low burst release followed by sustained release for 48 hours. The fast release of RHT as compared to RSV can be attributed to higher aqueous solubility of RHT. For both the drugs, Tf-NLCs showed slightly slow release as compared to unconjugated NLCs which may be due to Tf conjugation that created a double barrier effect for the diffusion of drugs.

Conclusion: The functionalized lipidic nanocarriers showed sustained release of both the drugs for a prolonged period. Hence, it would decrease the dosing frequency thereby reducing systemic toxicity. The dual drugs loaded Tf-NLCs may evolve as a superior treatment outcome for AD.

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Exploring the Permeation Potential of Piperine in Insulin Loaded Multiple Emulsion Containing Albumin as Suicidal Inhibitor for Oral Delivery

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Background and Rationale: The major issue with subcutaneous insulin (INS) delivery is patient compliance and precaution the patient has to take while administration. Thus, oral route is the most favoured route for INS administration but has issues pertaining to GI stability and permeability[1]. Hence, we developed W/O/W microemulsion (ME) containing piperine (PiP) as a permeation enhancer and albumin (Alb) as a stabilizer for oral INS delivery.

Method: INS loaded ME (ME(INS)-PiP-Alb) was prepared via two step method, using sunflower oil, Span®20/80 and Tween®20/80 along with PiP and Alb. Different stability study for INS and prepared NPs were performed to examine their stability[2]. *In vitro* release of INS was performed using dialysis bag method (cellulose acetate 12 kDa) in SGF (2h), SIF (6h) and PBS (till 24h) at 37°C and 80 rpm in shaker bath and samples were analysed using validated RPHPLC method. Further, *ex vivo* permeability, Caco-2 permeability and uptake was also performed along with pharmaco-kinetic (% relative bioavailability (BA_R)) and –dynamic (hypoglycaemia) studies using SD rats.

Results and Data Analysis: The ME(INS)-PiP-Alb rendered droplet size of 3.35±0.25 µm and PDI of 0.302±0.10 with ~98% of INS content. In presence of pepsin and trypsin formulation was able to restrict INS degradation to ~49 and 40% till 1h whereas, ME(INS)-PiP revealed INS degradation till ~71 and 65% respectively. This authenticated the role of Alb as a suicidal inhibitor in preventing the INS degradation. The storage and accelerated stability studies showed that ME(INS)-PiP-Alb was stable till 12 months at 4°C. The *in vitro* release for ME(INS)-PiP-Alb showed ~19%, 31% and 22% release in SGF, SIF and PBS respectively with ~74 % final cumulative release. Lower release in SGF was desired to prevent INS from degradation before absorption. The *ex vivo* and Caco-2 permeability data for ME(INS)-PiP-Alb revealed ~4 and 1.5-fold higher INS permeation than free INS and ME(INS) without PiP respectively. Also, qualitative uptake showed higher permeation for ME(FITC-INS)-PiP-Alb over FITC-INS. The pharmacodynamic studies revealed ~3.2-fold higher hypoglycaemic effect in animals treated with ME(INS)-PiP-Alb in comparison to ME(INS)-PiP. The pharmacokinetic studies revealed ~1.6 fold higher AUC for ME(INS)-PiP-Alb than ME(INS)-PiP.

Conclusion: The ME(INS)-PiP-Alb was able to maintain the chemical and conformational stability of INS in biological fluids and in presence of pepsin and trypsin. *In vivo* results also suggested that Alb as a stabilizer can assist in improving the hypoglycemic effect of the developed ME with PiP. Hence, this strategy can also be extrapolated for delivering other bio-macromolecules orally.

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High Permeation Vesicles Mediated Localized Transdermal Delivery of Docetaxel for the Management of Breast Cancer

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Background and Rationale: Breast cancer is the most commonly diagnosed life-threatening disease in women after lung cancer. The use of systemic chemotherapeutics for treating breast cancer causes serious systemic side effects and lower drug exposure to breasts. The distinct anatomical features of human breasts (e.g. embryological origin of breast skin, presence of mammary fat layers and highly developed internal venous and lymphatic circulation) help in preferential accumulation of drugs into breasts after topical application on breast region (1). However, the skin poses a major barrier for permeation of drug molecules. High permeation vesicles (HPVs) are novel vesicular carriers with dual benefits of nanocarriers and synergistic permeation enhancer cocktail to improve skin permeation (2). The aim of the current study was to evaluate the potential of HPVs in localized transdermal delivery of docetaxel for the management of breast cancer.

Methods: A) Preparation and characterization of HPVs and HPVS gel: HPVs (composed of Leciva S90 and permeation enhancers sodium oleate, sodium lauryl ether sulphate and propylene glycol) in 8:2 w/w ratio was prepared by thin film hydration method and evaluated for various physicochemical attributes. For ease of application, the prepared formulation was further loaded in Carbopol 934 gel.

B) *In vitro* release and permeation study: The *in vitro* release of prepared formulations was conducted via dialysis bag method (MWCO 12kDa) in phosphate buffer pH 5.8 (to mimic skin pH) with 0.5% tween 80 to maintain the sink conditions and compared with free drug, scope mixture and liposomal formulation. Further, the permeation efficiency of prepared formulation across pig ear skin was evaluated using Franz diffusion cell.

C) *In vitro* and *in vivo* study: The cytotoxic potential of prepared HPVs was analysed in MCF-7 and MDA MB-231 cell lines. Further the formulation was evaluated *in vivo* for therapeutic efficacy and systemic toxicity.

Results and Discussion: The optimized formulation of HPVs resulted in vesicle size of 124.2±7.6 nm, PDI 0.21±0.12, zeta potential -35.2±3.1 mV and 11.2 ± 1.3 % drug loading. TEM images revealed the spherical structure of DTX loaded HPVs. The free drug and SCOPE mixture showed rapid release profile. The encapsulation of DTX in nanocarriers helped in attaining sustained drug release. HPV and liposomal formulation exhibited 86% and 94% drug release, respectively at 48 h. The incorporation of HPVs in gel matrix further assisted in sustaining the drug release pattern and showed 76% drug release in 48 h. Drug release kinetic from HPVs and its gel formulations exhibited the highest linearity for the Higuchi model that explains diffusion-based release of the drug from the formulation. The skin permeation and deposition study were performed to determine the transdermal DTX permeation and amount of DTX present in skin layers. Out of all groups, HPVs showed highest percent of skin permeation with ~29% DTX permeation. While, SCOPE mixture and liposomal formulations exhibited ~12% and ~17% DTX permeation, which was substantially lower than HPV formulation. The drug skin deposition profile showcased 19.89% & 25.79% intradermal drug accumulation for SCOPE mixture and liposomal groups. On the other hand, HPV group marked strikingly improved drug permeation with 40.75% intradermal distribution. The dree drug and DTX in gel showed very poor drug penetration in skin layers as well as transdermal permeation. The reduced IC50 values of DTX HPVs in MCF -7 and MDA-MB -231 cells assured the therapeutic effectiveness of HPV based therapy. The topical application of DTX HPV gel in tumor bearing mice showed significant inhibition of tumor growth and no systemic toxicity. The greater permeation and higher intra-tumoral accumulation (as evidenced by bioimaging analysis) of drug with HPV based gel formulation prove to be effective in achieving significant tumor burden reduction as equivalent to Taxotere® therapy.

Conclusions: Overall findings of this study supported the effectiveness of using HPVs as a carrier of anticancer agents in topical breast cancer chemotherapy.

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Permeation Studies of Transungual Drug Delivery System Across Porcine Hoof Membrane for Onychomycosis

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Background & Rationale: Onychomycosis is recognised as dermatophytic fungal ailment of fingernails and toes that causes thickening and discoloration of nail bed, folds, and nail plate. The ailment is much more than a cosmetic issue; it shows major impact upon life of an individual. It is an exploitative infection that occurs in specific sub - populations of diabetic patients, HIV/AIDS, psoriasis, and other diseases. Current therapeutic approaches include systemic administration of oral antifungals like allylamines and azoles that are conveyed towards the nail plate from nail bed. Like an alternative to oral antifungals, topical drug delivery like amorolfine, ciclopirox 8% nail lacquer, and 10% solution of Efinaconazole are available. Topical antifungals delivered through human nail have several benefits over oral treatment, along with a decreased prevalence of side effects and a reduced risk of drug-drug interactions with medications to treat AIDS/HIV, psoriasis and diabetes. Moreover, permeation rate of topical agents is low. Thus, the primary goal in developing a topical preparation for Onychomycosis therapy is to achieve antifungal drug permeation and *in vitro* transungual release through the nail to reach inside nail bed.

Methods: A) **Screening of Permeation Enhancers**-Human fingernail clippings were obtained from healthy participants. The clippings were washed with ethanol, then distilled water. These then were cleaned and dried at room temp. The clippings were stored in glass containers at a monitored temperature of 25 ±2°C. The clippings' length and thickness were 12 mm ± 0.2 and 0.4 mm ± 0.03 and respectively.

N-acetyl-L-cysteine, urea, hydroxy propyl cyclodextrin (HPβD), thioglycolic acid, water, 2-mercapto ethanol, propylene glycol, sodium lauryl sulphate (SLS) and sodium hydroxide had been used to see how they affected hydration and swelling of nails. Each glass vial contained 1 mL of water: ethanol (20:80), 10 mg of Efinaconazole and permeation enhancer (5%). Nail clippings were prepared by weighing in vials with various enhancers, including one vial serving as a control with no enhancer. The clippings were enabled to swell for 24hrs in sealed glass vials at 32° before being separated, washed, and again weighed. The hydration enhancement factor (HEF) was calculated as: HEF = W1/W2,

where, W1 = % weight gain of clippings with enhancers and W2 = % weight gain of clippings with water. Enhancers with highest HEF will be selected for further screening.

B) **Formulation and characterization of nail lacquer**-The amalgamation method for nail lacquer was created by mixing hydrophilic (HPMC E5) polymer (5%) and hydrophobic (Eudragit RL 100) polymer (5%) and in ethanol (solvent) upntil a clear solution is achieved. At 450 rpm, tween 80, drug (Eficonazole), and PEG 400 were added to a clear solution. After stirring for 60 minutes with a chosen penetration enhancer (5%), the combination was stored in sealed containers till further use. To optimise the formulation, a 3^2-factorial design with various polymer and solvent ratios were used. The optimized batch was chosen based on flux, viscosity, drying time, and then tested for film adhesion, water resistance, non-volatile content, scanning electron microscopy(SEM) blush test, and Fourier transform infrared spectroscopy (FTIR).

Table: dependent and independent variables

Factors (Independent Variable)	**Levels Used**			**Responses (Dependent variable)**
	-1	0	+1	
X_1= ratio of polymers (Eudragit RL 100/HPMC E5)	30:70	50:50	70:30	Y_1 = drying time (s) Y_2 = flux (µg/cm^2/h) Y_3 = viscosity (cPs)
X_2= ratio of solvent system (ethanol/water)	70:30	80:20	90:10	

C) *In vitro* transungual release study- Hooves were cleaned, washed, and hydrated for 24hrs in phosphate buffer solution pH 5.8 (PBS). The soft tissues of hooves was removed with a blade. These were cut into thin slices and saved for later use. *In vitro* dissolution experiments were carried out using a Franz diffusion cell. The length and thickness of porcine hooves were 15mm ±0.8 and 0.8mm ±0.5 respectively, as measured with a micrometre. The nail adapter and horseshoe clamp were used to secure the hoof between receptor and donor compartments of Franz diffusion cell. The membrane was treated with 1 mL of lacquer. To activate nail plate situations, a phosphate buffer (pH 5.8): ethanol (3:1) mixture was placed in the receptor section. At 37°C, assembly was stirred continuously for 24hrs. 1 ml of the sample was retracted for 24 hour periods and interchanged with the new medium. The total drug released per unit area (n=3) (Qn) across the porcine hoof had been calculated using a UV spectrophotometer at 259 nm. The flux has been determined by calculating as slope between total overall amount of drug released per unit area (µg/cm^2) and time (h) (n=3), and it was then compared to a flux of a commercial dosage form.

Results and Discussion: Thioglycolic acid, 2-mercaptoethanol, N-acetyl-L-cysteine had the HEF value, also 2-mercaptoethanol chosen for integration in nail lacquer composition because it had deeper permeation than some other enhancers. The optimised preparation has a solvent-to-polymer ratio of 70:30. The preparation achieved a flux of 181.98 ± 3.19 g/cm^2/h compared to 52.88 ± 3.11 g/cm^2/h for commercial preparation. Scanning electron microscopy analysis demonstrated the nail lacquer's promising potential. SEM analysis showed that nail surface which is untreated shows smooth surface area with few fractures whereas preparation with no permeation enhancers results in uneven surface with irregular pores.

Conclusions: Onychomycosis is a type of nail fungal infection which could be difficult to cure. A topical anti - fungal must be highly effective and tolerable at killing the fungi while also being capable of crossing the complex system of nail plate to provide an acceptable remedial impact. Lower keratin binding efficiency of Efinaconazole maintains both subungual and transungual conveyance towards the contamination site inside nail grid, plate, and nail bed. To determine the effect of polymer and solvent ratios, a 3^2 factorial design was used. Efinaconazole exhibited superior nail permeation even without using penetration enhancers. As a result, it is reasonable to conclude that nail lacquer has the potential to be a potential intervention for onychomycosis, also for reducing side effects associated with medicines and improving patient compliance.

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Solidified Self-nano Emulsifying Drug Delivery System For Enhanced Stability and Oral Bioavailability of Erlotinib

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Background and Rationale: Erlotinib (ERL) (BCS class II), needs to be formulated for the enhancement of stability and bioavailability (BA). Self-nano emulsifying drug delivery systems (SNEDDS) have significant potential in increasing the oral BA of drugs via bypassing first pass metabolism through lymphatic absorption. Conventional SNEDDS have limitations like precipitation of drug during storage, interaction with capsule shell, and stability. To alleviate these limitations, development of ERL-sSNEDDS was done by adsorption method combining both technologies of emulsified liquid formulation (for improving solubility) and solidification process for enhancing the oral BA, stability and therapeutic efficacy.

Methods: Different oils, surfactants and co-surfactants were screened out based on the emulsification ability to find out Capmul MCM EP (CPM EP), Cremophor RH 40 (CMR RH 40) and Labrafil CS (LBF CS) as suitable candidate. Ternary phase diagram was used for plotting different ratios of CPM EP, CMR RH 40 and LBF CS for identifying self-nano emulsifying area. Liquid formulation was optimized by using extreme vertices D-optimal mixture design of constrained region. Preparation of Erlotinib sSNEDDS from liquid was done by adsorption method to selected solid carriers. The prepared sSNEDDS were evaluated for various quality attributes (Solid state characterization, morphology), stability in simulated GI fluids, accelerated stability studies, *in vitro* drug release, qualitative uptake, cell cytotoxicity, apoptosis assay and *in vivo* pharmacokinetics.

In vitro release study was performed by dialysis method (MWCO 14,000 Da) in SGF (pH 1.2; 2 h) and SIF (pH 6.8; 6 h) to mimic the physiological conditions. Free drug and formulation (equivalent to 1mg drug) in 2 ml release media kept within a dialysis bag and was suspended in 20ml release media (sink condition maintained with Tween® 80). Total assembly was kept in shaker bath (100 rpm) with temperature of 37±0.5°C. At predefined time intervals, the samples (1 ml) were collected and analysed using validated HPLC method.

Results and Discussion: Screening of oils, surfactant and co-surfactants were based on droplet size, PDI and % transmittance. CPM EP, CMR RH 40 and LBF CS in the ratio of 59:11:30 as the optimized composition was chosen based on desirability value from the desirability graph. The release properties of Aerosil 200 (A200)-ERL-sSNEDDS in biorelevant media showed ~69% release in SGF upto 2 h and ~82% release in SIF till 8 h which was higher (followed Higuchi kinetics with non- Fickian transport) than free ERL. The *in vitro* cytotoxicity assay revealed that A200-ERL-sSNEDDS showed higher cytotoxicity (PANC-1 and MIA PaCa-2 cells) than free ERL. In comparison to free drug the A200-ERL-sSNEDDS showed higher apoptotic index. Stability evaluation in simulated gastric fluids of A200-ERL-sSNEDDS had shown insignificant difference ($p>0.05$) in quality attributes. Pharmacokinetic study of A200-ERL-sSNEDDS showed ~2.4 fold ($p<0.05$) increment in C_{max} as compared to the free drug.

Conclusion: Higher bioavailability in case of ERL sSNEDDS as compared to free drug was obtained along with better stability in simulated GI conditions and accelerated storage conditions.

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Solubility Enhancement and Establishment of In Vitro–In Vivo Correlation (IVIVC) for the Optimized Efavirenz Nanosuspension

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Background and Rationale: Efavirenz is an effective antiretroviral medication used to treat HIV-1 infection. Owing to its poor aqueous solubility, the rate and extent of absorption are largely dependent on its dissolution characteristics. Thus, the current research aims for solubility enhancement of the developed nanosuspension, with specific emphasis on establishing an IVIVC for nanosuspension.

Methods: Efavirenz nanosuspension was prepared using the anti-solvent precipitation ultrasonication method. The effects of concentration of PVA in the anti-solvent, the concentration of efavirenz in the organic phase, and the ultrasonication time duration were studied on particle size and polydispersity index. Characterization of nanosuspension was performed. *In vitro* drug release of the formulation and *in vivo* oral bioavailability of nanosuspension was determined using an animal model (Wistar rats, n=3). Various pharmacokinetic parameters were evaluated from the plasma drug conc. time profile. For the establishment of IVIVC, the *in vitro* data was compared with the *in vivo* data and three levels (level A, B, C) of correlation were tried.

Results and Discussion: The optimized formulation exhibited good stability. The drug showed complete release in 90 minutes, compared to just 10% release by pure drug over the same time period. Tmax, Cmax, and AUC 0-48 h of optimized nanosuspension were found to be 1.5 h, 7.46 µg/ml, and 87.27 µg/ml*h, respectively. The oral bioavailability of Efavirenz nanosuspension was improved *in vivo.* IVIVC screening demonstrated that Level A correlation could not be established across the entire study period. Furthermore, the correlation until the absorption phase (up to Tmax) of *in vivo* data could not be established (R2 value of 0.548). Maximum absorption occurred 1 hour after drug release (R2 value of 0.999) implying dissolution-related absorption in the preliminary points of the absorption phase. Level B correlation could not be achieved.

In Level C correlation, a fixed *in vitro* time point (1.5 h) was compared to *in vivo* Tmax. Thus, the efavirenz nanosuspension was found to have a Level C correlation.

Conclusions: The present study demonstrated the substantial potential of nanosuspension in improving efavirenz solubility and bioavailability. Though, we were unable to establish a significant IVIVC level A relationship, despite the FDA recommending and considering the Level A approach to be the most informative. However, a partial link between absorption and dissolution was used to create a level C correlation. Level C, on the other hand, is unable to accurately reflect the full profile of the plasma concentration-time curve. Therefore, obtaining a waiver for bioequivalence isn't enough. Forecasting Cmax and AUC, on the other hand, can assist in determining BA and BE, which is critical in the early phases of development.

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Understanding pH-Responsive Drug Release Behaviour from Adenosine-Functionalized Paclitaxel-Loaded pH-Sensitive Stealth Liposomes Targeted for Triple Negative Breast Cancer

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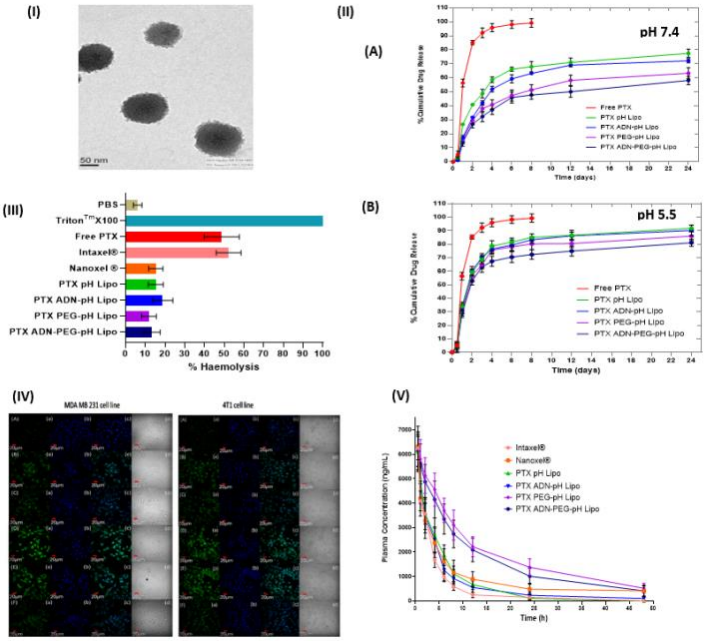
Background and Rationale: Paclitaxel (PTX) is a highly potent wide spectrum anticancer agent. However, its hydrophobic nature with poor water solubility limits its clinical application. Its marketed formulations contain non-targeted drug carriers and accumulate in tumors by the enhanced permeability and retention effect (EPR) in tumors. The absence of selective targeting to the tumor usually results in low anti-tumor activity owing to non-specific tissue distribution. Therefore, in the present work, both active and passive targeting was achieved by developing adenosine (ADN)-conjugated pH-sensitive liposomes (pH Lipo) where adenosine was presented as a targeting ligand. Also, TPGS was used here to improve the circulation half-life of the liposomes.

Methods: PTX-loaded pH Lipo were prepared by thin film hydration method using DOPE and CHEMS which impart pH-sensitive properties to liposomes. Different conjugates were synthesized (ADN-CHEMS and TPGS-ADN) by carbodiimide coupling and further used for preparation of ADN conjugated PEGylated and non-PEGylated pH Lipo. Different formulation parameters like molar ratio of lipidic components, sonication cycle and drug loading were optimized. The pH Lipo were characterized and further different *in vitro* and *in vivo* studies were performed.

Results: The optimized pH Lipo contained DOPE:HSPC:CHEMS:Cholesterol at molar ratio of 3:3:2:2 with 7.5% w/w drug loading. The synthesized conjugate were used for the preparation of different pH Lipo (PTX ADN-pH-Lipo, PTX PEG-pH-Lipo and PTX ADN-PEG-pH-Lipo) which possessed particle size below 130 nm, PDI below 0.205 and % entrapment efficiency more than 60%. The TEM analysis of pH Lipo showed spherical shaped liposomes [Fig. 1(I)]. *In vitro* release study showed biphasic release pattern of PTX at pH 7.4 and 5.5. Moreover, the pH Lipo showed substantially greater % drug release at pH 5.5 owing to their pH sensitive nature [Fig. 1(II)]. This indicated faster intracellular PTX release after receptor-mediated endocytosis. The various pH Lipo were hemocompatible in nature [Fig. 1(III)]. The MDA MB 231 and 4T1 cell lines depicted improvement in cellular uptake of pH Lipo with significant reduction in IC_{50} value [Fig. 1(IV)]. Moreover, higher apoptosis index was observed as compared to free PTX. Pharmacokinetic profile of PTX ADN-PEG-pH Lipo revealed 3.98-fold and 3.41-fold higher AUC and $T_{1/2}$ values of PTX as compared to Intaxel®, respectively [Fig. 1(V)]. Significant reduction in tumor burden and serum toxicity marker levels were achieved from the developed pH Lipo depicting efficacy and safety of the formulation.



Conclusions: PTX ADN-PEG-pH Lipo possessed improved *in vitro* and *in vivo* performance with enhanced pharmacokinetic, bio-distribution and safety profiles. Also, the efficacy of this formulation was better than the marketed formulation, Intaxel®. Since, ADN receptors are overexpressed on many other cancers, it would be interesting to further explore the developed formulation for other types of cancers as well.

Figure 1. Characterization of pH Lipo. (I) TEM image of PTX ADN-PEG-pH Lipo; (II) % Cumulative drug release vs time plot at (A) pH 7.4 and (B) pH 5.5; (III) Graphical representation of %hemolysis of different formulations along with positive and negative control; (IV) CLSM images of cell lines treated with different formulations; (V) Area under the curve profile for various groups of pH Lipo.

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"Glutamine trap" Driven Mixed Micelles of Lapatinib with Amplified Apoptosis Inducing Potential for Targeting Triple Negative Breast Cancer

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Background and Rationale: Triple negative breast cancer (TNBC) have an amplified demand for nutrients such as glucose, amino acids, vitamins to support their malignant proliferation. Clinically, many cancers like the aggressive TNBC require large amount of glutamine for their continued growth and survival. This results in circulating glutamine extraction by the tumor being much greater than that for any organs, behaving as a "glutamine trap". The present work sought to elucidate whether the glutamine trap effect could be exploited to deliver lapatinib (LPT) to selectively kill TNBC cells dependent on glutamine. Further, it is also reported that the glutamine transporter ASCT2 is highly expressed on TNBC. Therefore, glutamine stapled mixed micelles (LPT G-MM) can selectively facilitate their ASCT2 transporter mediated cellular uptake thereby improving the efficacy and reducing the dose dependent toxicity of LPT.

Methodology: Two different polymers i.e., glutamine-Pluronic® F127 conjugate (PG) and docosahexaenoic acid- Pluronic® P123 conjugate (P-DHA) were firstly designed and synthesized. Further, LPT G-MM were prepared using thin film hydration technique and employing PG and P-DHA. The prepared mixed micelles (MM) were evaluated for various quality attributes [particle size, % entrapment efficiency (% EE), % drug loading], *in vitro* drug release, hemolytic toxicity study, TNBC cell uptake (simulated glutamine depleted condition), cell cytotoxicity, *in vivo* pharmacokinetics, anti-tumor efficacy and toxicity studies.

Results and Discussion: The PG and P-DHA were synthesized by carbodiimide chemistry and characterized by FT-IR and ^{1}H-NMR spectroscopy. Further, LPT G-MM were prepared displaying appreciable quality attributes (particle size: 109.50 ± 10.12; PDI: 0.144 ± 0.045; % EE: 91.50 ± 3.32). The transmission electron microscopy revealed the spherical shape of LPT G-MM. The *in vitro* release study showed biphasic and sustained release pattern of LPT from LPT G-MM and were compatible for intravenous administration (no hemolytic potential). In case of LPT G-MM, the cellular uptake (simulated glutamine depleted condition) in MDA-MB-231 and 4T1 cell lines was augmented as compared to free LPT. Further, LPT G-MM displayed greater cytotoxicity in MDA-MB-231 and 4T1 cell lines and decrease in the IC_{50} value as compared to free LPT. The apoptotic index observed in case of LPT G-MM was significantly higher than that of free LPT. Furthermore, the pharmacokinetic profile of LPT G-MM revealed an increase in $t_{1/2}$ and AUC ($0 \rightarrow \infty$) compared to free LPT. Finally, treatment with LPT G-MM demonstrated significant cutback in the % tumor volume and serum toxicity markers as compared to free LPT.

Conclusion: The glutamine stapled mixed micelles displayed promising therapeutic potential, paving a new path for efficient LPT delivery.

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Acknowledgement: The authors acknowledge Director, NIPER S.A.S. Nagar for providing necessary facilities and infrastructure. Technical assistance rendered by Mr. Rahul R Mahajan is also duly acknowledged.

Development, Optimization and Characterization of Glibenclamide Loaded Nanostructured Lipid Carriers Using Design Paradigm

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Background & Rationale: Glibenclamide, an oral hypoglycaemic agent is a sulfonylurea, which increases the liberation of endogenous insulin and enhances its peripheral effectiveness. Glibenclamide is used as an oral dosage form in the treatment of type II diabetes mellitus and gestational diabetes. Frequent dosing, associated hypoglycaemia, gastrointestinal disturbance are the major drawbacks accompanying oral Glibenclamide therapy. Loading Glibenclamide into a nano formulation may pave way for many alternative routes of administration, like transdermal delivery system. The main drawback of transdermal delivery is the presence of stratum corneum whose molecular design allows only specific materials to diffuse through it. Nanostructured lipid carriers can gain access across the stratum corneum due to their nano size and inherent lipoidal composition. Thus, the present investigation is focused on preparing glibenclamide nanostructured lipid carriers and assessing its suitability for transdermal administration.

Methods: A) Preparation of nanostructured lipid carriers: The melt dispersion technique was used to prepare the nanostructured lipid carriers. The lipid ratios were optimized using central composite design using the software design expert. The optimised formulations were evaluated for various physicochemical, morphological, *in vitro* and *ex vivo* release profile, histological, and cytotoxicity parameters.

B) *In vitro and ex vivo* permeation study: The Franz diffusion assembly was used for the permeation study. For the *in vitro* study, cellophane membrane was placed between the donor and receptor compartment assembly and for the *ex vivo*, Wistar rat's newly obtained abdominal skin sample, with the stratum corneum side facing the donor compartment was used. Glibenclamide dispersion and optimized Glibenclamide nanostructured lipid carriers suspended in phosphate buffer pH 5.5 (skin pH) were placed in donor chamber and samples in receptor compartment were analysed spectroscopically.

Results and Discussion: The study comprehended the practicability of the design paradigm in optimization and estimation of the influence of solid and liquid lipid concentrations on the responses. The optimum formula was selected from the contour plot at the factor levels of 70 % solid lipid and 16.657 % liquid lipid. The predicted responses were 180 nm for particle size and drug entrapment 91.796 %. The *in vitro* release study from the optimized formulation showed that release of drug was prolonged to 89.5% ± 0.707 up to 8 h and the the cumulative skin permeation was 499.70.98 g/cm^2. The release kinetic reported that drug release from the nanoparticles followed the Higuchi model and the mechanism of release from the particles showed a Fickian diffusion. The histological study of the excised rat skin treated with optimized nanolipid depicted a significant change in the morphology thus supporting the *ex vivo* permeation outcome.

Conclusions: From the histological and cell toxicity study of the optimized NLCs it can be concluded that the Glibenclamide loaded nanostructure lipid carriers can be proposed to be an assuring transdermal drug delivery scheme which is non-toxic, and biocompatible with a good biological performance.

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Industrially Feasible and Scalable Approach in the Manufacture of HPMCAS-Stabilized Amorphous Solid Dispersion of Abiraterone Acetate

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Background and Rationale: Abiraterone acetate (AbA) is used as a first-line treatment for metastatic castration resistance prostate cancer. One of the major problems with AbA is its low aqueous-solubility (< 0.5 µg/mL) giving rise to slow and inadequate dissolution of the crystalline AbA in the gut, leading to poor absorption and therefore low oral bioavailability (< 10 %). The AbA (currently marketed product Zytiga) is administrated orally with a high dosage of 1000 mg/day (four 250 mg tablets) due to the low aqueous solubility. Because of the high dose, this is unsuitable for patients owing to the risk of toxicity [1]. On considering these issues, the purpose of the current work is to design an amorphous solid dispersion (ASD) with a polymeric carrier, hydroxypropyl methylcellulose acetate succinate (HPMCAS) that allowed for improving the solubilization, dissolution, and oral bioavailability, decreasing the clinical dose and diminishing the food effect. Apart from that, in the case of AbA the precipitation can take place upon transfer of dissolved AbA from the gastric media to the pH neutral intestinal media which leads to poor absorption. To accomplish the optimum absorption of AbA, the polymeric carrier (HPMCAS) acts as a precipitation inhibitor which inhibits the precipitation of AbA [2].

Methods: The solvent evaporation method was employed for the preparation of ASD using different ratios of AbA and HPMCAS (1:1, 1:2, and 1:3). A saturation solubility study was performed for the ASD in distilled water, pH 6.8, 0.1N HCl, FaSSIF (pH 6.5), and FeSSIF (pH 5.0). For AbA precipitation inhibition studies, HPMCAS was studied at a weight ratio of 1:2 (AA/HPMCAS) in a binary mixture. In-vitro dissolution studies were performed for each ASD and pure drug (AbA) in pH 6.8, 0.1N HCl, FaSSIF (pH 6.5) and FeSSIF (pH 5.0).

Results and Discussion: From the saturation solubility studies, ASD containing AbA: HPMCAS (1:2) exhibited high solubility among all ASD. The solubility of ASD in distilled water, 0.1 N HCl, pH 6.8, FaSSIF (pH 6.5), and FeSSIF (pH 5.0) were observed to be 24-fold, 8.5 fold, 21-fold, 2.42-fold, and 1.32-fold higher than the solubility of crystalline AbA. Upon generating supersaturation of AbA without the presence of HPMCAS instantaneous and complete precipitation was observed. The presence of pre-dissolved HPMCAS provides prominent and stable supersaturation. The in-vitro dissolution profile of the optimized ASD formulation in 0.1 N HCl, pH 6.8, FaSSIF (pH 6.5), and FeSSIF (pH 5.0) were observed to be 1.2-fold, 9-fold, 3-fold, and 1.5-fold higher than the crystalline AbA. This may be attributed to the reduction in particle size, increase in the surface area, increases the wettability due to the interaction of the drug with the amphiphilic polymer, and change in the crystalline state to the amorphous state.

Conclusions: In conclusion, the ASD of AbA in the presence of HPMCAS polymer was accomplished to enhance the solubility and in-vitro dissolution of AbA significantly. In the ASD, the AbA maintains the supersaturation state for a longer period due to the presence of the HPMCAS (precipitation inhibitor). These approaches may offer the great advantage of reducing the dose of the drug, which help in lowering the cost of the formulation and unwanted side effect.

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Modulating the Dissolution Behaviour of Sulfamethoxazole by Mechanochemical Cocrystallization

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Background & Rationale: Sulfamethoxazole is a sulphonamide bacteriostatic antibiotic that is most commonly used to treat ear infections, urinary tract infections, bronchitis, traveller's diarrhoea, shigellosis, and pneumocystis juroveci pneumonia. Sulfamethoxazole (SMX), being a BCS Class II drug, have poor solubility (~0.5 mg/mL), which results in a high prescribed dose of 800 mg/day[1]. Accordingly, these high doses relate to antibiotic resistance along with an increased risk of adverse effects like gastrointestinal disturbances, skin reactions, and crystalluria[2]. We explored the applicability of cocrystals to modulate the poor physicochemical properties like solubility and dissolution with a highly soluble coformer, succinimide (SUC). In this contribution, we prepared SMX-SUC cocrystals by mechanochemical synthesis with improved physicochemical properties. The study also explored the reasons for the associated changes in physicochemical properties like solubility and dissolution of SMX-SUC cocrystals.

Methods: (A) SMX-SUC cocrystals was prepared by mechanochemical synthesis in a planetary ball mill and subsequent characterization studies were performed.

(B) Equilibrium solubilities of SMX and cocrystals were performed in aqueous media by shake flask method.

(C) Powder dissolution studies of SMX and cocrystals were performed using USP Apparatus II at 50 rpm by adding ~500 mg SMX and equivalent cocrystals in FDA recommended dissolution medium (0.2 N HCl in water)[3].

Results and Discussion: A new cocrystal of the antibiotic drug sulfamethoxazole and succinimide, namely the SMX-SUC cocrystal, was prepared by mechanochemical synthesis of 1:1 stoichiometric amount of the materials. The formation of the SMX-SUC cocrystal was confirmed by SCXRD, PXRD, and thermal analysis. Analysis of the cocrystal structure showed the presence of strong hydrogen bonds and other auxiliary interactions, which provided the structural insight and the reasons associated with the modulation of the physicochemical properties.

In the equilibrium solubility studies, it was observed that the cocrystal is better soluble than SMX. Also, the powder dissolution studies established an improvement in the dissolution behaviour of the cocrystal. The improvement in the solubility and dissolution behaviour could be associated with the presence of a highly soluble coformer (SUC) in the crystal lattice. As SUC is liberated into the solution due to solute-solvent interactions, the H-bond associated cocrystal dissociates in the aqueous media, and the less soluble SMX molecules agglomerate as a metastable phase due to the changes in structural conformation. Meanwhile, the rapidly dissolving metastable state tends to influence the physicochemical properties due to the changes in crystal packing and hydrophilic properties of the coformer.

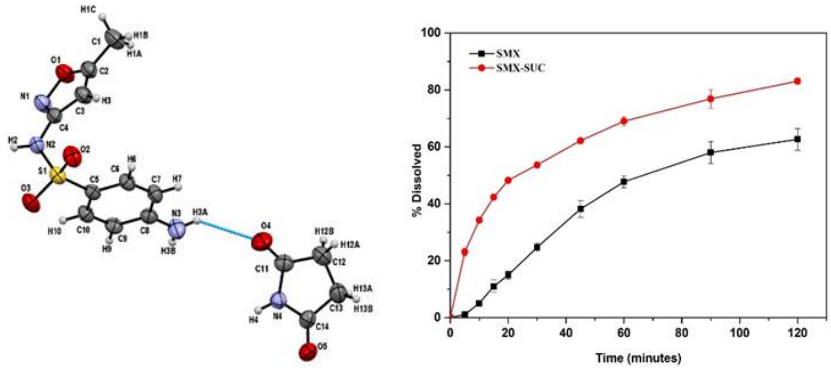

Figure: Cocrystal structure and Powder dissolution profiles of SMX and SMX-SUC.

Conclusion:

The present study proposes that the cocrystallization of an existing antibiotic could develop a medication with improved physicochemical properties like solubility and dissolution, which could alter the dosage regimen and subsequently improve the therapeutic efficacy of this existing pharmaceutical by property-based design.

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Solid State Modification of Etodolac to Target its Limiting Solubility and Dissolution Profile

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Background and Rationale: Most active pharmaceutical ingredients (APIs) suffer from poor physicochemical properties like aqueous solubility, dissolution rate, permeability, stability, hygroscopicity, and manufacturability. Apart from conventional strategies to target such physicochemical properties, crystal engineering has emerged as an alternative to manipulate the poor physicochemical properties of APIs without compromising their therapeutic benefits. This strategy includes various solid state modification techniques such as the formation of salts, polymorphs, coamorphous systems, cocrystals, hydrates, solvates and eutectics.[1] The present study deals with the formation, characterization and evaluation of dissolution properties of pharmaceutical eutectic of Etodolac (ETD) and Theophylline (THE). ETD belongs to NSAIDs category and is an indication for rheumatoid arthritis and osteoarthritis. Due to its limiting aqueous solubility and fair permeability profile, it is categorized as BCS II drug. In literature, other solid state modification techniques have been reported to address the issues related to its poor solubility and dissolution.[2,3]

Methods: (A) 1:1 ETD-THE eutectic was prepared by mechanochemical grinding in a planetary ball mill and characterized by Differential scanning Calorimetry (DSC) and Powder X-ray diffraction analysis (PXRD).

(B) Powder dissolution studies of drug and eutectic were performed using USP Apparatus II at 50rpm by adding 200mg equivalent ETD in 900mL distilled water.

(C) Equilibrium solubilities of drug and eutectic were performed in distilled water by shake flask method for 24hrs.

Results and Discussion: DSC endotherm of 1:1 ETD-THE was found at 142.3°C which was distinctive to that of the both parent components (ETD, 151.3°C and THE, 272.9°C). DSC data was empirically supported by PXRD patterns where signature peaks of components retained in 1:1 ETD-THE eutectic. Equilibrium solubility and powder dissolution studies were measured for the eutectic in contrast to pure ETD. The relative improvement of equilibrium solubility and powder dissolution studies were turned to be 1.4 and 1.5 folds respectively. The betterment can be attributed to the factors such as particle size reduction due to mechanochemical grinding and the use of THE as a hydrophilic carrier.

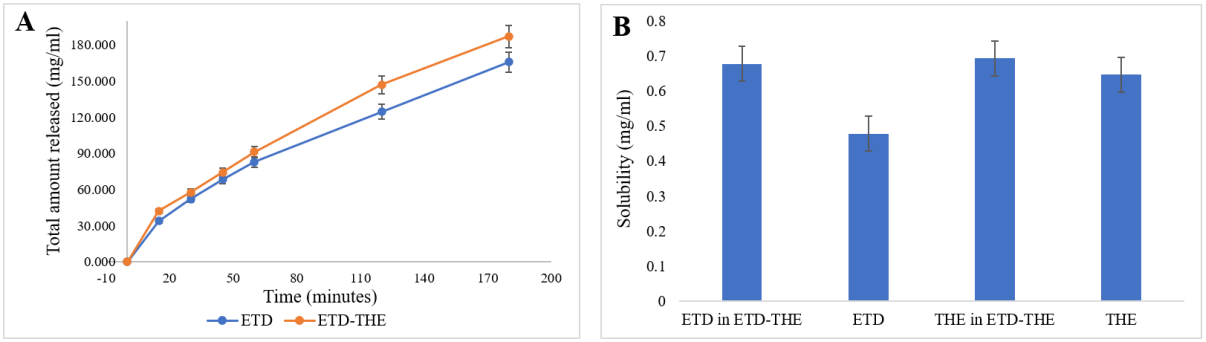

Figure1. (A) Powder dissolution profiles of ETD and ETD-THE in water at 37°C; (B) Aqueous equilibrium solubility comparison graph of pure ETD, pure THE and their respective concentrations in ETD-THE system.

Conclusion: The present study targets the poor solubility and dissolution properties of ETD by synthesizing 1:1 ETD-THE eutectic and its comprehensive thermal and X-ray diffraction characterization. Equilibrium solubility and powder dissolution studies of ETD-THE eutectic have been improved by 1.5 and 1.4 folds, respectively in comparison to parent ETD.

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Topical Active Dermal Targeting of Tofacitinib Loaded Hyaluronic Acid-Coated Proglycosomes to CD44 on Activated Macrophages in Rheumatoid Arthritis Condition


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Background and Rationale: Tofacitinib (TF) is a selective oral Janus kinase inhibitor approved by the USFDA for the treatment of rheumatoid arthritis (RA). Long-term oral TF administration has been linked to serious side effects such as a rise in cholesterol level, a decline in neutrophil count (upon 3 months of continuous usage), gastrointestinal perforations, systemic effects, and immunological suppression [1]. To overcome these oral adverse effects, topical administration of TF can be a good approach. The therapeutic efficacy of tofacitinib can be improved through the high affinity of natural ligands (hyaluronic acid and chondroitin sulphate) to CD44 receptors on the macrophages or other immune cells in the dermal region. Thus, the present research work was inspired by the possibility to develop and evaluate the potential of hyaluronic acid-coated proglycosomes (HA-TF-PG) as the carrier for site-specific dermal delivery.

Methods: Proglycosomes were prepared by the thin-film hydration (TFH) method. The Normal proglycosomes (N-TF-PG) and HA-TF-PG formulations were evaluated for *in vitro* drug release in media consisting of phosphate buffer saline pH 7.4 and 0.15% w/v sodium lauryl sulphate. The gelling agent SEPINEO™ P 600 was incorporated into the optimized formulations under constant stirring to enhance the topical applicability. The *ex vivo* permeation and dermatokinetics studies were performed in phosphate buffer saline (pH 7.4) using modified Franz diffusion cell apparatus for 36 h. Further *in vivo* efficacy studies were carried out in Freund's complete adjuvant (CFA) induced arthritis model.

Results and Discussion: The N-TF-PG and HA-TF-PG showed particle sizes of ≤ 250 nm with PDI of < 0.30. The *in vitro* drug release studies demonstrate that TF solution diffused completely (100%) across membrane within 2 h, whereas the N-TF-PG and HA-TF-PG controlled the release up to 7 h. Initial burst release was observed in the initial 1 h from N-TF-PG (38 %) and HA-TF-PG (48 %); this could be due to the surface-bound drug on the proglycosomes. The R^2 values of N-TF-PG (0.9981) and HA-TF-PG (0.9982) confirm the Korsmeyer Peppas model mechanism with quasi-fickian diffusion transport. The *ex vivo* studies demonstrated that N-TF-PG gel exhibited 1.76-fold high flux compared to HA-TF-PG gel. The *in vivo* efficacy study revealed that HA-TF-PG showed a significant ($P < 0.001$) reduction in inflammation in arthritic rat paws compared to the conventional TF.

Conclusion: The current study ensured that the HA-TF-PG-loaded SEPINEO P600 gels systems would provide a safe and effective formulation for localization of TF at the RA site and overcome the adverse effects associated with the TF.

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Goregaon (East), Mumbai - 400063

Phone : 022-26851903
sotaxindia@sotax.com
www.sotax.com

PLATINUM PARTNERS

www.sotax.com

SOTAX leads the way in the development and manufacture of high-quality pharmaceutical testing equipment and associated services. Our equipment is used worldwide in the development and production processes of our customers and the pharmaceutical and science industries. SOTAX develops, produces and markets system solutions for pharmaceutical testing and does so in close cooperation with pharmaceutical and scientific partners. Our extensive market and process know-how enables us to meet our customers' requirements and comply with the key directives relevant to them. We are also open to cooperation with new industries. SOTAX is a leading independent company for pharmaceutical testing equipment.

Providing high-quality testing solutions for pharmaceutical dosage forms such as tablets has been our expertise and passion for more than 4 decades. Strongly committed to local service and driving innovation, we are proud to be the preferred choice of pharmaceutical companies world-wide. SOTAX develops and manufactures equipment for dissolution testing and automated sample preparation. The SOTAX brand is known for having pioneered the USP 4 flow through dissolution testing method and for being the industry's benchmark brand for fully automated dissolution testing solutions since 1993.

SOTAX has manufacturing plants in Switzerland (Aesch), US (Westborough) and India (Navi Mumbai), for manufacture of innovative, sophisticated, and long-lasting instruments and systems for pharmaceutical testing, establishing SOTAX as the leader in this technological field.

For more details, please visit www.sotax.com

Contact Details:

Dr. L. Ramaswamy
Managing Director, SOTAX India Pvt Ltd

✉: lakshmanan.ramaswamy@sotax.com
✆: 98201 26185

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

CAPSULES / ENGINEERING / FILMS & FOILS / INSPECTION

ACG

Make it better.

PLATINUM PARTNERS

www.acg-world.com

We know how hard it can be to get better. That's why, for sixty years, we've been getting better at helping our pharmaceutical and nutraceutical partners make people better.

Founded in Mumbai in 1961, ACG now serves companies all over the world, touching almost every aspect of solid dosage manufacturing.

With a presence in 138 countries on six continents, ACG is now the world's largest integrated supplier of solid dosage products and services – providing hard-shell capsules, film and foil barriers, track and trace systems, and process, packing and inspection equipment.

We make it better, so you make it better, so together we can make people better.

Our Businesses Include:

ACG Engineering
Medicine is only as good as the equipment that manufactures it.

ACG Inspection
Medicine is only as good as the systems that ensure it arrives safely at its destination.

ACG Capsules
Medicine is only as good as how well it's delivered to the body.

ACG Films & Foils
Medicine is only as good as the barriers that protect their integrity.

Our Approach:

A healthier world through partnership.

While pharma and nutra companies develop the formulations that go into medicines and supplements, we provide the equipment and consumables to produce and deliver those formulations at scale – always ensuring the highest levels of efficacy are maintained.

A healthier world through integration.

Things work better (and easier) when they're designed to work together. Fewer suppliers also means simpler accountability when things go wrong. We are the world's most integrated solid dosage manufacturing provider, and are continually finding new ways of making everything work better together.

BASF
We create chemistry

Solubilization

Our functional ingredients unlock the potential of your challenging API through our Solubilization platform:

- Effective solubilization in solid & liquid dosage forms
- Comprehensive range of cutting-edge solubilization polymers for greater solubility and bioavailability
- Hot-melt extrusion application technology for effectiveness and cost efficiency

Product Highlights:

- **Kollidon® VA 64 / VA 64 fine**
- **Soluplus®**
- **Kolliphor® EL / ELP**
- **Kolliphor® P 188 / P 188 micro and P 407 / P 407 micro**
- **Kolliphor® SLS fine**
- **Kolliphor® HS 15**

More information

Contact us: pharma-solutions@basf.com

https://www.basf.com

BASF Pharma Solutions produces innovative excipients and active ingredients of outstanding quality and performance. With a global team of industry experts and digital solutions, such as the Virtual Pharma Assistants, BASF supports its customers in developing efficient, cost-effective and reliable formulations. Equipped with an in-depth understanding of multiple technologies and applications, BASF has the knowledge and resources to make drug delivery and drug and biologics manufacturing safer and more sustainable.

BASF's pharmaceutical ingredients are produced in line with relevant quality requirements at our state-of-the-art-production sites. With more than 75 years of expertise, we offer the continuity and experience to provide solutions for your pharmaceutical business needs. Headquartered at our Florham Park site in the United States, BASF's Pharma Solutions operations span across the globe. With production facilities spread in different continents and a global team of experts, we are able to support pharmaceutical industries in any location.

ImageProVision Technology
Leaders in Image Analytics

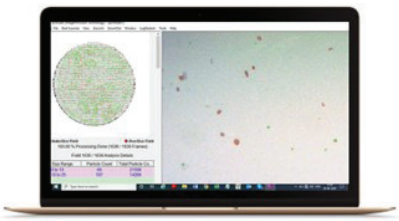
ImageProVision's ipvAutoClass

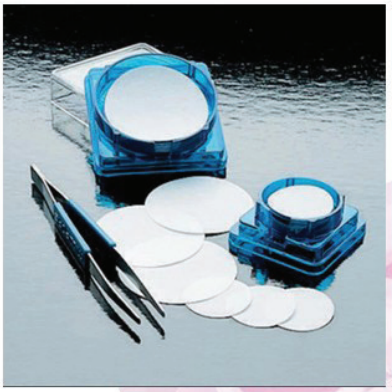
Automatic Microscopic Particle Classifier

ImageProVision Technology
Leaders in Image Analytics

ImageProVision's ipvAutoCount

Automatic Particulate Matter Counter





SESSION PARTNERS

www.imageprovision.com

ImageProVision Technology is a leading Indian company in physical testing space with an emphasis on Image Analytics. ImageProVision's products and services cater to Pharmaceutical, Life Sciences, Bio-Technology, Medical, Chemical, Defence segments.

In a very short period of time, ImageProVision has created a dominant position in Microscopic Image Analysis and has developed some path-breaking solutions for optical, polarized, hot stage, scanning electron microscopy. Some popular products like "Microscopic Particle Analyser", "Particle Classifier", "Particulate Matter Counter", "Nano Particle Analyser" "Smart Proof Reading System" etc are being used by major Indian pharma companies. ImageProVision has also developed high technology products powered by Machine Learning and Artificial Intelligence.

With more than 210 installations at 87 customers locations, ImageProVision is working with leading Pharma companies. These products are used in R&D for new drug development and in Manufacturing QA/QC during drug production. All products comply to regulatory requirements such as 21 CFR compliance.

ImageProVision has a strong team of technology & domain experts. Innovation being the core theme of ImageProVision's culture, ImageProVision has won prestigious awards like India Pharma Award, Startup Masterclass Award, NASSCOM Emerge-50 award etc. ImageProVision is a true success story of Indian Startup & Make in India community in technology segment of Pharma & Healthcare.

ABITEC LIPID EXCIPIENTS

OPTIMIZED FOR CONTROLLED RELEASE

STEROTEX®
CAPMUL® GDB
ACCONON®

WWW.ABITECCORP.COM

ABITEC
AN ABF INGREDIENTS COMPANY

SESSION PARTNERS

ABITEC
AN ABF INGREDIENTS COMPANY

www.abiteccorp.com

ABITEC Corporation, an ABF ingredients company, is a leader in the development and manufacture of specialty lipids and surfactants. Through world-class technical, scientific, regulatory, and manufacturing expertise, they deliver the highest quality solutions in solubilization, emulsification and lubrication to a range of markets globally.

ABITEC is dedicated to the advancement of drug delivery through essential bioavailability enhancement and formulation development technologies.

ABITEC's functional excipients can be incorporated into a broad range of pharmaceutical formulations and dosage forms including but not limited to; soft-gelatin capsules, tablets, parenteral, topical, transdermal, ophthalmic and suppository bases. These high quality excipients are utilized in the formulation of Self-Emulsifying Drug Delivery Systems (SEDDS) specifically designed for meeting the solubility challenges of the pharmaceutical industry. In addition, ABITEC's excipients are employed as carriers, emulsifiers, solubilizers, lubricants and more in a wide range of applications.

Since the acquisition of Larodan in 2020, a manufacturer and international marketer of state of the art, high-purity research grade lipids, the ABITEC-Larodan team of dedicated chemists and scientists have continued to advance their approach to innovation. This partnership along with others across the globe has allowed ABITEC the opportunity to expand their focus towards basic science, as opposed to historic short-term commercial drivers. This directional approach towards innovation is paramount to the development of impactful lipid products and their associated applications to further understand and address the scientific and biological challenges facing the market sectors that we serve today and tomorrow.

For more information on ABITEC's ongoing innovation developments and partnerships please visit our website at www.abiteccorp.com

HMES
HOT MELT EXTRUSION SYSTEM

HME: Effective Processor of Dissolution Enhancement

- Innovatively built HME with Patented elements of Pharmaceutical Industry
- cGMP AND Regulatory complied
- Precise Control over CPP and CQA
- Modular, clean and scalable technology
- Continuous Processor for 10gm to 200kg/hr
- integrated solution for feeding to Flaking/Pelletizing
- Used in OEB 1-OEB 5 formulations
- PAT Integration

STEER A NEW WORLD

STEER

Integraal®

All-in-one True Continous Granulator

- **Versatile** — Wet granulation; Melt granulation; Moisture activated granulation; Dry granulation
- **Multifunctional** — Single step Granulation for Granulating, drying, and sizing
- **Controlled** — It provides controlled process condition for CPP and CQA
- **At Scale** — Research to Manufacturing scale Technology -0.1 Kg to 100kg/hr output
- **Clean** — Quick batch changeover due to self-cleaning capability. Reduced solvent requirement
- **Monitored** — Monitored- Process Analytical Technology Temperature, NIR, PSD

STEER A NEW WORLD

STEER

SILVER PARTNERS

steerlife.com

Founded in 1993 by Dr. Babu Padmanabhan, STEER ENGINEERING PVT. LTD, is committed to the design, creation and implementation of advanced materials platform technology that effectively transforms and functionalises materials in the field of pharmaceuticals, plastics, food & nutraceuticals, biomaterials and biorefining. Operating 4 global offices, 10 satellite offices, 4 Application Development Centres and supported by a talented workforce of over 500 engineers, scientists and technicians, the STEER Group serves over 35 countries across the globe.

STEER is driven by innovation and holds 71 granted patents along with 87 under review that have been applied for. With a vision to 'steer a new world', the Group remains focused on the development of advanced platform technologies and processes to improve the quality of life and change the way people live, eat and stay healthy.

STEER is in unique position to support Pharmaceutical Industry with Technology, Process and Product expertise in the oral solid continuous manufacturing.

STEER manufactures Twin screw extruders for Hot melt and Conventional Granulation in sizes ranging from 10mm, with the capability to run feed rates as low as 10-15 grams per batch to 70mm models with the capability to run rates as high as 100-150 kg/hr.

All extruders are cGMP compliant. STEER is the only supplier in the industry to offer all extruders in both clam shell and segmented barrel configurations. All STEER pharma extruders are scalable making it possible to accurately translate R&D projects to a manufacturing scale or produce a manufacturing process on an R&D scale extruder. STEER also provides ancillary equipment's to the

industry such as feeders, chill roll units, cooling belts, flakers, pelletizers, etc.

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

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

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 2023

First Announcement

We are happy to inform you that **DRPI 2023** is already being planned.

DRPI 2023 activities will begin in the month of April 2023 with a '**CALL FOR ABSTRACTS**.'

Exact dates and schedule for **DRPI 2023** 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

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