Society for Pharmaceutical Dissolution Science

DISSO INDIA - CHANDIGARH 2019

7th International Annual Symposium

Date : 12th & 13th September, 2019

Venue : Radisson® Hotel,
Chandigarh Zirakpur Patiala Road,
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phone: +91-22-42950191/92
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sotaxindia@sotax.com
www.sotax.com

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Prof. Raghuram Rao Akkinepally
Director - NIPER

S.A.S. NAGAR
प्रो. रघुराम राव अक्किनेपल्ली
निदेशक
Prof. Raghuram Rao Akkinepally
Director

राष्ट्रीय औषधीय शिक्षा एवं अनुसंधान संस्थान
NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH (NIPER)
(औषध विभाग, रसायन एवं उर्वरक मंत्रालय, भारत सरकार)
(Deptt. of Pharmaceuticals, Ministry of Chemicals & Fertilizers, Govt. of India)
सैक्टर 67, एस.ए.एस. नगर (मोहाली)–160 062, पंजाब, भारत
Sector 67, S.A.S. Nagar (Mohali) - 160 062 Punjab, India

MESSAGE

I am extremely happy that Disso India 2019 is being organized by NIPER - SAS Nagar, in association with Society for Pharmaceutical Dissolution Science (SPDS) from September 11th to 13th, 2019. I had the opportunity to attend Disso India 2018 at Hyderabad in June last year. The event offered an impressive gathering of pharmaceutical professionals and the deliberations were of the highest standards. This year's event promises to be even better with participation of eminent speakers in the area of dissolution science. Dissolution has evolved from being a quality control tool to a pivotal methodology for ensuring safety and efficacy of the pharmaceutical products. Progress has been made in the area of bio-relevant dissolution media, advanced dissolution equipment and computer modelling. This has opened up new avenues for accelerated development and approval of drug products. Advancements in robotics and automation are creating more sophisticated dissolution apparatus, for generating more meaningful data.

NIPER, SAS Nagar is an institute of national importance which was created by an act of parliament. One of the primary mandate of the institute is to organize national and international meetings in the area of pharmaceutical education and act as a nucleus for interaction between academia and industry. We are excited about organization of Disso India 2019 in collaboration with SPDS. It shall provide a right platform for furtherance of ideas of mutual interest for the benefit of students and pharmaceutical professionals. The organizing committee has made praise worthy efforts for the success of the event.

My best wishes for the event and we look forward to expanding the collaboration with SPDS in future.

रघुराम राव अक्किनेपल्ली

(Prof. Raghuram Rao Akkinepally)

Message from Organising Secretary - DISSO INDIA - CHANDIGARH 2019

Arvind Kumar Bansal
M.Pharm, Ph.D., FAAPS, Scientific Chair - SPDS, Organizing Secretary - Disso India Chandigarh 2019

On behalf of the organizing committee and National Institute of Pharmaceutical Education and Research (NIPER), S.A.S Nagar, I welcome you all to **Disso India Chandigarh 2019**, to be held from 11th Sept 2019 to 13th Sept 2019.

Dissolution science has acquired a critical role in development, regulation and performance evaluation of various pharmaceutical products. Important developments have taken in the field of automation of dissolution equipment, bio-relevant media, dynamic dissolution testing, physiologically based pharmacokinetic (PBPK) modelling, and dissolution testing of non-oral drug products. The conference shall focus on these important developments and we are fortunate to have a galaxy of eminent speakers who are globally recognized authority in their respective areas. This year we have included a module on the "Importance of Dissolution during formulation development". BCS and biowaiver continue to evoke immense interest in the pharmaceutical industry, as they provide a scientific framework for simpler regulatory approvals. Additionally, we have laid emphasis on the role of material properties of API, excipients and process parameters on dissolution performance. I am sure the deliberations during the conference shall enhance the knowledge of scientists from industry, academia and regulatory bodies, on various aspects of dissolution science.

Society for Pharmaceutical Dissolution Science (SPDS) was formed on 16th July 2012 with a vision to promote the developments in dissolution sciences among the pharmaceutical professionals, regulatory bodies and academia. Mission and vision of SPDS is to gather the professional experts of dissolution sciences, on a global platform and dissipate the current science and advancements. It is an honour for NIPER to organize **Disso India**-Chandigarh **2019**, in association with SPDS. We are thankful to SPDS for reposing faith in us for hosting this prestigious event in association with NIPER, S.A.S Nagar. We are fortunate to receive support from drug regulatory bodies of Punjab, Haryana and Himachal Pradesh. It will help us to reach a wider spectrum of stakeholders in the pharmaceutical industry. It will be our endeavour, to maintain the highest technical standards and provide a conducive environment to make "Disso India-Chandigarh 2019" a memorable meeting for all the participants.

With Warm Regards

Arvind Kumar Bansal, M.Pharm, Ph.D., FAAPS
Scientific Chair, SPDS
Organizing Secretary - Disso India Chandigarh 2019

Message from Chairperson - DISSO INDIA - CHANDIGARH 2019

Pardeep Mattu
Drug Controller - Punjab

Food And Drugs Administration Punjab
Near Civil Hospital, Kharar, Sahibzada Ajit Singh Nagar-140301 (INDIA)

I am happy to learn that NIPER, SAS Nagar in collaboration with Society for Pharmaceutical Dissolution Science (SPDS) is organizing an international conference on dissolution science. There has been increasing emphasis on product quality for the products being sold in India. Bioequivalence studies have been made mandatory from the year 2018 to ensure safety and efficacy of the products. Dissolution is a very important pharmacopeial parameter for ensuring release of the drug substance and ensuring batch to batch uniformity. A special expert committee constituted by the CDSCO has proposed guidelines for formulation development of various formulations, with the objective that each drug produced in the country shall be safe, efficacious and of standard quality. Dissolution finds an important place in the development of oral solid dosage forms. The equipment suppliers should develop more economical dissolution apparatus to increase access of this important tool to small and medium enterprises as well.

The FDA Punjab extends its full support for the success of the event so that maximum number of stake holders can benefit from the event.

(Pardeep Kumar)
Joint Commissioner (Drugs)
Food & Drugs Administration, Punjab

NK Ahooja

Drug Controller - Haryana

State Drugs Controller-cum-Licensing Authority
Food & Drugs Administration, Haryana
SCO No. 94, Sector-5, Panchkula (Haryana)

I am very happy to note that Society for Pharmaceutical Dissolution Science in collaboration with NIPER, SAS Nagar is organizing Disso India 2019 at Chandigarh. I as the Chairperson for the event welcome all the speakers, participants and sponsors to this important event.

Dissolution is an extremely important regulatory test for Pharmaceutical products and ensures not only the batch to batch variability but also the product performance. The regulatory scenario is evolving at a fast pace and dissolution is going to play an increasingly important role. The deliberations in Disso India promise to be exciting and shall bring forth deep insights of science of dissolution.

The local organizing committee has made extensive efforts to ensure a successful conference. I am sure this event shall be an enriching experience for all the participants. Once again I welcome you all to City Beautiful and Disso India 2019.

(Narender Kumar Ahooja)
State Drugs Controller
Food & Drugs Administration, Haryana

Message from President - SPDS

Vijay Kshirsagar
Director & CEO, TRAC Pharma Consulting, Mumbai

Friends, a very warm welcome to Disso India Chandhigarh 2019 being held at Chandigarh. It is a matter of great satisfaction that Society for Pharmaceutical Dissolution Science (SPDS) has taken significant strides since it's inception about 7 years back. Thank you all for your support without which it is just not possible.

Year after year we have getting very good feedback from all of you which motivates us to still better to help global industry develop/ control safe & efficacious drugs. Every year, we had a mega annual conference in India apart from occasional conferences outside India. Next year i.e. in 2020 we will reach the new glory by hosting Dissolution Conference in USA. Our local organising committee with Dr Arvind Bansal as the primary driver for things to happen, has taken every possible care to see that you enjoy the program .

This abstract book shall reveal that we have been able to get the contribution from global dissolution experts like Dr. Vinod Shah, Dr. Umesh Banakar, Dr. B. S. Bhoop, Mr. Samir Haddouchi, Dr. Padma Devrajan & several others. The topics are wide ranging from testing, BCS, TCS, Biowavers, QbD for Dissolution, automation, Dissolution of Nano Formulations etc.

We are indeed lucky to have best available subject matter experts in our committee. We appreciate the efforts taken by entire local organising committee with Dr. Raghuram Rao as the Chief Patron. We cannot forget the man behind the scene i.e. Dr. L. Ramaswamy, our most dynamic General Secretary.

We express heartfelt thanks to all our national and international speakers of Disso India Chandigarh 2019 who have always contributed without any hesitation/expectation, which shows their love for the Science of Dissolution. So happy learning and enjoy the conference and do give us your feedback. Finally, an appeal to you to join us in the journey towards excellence in Dissolution.

Vijay U. Kshirsagar
President-SPDS
11th August 2019

Message from General Secretary - SPDS

Dr. L. Ramaswamy
Managing Director, Sotax India Pvt Ltd, Mumbai

Dear Colleagues,

It is indeed a pleasure and privilege for me to be the General Secretary of SPDS and coordinate Disso India - Chandigarh 2019 with LOC and the Scientific Committee. This is the first time we are organizing Disso India at Chandigarh. Collaborating with NIPER, SAS Nagar, Punjab, one of the most prestigious Pharma research Institutes of the Country and conducting this event in Chandigarh is a matter of great pride for SPDS. I would like to express my deepest gratitude to Dr. Raghuram Rao, Director of NIPER for accepting our proposal and supporting us unconditionally.

The key role performed by our Scientific Chair and the Organising Secretary- Dr. A. K. Bansal, Professor of Pharmaceutics, NIPER, SAS Nagar together with his team of LOC, has been critical in successfully organising Disso India - Chandigarh 2019.I must mention here that the response received from the Pharma Industry and academia has been very encouraging.

Under the guidance of two able Chairmen, Pardeep Mattu and NK Ahooja, the organizing committee has provided an extremely conducive environment for such a high-level conference at Chandigarh. I wish to also thank both the Local Organizing Committee and the Scientific Committee for all their efforts in making this possible.

I am sure that all the delegates of Disso India - Chandigarh 2019 shall find their time spent at the conference enriching and enlightening. My sincere thanks to all the delegates and their managers who have given their approval for their participation in this conference. Most importantly, a conference 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 President, Vijay Khirsagar and all other trustees made my functioning very easy and enjoyable at SPDS.

Encouraging young scientists and academicians has always been our way of life at SPDS. Thus, Posters Exhibit on Dissolution Testing is an added feature of Disso India. My sincere appreciation to all the poster presenters and their teachers who have encouraged their Students / Scholars to present nearly 50 posters on Dissolution Testing and its applications in this conference. The Poster management committee under the leadership of Prof Mala Menon BCP, Mumbai and Dr. Sanyog Jain, NIPER, SAS Nagar have greatly managed in ensuring this is done in the most optimum manner.

I wish you all a great conference of Disso India - Chandigarh 2019 over these two days, 12th and 13th September 2019 at Hotel Radisson.

Best Regards

Dr. L. Ramaswamy
Managing Director, Sotax India Pvt Ltd, Mumbai

Message from President - North Chapter

Prof. B S Bhoop

Prof. Emeritus, Panjab University

Professor Bhupinder Singh Bhoop
M Pharm, Ph D, D St, FPAS, FIPA
Coordinator, UGC Centre of Advanced Studies in Pharmaceutical Sciences
Founder Coordinator, UGC Centre of Excellence in Nano Biomedical Applications
Chairman, University Institute of Pharmaceutical Sciences (2014-2017)
Dean, Faculty of Pharmaceutical Sciences (2011-2013)
Dean Alumni Relations, Panjab University (2007-11)
Fellow & Member University Senate (2012-16); Syndicate Member (2013-15)
Panjab University, Sector 14, Chandigarh 160014 INDIA
☎ 91-172-253-4103, Cell: 91-981-560-2785 *Telefax* : 91-172- 254-3101
E-mail: bsbhoop@yahoo.com, bsbhoop@gmail.com, bsbhoop@pu.ac.in

227/2019/UIPS/BSB 8/27/2019

MESSAGE

I am quite fascinated to know that the Society for Pharmaceutical Dissolution Science (SPDS) is organizing **Disso India 2019,** an International Conference on Dissolution Sciences and Applications, in Chandigarh, on the theme, "***Ensuring Built-in Quality through Dissolution Studies***" on 12-13th September, 2019, preceded by a Pre-Conference Workshop on 11th September, 2019 at NIPER, Mohali.

Dissolution verily is the pivot to successful development of drug products, oral as well as non-oral, for plausible enhancement in the bioperformance of drug candidates. Establishment of SPDS in 2012 has brought the much-needed shot in the arm for disseminating and propagating assorted vistas of drug release and dissolution testing among the scientists across the globe. SPDS, since its inception, has been successfully making pioneering strides under the able tutelage of global stalwarts like, Dr Vinod P Shah and Dr Umesh Banakar, and dynamic execution by Dr Vijay Kshirsagar and Dr L Ramaswamy as its President and General Secretary, respectively.

In this context, the vision of the SPDS and Disso India 2019 Organizing Team, with Professor Arvind Bansal as Organizing Secretary, needs to be applauded for bringing out a panoramic portrayal of this vibrant and vital domain of dissolution science through this conclave. This would offer an excellent opportunity for the young scientists to share a common platform to exchange their knowledge and know-how, and to learn and update their professional skills from the experts gathered from far and wide.

I, as the President of North India Chapter, and a humble member of National and Local Organizing Committees, take pride and privilege in welcoming the delegates to the City Beautiful - Chandigarh.

I sincerely hope that the Disso India 2019 would provide a conducive forum for information sharing on the nuances in the domain and for networking among fellow delegates. We are grateful to the esteemed guests for having acceded to our invitation to grace the occasion. May it be a highly useful, fruitful, meaningful and memorable event!

Bhupinder Singh Bhoop
Professor & Coordinator

Res: 2321 GF, Sector 38C, Chandigarh 160 036, INDIA. ☎ 91-172-2697575

Society for Pharmaceutical Dissolution Science

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

SPDS is the only professional body dedicated to Dissolution and its application worldwide.

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.

ORGANIZING COMMITTEE

Core-Committee

Chief Patron : **Prof. Raghuram Rao Akkinepally**
Director, NIPER - SAS Nagar

Chairpersons : **Pradeep Mattu**
Drug Controller - Punjab
NK Ahooja
Drug Controller - Haryana,

Vice Chair : **Atul Nasa**
Drug Controller, Delhi, Delhi Drug Controller Office

President : **Vijay Kshirsagar**
Director & CEO, TRAC Pharma Consulting, Mumbai

General Secretary : **Dr. L. Ramaswamy**
Managing Director, SOTAX India, Mumbai

President-North Chapter : **Prof. B S Bhoop**
Prof. Emeritus, Panjab University

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Professor & Head (Department Of Pharmaceutics)
NIPER SAS Nagar, Punjab

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- **Dr. Raghunandan HV,** Consultant, RC2 Pharma Solutions
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- **Samir Haddouchi,** Managing Director, SPS Pharma Services
- **Dr. Sandip Tiwari,** Manufacturing Science and Technology, Actavis Laboratories FL, Inc., Florida, USA

Scientific Committee for Disso India - Chandigarh 2019

Chairperson : **Prof. Arvind Bansal**
Professor & Head (Department Of Pharmaceutics)
NIPER SAS Nagar, Punjab

Co-chair : **Dr. Vinod Shah**
Ex-USFDA, Pharmaceutical Consultant, USA

Dr. Deepak Haldankar
President Technical, Akums Pharmaceuticals, Haridwar

Local Organizing Committee

- **Dr. Abhay Sangamwar,** Assistant Professor, NIPER - SAS Nagar
- **Prof. Ashok Tiwary,** Professor and Former Dean, Panjab University, Patiala
- **Avtar Singh,** Associate Director - Quality, GMP Affairs & RA, Centrient Pharmaceuticals, Punjab
- **B. K. Samantray,** Deputy Drugs Controller, Baddi, CDSCO, Baddi
- **B. S. Grover,** Vice President Quality Assurance, Alkem, Baddi
- **Dr. Deo Narain Dikshit,** Director, Aqex Pharmasolutions
- **Devender Solanki,** Director, Abbott, Panchkula, Haryana
- **Prof. Farhan J Ahmed,** Prof. Pharmaceutics, Jamia Hamdard, New Delhi
- **Dr. Gautam Singhvi,** Assistant Prof., BITS, Pilani, Rajasthan
- **Dr. Lalit Wadhwa,** President R&D, Ind Swift Labs, SAS Nagar
- **Dr. Manish Goswami,** Head of Dept., Chandigarh University, Landran
- **Praveen Khatry,** AVP-MSTG, Sun Pharma, Mohali
- **Rajesh Aggarwal,** Dy. General Manager R&D, Modi-Mundipharma
- **Dr. Sandeep Arora,** Dean, Chitkara University
- **Dr. Sanyog Jain,** Associate Professor, NIPER - SAS Nagar
- **Prof. S. P. Goel,** Principal, Sachdeva College of Pharmacy, Chandigarh
- **Dr. Sukhjeet Singh,** Sr. Vice President - R&D, Panacea Biotec
- **Prof. V. R. Sinha,** Prof. Pharmaceutics, UIPS, Panjab University

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- **S. D. Joag**
  Consultant, SynergyPharma Formulation India Pvt. Ltd.

Disso India - Chandigarh 2019 Programme Schedule

TIME	TITLE & SPEAKER
	DAY 1 : 12/09/2019
09.00 am - 10.00 am	**Inaugural Session of Disso India 2019**
	Module 1 : Importance of Dissolution during formulation development
10.00 am - 10.30 am	**BCS, Dissolution and Biowaiver** **Dr. Vinod P. Shah,** Ex-USFDA, Pharmaceutical Consultant, USA
10.30 am - 11.00 am	**Dissolution enhancement by modulating the physical form of the API** **Dr. Raj Suryanarayanan,** PhD, Professor and William and Mildred Peters Endowed Chair, Departmentof Pharmaceutics, College of Pharmacy, University of Minnesota
11.00 am - 11.30 am	**MORNING TEA**
11.30 am - 12.00 pm	**Effect of surface anisotropy of crystal habits on dissolution performance** **Dr. Arvind Bansal,** Professor & Head (Dept. of Pharmaceutics) NIPER SAS Nagar, Panjab
12.00 pm - 12.30 pm	**PANEL DISCUSSION 1**
12.30 pm - 01.00 pm	**Excipients' Role in Modifying Dissolution** **Ms. Seema Trivedi,** GM Technical, Anshul Life Sciences, Mumbai, India
01.00 pm - 02.00 pm	**LUNCH (PARALLEL POSTER SESSION)**
02.00 pm - 02.30 pm	**Critical process parameters affecting dissolution** **Dr. Deo Narain Dikshit,** Director, Aqex Pharmasolutions
02.30 pm - 03.00 pm	**Implementation of QbD for dissolution testing** **Dr. B S Bhoop,** Prof. Emeritus, Panjab University
03.00 pm - 03.30 pm	**Solubility to permeability to bioavailability : Connecting the dots** **Dr. Namita Tipnis Varde,** Ph.D., Application Scientist, Electrolab India Pvt Ltd.
03.30 pm - 04.00 pm	**EVENING TEA**
04.00 pm - 04.30 pm	**Dissolution Qualification: general concerns and indirect importance of automation** **Michel Magnier,** Product Manager and Application specialist, SOTAX AG, Switzerland
04.30 pm - 05.00 pm	**PANEL DISCUSSION 2**
05.00 pm - 05.30 pm	**CULTURAL PROGRAMME**

TIME	TITLE & SPEAKER
DAY 2 : 13/09/2019	
Module 2 - Dissolution of Novel Drug Delivery Systems	
09.00 am - 09.30 am	**Poster Awards and Felicitation**
09.30 am - 10.00 am	**Topical drug classification system (TCS)** **Dr. Vinod P. Shah,** Ex-USFDA, Pharmaceutical Consultant, USA
10.00 am - 10.30 am	**Importance of dissolution studies in evaluation of DPIs** **Dr. Paul W S Heng,** GEA-NUS Pharm Processing Res Lab, Dept of Pharmacy, National University
10.30 am - 11.00 am	**Dissolution of topical products** **Dr. Rajeev Raghuvanshi,** Dr. Reddy's Lab
11.00 am - 11.30 am	MORNING TEA
11.30 am - 12.00 am	**Practical approaches for dissolution testing of nano formulations** **Prof. Dr. Padma Devarajan,** Institute of Chemical Technology, (ICT), Mumbai, India
12.00 pm - 12.30 pm	**Other NDDS / differentiated products + Long acting parenterals** **Samir Haddouchi,** Managing Director, SPS Pharma Services, Orleans, France
12.30 pm - 01.00 pm	PANEL DISCUSSION 3
01.00 pm - 02.00 pm	LUNCH
Module 3 - Regulatory and IP considerations	
02.00 pm - 02.30 pm	**Regulatory aspects of dissolution** **Vijay Kshirsagar,** Director and CEO, TRAC Pharma Consulting, Mumbai, India
02.30 pm - 03.00 pm	**Patent opportunities with dissolution studies** **Dr. Umesh Banakar,** Professor and President, Banakar Consulting Services, USA
03.00 pm - 03.20 pm	**Efficiently Automated UV/VIS Spectroscopy** **Atul Yelpale,** Product Specialist- Anachem Mettler-Toledo India Pvt. Ltd.
03.20 pm - 03.50 pm	PANEL DISCUSSION 4
03.50 pm - 04.00 pm	VOTE OF THANKS
04.00 pm - 04.30 pm	EVENING TEA

Dr. Vinod P. Shah

Ph.D., FAAPS, FFIP, Pharmaceutical Consultant, North Potomac, MD, USA

Dr. Shah is a pharmaceutical consultant. He retired from US FDA (Food and Drug Administration) as a Senior Research Scientist after 30 years of service in July 2005. At FDA, he has developed several Regulatory Guidances for Pharmaceutical Industry in the area of dissolution, SUPAC, bioequivalence and biopharmaceutics. He has received several FDA Awards including Award of Merit, Scientific Achievement Award and Distinguished Career Service Award.

Dr. Shah is an Honorary Member of Indian Pharmaceutical Association (2003), a recipient of IDMA and SPDS Excellence Award Dr. Shah is author/co-author of over 300 scientific papers and a co-editor of four books. He 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 FIP Lifetime Achievement Award in Pharmaceutical Sciences, Honorary Doctorate from Semmelweis University, Budapest, Hungary and from University of Medicine and Pharmacy Carol Davila Bucharest, Romania, AAPS Distinguished Pharmaceutical Scientist Award, AAPS Global Leader Award and Marquis Who's Who Albert Nelson Marquis Lifetime Achievement Award.

E-mail : dr.vpshah@comcast.net

BCS, Dissolution and Biowaiver

Biopharmaceutics Classification System (BCS) is a framework for classifying drug substance based on its solubility and permeability. The evolution of the BCS and related dissolution guidance, biowaiver monographs and its implications, and other dissolution-based biowaivers will be briefly discussed. Drug products under BCS Class 1 and 3 are eligible for biowaiver if it meets appropriate dissolution test criteria when compared with the brand name (innovator) drug product. The concept of BCS-based biowaiver is now generally globally accepted and attempts are on its way to harmonize the regulatory requirements. To help firms submit BCS based biowaiver applications, FIP/SIG/BCS focus group has undertaken the task of preparing biowaiver monographs. The biowaiver criteria reduce regulatory burden without sacrificing the drug product quality.

7th Annual International Conference on Dissolution Science and Applications, Ensuring Built-in Quality through Dissolution Studies, Punjab, India, September 12, 2019. Disso India – Chandigarh 2019.

Topical Drug Classification System (TCS)

Determining the bioequivalence of topical drug products is challenging, complicated and cumbersome. Topical Drug Classification System (TCS), based on established scientific principles of SUPAC-SS and *in vitro* release (IVR) has been developed to simplify regulatory pathway for generic topical drug approval. TCS classification is similar to well-established Biopharmaceutics Classification System (BCS). TCS considers qualitative (Q1) and quantitative (Q2) composition of inactive ingredients and microstructure arrangement (Q3) of topical products. IVR reflects the combined effects of several physico-chemical characteristics, particle or droplet size, viscosity, microstructure arrangement of the matter (Q3) and state of aggregation of dosage form. Based on Q1, Q2 and IVR similarity (Q3), topical drug products are classified as TCS class 1, 2, 3 and 4. Only TCS class 1 and 3 drug products are eligible for biowaiver. Validation of TCS concept using Acyclovir 5% cream product will be presented. TCS simplifies the regulatory requirements and reduces the regulatory burden, maintains drug product quality and make drug products more affordable to consumers.

7th Annual International Conference on Dissolution Science and Applications, Ensuring Built-in Quality through Dissolution Studies, Punjab, India, September 12, 2019. Disso India – Chandigarh 2019.

Raj Suryanarayanan (Sury)

PhD, Professor and William and Mildred Peters Endowed Chair, Department of Pharmaceutics, College of Pharmacy, University of Minnesota

Raj Suryanarayanan (Sury) is Professor and William and Mildred Peters Endowed Chair in the College of Pharmacy, University of Minnesota. He obtained his B.Pharm. and M.Pharm. degrees from Banaras Hindu University, India and M.Sc. and Ph.D. degrees in Pharmaceutics from the University of British Columbia, Vancouver, Canada. The overall goal of his research is to apply principles of pharmaceutical materials science to the design of robust pharmaceutical dosage forms with reproducible and predictable properties. His research group has developed low temperature powder X-ray diffractometric techniques to study frozen and freeze-dried pharmaceutical systems. He is a consultant to numerous pharmaceutical companies and was a member of the USP Expert Committee (Excipients test methods). He is a fellow of the American Association of Pharmaceutical Scientists (AAPS) and is a past chair of the Teachers of Pharmaceutics Section of the American Association of Colleges of Pharmacy. Sury is a member of the Academy of Distinguished Teachers at the University of Minnesota, is the recipient from AAPS of the Outstanding Educator Award and the David Grant Research Achievement Award in Physical Pharmacy and the PhRMA (Pharmaceutical Research and Manufacturers of America) Foundation Award. He is an Associate Editor of Molecular Pharmaceutics.

E-mail : surya001@umn.edu

Dissolution Enhancement by Modulating the Physical form of the API

Modifying the physical form of an active pharmaceutical ingredient (API) provides an avenue to enhance the solubility and dissolution rate of a drug. For example, while amorphization can result in an increase in apparent solubility, maintaining the supersaturated state for a sustained time period so as to translate to a bioavailability enhancement can be a challenge. Amorphous solid dispersions (ASD), wherein the API is molecularly dispersed in a polymer, is a popular and effective strategy for stabilizing APIs and sustaining supersaturation in solution. A second strategy is to prepare coamorphous systems, for example, of a weakly basic drug ketoconazole (KTZ) with each oxalic, tartaric, citric and succinic acid. The systems were physically stable and resisted crystallization. The dissolution performances of the coamorphous systems were compared using the area under the curve (AUC) obtained from the concentration- time profiles. The enhancement in dissolution appeared to become more pronounced as the strength of the acid increased. Coamorphization with acid caused at least a twofold increase in AUC when compared with amorphous KTZ. The decrease in pH of the diffusion layer of the dissolving solid, brought about by the acid, is at least partially responsible for the dissolution enhancement. Further enhancement in AUC was accomplished when ternary drug-polymer-acid ASDs were prepared with KTZ, polyvinylpyrrolidone, and each acid. Drug-polymer- acid ASDs take advantage of the solubility enhancement brought about by the counterion as well as the stabilization effects of the polymer. Hence, ternary ASDs exploit the solubility advantage of both salt formation and amorphization.

Dr. Arvind Bansal
Professor & Head (Department Of Pharmaceutics) NIPER SAS Nagar, Punjab

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 has 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 India being awarded this Fellow status. He has won prestigious awards like AAiPS Distinguished Educator and Researcher Award, Innocentive Award and OPPI Award. Prof Bansal's research group has completed more than 550 industry sponsored projects, granted 08 patents, filed 27 patents, and published 180 research articles and 26 review articles. He is an editorial board member of Journal of Excipients and Food Chemicals and Pharmaceutics. He is also an Advisor to the editorial board of Journal of Pharmaceutical Sciences and on Editorial Board of Molecular Pharmaceutics. Recently his lab has out-licensed a platform technology on “Nano crystalline solid dispersions – NanoCrySP.

E-mail : akbansal@niper.ac.in

Effect of Surface Anisotropy of Crystal Habits on Dissolution Performance

Dissolution and / or solubility may be the limiting parameters for oral bioavailability. Dissolution is a surface-mediated kinetic process and is affected by the solid form of the API. There is a vast body of information on the impact of solid forms like polymorphs, amorphous form, co-crystals and salts, on dissolution rate and solubility. However, the role of different crystal habits of the same polymorphic form of an API on dissolution behavior, is less explored. Different crystal habits contribute differential molecular surface environment, which can affect dissolution. A case study of acicular and plate shaped crystals of form III of celecoxib, shall be presented. Crystals habits were characterized by thermal techniques, microscopy and PXRD. Face indexation studies, surface chemistry using X ray Photon Spectroscopy were carried out on both the crystal habits. Crystal morphology prediction and visualization of surface molecular environment of different crystallographic planes was carried out using Mercury software. Significant differences were observed in wettability, powder dissolution and Intrinsic Dissolution Rate (IDR). These could be explained on the basis of anisotropic surface chemistry of the crystal habits and differences in relative abundance of various crystal facets. We recommend to consider crystal habit, apart from polymorphic form, as a Critical Material Attribute (CMA) for dissolution of BCS class II drugs.

Seema Trivedi
GM Technical , Anshul Life Sciences, Mumbai, India

Qualification : B.Pharm from C.U Shah college of pharmacy, SNDT University in 1988

Experience: Fem Care Pharma Ltd for 4 years. in product development of Personal care, Performance chemical. Had an opportunity to work on fragrance encapsulation through liposomes, cyclodextrin for Fabric softener. Also worked on liquid detergents. Stabilised the Instobleach Hydrogen Peroxide cream

Ipca Laboratories Ltd. : Tenure of 12 years

Initially 2 years in Analytical and then transferred to Formulation developments for Domestic market. ROW, EU generics and US market (ANDA projects). Lead a team of approx 12-15 formulation scientist. She was also a mentor to M. Pharm student of BITS, Pilani for their dissertation programme In the tenure got an opportunity to develop all dosage form like Liquid orals, Semi solid preparation, Oral solids, and injectables. Developed more than 50 formulations mainly in oral solid dosage forms. Also developed few Modified release formulations and formulation for EU generics from Pre-formulation studies right upto the Exhibit batches.

Nicholas Piramal Ltd. Worked for two years as Senior Group Leader. Developed and launched about 4 US generics Projects. Involved in Lab Management and Pilot Scale areas for Audits

Anshul Life Sciences As a General Manager Technical, leading an application Lab Team. Application Lab caters to the needs of customer on the formulation development. Data generation for application of Excipients. Regulatory support to the customer and Manufacturers.

Email : seema.trivedi@anshulindia.com

Excipient's Role in Modifying Dissolution

Dissolution is an important testing parameter in the oral dosage form. It can discriminate between the formulations. The inherent characteristics of the API cannot be changed i.e its solubility and Bioavailability. But Excipients can play an important role in increasing the bioavailability of API by various methods like Solid dispersion, complexations etc.

For Immediate Release Tablets, Super- Disintegrants will improve the rate of dissolution by disintegrating the Immediate Release tablet at faster rate and thereby exposing the API to the media. Contrary there are some super-disintegrants which forms complex with API and can slow the release. The diluents can also change the rate and extent of dissolution of all the formulations based on the solubility, pH of the excipients in the media.

For Controlled/ Modified Release formulation the dissolution is controlled solely by the excipients. Various polymers and waxes are used to modify the dissolution over a period. The different grades of Excipient can give a different dissolution rate. Hypromellose is available in various grades of viscosity for Modified release formulation from 100 cps to 200,000 cps. The viscosity is selected based on the Bio Classification of the API.

In the presentation we will discuss the excipient role in improving the dissolution where is it limiting factor for bioavailability and for modifying the release of controlled release formulation over a period.

Dr. Deo Narain Dikshit

Director, Aqex Pharmasolutions

- Dr. Deo Narain Dikshit, MSc (Organic Chemistry), PhD. is founder, President and CEO of AQEX PHARMASOLUTIONS PVT. LTD. AQEX stands for Advance Quality Excellence in services to Pharmaceutical Industry in field of Quality , Compliance Process Excellence , new green field project
- Dr. Deo Narain Dikshit is a Qualified and Certified Auditors in ISO 14000, GXP Audit and Certified Trainers for TQM, cGMP trainings. He has attended more than 500 trainings and has been trainer on various plateforms – such as CPHI, ISPE, IPA, Quality Excellence (Flemingo Europe), FICCI and Indian Pharmacopoia commission and CDSCO driven trainings
- Dr. Deo Narain Dikshit is having experience of more than 36 years in Pharmaceutical industry in Quality Assurance, He has worked as Regional corporate Quality Head of Asia of Indian multinational company and has proven managing ability in Quality Function.
- In his carrier of three and half decades, Dr. Deo has worked in various leadership positions of Sunpharma (i) Ltd, Ranbaxy Laboratories Ltd, Alkem Laboratoroies, Nicolas Piramal Health Care (I) Ltd, Unichem Laboratories Limited, IPCA laboratories Ltd, Natco Pharmaceuticals Ltd, Bio Vaccines Ltd amd Aristo Laboratories. Dr. Deo has been Responsible for Plants in Shenghai, Malaysia and Bangladesh
- He was responsible for Quality and compliance for multiple sites in India and other Asian Countries which were manufacturing pharmaceuticals products being marketed to advance markets like United States of America, Canada, entire Europe, Russia, Ukraine, Japan, Middle East, South east Asia, Australia, South Africa, Brazil and many other. Hence he has been managing directly responsible for Quality function and compliance to GxP requirements, managing Regulatory audit, Multi site Technology transfers, new projects new Product Filing, hosting and managing Regulatory inspections of various Regulators – FDA , IMB , MHRA, MCA, MCC, TGA, ANVISA, HSA, KIKO, AFFSAP, ANVIMA, FDA RUSSIA, Health CANADA , WHO
- Dr. Deo Narain Dikshit has worked in many green field projects of setting new Dosage form plants of OSD, Parenterals, Liquid, Ointment and Creams from Conception to Approval of Plant, Remediation of Quality Management, Improvement of efficiencies, Quality Risk Management, Laboratory data Compliance, Data Integrity remediation, Product Quality issues provides the overall leadership, business strategy and day to day management of organization.

E-mail : deo.dikshit@aqexpharmasolutions.com

Critical Process Parameters Affecting Dissolution

The manufacturing process development programme or process improvement programme should identify any critical process parameters that should be monitored or controlled (e.g., granulation end point) to ensure that the product is of the desired quality The process control strategies that provide process adjustment capabilities to ensure control of all critical attributes should be described.

The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Q8 guidance,

It is of great significance to realize that the quality is a systemic approach for drug development that begins with the predefined object and emphasizes product and process understandings based on sound science and quality risk management.

On the basis of the view of FDA to have understanding of Variability is process, It is very Critical and important to understand the sources of the Variation in Process performance

A pharmaceutical process is considered to be well understood when all sources of variability are identified and explained, and variability is managed by the process while product quality attributes can be accurately and reliably predicted.

However, pharmaceutical production processes are complex and multivariate by nature. The relationships between the critical quality attributes (CQAs) and the critical process parameters (CPPs) affects the Quality attributes such as Drug Release profile and thus affecting the Dissolution.

Dr. B S Bhoop
Prof. Emeritus, Panjab University

Acclaimed globally for his scientific work, esp. on QbD-based development of novel and nanostructured drug delivery, advanced pharmacokinetic and drug release kinetic modelling, Prof Bhoop has contributed over 35 years of dedicated service towards Pharmaceutical Education and Research.

Professor Bhoop has to his credit over 370 original publications, 15 books by prestigious international publishers and 68 book chapters. A widely travelled scientist, he has delivered more than 300 plenary, keynote and invited talks in India and overseas, including USA, Canada, UK, Germany, China, Thailand, Hong Kong, Kuwait, Dubai and Bangladesh. Several thousands of industrial scientists from leading pharma companies of India, of the likes of Mylan, Zydus, Ranbaxy, Cipla, Cadila-Pharma, Sentiss, Sun Pharma, IPCA, Glenmark, Sanofi-Aventis, Ajanta, Alkem, Jubilant, Bharat-Serums, Panacea Biotec, Beximco Pharma (Dhaka) and BioVectra (Canada) have been duly trained by him on QbD, Biowaivers and Nanomedicine. He has guided/guiding over one hundred researchers including 31 Ph.D.'s and 6 post-doctorates, completed 6 industrial consultancy assignments, and has 6 patents and 2 tech. transfers of nanotech-based drug delivery products. He has earned research grants over 7.30 crores from government and corporate sectors.

His work has fetched Prof Bhoop with numerous awards & accolades.

At Panjab University, Professor Bhoop has been Chairman - University Institute of Pharm. Sciences (2014-17), Fellow & Member - University Senate & Syndicate (2012-16), Dean - Faculty of Pharm. Sciences (2012-14), and Dean Alumni Relations (2007-11). He is currently the Coordinator of UGC Centre of Advanced Studies (CAS) in Pharm. Sciences, and Founder-Coordinator of National UGC Centre for Excellence in Nano Biomedical Applications (2011-).

On the basis of his exemplary accomplishments, Mr Hamid Ansari - then Vice President of India, Prof Ved Prakash - then Chairman-UGC, and Indian Pharmaceutical Association (IPA) conferred upon him Professor Bhoop the Honorary Fellowship Awards of Panjab University 2011, Punjab Academy of Sciences 2017, and of IPA 2018, respectively.

Email : bsbhoop@gmail.com

Dissolution as a Pivot in Implementing Quality by Design (QbD) for Drug Products

With escalating number of patients afflicted with diverse diseases and corresponding enforcement of stricter regulatory requirements, the need and demand for quality pharmaceuticals remain an imminent concern and challenge for manufacturers and scientists.

Design and development of an impeccable generic drug product, in this regard, involves a plethora of functional and non-functional excipients, processes and unit operations, besides API itself. The major cause of inconsistent quality of pharmaceuticals has been ascertained as the variability associated with these (active and inactive) raw materials, processes and packages, and associated interactions among them. Owing to such high intricacy and wide diversity of multi-step processes involved during pharmaceutical manufacturing, the federal agencies have been bringing out newer regulatory requirements to monitor and assure the quality compliance. Recent paradigm shift has been through regulatory initiatives by ICH, USFDA, EMEA, etc. in implementing systematic mindset of Quality by Design (QbD). Today, the regulators require thorough scientific and risk - based understanding of product and process development strategies to meet the efficacy and safety demands of pharmaceuticals, not merely to live up to patient satisfaction, but to avoid potential product rejects and recalls too.

Dissolution, in this regard, has proved to be a pivotal tool, providing a definitive clinical marker for regulatory applications in the light of BCS perspectives. Application of these concepts in QbD context, however, requires a certain level of understanding especially during regulatory documentation. Vital aspects include identification of rate-limiting steps in drug absorption process, linking with apt pharmacokinetic variables, prognostic abilities of *in vivo* bioavailability from *in vitro* dissolution test conditions, and interpretation of critical product/process variables. The current talk would succinctly provide a bird's eye view on such paradigms, challenges thereof, and plausible remedial measures.

Namita Tipnis Varde
Ph.D., Application Scientist, Electrolab India Pvt Ltd.

Namita Tipnis Varde received a B.Pharm from Gahlot Institute of Pharmacy, Navi Mumbai in 2010. She received an M.S. in Pharmaceutics and Drug Delivery Systems from Northeastern University, Boston in 2013. She received a Ph.D in Pharmaceutics from University of Connecticut in 2018. She has received several awards for her dissertation research 'Formulation Development and Sterilization of Drug Coatings for Implantable Biosensors'. She has authored 2 book chapters, 1 review article and 4 research articles and has presented her research at AAPS, CRS and Diabetes Technology Society. She is presently working as an Application Scientist in Electrolab India Pvt Ltd. Her area of focus is simultaneous dissolution and permeability determination and in vitro release testing of novel drug delivery systems using compendial and non-compendial apparatus.

Email : namita.varde@electrolabgroup.com

Solubility to Permeability to Bioavailability : Connecting the Dots

In case of drug product development, *in vitro* dissolution and/or release testing is of critical importance, as it facilitates prediction of *in vivo* product behaviour. There exists a need to develop a discriminatory, reproducible and robust dissolution method using compendial dissolution apparatus and physiologically relevant medium. In case of generics, following *in vitro* testing, *in vivo* studies need to be performed showing bioequivalence of the test product to the reference product, especially mandatory in case of products containing BCS class II and IV drugs. In order to prove bioequivalence, there should be no significant differences in the bioavailability between the two products. The key factors controlling the *in vivo* bioavailability are solubility, dissolution and permeability. During generic formulation development, several excipients are utilized to modify the solubility and permeability of the drug in the dosage form to increase bioavailability. This excipient effect on formulation solubility and dissolution rate can be demonstrated using a discriminatory dissolution test performed on formulations containing different solubility modifiers. However, the excipient effect on drug permeability requires further understanding as similar dissolution profiles may not warrant for similar permeability patterns. Disso*flux*™ is a tool to measure dissolution rate and permeability flux simultaneously, which can aid rank-ordering of formulations based on both solubility and permeability. Understanding *in vitro* solubility and permeability together can aid in accurate predictions of *in vivo* bioavailability. Formulation selection for bioavailability - bioequivalence studies remains crucial as failures can lead to huge losses in terms of timelines and costs to companies and having a tool to facilitate and validate formulation selection prior to bioequivalence studies can be largely benefitting.

Michel Magnier
Product Manager USP4, SOTAX AG, Switzerland

After a Master of biochemistry in University of Paris XI ORSAY, Michel Magnier started to work on scientific instrumentation as a Product Specialist on analytical equipment, training users of several industries including dissolution testing users in the pharmaceutical industry. After these two years, Michel Magnier has been Product Manager in FISHER SCIENTIFIC France during seven years supporting different product lines as UV-Vis spectrophotometry, Climatic chambers, and viscometers. End of 1999, Michel Magnier joined the SOTAX Company to come back to the dissolution testing market and to cover this specific field in France in a dedicated team. After six successful years, Michel moved to SOTAX AG headquarters, Basel, in 2005, to become Product Manager for dissolution testing. Since 2005, Michel Magnier has played different roles within SOTAX AG: Product Management, Marketing and Business Development. He is now Product Manager for Flow-Through Cell Dissolution testing (USP 4)

E-mail : michel.magnier@sotax.com

Dissolution Qualification: general concerns and indirect importance of automation

If a neutral observer would engage into a dissolution conversation in a solid dosage form QC laboratory the probability is high that somebodywill come to him with anecdotes about the challenges and burdens of qualifying a USP 1, 2 dissolution instrument… For decades, it is a fact that testing tablets, in accurate conditions to obtain results inside specifications (what a dissolution PQ is, in a nutshell) - before using a dissolution instrument to release batches on the market - is sometimes perceived by users as problematic.

But testing tablets in accurate conditions to obtain results inside specifications is indeed what this dissolution instrument is designed and manufactured for… and consequently what it will be daily used for…isn't it? Therefore, this observer will wonder why a high-level athlete would complain about a serious warm-up in the stadium before starting the competition…while it can only help.

Now from an insider point of view, the real question is: does this « competition » only starts after a positive PQ result? It started much earlier…So why not considering the dissolution qualification as a single step of a continuous partnering process - as the USP informative chapter <1058> Analytical Instrument Qualification does. Even now when continuous manufacturing and batch manufacturing are compared, it remains obvious that no pharmaceutical testing effort will ever be short-term driven, or considered as mainly punctual. QC dissolution data are considered in relation to those initially submitted. Dissolution data matter long-term as a supra-indicator, as a trend, andin the case of continuous manufacturing as a model.

Releasing a pharmaceutical dosage form on the market remains a long and expensive process, targeting highly demanding customers: us.

Qualification means also literally the qualification of users. As university examinations: passing is the door opener but understanding why one passed (and why the test was what it was) lead to deeper conclusions. This is what being « discriminant » is about Knowing what is *actually* mandatory matters also. « What is critical? » This is what dissolution users have to accomplish daily: understanding and judging their data in the light of guidelines and recommendations. Data can be generated by the system. However, data have to be judged by the users.

To help them, traceability - due to the power of automation - is reaching a new milestone in which data are now securely acquired, gathered and stored. The access to information has improved while the volume of information was significantly expanding. This challenge also would not have been realized without the help of software driven automated systems.

Therefore, to add to this initial conversation about dissolution qualification it may make to sense to precise that qualification - rather than being a challenge or a burden- is also the great moment when the user can start to use its instrument *on purpose*.

Paul W S Heng
GEA-NUS Pharm Processing Res Lab, Dept of Pharmacy, National University of Singapore

Dr. Paul W S Heng has a basic degree in pharmacy and obtained his PhD from the National University of Singapore in 1985. He has since joined the Department of Pharmacy, National University of Singapore as a faculty member, and teaches pharmaceutical technology for three decades. He served as Head of Department for two terms, 2000-2004 and is the Principal Investigator for GEA-NUS Pharmaceutical Processing Research Laboratory, a research laboratory focused in process and product development related to pharmaceutical technology. Dr Heng has served several terms as Chairman of the Singapore's Quality Control Advisory Committee which saw the acceptance of Singapore as a member of the PIC/S. Dr Heng has undertaken several consultancy appointments in product manufacturing companies and has been involved in many new product developments and personnel training. His research interest is in pharmaceutical technology, especially research related to solid dosage forms, pellets and tablets. He has expertise with excipients, design of controlled release systems as well as in encapsulation technologies. He has successfully supervised or co-supervised over fifty doctorate program students, several masters students, authored or co-authored over 280 international refereed research journal articles and has also written several book chapters and patents. He is the editor-in-chief of the Asian J Pharm Sci and is in the editorial boards of the Pharm Dev Tech, J Microencapsulation, Drug Dev Ind Pharm, Therapeutic Delivery, AAPS PharmSciTech, J Pharm Sci, Int J Pharm, among others.

E-mail: phapaulh@nus.edu.sg

Importance of Dissolution Studies in Evaluation of DPIs

Pulmonary drug delivery is a non-invasive drug delivery system that provides the option of either local or systemic therapy for drugs that are otherwise not desirable or possible by the oral route. For pulmonary diseases such as asthma and chronic pulmonary obstructive disorder, treatment would be best if drugs are delivered directly to the site of action. The highly vascularised lungs provide a large surface area for rapid absorption of drugs and together with the low enzymatic activity present, the lungs also present an excellent alternative site for drug absorption to systemic system especially for drugs that bioavailable when administered orally, such as proteins and hormones, among others.

Dissolution testing of oral solid dosage form is a well-accepted requirement in the pharmaceutical industry. However, there is still a lack of a universally accepted dissolution methodology for the estimation of dissolution behaviour of orally inhaled product to date. The design of a dissolution system representative of drug particles dissolving in the lungs is challenging due to difficulties for replicating conditions within the lungs. Estimates of pulmonary fluid of around 20 mL over about 70 m^2 lung surface is highly difficult along with the more stagnated pulmonary fluid of uncertain composition may be challenging to replicate, for preparing the suitable dissolution medium.

For a dissolution test to better reflect the *in vivo* conditions, only drug particles which reach the site of action or fine particle fraction should be used for dissolution testing. However, there are challenges to obtain the fine particle fraction for dissolution testing. After collection, dispersing the dry powder in the dissolution medium can be problematical. This presentation will discuss the various dissolution methods proposed and our solution to design a system to collect the full fine particle fraction for dissolution testing, and using the enhancer cell unit for the purpose.

Permeability through pulmonary epithelial cells is a prerequisite for drug absorption into the blood stream. Assessing *in vivo* events of lung deposition and pulmonary pharmacokinetics is still an experimentally challenging task. Chick chorioallantoic membrane is a thin and transparent, highly vascularized membrane within a fertilized egg. It acts as both a respiratory and excretory organ for the growing embryo, similar in function with the lungs. The chorioallantoic membrane lacks keratin, not stratified and do not have mucus or ciliabut with structural similarities with the lung surfaces. Thus, it can serve as the *in vitro* biological tissue for permeability studies. The presentation will briefly discuss the opportunities with the use of the chorioallantoic membrane for dissolution and permeability evaluation the fine powder fraction from the dry powder inhaler.

Dr. Rajeev Raghuvanshi

Dr. Reddy's Lab

DESIGNATION : Senior Vice President, Global Head for CMC, Proprietary Products R & D and Global Head for Dermatology F R & D, Dr. Reddys Labs Ltd., Hyderabad

EDUCATION : Ph.D. – National Institute of Immunology, New Delhi, M.Pharm. – IIT-BHU (Formerly IT – BHU), B.Pharm. - IIT-BHU (Formerly IT – BHU)

EXPERIENCE : 28+ yrs, in global innovative, 505b(2), complex generic, super generics, generic, NDDS and NCE formulation development, scale-up and technology transfers. Hands on experience with Oral, Nasal, Injectable, buccal, semisolid and other dosage forms. Extensive work on "open innovation" model, global alliances, out-sourcing, collaborative product development, R & D Strategy, organizational development, change management, leadership development etc. Widely travelled to US, Europe, South East Asia, Japan, and South Korea. F2F interaction with global regulators like US FDA, MHRA, MPA-Sweden, South Korean FDA, Romanian FDA& DCGI, India. Academically active through thesis advisory and evaluation and teachingat premier institutes in the country.

WORKED WITH :
Current – Dr Reddys Labs Ltd, Hyderabad since April 2010 1998 – 2010 : Ranbaxy Labs Ltd, Gurgaon
1990 – 1998 : National Institute of Immunology, New Delhi
1989-1990 : Dabur Research Foundation, Ghaziabad

PUBLICATIONS: 54 + Filed/granted Patents, 3 Book Chapters, 16 Publications in peer reviewed journals, > 10 Presentations on International Forums

ACHIEVEMENTS :

1. Lead member of team responsible for 1st cycle approval of 6 505b(2) NDAs in US
2. Developed and filed > 75 ANDAs/Generics globally [US, EU, China, LATAM / WHO (ARVs)]
3. Launched multiple "First to Market" NDDS products in Indian market
4. Member of the team who filed 1st Nasal USIND from India
5. Leader of the team recipient of 'Most Innovative Team" award for DRL in 2012
6. > 10 Face to Face meetings with USFDA/EU Reg agency on 505b(2) strategy and filing

E-mail: rraghuvanshi@drreddys.com

Complexity Of Predicting Skin Permeation For Topical Products

Skin is designed to protect transfer of materials from outside to in and from inside to out of the body. It has strong barrier properties to perform this function the skin is structured accordingly. Stratum Corneum, outermost horny layer is identified as principal barrier for the skin.

Assessment of topical products may be difficult as compared to transdermal preparations because of the need for the drug to be stationed in one of the skin layers as against crossing the skin and reaching systemic circulation in case of Transdermal.

Different need from different topical products to match the need of the therapy requires assessing the drug transport / permeation through different skin layers. This makes the assessment and understanding of drug permeation / transport through skin to be important but is more complex than simple. The complexity comes from the 3 components – 1) nature of the formulation2) skin structure and condition & 3) continuous interaction between formulation and the skin

This area has shown great advancement in recent times. Techniques like in-silico modelling, NMR, Raman, IR, micro-dialysis, artificial skin permeation (e.g. HSEs), biomarker analysisetc. are being used to map the drug movement though the skin layers. Using artificial skin provides added advantage of getting skin with different properties to mimic diseased skin.

Still the IVIVC predictions are eluding us in case of topical preparations. This gets compounded by complexity of the formulation matrix and skin structures. Scientists are using combination of different techniques to find the correlation between *in-vitro*, *ex-vivo*, animal models and in-vivo performance.

Case study to demonstrate the understanding of linkage between topical formulation, its permeation potential and PK will be discussed.

Prof. Dr. Padma Devarajan

Head and Professor in Pharmacy Dept. of Pharmaceutical Sciences and Technology, Institute of Chemical Technology, Mumbai, India

Dr. (Ms) Padma V. Devarajan is Professor in Pharmacy and ex-Head, Department of Pharmaceutical Sciences and Technology at the Institute of Chemical Technology, Mumbai, India. She is a member on the Board of Governors of ICT and Coordinator of the world Bank TEQIP programme and M.Tech Pharmaceutical Biotechnology. Her research interests include colloidal carriers for targeted delivery in cancer and infectious diseases, Veterinary Drug delivery, Bioenhancement strategies, Mucosal DDS and QbD in drug development. won her the Prof. N. R. Kamath Book Award at ICT.

She has over 100 publications and presentations, has edited a book on "Targetted Drug Delivery- Concepts and Strategies" published by Springer and is Editor and author of a book on Receptor Mediated Endocytosis which is in press. She has filed over twenty patents international / national, has seven patents granted and five licensed. Her research is funded through Government Grants 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, and is currently 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 and European Journal of Drug Metabolism and Pharmacokinetics.

Prof. Devarajan is a gold medallist of Mumbai university at B.Pharm, and President of the Alumni Association of 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, Eudragit Award 2015, the Bengalauru Nano Innovation Award for a Nanosystem developed for Veterinary Infection and the IPA-ACG Scitech award 2017 for innovation in Solid Dosage form and the OPPI Sientist Award 2018.

E-mail : pvdevarajan@gmail.com

Practical Approaches for Dissolution Testing of Nano-Formulations

Nano drug delivery systems (DDS) have acquired great importance especially for targetted therapeutics of cancer and infectious diseases. Nano DDS can address the need for high efficacy while enabling decreased toxicity and therefore consitute an important armamentarium in drug therapy. A major requirement for any formulation development is understanding release from the formulation developed and also designing *in vitro* release as a final product quality parameter. A robust method which could be discriminating and practical is an important need. Number of methods are reported in literature for *in vitro* release testing of nano-formulations and include sample and separation methods, dialysis methods, methods based on modified compendial dissolution apparatus and combinations. Nevertheless till date there is no standard or compendial method. This lacuna poses immense challenges in the development and standardization of nano-formulations. The talk would briefly discuss the various approaches that are being evaluated and highlight the challenges therein. A major focus of the talk would be application of the USP IV dissolution apparatus as a practical approach for evaluation of in vitro drug release of nano-formulations. The same will be discussed with case studies highlighting advantages and limitations. Suggestions for future developments would also be discussed.

Samir Haddouchi
Managing Director, SPS Pharma Services, Orleans, France

Prior to joining SPS Pharma Services in 2005, Samir spent more than 10 years in the pharmaceutical industry.

As a chemist, he started working on the analytical development of agrochemical compounds at Sandoz Agro in the region of Basel (Switzerland).

During the Novartis merger, he moved to Orléans (France) in 1998 to join the analytical group in the technical development department where he became responsible for dissolution.

In 2005, he resigned from Novartis to create SPS Pharma Services in Clermont Ferrand which is the first and only CRO specialized in Dissolution and Release Testing.

Since then, Samir manages SPS facility and is in charge of projects management.

In April 2013, SPS Pharma Services moved to a new larger facility in Orleans (France) in order to ensure better efficiency and provide a broader range of services to its clients, including cGMP routine testing.

The facility has been successfully inspected by US FDA and is registered as Pharmaceutical Establishment for both US and Europe.

Fields of interest and expertise: analytical development (LC), *in vitro* dissolution and release testing (all techniques from USP1 to USP7), *in vitro-in vivo* correlations (IVIVC), formulation development, laboratory automation.

Samir is regularly invited as speaker in international conferences as well as expert for various organizations (scientific societies and Health Authorities).

Email : samir.haddouchi@sps-pharma.com

Drug Release from Long Acting Products : What are the Solutions?

New types of formulations and drug delivery technologies call for a new approach to *in-vitro* drug release testing and traditional dissolution methods are not tailored to these novel dosage forms.

Products such as medical devices, combination products, injectable suspensions, microspheres and other parenterals can be challenging when it comes to the development of an *in vitro* release or dissolution method. More flexible techniques such as the flow through cell may be needed to fulfill the requirements of such complex formulations.

It is of importance to use suitable method development strategies to characterize the release properties of the formulation as well as the dissolution properties of the Active Ingredient (API). That way, *in vitro* methods may serve either as formulation screening tool, to correlate *in vitro* results with *in vivo* performance or to control the quality of commercial products thus ensuring batch-to-batch consistency.

This lecture will discuss current and new applications related to non-conventional dosage forms.

Keywords

Drug release, Dissolution, Flow through cell, parenteral

Vijay Kshirsagar
Director - TRAC Pharma Consultancy, Mumbai, India

Vijay is an accomplished Quality, Regulatory & Analytical professional with around 40 years of rich experience of working for reputed Indian & MNC Pharma firms. He has worked for Unichem / Ranbaxy / Sun / Lupin / IPCA / German Remedies in Senior Capacity as Executive Vice President/Director/General Manager etc for CQA, Regulatory & Analytical Research.

Vijay has led from front for successful completion of several regulatory inspections by US FDA, MHRA, EDQM, ANVISA, WHO, PICS, PMDA, Health Canada, TGA etc. both for Drug Products (Non-Sterile & Sterile) & API's. He has been a frequent trainer in India & abroad having spoken on wide range of topics related to cGMP / GLP / QbD / Validations etc. He is the founder President of 'SPDS'. He is also working on the board of Directors of ISPE-India. IDMA has conferred upon him an 'Outstanding Analyst Award 2011' for his contribution towards pharmaceutical analysis. He is a Lead Trainer for USP's training programs for young pharmaceutical professionals. He has successfully represented his company in US and UK courts regarding IP related matters (Para IV filings).

He has published articles on topics like OOS, QbD & cGMP in reputed journals/books. Guideline written by him on CAPA is published by IDMA. He is M.Sc. by Research in Organoanalytical Chemistry from Mumbai University. He is a Mentor to two reputed pharmacy colleges in Mumbai including BCP.

Post retirement, he has formed his own Consulting firm called TRAC offering specialized services globally, for cGMP Training, Regulatory Filings, Auditing & Compliance. As a consultant, he has helped number of companies to get their first time international regulatory approvals & also sustain them over a long period. He is also advising some companies for their remediation plans to revive their regulatory approvals.

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E-mail : vukshirsagar@gmail.com

Regulatory Issues Related to Dissolution Studies

Dissolution is more a Science than mere testing. Paradigm shift has happened and it is getting linked to life cycle management of drug products. Regulatory expectations are going up day by day due to new emerging risks. As a result, we find many dissolution related observations emerging from regulatory inspections. These issues are related to non-discriminatory test methods, lack of automation & traceability, improper specifications, non-integral testing, data management etc.

Dissolution studies is a surrogate for *in vivo* testing. Dissolution Science calls for QbD implementation for development of discriminatory method development, associated risk assessment, establishing a good IVIVC and further deciding realistic test limits based on IVIVC/ life cycle management principles and certain guidance discussed above. The biggest benefit is that we will give a good effective & safe product for the patient. Investigation too needs to be done by subject matters experts using various scientific tools to identify a root cause and have robust CAPA for the same. Regulatory observations related to dissolution can thus be minimised. All these topics are going to be a part of presentation on this topic.

Prof. Dr. Umesh Banakar

Professor and President, Banakar Consulting Services, USA

Umesh V. Banakar, Ph.D. is Professor of Pharmaceutics and an Independent Consultant/Advisor to Pharmaceutical Industry and Academia worldwide with extensive contribution in drug product development and evaluation (*in vitro* and clinical).

He is on the **International Scientific Advisory Board** of several pharmaceutical corporations worldwide. Of date, he has –

- Successfully completed several Pharmaceutical Product Development Technology Transfer through education assignments sponsored by the UN/IESC and other pharmaceutical corporations worldwide
- Planned and executed the development, both *in vitro* and clinical, of **several NDAs [including 505(b)(2)] and ANDAs (both IR and MR products)**
- Served as **testifying/non-testifying expert in over 60 patent litigations** in the disciplines of pharmaceutical formulations/technology, clinical investigations and dissolution testing
- Founding **Chairperson of 2 International CROs** and has executed over 500 clinical trials (Phase I-IV including BE studies)
- Founding Board Member and Principal Scientific Adviser of **Society for Pharmaceutical Dissolution Science [SPDS]**
- Founder of **Goa – Center for Excellence in Intellectual Property [G-CEIP]**

He has authored over 100 publications, over 100 published abstracts and presentations, numerous specialized workshop manuals, several chapters and monographs, over 45 expert book reviews and 5 guest editorials. The texts that he has authored and/or edited include:

- **Pharmaceutical Dissolution Testing, Drug Development Process: Increasing efficiency and cost effectiveness**, and co-edited include:
- **NanoBioMedicine (6 volume; 91 chapters series),**
- **Desk Book of Pharmaceutical Dissolution Science and Applications,**
- Electronic text: **Basic Pharmacokinetics**
- **Others.**

He is the founding Editor-in-Chief and on Editorial Boards of several scientific journals. He has **received numerous awards** for :

- excellence in teaching, research/scholarly activity,
- two **Service to Country Awards from the UN** and
- nomination for the distinguished **Fulbright Scholar Award for Teaching**

He is on the **roster of experts** with WHO, United Nations – TOKTEN program and International Executive Service Corps (IESC). He is **listed in ?** Who's Who in Biotechnology, Who's Who Among Asian Americans, and American Men and Women of Science.

E-mail : ubanakar@gmail.com

Patent Opportunities with Dissolution Technology: *Understanding the relation !!*

Dissolution testing and technology have now forayed into the discipline of intellectual property (IP) wherein the novel as well as innovative considerations of the invention have been secured. Often these inventions, i.e., the pharmaceutical product(s), are worth 'multi-million dollars' and their ratification through (in) validity and/or (non) infringement focuses on convincing and compelling rationale based on principles of dissolution science and applications. Additionally, it is generally accepted that the 'new' product is patentable, however, the patentability of this 'new' product is more than often based on its some unique aspect – functional and/or outcome. The patentability of the product depends heavily on understanding the underlying dissolution performance of the product through specifications which define the invention. Furthermore, and perhaps more important is the necessity to prove, beyond reasonable doubt, the novelty, innovation and (non) obviousness considerations of this very dissolution performance and its relation to the product (invention) in question. The presentation will address the emerging *et* fascinating role of dissolution testing in intellectual property with respect to patentability of the resultant invention, i.e., the product.

Atul Yelpale

Product Specialist- Anachem Mettler-Toledo India Pvt. Ltd.

Technical and Academic Qualification:

- **M-Tech. in Pharmaceutical Sciences & Technology,** fromInstitute of Chemical Technology (ICT) University of Mumbai.
- **B-Tech. in Chemical Technology**

Professional Experience: (7+ Years)

- **Product Specialist -** Anachem Mettler-Toledo India Pvt. Ltd. (Current) PAN-India role for Analytical instrument range
- **Product Specialist -** Molecular Spectroscopy & Chromatography (Product/Application)

Background:

- Completed masters study from ICT in Pharmaceutical Sciences and technology.
- Started professional career with PerkinElmer as Technical specialist for West region for Chromatography and Molecular Spectroscopy.
- Further promoted in PerkinElmer for PAN-India product and application management in molecular spectroscopy.
- Joined Mettler-Toledo in 2016 as Product Specialist for Spectroscopy.
- Currently managing product portfolio for entire analytical chemistry range of products.
- Having core expertise in UV-Vis and UV/Vis/NIR spectroscopy, FTIR spectroscopy, microscopy & imaging, fluorescence, mass spectrometry etc.
- Also have significant experience on chromatography, DSC, TGA, and inorganic spectroscopy (AAS, ICP-OES,ICP-MS) etc. analytical techniques.

Email: atul.yelpale@mt.com

Efficiently Automated UV/VIS Spectroscopy

Efficient automation of analytical techniques, such as optical spectroscopy, is an essential aspect in optimizing **time to result**. It requires not only a fast analytical technique but also automation of time-consuming, laborious and error-prone analytical workflow steps such as sample/standard preparation. Array-based spectrophotometers scan complete spectra within seconds, enabling fast and reliable measurements, including simultaneous identification of impurities. A cuvette changer takes a first step towards efficient automation of samples series and reference standards, yet steps, such as dissolution/ dilution and the transfer of sample into cuvettes, are nevertheless carried out manually. Efficiency can be increased further with an analytical system that automates the preparative steps and enables accurate, direct, cuvette-avoiding optical measurements. In this presentation, new automation solutions in analytical spectroscopy are discussed and assessed with respect to efficient and reliable result generation.

P1 - "*In Vitro* Dissolution Simulations for Formulation Development"

Divyen Shah[i], **Bhupesh Pratap**[i], **Sethu Kavuri**[ii]
[i]Perrigo Laboratories India Private Limited, Plot No. N 39/N 39-1, Additional MIDC, Anand Nagar, Amernath (E), Dist.- Thane, Maharashtra, India- 421506.
[ii]Perrigo Research and Development Company, Global Scientific Affairs, Perrigo R&D Company, 515 Eastern Avenue, Allegan, MI 49010, USA
Email ID : divyen.shah@perrigo.com

Key words:

DDDPlus, *In vitro* simulation, % Prediction error (%PE)

Introduction:

For early formulation development, decision on strategies could be made faster with minimal resources usage through integration of simulation tools. Regulatory bodies routinely advise industry on using modeling and simulation to predict clinical outcomes as well as support formulation changes through IVIVC. Integration of *in vivo* and *in vitro* simulation tools could also reduce formulation trials, *in vitro* dissolution trials for selection of discriminatory / biorelevant dissolution method and *in vivo* studies. The concept of PBPK modeling is well established but still the *in vitro* modeling is not widely used by industries. A newer tool for prediction of *in vitro* dissolution -DDDPlus (Dose Disintegration and Dissolution Plus) is useful to evaluate disintegration and dissolution pattern of dosage form. DDDPlus uses traditional dissolution models as well as Mass Transfer model.

Method:

Simulated dissolution model developed for a matrix-based ER tablet formulation containing BCS Class I drug. The plan for the development was to build a PBPK model and then generate a target bio-indicative dissolution profile.

DDDPlus was used to evaluate various formulation compositions. Simulation model using DDDPlus software was used to evaluate formulation changes required to meet desired dissolution profile. Minimum inputs required to build model were predicted using ADMET predictor or generated in-house data.

The formulation contained BCS class-1 API and components commonly used in extended release formulations. Calibration constant, Polymer-drug interaction constant and release exponent were optimized while building the model using mass transfer as dissolution model. The model was verified with the experimental dissolution data[1].

Result:

The amounts of various formulation components were predicted for target dissolution profile using developed *in vitro* dissolution model. The suggested changes in formulation through simulation was able to match the targeted dissolution profile. The predicted dissolutions were within 5% against observed experimental dissolution data.

Conclusion:

The developed model was not only able to predict/ simulate *in vitro* drug release for formulation but also suggest changes in formulation composition. Further, the model can also be used to evaluate change in dissolution test conditions. Simulated dissolution model can be used further to optimize formulation for target drug release to establish clinical relevance

References:

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P2 - Formulation of nanolipid carriers for solubility enhancement of poorly soluble drug

Bhagyashree M. Chande, Nihal A. Shaikh, Rita R. Lala
Prin. K. M. Kundnani College of Pharmacy, Cuffe Parade, Mumbai - 400 005, Maharashtra, India
Email ID : bmchande@gmail.com

Keywords:

Nano lipid carrier, Bioavailability, Solubility, Antiretroviral agent

Introduction:

Nano lipid carriers are the newer generation of solid lipid nanoparticles consisting of solid lipid and liquid lipid which are used to enhance solubility of most poorly soluble drugs[1]. Antiretroviral drugs exhibit solubility problems and hence incorporating them into nano carriers may show promising results in the treatment of HIV infection.

Aim:

In the present work, attempts were made to improve the bioavailability of DTG an antiretroviral drug which is an HIV-1 integrase inhibitor belonging to BCS class II by formulating a Nano Lipid Carrier (NLC) suspension.

Method:

The work presented describes the development of NLC suspension based on a combination of various lipids by melt emulsification sonication technique[2]. The influence of solid to liquid lipid ratio, surfactant concentration and sonication time was studied on particle size and percent entrapment by 2^3 factorial design. *In-vitro* release was estimated using dialysis membrane (MW cutoff 12000-14000) and *ex-vivo* studies were carried out using rat intestine.

Results and discussion:

The developed NLC were evaluated for particle size distribution, zeta potential, entrapment efficiency, SEM, *in-vitro* and *ex-vivo* release studies. It was found that among all the batches formulated, batch 2 of NLCs showed better entrapment efficiency (88%), particle size(123.1nm).*In-vitro* release was found to be 94.51% in 24hrs. The *ex-vivo* release in 6hrs was 75.95% as compared to 55.62% for the drug suspension. NLC showed an increase in permeability of about 1.37 fold as compared to the drug suspension.

Conclusion:

NLC loaded with DTG were successfully developed. The optimized formulation had particle size in the nano metric range with better entrapment efficiency and showed improved drug release.

Acknowledgement:

Sprint Testing Laboratories for SEM testing and BVP, Belapur for DSC testing.

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P3 - Novel Amphotericin B - Lipid Conjugate Loaded Enteric coated Liposomes for Improved Gastric Stability and Oral Bioavailability of Amphotericin B

Akansha Goel, Navneet Singh, Tushar Date, Dasharath Chaudhari, Sanyog Jain*
*Centre for Pharmaceutical Nanotechnology, Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research (NIPER), SAS Nagar , Punjab - 160062, India
Email ID : sanyogjain@niper.ac.in; akanshagoel250@gmail.com

Keywords*:*

Amphotericin B, intestinal permeation, prodrug, oral bioavailability

Introduction:

Amphotericin B (AmB) is a broad spectrum polyene antibiotic with poor permeation and gastric instability which poses a problem in its oral delivery. To overcome these issues, the present study was carried out to design a novel lipid conjugate of amphotericin B (AmB) with improved gastric stability and intestinal permeation followed by development of nanoformulation for effective oral delivery of developed conjugate [1].

Methods:

The working strategy involved preparation of drug lipid conjugate wherein AmB was conjugated with Tocopherol-α-succinate (TOS) by carbodiimide coupling reactions [2]. The conjugate was characterized by techniques like FTIR, MS, NMR spectroscopy and UV visible spectrophotometry. The AmB-TOS conjugate was encapsulated into liposomes followed by coating of liposomes with Eudragit S100 for improved gastric stability and to impart pH sensitive release [3]. The prepared nanoformulation was then optimised and characterised for its size, redispersibility, morphology, entrapment efficiency, *in-vitro* drug release, stability studies in simulated gastrointestinal fluids and permeability studies using Caco-2 cell lines.

Results:

The AmB-TOS conjugate was found to improve the permeability across biological membranes, impart better gastric stability and enhanced drug loading into delivery carriers like liposomes. The *in-vitro* release profile displayed a delay in drug release (2h) attributed to pH-sensitive Eudragit coating. The apparent permeability of conjugate was also enhanced attaining a maximum value of $9.37*10^{-5}$ cm/s, with Caco-2 uptake >90%. Moreover, the prepared liposomal formulation demonstrated lower nephrotoxicity potential as evident by % cell viability assay in HEK cells (>90%). Evaluation of *in-vivo* pharmacokinetic parameters in female Sprague Dawley rats also highlighted the superiority of AmB-TOS liposomal formulation with higher area under curve (AUC) and half-life ($t_{1/2}$) as compared to free drug (2.41 and 2.35 fold respectively).

Conclusion :

The prepared liposomal nanoformulation of AmB-TOS conjugate demonstrated improved oral bioavailability, better gastric stability and reduced side effects as compared to AmB, and could be a promising approach for enabling the oral delivery of AmB.

Acknowledgments :

The authors are thankful to Department of Science and Technology (DST), Government of India for providing funding to the research project.

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P4 - Enhanced Stability and Prolonged Drug Release of Temozolomide through Lipid based Nanocarriers

Tejashree V. Waghule, Vamshi Krishna Rapalli, Srividya Gorantla, Sunil K. Dubey, Ranendra N. Saha, Gautam Singhvi*
Industrial Research Laboratory, Department of Pharmacy, Birla Institute of Technology & Science (BITS), Pilani, India-333031.
Email ID: gautam.singhvi@pilani.bits-pilani.ac.in. • tejashreewaghule22@gmail.com

Key Words:

glioblastoma, prolonged release, temozolomide, lipidic nanoparticles

Introduction:

Glioblastoma forms about 80 % of all the brain tumours and is a challenge to treat because of its unique features like indistinct tumour margins, high infiltrative nature, higher degree of endothelial cell hyperplasia and vascular proliferation. The existing treatment which is surgical resection followed by radiotherapy and chemotherapy shows certain limitations like systemic side-effects and tumour reoccurrence. Blood brain barrier forms a major obstacle in the treatment. Temozolomide is a drug approved for treating glioblastomas. The drug has 100 % oral bioavailability but gets degraded at physiological pH thus having very short half-life and only 20-30 % brain bioavailability. Due to its hydrophilic nature, reported nanoformulations exhibits poor drug loading. The objective of the present work was to formulate lipid based drug delivery system which could help to enhance the brain bioavailability by prolonging the drug release and increasing the circulation time of the drug so as to overcome the limitations of the existing therapies and reduce the side effects.

Methods:

Two different types of lipid based nanocarriers- bilayered vesicles and cubosomes were prepared. Bilayered vesicles were prepared by coating the lipid and the drug on mannitol and subsequent hydration with aqueous phase. Cubosomes were prepared by heating the lipid phase and aqueous phase to 80°C and adding the melted lipid phase to the aqueous phase followed by stirring. These nanocarriers were characterized for size, zeta potential, entrapment efficiency and drug loading. The *in-vitro* drug release studies were conducted and the release of the drug from the lipid based nanocarriers was compared with the free drug. Further stability studies were conducted to evaluate the stability of the nanocarriers at plasma pH 7.4 and thus the circulation time of the drug.

Results:

The size of the nanocarriers obtained was less than 300 nm and the PDI obtained was less than 0.3. The entrapment efficiency was found to be enhanced as compared to the conventional nanocarriers. The designed formulations showed prolong drug release from 12 to 20 h whereas free drug showed 100 % drug release within 6 h. The drug loading and stability of Temozolomide were significantly improved with developed lipid based nanocarriers.

Conclusion:

The entrapment of the drug in the lipid based nanocarriers successfully protected the drug from degradation at plasma pH, showed prolonged release and enhanced circulation time of the drug. Further pharmacokinetic and biodistribution studies can be conducted to confirm the enhanced brain bioavailability.

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P5 - Topical Delivery of Curcumin Loaded LipidicNanocarrier for Improved Efficacy towards Pivotal Microbes and Inflammation in Psoriasis and Atopic Dermatitis Skin Conditions.

Vamshi Krishna Rapalli, Tejashree Waghule, Srividya Gorantla, Sunil K. Dubey, Ranendra N. Saha, Gautam Singhvi*
Industrial Research Laboratory, Department of Pharmacy, Birla Institute of Technology & Science (BITS), Pilani, India – 333031.
EmailID: gautam.singhvi@ pilani.bits-pilani.ac.in. / p20170004@pilani.bits-pilani.ac.in.

Key Words:

Antibacterial, Atopic-dermatitis, Curcumin, Psoriasis, Skin Permeation

Purpose:

Psoriasis and atopic dermatitis are autoimmune disorders, act by down signalling pathways in immune cells, and non-immune cells keratinocytes, and fibroblast cells. Microbes play one of the key role in worsening the skin condition in case of psoriasis and atopic dermatitis. Curcumin is the major constituent of curcuma longa which exhibit anti-inflammatory, anti-bacterial and anti-oxidant properties. Curcumin belongs to class-II molecule, and the compromised skin disease condition inhibits the permeation of curcumin through skin in case of psoriasis and atopic dermatitis. Topical delivery of curcumin loaded lipidic nanocarriers are expected to improve the therapy with improved permeation in both disease conditions. Therefore, the objective of the present study was to formulate curcumin loaded lipidic nanocarriers for topical delivery and its *in-vitro* and *ex-vivo* characterization.

Method and Results:

For formulation optimization, lipids (solid and liquid lipids) were selected based on the solubility of curcumin and, surfactant screening was performed based on suitable HLB value for the preparation. Lipidic nanocarriers were prepared by hot emulsification followed by size reduction. The optimised nano dispersion was converted into hydrogel using carbOpol 974P. The optimised formulation was characterized for particle size, zeta potential, entrapment efficiency, *in-vitro* drug release, *ex-vivo* skin permeation study and occlusive effect of the formulation. The optimized formulation exhibited mean particle size lesser than 100 nm with PDI 0.25 and zeta potential -15 mV. The *in-vitro* drug release study showed controlled release up to 48 h. The *ex-vivo* tape stripping studies of lipidic nanocarriers showed significant increased permeation and skin retention compared to free drug. The *in-vitro* anti-bacterial study showed high zone of inhibition compared to free curcumin solution which revealed the curcumin entrapped in lipidicnanocarrier has improved the permeation through bacterial cell wall.

Conclusion:

Curcumin loaded lipidic nanocarriers based topical formulation was prepared and investigated for *in-vitro* and *ex-vivo* characterizations. The developed formulation exhibited improved permeation; prolong release and better anti-bacterial effect compared to free drug solution. These lipidic nanocarriers are expected to be patient friendly with reduced side effects and easy to apply topically.

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P6 - Formulation Of Ionisable Model Drug in Pellet Dosage Form :Effect of pH Modifying Starter Pellets on Release and Dissolution

Paras P. Kothari, Junaid W. Ansari, Ankita D. Malwar, Vinita V. Kale
Gurunanak College of Pharmacy, Dixit Nagar, Nari Road, Nagpur - 440026, Maharashtra, India.
Email ID: kothariparas46@gmail.com

Key words:

Ionisable Model Drug, Starter Pellet, Tartaric acid, Calciumcarbonate

Introduction:

Various approaches have been made to improve the bioavailability of drugs with pH dependent solubility. One of the possible strategies is the incorporation of pH modifiers in the dosage form. Release of pH dependent drug from solid dosage form can be successfully enhanced by maintaining the pH of the formulation in the immediate environment.[1-2]

Aim:

The aim of this work was to prepare spheronized starter pellets of tartaric acid and calcium carbonate and to study the effect of microenvironment pH on release of ionizable drug.

Methods:

The starter pellet were manufactured using extrusion spheronization method. The formula for starter pellet was statistically optimized using Minitab. Coated pellets of model drugs (Diclofenac Na and Paracetamol) were prepared by Layered coating on starter pellets in pan coater. The influence of tartaric acid and calcium carbonate on the dissolution and release of Diclofenac Na and Paracetamol was determined by conducting dissolution studies at pH 1.2 and pH 6.8.[3-5]

Result:

It was observed that Diclofenac Na being weakly acidic drug showed no effect on dissolution and release of drug at physiological pH 1.2 and pH 6.8 when acidic starter pellet was used. The reason could be attributed to the weak acidic nature of drugand creation of diffusion layer in acidic microenviroment. However diclofenac when coated on carbonate starter pellet showed enhancement in dissolution due to alkaline microenvironment. No significant difference in release of Paracetamol was noted at physiological pH when either acidic starter or alkaline starter pellets were used.

Conclusion:

The study concludes that vicinity (diffusion layer) environment can affect drug release of ionizable drugs and acidic material or alkaline material starter pellets can be used to modify and control the dissolution and release of weakly acidic or weekly basic drugs.

Acknowledgement:

We are thankful to Sikh Education Society, Nagpur for providing necessary research facilities.

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P7 - Transdermal Patch of Trazadone containing Medium Chain Triglycerides as Permeation Enhancer

Ankita K. Soni, Mohd. Atif Ansari, Shubhangi S. Mohije, Vinita V. Kale
Gurunanak College of Pharmacy, Dixit Nagar, Nari Road, Nagpur - 440026, Maharashtra, India
Email ID: ankitasoni2481996@gmail.com

Key words :

Medium Chain Triglycerides, Permeation enhancers, Trazadone, Transdermal patch

Abstract :

Introduction:

The model drug used is Trazadone (TZN) which is a psychoactive compound with sedative and anti-depressant properties. The solubility of TZN is pH dependent and has pKa of 6.74 in water. As a result, it is highly soluble in acid media i.e. when below its pKa. In contrast, when above pKa, its solubility is very low i.e. in the neutral and basic conditions of lower intestine. The undesirable effect of TZN administered orally can be eliminated using transdermal route. To increase the rate of permeation of drug across skin, triglycerides are used as permeation enhancers. Medium chain triglycerides (MCTs) are known for being quickly absorbed by body.[1-2]

Aim:

The aim of the present work is to develop and evaluate MCT as permeability enhancer for transdermal formulation using TZN model drug.

Method:

The partition coefficient of drug TZN was determined by separating funnel method. The solubility of TZN was determined by shake-flask method in different pH media 5.0, 6.8 and 7.4 respectively. Different batches of transdermal patches containing TZN and MCT as permeation enhancer were prepared. The variations in batches were made relatable with concentration of polymers and plasticizers used. Skin permeation profile of MCT containing TZN was studied using Franz-diffusion cell.[3-4]

Result:

Partition coefficient was found to be 0.87 of drug TZN and 0.91 of TZN-MCT combination in n-octanol:water phase. TZN was found to be highly soluble in acidic pH media and less soluble in neutral and basic pH media. Batch of TZN transdermal patch containing 10% pectin, 2% glycerol and 4% MCT passed all the desired evaluation tests. This transdermal patch showed uniform surface texture, good adherence and tacking property. The transdermal patch containing TZN in combination with MCT shows permeation enhancement (amount of drug permeated) by 20%.

Conclusion:

In the present study, the effect of MCT was studied for its permeation enhancing and solubility enhancing properties in different pH media. The *in-vitro* permeation study of transdermal patch using Franz diffusion cell and dissolution study of tablets showed that MCT can remarkably enhance the permeation and solubility of model drug TZN in transdermal patch.

Acknowledgement:

We are thankful to The Sikh Education Society, Nagpur for providing necessary research facilities.

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P8 - Development of Discriminating Dissolution Method for Sildenafil Citrate Tablets.

Shubham S. Gupta, Priya V. Vaswani, Priyanka T. Bhaisare, Vaishali A. Kilor
Gurunanak College of Pharmacy, Dixit Nagar, Nari Road, Nagpur-440026, Maharashtra, India.
Email ID: shubhamgupta0918@gmail.com

Key words:

Discriminating dissolution, sildenafil citrate tablets, BCS class II, similarity factor

Introduction:

Discriminatory dissolution method is used to describe that a dissolution test is capable of differentiating or discriminating between products based on formulation and/or manufacturing differences. However these differences may reflect products *in-vivo* differences, thus their quality in humans.The discriminating power of the dissolution method is the method's ability to detect changes in the drug product. The systematic development of discriminatory dissolution method is required for starting full-fledged product development. Demonstrating the discriminatory power of the dissolution method is used in monitoring API or formulation parameters of the poorly soluble compound.Sildenafil citrate has a pH dependent solubility thus it is categorized as BCS class II drug. As BCS class II drug possess poor solubility it eventually affects drug absorption. Therefore it is important to develop suitable dissolution method as a quality control parameter for such drugs, which correlates with the rate of absorption of the drug *in-vivo*. Also developing discriminating dissolution method helps in generic drug development as per US-FDA guidelines.

Aim:

Aim of proposed work is to develop a discriminating dissolution method for Sildenafil Citrate tablet formulations.

Methods:

To quantify the Sildenafil in dissolution samples, UV spectrophotometric method was developed using 0.01M hydrochloric acid as solvent at λmax 294 nm. Saturation solubility, pH dependent solubilityof Sildenafil citrate bulk drug was evaluated. Sildenafil citrate tablets were developed by using wet granulation method. Sildenafil tablets IP (100mg) from Cipla was used as reference. All the specifications of the formulated Sildenafil citrate tablets were comparable to the marketed tablet as per IP including dissolution profile. For developing discriminating dissolution method, dissolution profile of formulated tablets was compared with marketed tablets of sildenafil citrate (100mg) by varying pH of the dissolution medium, rpm as well as volume of the dissolution medium. Effect of run to run variability as well as change in type of dissolution apparatus was also studied.

Results & Conclusion:

Dissolution method was optimized using USP type II (paddle) apparatus at 50 rpm rotation speed and 900 ml phosphate buffer (pH 6.8) at 37±0.5°C as discriminating dissolution medium. The similarity factor (f_2) was calculated for formulations with changes in composition and manufacturing variations, values revealed that dissolution method having discriminating power. The proposed dissolution method can be effectively applied for routine quality control *in- vitro* dissolution studies of Sildenafil citrate in tablets.

Acknowledgement:

Authors are thankful to the management and Principal, GurunanakCollege of pharmacyDr. A. M. Ittadwar (Sikh Education Society) for providing necessary research facility. We acknowledge the cooperation fromZim Laboratories Ltd., Kalmeshwar in providing the gift sample of Sildenafil citrate for the present research work.

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P9 - Predictive Modelling using Simulation Techniques to set Dissolution Specifications for Sustained Release Tablets

Pooja Ochani B., Niraj Murle, Chirag Shah, Sumedha Nadkar, Chaitanya Channe, Divyen Shah
Perrigo Laboratories India Pvt. Ltd., N 39/ N 39-1, Addl. MIDC, Anand Nagar, Ambernath, Thane, Maharashtra, India.
Email ID: Pooja.OchaniBhagat@perrigo.com

Keywords:

Predictive Modelling Tools, Controlled Release Formulation.

Introduction:

The objective of the study was to evaluate the applicability of predictive modelling tools to set the dissolution specifications for a controlled release formulation. The study was carried out on a decongestant with high solubility and moderately high permeability which required a sustained release of over 12 hours.

Main Section:

In vitro dissolution has been recognized as an important profile of a formulated drug candidate, it determines the rate and extent of the drug release and could be used as a surrogate for bioequivalence (BE) studies. *In vitro* dissolution in appropriate biorelevant media assures that each batch of the same product will perform identically *In vivo*. One of the challenges of biopharmaceutics research is *In vitro - In vivo* correlation (IVIVC). Thus, the need for a reliable tool to correlate *In vitro* and *In vivo* drug release data has exceedingly increased. Such a tool shortens the drug development period, economizes the resources which leads to improved product quality.

With the proliferation of modified-release products which facilitate improved patient compliance, it becomes necessary to examine the concept of IVIVC in greater depth.

Methods:

A controlled release tablet formulation of the decongestant was developed using various combinations of hydrophilic/hydrophobic polymers to obtain a release which was based on the predictive modelling tools viz. GastroPlus and WinNonlin software. Literature based *In vivo* data was used to perform IVIVC via software and a dissolution range was predicted. Test formulations were developed to have a sustained release of over 12 hours and to release the drug within the predicted dissolution range which would result in T/R ratio of 90-110. OGD medium, 0.001 N HCl, 900 ml, 50 rpm was selected for correlating *In Vitro* fasted conditions. Acetate buffer, pH 4.5, 900 ml, 150 rpm was selected for correlating *In Vitro* fed conditions. In both, fasted and fed dissolution conditions, Test 1 formulation was faster and drug release from Test 2 formulation was within the set specifications and similar to Reference Listed Drug.

Results:

Results of Bioequivalence study inferred that, IVIVC established through literature was able to predict the outcome for the developed formulation and T/R ratio of Test 2 formulation for both Cmax and AUC parameters were within 10% of observed results.

Conclusion:

Use of predictive modelling using Gastro Plus and WinNonlin for setting specifications for a controlled release tablet development process showed good correlation from the initiation of development. Observed T/R ratios for fasting and fed study are reasonably comparable to predicted outcome. Therefore, applicability of predictive softwares in early development is highly recommended and would significantly shorten the development cycle of controlled release dosage forms.

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P10 - Degradation of Released Drug During the Course of Dissolution Studies

Sonia Verma, Anuradha Gupta, Jitender Madan, Manish Chourasia, Amit Misra
CSIR-Central Drug Research Institute, Lucknow
Email ID: vermasonia006@gmail.com

Keywords:

Correction factor; first order rate constant;

Introduction:

The study of *in vitro* drug release from sustained release preparations intended for drug delivery over several days or weeks faces the challenge of the released drug degrading in the receptor medium. Thus, apparent cumulative amounts permeated require dynamic correction if they are to reflect the true picture. The present study describes calculation of the true amount of rapamycin (RAP, sirolimus) released from inhalable particles in a long term study.

Methods:

The degradation profile of RAP inphosphate buffer containing 1% sodium dodecyl sulphate was established by estimating amount remaining after 1 to 13 days. A first-order degradation rate constant was derived. *In vitro* drug release from inhalable particles was studied using USP 24 Tablet dissolution apparatus II. A rate equation describing dynamic degradation of RAP during the drug release was established based on observation of first-order degradation of free RAP . This equation had the form:

$$C_r(t) = \frac{Dose}{V} * \left| \frac{k_d}{(k_d - k_s)} \right| * (e^{-k_s * t} - e^{-k_d * t})$$

media at any time; k_s, release rate constant; k_d, degradation rate constant; V, volume of dissolution media. Estimates of *in vitro* rate constants (k_s and k_d) were computed by fitting *in-vitro* release data into the equation. The amount released at any given time (A_r) was then calculated from the equation:

$$A_r = Dose * (1 - e^{-k_s * t})$$

Result:

Table 1: Determination of RAP degradation kinetics

Modelling	R2	
	pH=5.2	pH=7.4
Zero order kinetics	0.9046	0.9002
First order kinetics	0.9367	0.951

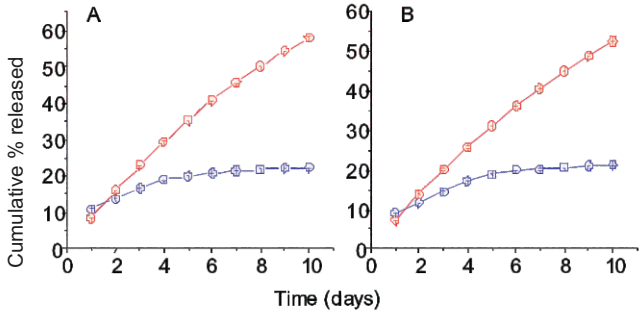

Figure 1: Uncorrected (*blue line*) and corrected (*red line*) *in vitro* drug release from microparticles at pH 5.2 (*A*) and 7.4 (*B*), with first-order curves fitting the data (R^2> 0.99). Means (*scatter points*) ± standard deviations (*error bars, internal*) of duplicate experiments are plotted.

Conclusion:

In vitro drug release from the particles was first-order and extended beyond 10 days. This extended release is expected to be helpful in maintaining the intracellular drug concentration for prolonged periods.

Acknowledgment:

We are thankful to CSIR for providing Senior Research Fellowship.

Reference:

Chen H S et al. Concentration profile for the dissolution of drug tablets undergoing simultaneous degradation. *J. Pharmacokinet. Biopharm*. 1980, 8 (6), 621- 631

P11 - SMEDDs Formulation of Gliclazide with Enhanced Dissolution

Heta S. Vasani, Divya D. Jain, Rajesh M. Pople, Veena P. Chaudhari, Ujwala A. Shinde
Bombay College of Pharmacy, Kalina, Santacruz (East), Mumbai 400 098.
Email ID : hetavasani610@gmail.com

Key words:

Gliclazide (GLZ); solubility; SMEDDs*; in vitro* drug release.

Introduction:

Diabetes mellitus is one of the third world diseases that is an epidemic now, characterized by chronic hyperglycemia resulting from the combination of inappropriate insulin secretion and/or resistance to insulin[1]. GLZ, a sulphonylurea, is usually combined with metformin for the treatment. GLZ is a BCS class II drug which has good permeability and poor solubility. The meagre solubility contributes to poor dissolution rate, resulting in limited bioavailability. One of the approaches to improve bioavailability of such drugs is using lipid-based formulations such as SMEDDs[2]. The objective of the present study was to formulate and characterize SMEDDs of GLZ by *in vitro* techniques.

Methods:

Solubility of GLZ in different oils (Migliyol 812, Acconon, Capmul MCM, Maisine® CC, Capryol 90, Labrafil M1944, Labrafac lipophile WL1349, Plurol), surfactants (Labrasol, Tween 80, Cremophor EL) and co-surfactants (Transcutol HP, Ethanol, Butanol, 2-Propanol, Propylene Glycol, PEG 400) was assessed in order to prepare SMEDDs of GLZ using saturation solubility method[3].Various formulations were prepared using full factorial design keeping the amount of GLZ constant with varying amounts of other excipients. Using phase titration method and constructing pseudo-ternary phase diagrams, optimized liquid SMEDDs of GLZ were prepared and subjected to self-emulsification efficiency study, droplet size, polydispersity index, zeta potential and FTIR spectroscopy.[4] The optimized formulation was then filled in hard gelatin capsules (FLOFIT™ size 0; ACG Associated Capsules Pvt. Ltd.) and *in vitro* drug release was assessed using USP Type II apparatus (ELECTROLAB, INDIA) [Medium & Volume: 900mL of Phosphate Buffer Solution pH 7.4; Speed: 100 rpm] and the amount of drug released was determined using UV spectrophotometry.

Results & Discussions:

Of the screened excipients, Gelucire 48/16, Transcutol HP, Tween 80 and Capryol 90 showed good solubilizing power and hence were selected for formulation optimization. The droplet size of optimized GLZ loaded SMEDDs was found to be less than 200nm with PDI less than 0.5. GLZ release from SMEDDs was found to be greater than 80% as opposed to pure GLZ which gave less than 30% release at the end of60 min. This enhanced dissolution rate of GLZ may be attributed to reduced droplet size along with self-emulsification facilitated by SMEDDs.

Conclusions:

SMEDDs aided in improving the dissolution of GLZ by presenting it in a soluble form, and hence, can be a viable alternative for oral administration of GLZ.

Acknowledgements: ACG Associated Capsules Pvt. Ltd. for financial support for this project and gift of capsule samples. Gattefossé India Pvt. Ltd.,Indeus Life Science, Mumbai for gift samples of Transcutol HP, Capryol 90 and Gelucire 48/16 and Gliclazide respectively

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P12 - Evaluation of Site selective release of Probiotics from an HPMC Delayed release capsule

Ashish V. Sangve, Smita S. Bansode, Mala D. Menon
Bombay College of Pharmacy, Kalina, Santacruz (E), Mumbai- 400098
Email ID : asangve02@gmail.com

Keywords:

Probiotic, Cellulose Capsule, HPMC Capsule, Delayed release, Site specific release

Introduction:

Probiotics are "good or friendly bacteria" with several beneficial effects like improved lactose digestions, resist enteric pathogens and preventing infections, immune system modulation. *One of the major issues with probiotics is their viability in the GIT, mainly in the acidic gastric environment. Hence, probiotic bacteria / oral probiotic formulation needs to be protected by enteric polymeric coatings.* This increases the processing and cost of the final product. HPMC DR (ACGcaps™ HD) capsule is a novel capsule composition which ensures delayed release of the contents by a unique dual triggered mechanism (pH and time dependent) to ensure targeted delivery of contents in the intestine; these capsules can provide an alternative to the coating of probiotics.

Objective and Rationale:

To assess the suitability of HPMC DR capsules for probiotic powder and probiotic oil formulations with respect to protection from acidic environment of stomach and ensuring selective release in upper intestine.

Methods:

A) Filling of Probiotic formulations in HPMC DR capsules: Two formulations, viz. Freeze dried powder of the probiotic strain, *L. casei* (100mg equivalent to 2.3×10^6 CFU) and an oil formulation (dispersion in almond oil-0.5 ml equivalent to 2.3×10^6 CFU) were filled in regular HPMC capsules and the novel HPMC DR capsules. The liquid filled capsules were sealed by banding.

B) *In vitro* selective release and survival studies of probiotics: These studies were performed in simulated gastric fluid (SGF-pH 1.2) and simulated intestinal fluid (SIF-pH 6.8) [50 ml medium stirred magnetically-60-80 rpm], at 37±2°C. The capsules, after pre-exposure to SGF for 2 hrs, were transferred to SIF and study was carried out for additional 6 hrs. Aliquots were withdrawn at periodic time intervals during each exposure and, after suitable dilution, were assessed for probiotic release and viability by pour plate technique in MRS agar plates.

Results and Discussion:

The regular HPMC capsule disintegrated in SGF and very low survival of 7 to 8 % was seen for both powder and oil formulations. The HPMC DR capsules, filled with probiotics in powder form or as oil dispersion, were intact in gastric fluid throughout the two hour period, which prevented any probiotic cells from being released. This was evident by no growth in MRS agar plates inoculated with aliquots sampled at regular intervals. When transferred to intestinal medium, the capsules disintegrated releasing the probiotics; and the % survival was observed to be 70 to 90 % for up to 360 mins in case of both powder and oil probiotic formulations.

Conclusions:

HPMC DR capsules are suitable for protecting probiotics from gastric environment and targeting their release in upper intestine; further it is an alternative to costly and time consuming encapsulation or coating of probiotics.

Acknowledgement:

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P13 - Effect on Diffusion of Diclofenac Sodium from Emulgel Prepared by Hot-Melt Extrusion (HME) Technology

Prayas Acharya, Devanshi.S. Shah, Purnima.D. Amin
Department of Pharmaceutical Sciences & Technology, Institute of Chemical Technology, Matunga, Mumbai-19
Email ID : prayasacharya10@gmail.com

Keywords:

Hot-melt extrusion (HME); topical emulgel; continuous processing; Diclofenac sodium

Introduction:

Gels are semisolid systems consisting of either dispersion composed of small inorganic particles or large organic molecules interpenetrated by a liquid. The present work focuses on the development of a continuous manufacturing process fort these dosage forms using HME technology. HME has several advantages over the conventional methods for the preparation of gels in that it reduces the number of unit operations and the time required for the preparation of the same. Moreover, due to better homogenization in the extruder, the diffusion of the active is improved leading to increased efficacy [1].

Methods:

A) Preparation of Emulgel: A topical emulgel formula was developed conventionally which included Diclofenac sodium and counter irritants such as menthol, camphor and methyl salicylate. This active phase was then mixed with a hydrogel to finally yield an emulgel. This formulation was prepared conventionally, by separately preparing the active phase (Phase A) and adding it to a preformed carbomer gel (Phase B). Further, Phase A and Phase B were emulsified using Tween 20. The same formulation was prepared using HME wherein a uniform premix of all the ingredients (Phase A, Phase B and emulsifier) was prepared and fed to the extruder. The processing parameters which affect the product were the screw temperature, screw speed, feed rate and screw configuration (for twin-screw extruder). Both the products, conventional and those prepared by HME were evaluated for their various properties and compared with the marketed formulation.

B) Evaluation : The gels were evaluated for their organoleptic properties such as appearance, color, odor and homogeneity, pH**,** spreadability, viscosity, stability under thermal cycling and centrifugation and globule size using microscopy [1]. *In-vitro* diffusion studies through cellulose nitrate membrane were performed using vertical Franz diffusion cells.

Results and discussion:

All the properties of conventional and HME batches were compared with the marketed formulations. It was found that both the products had similar properties but because of several advantages of HME over conventional methods it is preferable to use HME as a continuous processing technology. Most importantly the diffusion of Diclofenac sodium was found to be higher for the emulgel prepared by HME than the conventional products. The maximum percentage diffusion through membrane for HME sample was found to be 78% whereas that of conventional and marketed products were found to be 55% and 47%, respectively. The HME emulgel showed superior homogeneity as compared to that made by conventional method because of better mixing. This was also confirmed by the reduced globule size which was found to 3.02 µm for the HME sample and 10.9 µm and 12.1 µm for the conventional and marketed products respectively.

Conclusion:

HME is an industrially feasible technology which provides several advantages over the conventional methods, most importantly improved diffusion of the drug along with continuous processing, fewer steps, uniform product and shorter processing time. This diffusion study shows the application of HME technology for emulgels.

Acknowledgement:

We are thankful to Jubeln Lifesciences for helping us to carry out the scale-up for this work.

Reference:

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P14 - Preparation of Ritonavir solid dispersion by hot melt extrusion technology for solubility and dissolution enhancement

Manindra Mahapatra, Divakar R. Jaiswar, Purnima D. Amin

[1]Department of Pharmaceutical Sciences & Technology, Institute of Chemical Technology, Matunga, Mumbai-19

Email id : manindrapharma2018@gmail.com

Keywords:

Hot Melt Extrusion (HME), Amorphous Solid dispersion (ASD), Ritonavir, Eudragit® EPO, Dissolution rate.

Introduction:

Poor aqueous solubility and dissolution rate became a major challenge for upcoming drugs in market. Melt extrusion process is currently applied in the pharmaceutical field for the manufacture of a variety of dosage forms and formulations such as granules, pellets, tablets, suppositories, implants, stents, transdermal systems and ophthalmic inserts[1]. Different strategies have been developed to address low drug solubility which includes salt formation, pH adjustment, co-crystal formation and co-solvent approach. Ritonavir (RTV) is a protease inhibitor used for the treatment of AIDS. One of the approaches for increasing solubility and hence bioavailability is preparation of amorphous solid dispersion. In the present work Hot- melt extrusion was used to prepare Amorphous Solid Dispersion.

Material & Methods:

Hot melt extrusion technology (HME) was used to prepare amorphous solid dispersion (ASD) of ritonavir using Eudragit® EPO as carrier polymer and TPGS (D- α tocopheryl polyethylene glycol succinate) as a plasticizer. Polymer selection was based on drug–polymer miscibility by film casting method, Hansen solubility parameters and molecular modeling study.

Evaluation:

Methods used for characterization of solid dispersions are saturation solubility study, contact angle measurement, flow property, DSC, FTIR, HSM, XRD, SEM, in vitro dissolution study and stability study.

Result and discussion:

Amorphization confirmed by XRD and good wettability as shown by contact angle measurements facilitated more than 95% drug dissolution within 15 min. Intermolecular hydrogen-bond interaction between RTV and Eudragit® EPO was investigated by FTIR and molecular modeling study which stabilized the amorphous nature of the RTV in polymer carrier[2]. DSC revealed drug polymer miscibility resulting in formation of homogenous one phase solid system. Live thermal events of the amorphous solid dispersion were observed under hot stage microscopy (HSM). The amorphous nature of RTV solid dispersion was stable for 6 months when stored at 30°C/65% RH and there was no significant change in the dissolution. Higuchi diffusion model was applied to the dissolution data to explain the release behavior of the drug from the amorphous solid dispersion. 216 to 225 fold increased solubility in case of all batches was found to be in pH1.2 when compared the solubility of plain RTV in water.

Conclusion:

This study revealed that Eudragit® EPO is suitable polymeric carrier for the preparation of stable amorphous RTV by hot melt extrusion which helps in improving dissolution and bioavailability of the drug.

Acknowledgement:

Author is thankful to Department of Biotechnology, Government of India for providing financial support to carry out this research work.

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P15 - Modulation of Microenvironmental pH for Enhancing Solubility and Dissolution rate of Efonidipine Hydrochloride Monoethanolate

Madhuri M. Kshirsagar, Ashish S. Rajput, Purnima D. Amin
Department of Pharmaceutical Sciences & Technology, Institute of Chemical Technology, Matunga, Mumbai-19
Email:madhurikshirsagar.mk@gmail.com

Keywords:

Hot-melt extrusion, Solid dispersions, Efonidipine Hydrochloride Monoethanolate, pH modulation, dissolution rate

Introduction:

Solubility and dissolution rate plays an important role in predicting bioavailability as well as therapeutic efficacy of a drug. Solid dispersions are one of the most successful strategies to improve dissolution rate of poorly water-soluble drugs [1]. Hot melt extrusion (HME) technique is an effective solvent-free and continuous process in the pharmaceutical industry for the formulation of molecular dispersions to improve the solubility and bioavailability of drug components [2].The purpose of this study was to increase the solubility and dissolution rate of Efonidipine hydrochloride monoethanolate (EHM) by using citric acid which modifies microenvironmental pH [3].

Methods:

A) Preparation of solid dispersions by HME: Candidate drug, EHM was subjected to the preformulation study. The miscibility of EHM and polymer was estimated based on the Van Krevelen solubility parameter. Solid dispersions of EHM with Eudragit EPO were prepared by HME. Citric acid was added which acted as both plasticizer and solubilizer.

B) Characterization: Physicochemical properties of the drug, polymer, extrudes, and corresponding physical mixtures were characterized by Thermo-gravimetric Analysis (TGA), Differential Scanning Calorimetry (DSC) and Infrared spectroscopy (FTIR), Energy-dispersive X-ray spectroscopy (EDX), Mass Spectroscopy (MS), solubility and dissolution rate [3].

Results and Discussion:

Preformulation studies suggested that low aqueous solubility could be the reason for low oral bioavailability. The optimized formula of solid dispersion comprises of 40% drug, 10% citric acid and 50% Eudragit EPO. XRD and DSC studies confirmed the existence of amorphous state of EHM in the solid dispersion. Interestingly, the obtained powders dissolved immediately (Q_{60}=90%) and demonstrated high apparent solubility, over forty-fold greater than pure EHM.

Conclusion:

Drug solubility and dissolution enhancement in water was achieved in HME formulations with polymer Eudragit EPO and citric acid, as microenvironment pH modulation agent.

Acknowledgement:

We are thankful to All India Council for Technical Education (AICTE) for providing fellowship.

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P16 - Study on *In Vitro* Dissolution Behavior of Poorly Soluble Drug Using Foldscope Microscopy

Hinge Nikita Subhash[a], **Murali Monohar Pandey**[a]
[a]Department of Pharmacy, Birla Institute of Technology and Science BITS, Pilani, India.
E-mail Id: 1810.niki@gmail.com

Keywords: Solid dispersions, foldscope, Soluplus®, macitentan, particle size

Introduction:

Macitentan (MCT), an endothelin receptor antagonist, is available as 10 mg film coated tablet for the treatment of pulmonary arterial hypertension. The drug belongs to BCS class II with very low aqueous solubility of 0.0066 mg/mL, which, is a major hurdle in its formulation development. In this research work, we prepared solid dispersion using a hydrophilic polymer, Soluplus® for the improvement in rate and extent of dissolution of the drug. Along with this, dissolution behavior of the drug and prepared solid dispersion was also studied using foldscope microscopy [1]. The advantages of ease to use and ability to observe liquid samples make foldscope a tool of choice for studying dissolution behavior of drugs. The aim of this study was to prepare solid dispersions of MCT with improved dissolution behavior, using the hydrophilic polymer Soluplus®, and investigate the dissolution behavior of these dispersions using foldscope microscopy. Foldscope is an easy to use tool of choice to study dissolution behavior of drugs.

Method:

A) Preparation of solid dispersions: Solid dispersions of 1:4, 1:6 and 1:10 ratios (drug: polymer) were prepared by solvent evaporation method, using ethanol as solvent, and termed as SD 1:4, SD 1:6 and SD 1:10.

B) Characterization of solid dispersions:

1. *In vitro* dissolution study: *In vitro* dissolution studies of pure drug, solid dispersions and physical mixtures were conducted using USP type-I dissolution apparatus in 500 mL phosphate buffer (6.8 pH) as dissolution medium containing 0.1% (w/v) Tween 80. Tween 80 was added into the medium to maintain sink condition. The dissolution samples were collected at predetermined time intervals (5, 10, 15, 30, 45 and 60 min) and analyzed by UV-Visible spectrophotometric method. Simultaneously, the above samples were also observed under foldscope microscope to study dissolution behavior of pure drug and SD 1:10.

2**. Physical characteristics of solid dispersions:** Images of pure drug, Soluplus® and SD 1:10 were captured to differentiate their physical characteristics using foldscope microscopy. The physical nature of the solid dispersion was also checked using differential scanning calorimetry (DSC).

3. **Wettability**: Decreased surface and interfacial tension results into increased wettability. The study was performed using pendant drop method (Kruss tensiometer). It was performed using 1 mL aqueous solution (1% w/v) of pure drug, SD 1:6 and SD 1:10.

Results :

The solid dispersions were obtained as hard flakes which produced colorless powder upon sieving (#60). *In vitro* dissolution study showed significant increase in dissolution of the drug from the prepared solid dispersion. Pure drug showed 40% dissolution in 60 min. SD 1:4, SD 1:6 and SD 1:10 showed 43%, 62% and 100% cumulative drug dissolution at the end of one hour respectively; whereas, physical mixtures of same ratio showed 26%, 32% and 35% dissolution in the same period of time respectively. Simultaneously, samples were withdrawn while performing dissolution study and observed under foldscope microscope. In case of SD 1:10, the number of particles and particle size was reduced significantly as compared to that of pure drug.

The physical appearance of pure drug, Soluplus® and SD 1:10 was studied using foldscope microscope; difference in appearance and size of particles present in the sample was evident. In DSC study, the drug was found to be crystalline and showed melting endotherm at 137 ^{0}C whereas, in all solid dispersions the endotherm was completely absent, which confirms the conversion of crystalline MCT into amorphous form in the solid dispersions. The surface tension for pure drug was observed to be 84.2 dynecm^{-1} while for SD 1:6 and SD 1:10, it was observed to be 54.3 and 26.7 dynecm^{-1} respectively.

Conclusion:

Dissolution study showed significant enhancement in dissolution of solid dispersions in comparison to pure drug and physical mixtures, which can be attributed to existence of drug in amorphous form in the solid dispersions, and is also evidenced by their decreased surface tension and hence improved wettability. Foldscope microscopy was also useful in providing an insight into the dissolution behavior in terms of number and size of particles, simultaneously during the course of the dissolution study.

Acknowledgement:

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P17 - Flow through Dissolution of Co-encapsulated Anti-Tubercular Drug Microparticles in Biorelevant Lung Media

Amit S. Lokhande, Padma V. Devarajan
Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology (Deemed University), Matunga (E), Mumbai, India.
Email ID : aslokhande29@gmail.com

Keywords:

Anti-tubercular,Biorelevant Lung Fluids, Float-A-Lyzer®, Flow through cell, Microparticles

Introduction:

Tuberculosis, challenged by drug resistance essentially necessitates multi drug therapy. Two challenges mainly exist, one is the co-encapsulation of all drugs together and the other is evaluation of such particulates for release. Currently, there is no official dissolution testing method for nano and micro systems. Flow through cell dissolution apparatus (USP Type IV) has been used for release testing of many particulate systems such as polymeric nanoparticles, liposomes [1,2]. We have evaluated our anti-tubercular combination drug microparticles in two biorelevant lung fluids using Float-A-Lyzer® in USP IV (SOTAX) dissolution apparatus.

Methods:

The co-encapsulated microparticles of three anti-TB drugs Rifampicin, Isoniazid and Ethambutol were prepared by simple one step precipitation method. The particles were characterized for physicochemical properties and for *in vitro* release in Flow through cell USP IV dissolution apparatus (CE7 SOTAX, AG) in a closed loop system, with a Float-A-Lyzer® (MW cut-off 20kD). The effect of flow rates (8mL/min, 16mL/min and 24mL/min) in two different biorelevant media namely Simulated Lung Fluid (SLF) pH 7.4 and Artificial Lysosomal Fluid (ALF) pH 4.5, was evaluated over 24h. The two drugs Rifampicin and Isoniazid were analysed by UV simultaneous equation method, whereas Ethambutol was analysed by Colorimetric method using Acetylacetone Reagent.

Results:

The microparticles showed average particle size of 2.0-3.0µm and 12% total drug loading, with %entrapment efficiency of >50% for all three drugs. The differential release rate was observed for three drugs based on their solubility, physicochemical properties, and pH of the release media. The dissolution rate was in the order of Ethambutol> Isoniazid >Rifampicin. The release rate for all three drugs was more rapid in ALF pH 4.5 compared to SLF pH 7.4. Lower release in SLF could allow particles to be efficiently phagocytosed by alveolar macrophages, while rapid release in ALF pH 4.5 proposes their efficient intracellular release delivery at site of action and hence efficacy.

Conclusion:

The USP IV Flow Through Cell Apparatus with Float-A-Lyzer® is an optimum method for *in vitro* release studies from nano and micro systems. Release of all the three drugs from the particulate system suggests their potential for anti-tubercular combination therapy.

Acknowledgements:

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P18 - Bioenhanced Spray Dried Curcumin Milk Powder - Effect of Permeation Enhancers on *Ex-vivo* Permeation of Curcumin

Vinod S. Ipar[1,2], Rekha S. Singhal[2], Padma V. Devarajan[1],
[1]Department of Pharmaceutical Sciences and Technology, [2]Department of Food Engineering and Technology, Institute of Chemical Technology(Deemed University), Mumbai, India.
Email ID : vinodipar11@gmail.com

Key words:

curcumin, milk powder, *Ex-vivo* permeation, spray drying, permeation enhancer.

Introduction:

Curcumin is a bioactive hydrophobic polyphenolic biopharmaceutical classification system (BCS) class IV nutraceutical compound that has attracted significant global attention due to multifaceted therapeutic actions [1]. Despite the promising therapeutic potential and safety, the oral bioavailability of curcumin has been strongly limited due to its poor aqueous solubility and low permeability [2]. To address these challenges different novel formulations such as solid dispersion, self-microemulsifying drug delivery system [3] andmicroemulsion[4]have been developed for bioenhancement of curcumin. Turmeric boiled in milk is an age-old home remedy for coughs and colds. Hence, we present a novel ready to use nutraceutical curcumin formulation in milk powder byscalable spray drying technique as a powder for reconstitution with water just prior to administration. In the present study, we evaluate the effect of different permeation enhancers such as quercetin, TPGS, lecithin, piperine and Labrasolon *ex-vivo* intestinal permeationby non-everted rat intestine sac method.

Methods:

A ready to use dried curcumin milk powder was developed using a suitable source of curcumin, carrier materials, solubilizers and stabilizers, milk powder as bulking agent and protein source and various permeation enhancers by high shear homogenization and spray-drying technology. Developed formulation was evaluated for *ex vivo* permeation by non-everted gut sac model to assess the effect of permeation enhancers on the efficiency of curcumin transport through the intestinal membrane. Rat intestinal sac was filled with 1 ml of dispersion (equivalent to 1 mg of curcumin), and placed in 50 ml of Krebs Ringer medium (pH 7.4) with 0.5% Tween 80 maintained at 37°C and aerated(10-15 bubbles/min) with oxygen. Sampling was carried out over time-period of 2h, samples centrifuged at 15000 rpm for 15 min, the supernatant was quantified by HPLC, and flux and permeability coefficient were calculated.

Results and Data analysis:

The spray dried curcumin milk powder was obtained as lemon yellow coloured, free flowing powder with 0.6%curcumin loading. Aqueous suspension of curcumin used as reference and s*pray dried* turmeric milk powder showed low permeation with flux of $0.003\mu g.cm^{-2}.min^{-1}$.Enhancement of flux in presence of permeation enhancers was in the order quercetin<TPGS<lecithin<piperine<Labrasol with Labrasol revealing a 13 fold enhancement.

Conclusion:

Ex-vivo permeation studies of curcumin confirmed maximum enhancement in permeability with Labrasol, suggesting Labrasol as a suitable permeation enhancer. Labrasol being FDA approved presents great promise for this Bioenhanced Nutraceutical Curcumin milk based formulation.

Acknowledgement:

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P19 - Spray Drying Process Optimization for the Preparation of Solid Dispersions of Itraconazole for Enhancement of Dissolution using Design of Experiments

Tamilselvan V., Durgesh K. Jha, Purnima D. Amin
Department of Pharmaceutical Sciences & Technology, Institute of Chemical Technology, Matunga, Mumbai-19.
Emai ID : selvantamil2122@gmail.com

Keywords:

Spray Drying, Design of Experiments, Itraconazole, Central Composite Design, Dissolution Enhancement

Introduction:

Design of experiments (DOE), a component of Quality by Design, is systematic and simultaneous evaluation of variables (process or formulation) to develop a product with predetermined quality attributes [1]. The objective of the current study was to evaluate the feasibility of making solid dispersions to enhance the dissolution behavior of low soluble drugs i.e., BCS Class II using Spray Drying Technique by employing DOE.

Methods:

(A) Preparation of Solid dispersions : Itraconazole (ITZ) was used as a modelBCS class II drug. The ITZ:Soluplus physical mixtures were prepared in the weight ratio of 1:1.5 and dissolved in a solvent system comprising Methanol and Dichloromethane (50:50).The prepared solutions were then spray dried to obtain free flowing powders. Based on a three-factor, three-level central composite design, the spray drying experiments were designed. The factors investigated were spray solution concentration, aspiration rate and atomizing pressure. The factors were optimized based on the dissolution time, process yield and powder properties. The optimum process conditions were obtained from Design-Expert® software to execute the process validation batches.

(**B) Characterization:** The solid dispersions obtained were evaluated for powder properties such as tapped density, bulk density, Hausner ratio, Carr's index, Differential Scanning Calorimetry (DSC), X-Ray Diffraction (XRD) and process yield [2]. *In vitro* dissolution studies were carried out in 900ml 0.1N HCl official media at 37±0.5°C in USP Type II dissolution apparatus.

Results:

The dissolution rate of drug from optimized solid dispersion has been increased significantly (Q60 is 90-95%) as compared with the pure drug (Q60 is 2-3%). Significant increase in process yields and improved powder properties were obtained by optimization of process variables using DOE. The desirability function used to optimize the response variables and observed responses were in agreement with experimental results [3].

Conclusion:

Thus, the study implies that DOE is a useful tool to optimize critical parameters of spray drying process to obtain products with desired quality attributes, like dissolution profile.

Acknowledgement:

We are thankful to All India Council for Technical Education (AICTE) for helping us to carry out this work. Also, we are thankful to Bajaj Life Sciences for providing gift sample of Itraconazole and BASF Limited for providing Soluplus sample.

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P20 - *In - vitro* Release Studies of Nanoparticle Loaded Novel Amoxycillin Gel for Periodontal Infections

Sameer C. Jain, Vishakha V. Surve, Saritha R. Shetty
Shobhaben Pratapbhai Patel School of Pharmacy & Technology Management,
SVKM's NMIMS, Vile Parle (W), Mumbai – 400056
E-mail ID: sarithabhandary@gmail.com

Key words:

Nanoparticles, periodontal, lyophilization, spray drying, amoxycillin.

Introduction:

Periodontal disease (PD) affects up to 50% of the global population and is one of the most common problems in oral healthcare [1]**.** Amoxycillin trihydrate, a broad spectrum, BCS class III antibiotic, having high solubility and low permeability is used to provide relief from PD. The aim of this research was to formulate amoxycillin loaded polymeric nanoparticles (NP) in gel base and to study its kinetic release profile.

Methodology:

Pre formulation studies were conducted to characterize the drug, excipients were screened and assessed for their compatibility with the drug**.** Eudragit grades, chitosan and carbomers were the polymers used for developing the polymeric NPs; various methods were adopted like spray drying, emulsion droplet coalescence, solvent evaporation and lyophilisation. Developed polymeric NPs were evaluated for percentage yield, particle size, drug entrapment efficiency, *in-vitro* drug release. Optimized batch was assessed based on the yield and entrapment efficiency, and loaded into chitosan gel base; the gel formulation was evaluated for assay, rheology and mucoadhesive strength. *In-vitro* release profile was performed on both the formulated nanoparticles and gel loaded nanoparticles batches. Franz diffusion cell was used for diffusion study; phosphate buffer pH 6.8 as medium, temperature 37ºC±2ºC, rpm was set to 50. Aliquots were withdrawn at 1 hr intervals for upto to 8hr and then at 24 hr and analyzed using UV spectrophotometer at 228.4nm. The obtained data was characterized for studying the drug release mechanism from the polymeric system hence various kinetic models were studied like Zero order, first order, Higuchi, Korsmeyer Peppas.

Results:

Of the various techniques employed to obtain the NPs, lyophilisation technique gave high yield of 70.37% with particle size of 443.4 nm and entrapment efficiency of 84.83%. At the end of 6 hours the formulated NPs exhibited cumulative drug release of 93.12%. Comparison of *in-vitro* drug release for 24 hrs between the plain Amoxycillin-loaded gel and NP loaded gel showed a marked enhancement in release from 26.02% and 67.67% respectively. Kinetic model fitting indicated that chitosan-NP gel obeyed Korsmeyer-Peppas model with slope (n=0.685), non-fickian transport mechanism was followed.

Conclusion:

Amoxycillin NP loaded gel can be used as an alternative for tablets and capsules which by passes first pass metabolism. Controlled release can be obtained thereby decreasing the dose from thrice a day to single application for localized action. The gel showed good permeability, spreadability and mucoadhesive strength. Future prospects include pharmacokinetic and bioavailability studies of the gel.

Acknowledgement:

Authors are thankful to Gujarat Dyestuff for their gift sample and Marine chemicals for chitosan polymers as gift samples. SVKM's NMIMS for constant support.

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P21 - Characterization and Kinetic Drug Release Study of Clotrimazole Vaginal Sponge Loaded Hydrogel

Ifeoma C. Ezeokafor, Ashika V. Padgaonkar, Saritha R. Shetty*
Shobhaben Pratapbhai Patel School of Pharmacy &Technology Management,
SVKM's NMIMS, Vile Parle (W), Mumbai – 400056
*E-mail ID : sarithabhandary@gmail.com

Keywords:

Micro-sponges, quasi emulsion technique, lyophilization, clotrimazole.

Introduction:

According to medical express [1], 138 million women worldwide suffer from recurrent thrush. Vaginal drug delivery is an important and potential route for vaginal candidiasis. The present study is an attempt to formulate and characterize novel vaginal sponge of clotrimazole for vaginal candidiasis. Clotrimazole is a BCS class II drug, and by formulating the vaginal sponge it is proposed to enhance the solubility of the drug and give controlled release by increasing the residence time at the site of application.

Methodology:

In preformulation, API and excipients were characterised for their compatibility, various types and concentrations of mucoadhesive polymers like carbomers, chitosan and HPMCs were tested for their ability to form sponges[2]. Vaginal sponges were developed using two techniques namely, quasi emulsion technique and lyophilisation. The formulated batches were optimised based on their product percentage yield, entrapment efficiency and particle size measurement. Rehydration study of sponge was carried out using simulated vaginal fluid. To evaluate the kinetic release profile, *plain drug loaded and sponges loaded hydrogels were evaluated using the* Franz diffusion cell; diffusion medium was phosphate buffer pH 4.0 maintained at 37°C; stirring rate was set at 50rpm, and dialysis membrane was used as the barrier between the donor and receptor compartments. Aliquots were withdrawn at one-hour intervals for up to 8hrs, and analysed by HPLC. This clotrimazole vaginal sponge loaded hydrogel release was compared with clotrimazole sponges and marketed product (Candid gel-Glenmark).

Results and discussion:

At the end of 8hrs, *in-vitro* release studies showed cumulative drug release of the optimized batch prepared by quasi emulsion technique to be 69.38% and for the lyophilisation batch it was 38.96%, while comparison with marketed product, it showed 80.475% drug release in just 60mins. The formulated polymeric system was characterised for the release kinetic mechanism for zero order, first order, Higuchi, Korsmeyer Peppas models. The kinetic study showed $r^2$of 0.9577 for Korsmeyer Peppas model, which predicts that the fractional release of drug is exponentially related to the release time. Mechanism of drug release can be attributed to instantaneous imbibition of water in the sponge matrix, swelling followed by drug diffusing out into the surrounding medium; non-Fickian behaviour is predicted.

Conclusion:

The *in-vitro* release from clotrimazole sponge-loaded hydrogel showed non-FickianKorsmeyerPeppas release mechanism, which can be a promising approach to constant rate drug delivery via the vaginalroute.

Acknowledgements:

Authors are thankful to Amoli Organics for their gift sample of drug clotrimazole and Evonik for Eudragit polymers as gift samples. SVKM's NMIMS for constant support.

Reference:

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P22 - Impact of Material Properties on Intrinsic Dissolution Rate of Efavirenz Sourced from Different Manufacturers

Srilaxmi G Rao, Ranjna Jain, Srushti Mahajan, Sandeep S Zode, Dnyaneshwar P Kale, Arvind K.Bansal*
Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research (NIPER),
Sector 67, Mohali, Punjab, India-160062
E-mai ID : akbansal@niper.ac.in

Keywords:

Material Properties, Source-to-source Variability, Surface chemistry, Hydrophilicity

Introduction:

Solid state properties of a drug substance such as particle size, shape, solid form, crystal habit, particle size distribution (PSD), surface area, porosity, surface morphology and surface free energy critically impact the dissolution and bioavailability of drug product [1, 2]. Sometimes source-to-source and lot-to-lot variations in material properties of an active pharmaceutical ingredient (API) could lead to variability in its biopharmaceutical properties. The present study focuses on impact of source-to-source variability in material properties of **Efavirenz** (EFV) on its intrinsic dissolution rate (IDR).

Objective:

To investigate the impact of material properties on intrinsic dissolution rate of Efavirenz sourced from different manufacturers

Material and Methods:

Efavirenz (EFV) samples were obtained from 3 different manufacturers and coded as I, II and III. For IDR study, powder compacts of EFV were prepared by compressing 200 mg drug at 20 kg/cm^2 in a hydraulic press for 30 seconds. Dissolution media of pH 6.8 buffer with 0.25%, and 0.5% SLS were selected based on its discriminatory power [1]. Powder X-ray diffraction (PXRD) on the powder compacts coupled with molecular modeling using Mercury software was performed to unveil the impact of surface chemistry on IDR.

Results and Discussion:

The samples showed similarity in their morphology and possessed plate-shaped crystals when examined under scanning electron microscopy. PXRD pattern revealed that all three samples were form I of EFV, while specific surface area (SSA) of samples I, II and III were 3.190 ± 0.08 m^2/g, 2.756 ± 0.08 m^2/g, and 2.973 ± 0.10 m^2/g respectively. IDR values were 258.93 ± 5.1 µg/min/cm^2, 171.43 ± 25 µg/min/cm^{2}and 211.73 ± 2.3 µg/min/cm^{2}of samples I, II and III, respectively. The trend of the IDR was I > III > II. Chemically EFV contains both hydrophilic (C=O, N-H groups), and hydrophobic (propane ring and benzene ring) groups. All samples showed dissimilar albeit close values for SSA. The percentage contribution of a hydrophilic (110) crystal facet was 31.3%, 26.7% and 26.8% for samples I, II and III respectively. As the IDR values are not affected by SSA of the samples, the differential IDR of the samples mainly was attributed to varied hydrophilicity of the samples caused by the most dominant crystal facet (110).

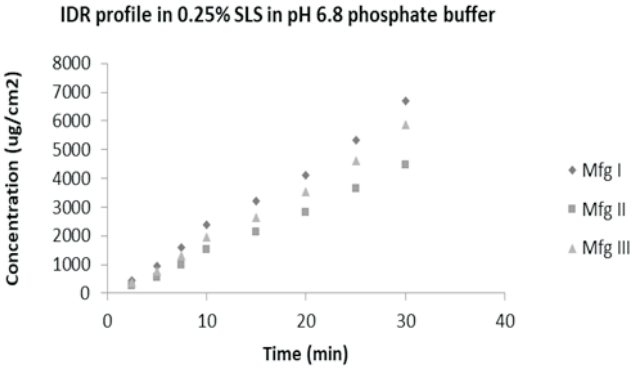

Figure 1. IDR profile of powder compacts of I, II and III in 0.25% SLS in pH 6.8 buffer

Conclusions:

The material properties play a vital role in governing the performance characteristic such as IDR. The present study investigated that EFV sourced from different manufacturers with relatively similar specifications led to variations in their IDR demonstrating the role of differential surface anisotropy (surface chemistry) of the samples. In pharmaceutical industry, the particle size, shape, and surface area are routinely investigated to understand their impact on the dissolution of API. However, the present study revealed that surface chemistry of samples can significantly affect the performance despite identical solid form and similarity in the other routinely monitored material properties.

Acknowledgment:

We would like to thank the Director NIPER, S.A.S. Nagar for providing research facility.

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P23 - *In vitro* Release Assessment of Thermoresponsive Intramammary *In Situ* Gelling Systems of Cephalexin Monohydrate for Dry Cow Therapy

Hemali Savla[1], Aarish Pithawala[1], Priyanka Alshi[1], Abdul Samad[2], Mala D. Menon[1]
[1]Bombay College of Pharmacy, Kalina, Santacruz (E), Mumbai- 400098
[2] Vetware Pvt. Ltd., Mumbai - 400102
Email ID: hemali.savla@bcp.edu.in

Key words:

Cephalexin monohydrate (CPM), bovine mastitis, intramammary *insitu* gel.

Introduction:

Bovine Mastitis, an inflammatory condition of mammary glands in cattle due to microbial infections, leads to decreased milk production and heavy economic losses in dairy industry. Conventional treatments (post-milking teat antisepsis, intramammary infusions and teat sealing) are cumbersome for daily administration in large herds[1]. Antibiotic therapy is employed either during lactation phase (300 days) or during dry period (60 days). Treatment during lactation phase leads to antibiotic residues in milk, which may be eliminated by treatment during dry period, which also allows for maintenance of uniform antibiotic levels in udder. Sustained release depot preparation of antibiotics as a more rational approach for drug delivery during dry period has been recommended by National Mastitis Control Board[2].

Aim:

Assessment of *in vitro* release profile and teat sealant efficacy of *in situ* gelling system of CPM in an *in vitro* model mimicking environmental conditions of cattle barns.

Methods:

Chitosan-based thermoresponsive *in situ* gelling system of CPM was prepared [3, 4] and characterized for physicochemical properties. ***In vitro*** release was carried out by static method. *In-situ* gel formulation (5ml) in dialysis bag was immersed in test tube containing prewarmed 40ml Phosphate Buffer pH 7.2 and maintained at 37ºC (± 1ºC). Whole contents of buffer were withdrawn at periodic intervals for upto 4 days and analysed by UV spectroscopy. An *in vitro* model replicating teat-like condition was developed in-house to assess sealant efficacy. A syringe assembly was filled with sterile blank/CPM-loaded gel. To mimic environmental conditions of cattle barns, the assembly tip was immersed for 30 mins daily in *S. aureus* broth culture / soil moistened with *S. aureus* culture. A loopful of gel was taken aseptically from surface of gelled formulation at periodic intervals and checked for microbial contamination.

Results and Discussion:

The developed *in situ* gelling system was found to gel within 7 mins at 37 ± 2°C and was thermoreversible for upto 4 cycles. The amount of drug released was found to be above the minimum inhibitory concentration (MIC) of 0.12 – 0.25 µg/ml for upto 3 days. In the sealant efficacy study, no microbial growth was observed in gel for upto 9 days, which indicated that the gel formed an effective barrier to entry of microbes into teat canal.

Conclusion:

Intramammary *in-situ* gelling system of CPM provided sustained drug release for 3 days, ensuring prolonged residence time in teat canal and can form effective barrier against microbial entry during dry period and can be proposed for twice a week administration.

Acknowledgements:

Gift samples **-** CPM (Saife VetMed Pvt. Ltd.), Chitosan (Nitta Gelatin).

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P24 - Drug Release studies from a Novel Wet Wipe formulation for veterinary application by Pay off stroke method

Pankaj Sontakke[1], **Unmesh Kharade**[1], **Juber Pendhari**[1], **Abdul Samad**[2], **Mala Menon**[1]
[1]Bombay College of Pharmacy, Kalina, Santacruz (E), Mumbai - 400098; [2]Vetware Pvt. Ltd. Mumbai.
Email Id: sontakkepankajmumbai@gmail.com

Key Words:

Repeat Breeding Syndrome (RBS), Anti-infective wet wipes, Silver nanoparticles (AgNPs), pay off stroke method, veterinary.

Introduction:

RBS is defined as cow's failure to conceive from 3 or more regularly spaced insemination services, in the absence of detectable abnormalities; this problem is mainly attributed to bovine genital infections. Tackling RBS problem is a challenging task and related to economics in dairy farming [1,2]. Current treatment approaches are systemic / local antibiotic therapy, which suffer from limitations of resistance development and issue of antibiotic residues in animal products (milk and meat). This has led to exploring other anti-infective agents like AgNPs, with good antimicrobial activity; antimicrobial resistance to elemental Ag is extremely rare due to multiple antimicrobial mechanisms. A wet wipe formulation loaded with AgNPs can achieve local delivery of antimicrobial to infected sites to achieve effective control over infections responsible for RBS.

Aim:

To assess *in vitro* release of AgNPs from the wet wipes by payoff per wipe stroke method [3], which simulates the actual administration procedure in animals before artificial insemination to disinfect the genital regions.

Methods:

A) Preparation of AgNPs-loaded wet wipe substrates- AgNPs were prepared bychemical reduction method and characterized for physicochemical properties. Wet wipes formulation solution was prepared with optimum concentrations of AgNPs, polymer, humectants; this solution was loaded on fabric material with micro pipette [(4 ml added to non-woven spunlace substrates (18×5 cm^2)] and characterized.

B) *In vitro* release of AgNPs from wipe fabric – *In vitro* release was assessed by payoff per wipe stroke method [3] on dialysis membrane (10×10 cm^2), soaked in distilled water for 24 hours, and placed in petriplate. The wet wipe was rubbed on dialysis membrane; payoff of AgNPs transferred to dialysis membrane after every wiping stroke and up to 4 wiping strokes was quantified by atomic absorption spectroscopy. Correspondingly, the antimicrobial activity of the AgNPs loaded wet wipes by pay off method against *S. aureus* and *E.coli* was also assessed on seeded agar plates.

Results and Discussion:

AgNPs were successfully prepared with mean particle size of 34.78nm and PDI of 0.487, zeta potential was -49 ± 11.2 mVand Ag content of 600 ppm. The AgNPs loaded wet wipes were brown in colour with smooth surface texture; Ag content was 82% and tensile strength was 59.187 g/cm^2.The *in vitro* release study of AgNPs from the wipe fabric revealed that Ag released increased with increase in number of wiping strokes [ranged from 0.61 mg (43.9%) in one stroke wiping to 1.103 mg (79.35%) in 4 wiping strokes], which is above MIC of silver (200 ppm). This was also reflected in antimicrobial study; no growth was seen in the wiped portions of *S. aureus* and *E. coli* seeded agar plates.

Conclusion:

Payoff stroke method, which simulates the end use of wet wipes was successfully applied to assess release of Ag from AgNPs loaded wet wipes.

Acknowledgements:

Gift samples-Non-woven fabrics (Ginni Filaments Ltd), Gellan gum (CP Kelco India Pvt. Ltd.)

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P25 - Lipid NanocapsulesStabilized using TPGS for Enhancing Permeability and Oral Bioavailability of Curcumin

Devaguptapu Prakash.,Pradnya Bapat, Rohan Ghadi, Dasharath Chaudhari, Sameer S. Katiyar, Sanyog Jain*
Centre for Pharmaceutical Nanotechnology, Department of Pharmaceutical Technology Formulation,
National Institute of Pharmaceutical Education and Research(NIPER), S. A. S. Nagar, Punjab- 160062, India.
E mail ID: prakash.devaguptapu1103@gmail.com

Keywords:

Curcumin, Nanocapsules, Permeability, Oral bioavailability

Introduction:

Curcumin (CUR), a drug with wide range of therapeutic uses is often underlined because of its low oral bioavailability as it belongs to BCS class -IV, having low solubility and low permeability.Present investigation highlights the development of Tocophersolan(TPGS) stabilized lipid nanocapsules (LNs) for enhancing the oral bioavailability and permeability of curcumin [1].

Method:

A) **Optimizing of LNs** for different lipids, different concentrations of TPGS and different drug: lipid ratio, followed by lyophilizing optimized LNs[2].

B) **Characterization ofthe prepared LNs-**PXRD, TEMentrapment efficiency (EE), *in vitro* release study, Caco-2 cell uptake study, *ex vivo* intestinal permeability and *in vivo* pharmacokinetic performance.

Results:

Optimized LNs exhibited desirable quality attributes (average particle size of 181.8±6.6nm, with PDIof 0.140± 0.01 and average % EE of 51.06 ± 7.27) employing MaisineTM 35-1 as a lipid carrier, 0.05% TPGS and CUR: lipid ratio of 5:10 and showed sustained release biphasic pattern. They showcased excellent stability in simulated GI fluids and storage stability. The CUR nanocapsules exhibited 14-fold higher Caco-2 cell uptake and 12.8-fold increased *ex vivo* intestinal permeability. Also, the AUC of CUR nanocapsules in SD rats was increased by 12 folds and MRT 2.47-folds as compared to aqueous CUR suspension.

Conclusion:

The prepared LNs possessed a positive impact on improving the permeability, oral bioavailability and maintaining the stability of CUR. The developed LNs can also be used as a prototype formulation for various difficult to deliver drugs, which exhibit poor solubility and poor permeability such as drugs of BCS Class IV. TheseLNs alsoreduce the frequency of oral administration for drugs, by providing sustained action for longer period of time.

Acknowledgments:

The authors are thankful to the Director of NIPER S.A.S. Nagar for providing necessary facilities and infrastructure.

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P26 - Solubility of Celecoxib-PVP Amorphous Dispersions: A Molecular Perspective

Vijaylaxmi Jain, Pooja Tiwari, Vishruth Reddy, Jaydeep Chormale, Piyush Gupta, Vasu Kumar Kakumanu, Arvind K. Bansal
Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research (NIPER), SAS Nagar, Punjab-160062, India
E mail: akbansal@niper.ac.in

Keywords:

Celecoxib, enthalpy relaxation, molecular dispersions

Introduction:

Celecoxib (CEL) is an anti-inflammatory agent having a solubility of 3.46 µg/ml and is reported to have dissolution rate limited oral bioavailability. Amorphous solid dispersion (ASD)is an attractive approach for overcoming solubility related delivery challenges. The present study investigates the solubility advantage from ASD of celecoxib with PVP-K30. Studies like solubility, isothermal recrystallization and enthalpy relaxation helped in unveiling the molecular basis of solubility advantage from ASDs. Mechanism of drug release from molecular dispersion was elucidated by drug release modelling.

Methods:

CEL molecular dispersions with PVP were prepared in the concentration range of 1-60% w/w by quench cooling method. Powder dissolution studies were performed in water; van't Hoff plots were generated in temperature range of 35-95°C; isothermal recrystallization study and enthalpy relaxation studies were conducted using DSC and various solubility studies were performed on 20 % PVP dispersion to establish the mechanism of drug release.

Results:

The peak solubility obtained with pure amorphous CEL was minimum i.e. 4.57 µg/ml and 60%w/w PVP dispersionexhibited the maximum value i.e. 24.35 µg/ml. The plateau phase solubilities for crystalline CEL, amorphous CEL, 5% ,10%, 20%, 40%, 60% w/w PVP dispersions were found to be 3.46 ± 0.17,3.50 ± 0.14, 7.70 ± 0.57, 12.10 ± 0.22, 12.54±0.36,12.67±0.51and12.59±0.17 µg/ml, respectively. The enthalpy relaxation was measured for CEL and its dispersions containing PVP inconcentrations ranging from 1% to 60% w/w. As the concentration of PVP increased, the magnitude of enthalpy relaxation decreased. After plateau phase appeared with concentration of 20% w/w PVP, a gradual decrease in enthalpy relaxation value was obtained with respect to polymer concentration. Amorphous CEL showedlesser decrease in ΔH_{sol} whereas PVP dispersion due to stabilizing effect of polymer shows a greater decrease in ΔH_{sol} and greater increase inΔH_{trans}. The lowerΔH_{sol} value of the PVP dispersion indicates the ease of solubilization process. The release of drug from amorphous molecular dispersions was found to be drug-dependent and independent of the carrier.

Conclusion:

Qualitative and quantitative choice of the carrier in an amorphous dispersion contributes crucially to the enhancement of solubility and optimal shelf life. The inverse correlation between the solubility enhancement and enthalpy relaxation helped in a better prediction of the role of carrier and optimization of the concentration of PVP for designing solid dispersions or amorphous systems.

Acknowledgment:

The authors are thankful to the Director NIPER S.A.S Nagar for providing infrastructure and facilities for research work.

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P27 - Enhanced Skin-Absorption and Anti-Acne Efficacy of Azelaic Acid loaded Microemulsions

Dhiman Tania1, Pathania Trishi1, Negi Poonam1*and Bisht Alpna1
School of Pharmaceutical Sciences, Shoolini University, Solan (H.P.)1
E mail id : taniadhiman78@gmail.com

Key words-

Microemulsion, *P. acne*, *Agar* well diffusion method, Broth microdilution assay, Skin permeation

Background:

Azelaic acid (AzA), a naturally occurring drug found in wheat, rye and barley, is used in the treatment of mild to moderate acne. Because of the poor aqueous solubility and low skin penetrability, it needs to be formulated at a higher dose, and leads to dose-dependent side effects. Therefore, to increase the permeation and retention of AzA, and to reduce its dose-dependent side effects, a dual strategy was followed. Firstly, to co-formulate AzAwith Tea Tree oil (TTO) which has been reported to be effective against acne vulgaris. Secondly, both AzA and TTO were co-loaded in the microemulsion system having high skin- permeation and retention characteristics.

Objective:

The objective of the current study is to develop AzA and TTO co-loaded microemulsions (ME) for the topical delivery, with a view to achieve enhanced permeation and retention for treatment of acne.

Methods:

A) Preparation and characterization of ME formulations - The first step involved construction of pseu do-ternary phase diagrams for the components- IPM as oil, Labrasol and Tween 80 as surfactant while Transcutol P, Phospholipon90G and Ethanol as cosurfactant used in S_{mix} ratio. Different ME compositions were selected from the microemulsion region. Droplet size and zeta potential of MEs were characterized employing Dynamic light scattering. Optimized ME was incorporated into hydrogel and evaluated for rheological and texture attributes, employing Rheometer, and Texture Analyzer, respectively.

B) Permeation and *in vitro* antimicrobial efficacy studies - The *ex vivo* permeation and retention of AzA and TTO co- loaded ME were evaluated in Wistar rat skin employing Franzdiffusion cell. Further, *in vitro* antibacterial efficacy of the developed systems were established in microbial strains i.e. *S. aureus, S. epidermidis and P. acne* using agar well diffusion method and broth microdilution assay.

Results: Optimized ME having S_{mix} (Labrasol: Cosurfactant in 4:1 ratio) 60%, oil (IPM) 35% and water 5% were used andexhibited nano size (357.4nm) with negative zeta potential (-1.42 mV). ME hydrogel exhibited pseudo plastic behaviour and appreciable firmness, work of shear, stickiness and work of adhesion. AzA and TTO co- loaded ME gel showed higher permeation and retention in Wistar rat skin *vis-a-vis* marketed formulation (Aziderm^{TM}) (Fig. 1).*In vitro* antibacterial efficacy of the AzA loaded ME system was better than AzA, in all the studied microbial strains. The zone of inhibition of AzA ME was 23±1 mm in *S. aureus*, *23.6±1.5* mm *in S. epidermidis, and* 22.3±0.5 mm in *P. acne*, whereas for AzA it was 24.6±5.5 mm in *S. aureus, 20.6±1.1* mm *in S. epidermidis, 11.3±0.5* mm *in P. acne*. Similarlylow MIC values of AzA loaded ME were observed- *0.19 for S. aureus,0.39 for S. epidermidis, 3.12 for P. acne; whereas MIC values for AzA were 0.78 for S. aureus, 0.78 for S. epidermidis, 3.12 for P. acne respectively.*

Conclusions:

The developed ME and ME hydrogel systems of AzA and TTO revealed superior permeation and retention characteristics, as well as better anti-bacterial efficacy against the studiedmicroorganisms vis-à-vis AzA and marketed formulation., and could be a promising drug delivery systemfor the topical therapy of *acne vulgaris*.

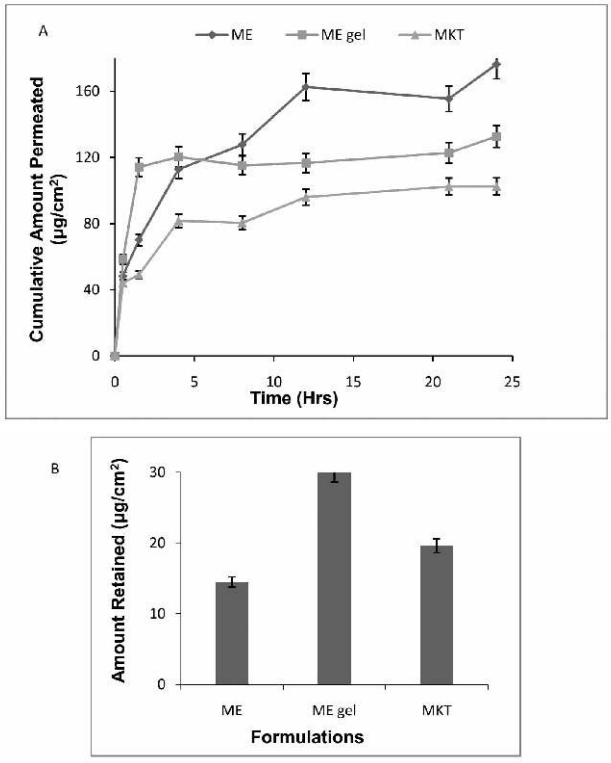

Fig. 1 *Ex-vivo* skin permeation and retention of AzA ME, AzA ME gel and marketed formulation A) Cumulative amount permeated B) Amount retained

Acknowledgement :

The authors are thankful to M/s Phospholipid GmbH, Nattermannallee, Germany, for the *ex gratis* supply of Phospholipon 90G, and M/s Gattefosse, Saint-Priest, France, for providing the gift samples of Labrasol and Transcutol P. The authors are also thankful to Shool ini University for facilitating the research work

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P28 - *In Vitro* Release Study of Rifampicin Solid Lipid Nanoparticles

MrunalBulbule, Maitri D. Amin, Vaishali A. Shirsat
Bombay College of Pharmacy, Santacruz East, Kalina,Mumbai-400098, India
E-mail ID : mrunal151992@gmail.com

Key Words:

Rifampicin, High Pressure Homogenization, Solid Lipid Nanoparticles, sustained drug release, QbD

Introduction:

Rifampicin (RIF), a first line anti-tubercular drug is chemically unstable in acidic environment of the stomach. Nanotechnology-based drug delivery systems have been reported to improve the antimicrobial efficacy by altering the pharmacokinetic processes. The main objective was to assess the formulation process parameters for incorporation of RIF in solid lipid nanoparticles (SLNs) to enhancegastric pHstability and high entrapment of RIF with sustained drug release.

Method:

RIF in present study was encapsulated into SLN's using Compritol ATO 888 as lipid and Tween 80, nonionic surfactant. Polyethylene glycol 400 (PEG 400) was used as a solubilizer for incorporating RIF in the lipid core. SLN's were prepared using High Pressure Homogenization (HPH) technique. Quality by Design (QbD) approach using 3^3 Box-Behnken model was constructed for the optimization of the formulation. RIF-SLN's were characterized using TEM, XRD and DSC. The *in vitro* drug release studies of RIF SLNs were performed using a dialysis membrane. SLNs of lyophilized RIF equivalent to 10 mg of RIF was placed inside the dialysis membrane and introduced into the basket of USP apparatus-I. The drug release was studiedat pH1.2 (0.1 M HCl) and pH 6.8 (Phosphate buffer)as the dissolution media. Aliquots withdrawn at specific time intervals were analysed using RP-HPLC method. The stability studies of RIF SLNs were conducted for 3 months.

Results:

RIF nanosuspension was successfully prepared using HPH technique. The entrapment efficiency of 78% was achieved. FTIR revealed no interaction between RIF and Compritol, TEM images showed spherical nanoparticles, DSC confirmed the encapsulation of RIF and XRD studies revealed the amorphization of drug. The average particle size achieved was 100.3 nm with polydispersity index (PDI) of 0.268 and zeta potential of -17.4 mV, indicating the stability of the developed nanosuspension. The drug release after 4 hours in pH 1.2 was around 8 % and is probably due to unentrapped drug. *In vitro* studies revealed retarded release of RIF from SLNs, with 16% drug release in first hour and 62% drug release in 24 hours. The *in vitro* drug release profile of lyophilized SLN's studied at pH 6.8 revealed best fit with Korsemeyer-Peppas model. Initial burst release was observed due to the unentrapped drug followed by the sustain release effect.The formulated RIF SLNs were found to be stable during the stability studies conducted for 3 months.

Conclusion:

High entrapment of Rifampicin in SLN was achieved by use of PEG and HPH technique. The *in vitro* release study of Rifampicin SLNs demonstrated the successful development of the sustained release formulation with improved gastric pH stability.

Funding:

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Acknowledgements:

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P29 - Assessing *in vitro* gastrointestinal Behaviour of Atorvastatin Calcium: Enhancing Caco-2 Permeability Using Eudragit EPO and PVP K30

Smeet Sorathia, Komal Shinde, Anshul Rohilla, Santhosh Sunnam, Prachi Joshi and Abhay T Sangamwar
Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research,
Sector-67, S.A.S. Nagar, 160062, Punjab, India.
E mail ID : smeetsorathia632@gmail.com

Keywords:

Supersaturation; gastrointestinal transfer model; drug-polymer interactions; supersaturation mediated permeability enhancement; Caco-2.

Introduction:

The aim of current study was to develop an understanding of drug - polymer interactions and its role in stabilizing the supersaturated state of a BCS class II drug, atorvastatin calcium (ATC) through gastrointestinal transfer modelling.

Methods:

Polymers, Eudragit EPO (EUD EPO) and polyvinyl pyrrolidone (PVP) K30 were assessed for their precipitation inhibition of the model drug, ATC based on solubility studies through semi-quantitative supersaturation assays. Gastrointestinal transfer modelling was done to understand the precipitation behaviour of ATC. The precipitates of ATC were subjected to Fourier transform-infrared (FTIR) spectroscopy analysis and ^{1}H Nuclear Magnetic Resonance (NMR) for insights on drug-polymer interactions leading to supersaturation stabilization. The transmembrane permeability of drug in its supersaturated state stabilized by polymers was also assessed through Caco-2 cell line study.

Results:

ATC showed greater supersaturation stabilization in EUD EPO than PVP K30. In gastrointestinal transfer modelling ATC concentration increases faster in PVP K30 than in EUD EPO. Also, the equilibrium concentration for analysis time was higher for PVP K30 than for EUD EPO.^{1}H NMR spectroscopy also showed stronger interaction with EUD EPO as compared to PVP K30. Caco-2 study showed almost 15-fold increase for PVP K30 and 20-fold increase for EUD EPO in the permeability enhancement when compared to saturated solution of atorvastatin.

Conclusions:

Analysis reveals that EUD EPO is able to maintain supersaturation under gastric conditions; however, PVP K30 is better at inhibiting precipitation throughout the transfer modelling. Polymer-stabilized supersaturated solutions of atorvastatin were determined to have better drug-polymer interactions and increased transmembrane permeability enhancement as compared to an equilibrium solution.

Acknowledgement

We are thankful to NIPER, SAS Nagar for fellowship and provision of infrastructural support for carrying out the study.

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P30 - Enhanced Biopharmaceutical Performance of Rivaroxaban through Polymeric Amorphous Solid Dispersion

Sumit Mukesh, Sunita Metre, Sanjaya K. Samal, Mahesh Chand, and Abhay T. Sangamwar*.
Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research, Sector-67, S.A.S. Nagar 160062, Punjab, India.
*Corresponding author. Tel:+91 172 2217682/87; E-mail: abhays@niper.ac.in

Key words:

Rivaroxaban, Polymeric amorphous solid dispersion, Apparent solubility, P-gp inhibition, Caco-2 permeability.

Introduction:

Rivaroxaban (RXB) is an orally active direct inhibitor of the activatedserine protease Factor Xa, given as monotherapy in the treatment of venousthromboembolism (VTE). It has been characterized *in vitro* as a substrate for theactive, nonsaturable efflux via P-gp transporter, limiting its high permeability. The present study aimed to use P-gp inhibiting polymers to prepare amorphous solid dispersions (ASDs) of RXB, with a view to achieve improved solubility and permeability of RXB and hence enhance its biopharmaceutical performance.

Materials:

RXBform I was obtained as a gift sample from Lupin Pharmaceutical Inc. (Lupin Research Park, Pune, India). Eudragit S100 (ES100) and Eudragit L100 (EL100) were received from Vikram Thermo Limited (Ahmedabad, India). Soluplus was obtained as a gift sample from BASF India Limited (Navi Mumbai, India).

Methods:

A) Preparation of ASDs of RXB with Soluplus, ES100 and EL100 by spray drying. B) Characterization of prepared ASDs by DSC, PXRD, FTIR, Microscopy, SEM, NMR spectroscopy, Dynamic vapor sorption. C) *In-vitro* dissolution in biorelevent media, solubility studies in water, *in vitro*permeability study using Caco II cells,*in-vivo* pharmacokinetic studies in male Wistar rats.

Results:

Superiorperformance of ASDs was observed upon dissolution and solubility studies over crystalline API. ASD prepared with Soluplus showed 10-fold increase in apparent solubility andmaintenance of supersaturation for 24 h compared to the crystalline RXB. Further, pharmacokinetic study performed in animalswas in good correlation with the solubility data. Increases of 5.7- and 6.7-fold were observed in AUC and C_{max}, respectively, forASDs prepared with Soluplus compared to those with crystalline RXB. The decreased drug efflux ratio was observedfor ASDs prepared with Eudragit S100 and Soluplus in Caco-2 transport study suggesting improvement in the absorption of RXB.

Conclusion:

ASD with Soluplus has shown better biopharmaceutical performance than crystalline drug. Therefore, ASD of RXB with Soluplus enhanced the overall biopharmaceutical performance through improved solubility and enhanced intestinal uptake of RXB.

Acknowledgments:

We are thankful to Prof. Arvind K. Bansal, Department of Pharmaceutics, NIPER, S.A.S. Nagar for providing DSC facility. We also thank Director, NIPER, S.A.S. Nagar for providing financial support and facilities.

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P31 - *In vitro* Release Assessment of Sustained Release Nanoliposome-based DPI of Ethionamide for Improved Therapy of Tuberculosis

Isha V. Naik[1], Rajesh R. Jain[1], S. Vaidya[2], Evans E. Countinho[1], Mala D. Menon[1]
[1]Bombay College of Pharmacy, Kalina, Santacruz (E), Mumbai, India
[2]Dept. of Clinical Pathology, Haffkine Inst. for Training, Res. &Testing, Parel, Mumbai, India
Email ID: naik.isha19@gmail.com

Keywords:

Nano-liposomes, Mannose, Pulmonary, Flow through cell, DPI

Introduction:

TB, caused by the intracellular pathogen, *Mycobacterium tuberculosis (M.tb*), is a global challenge; major problem is to achieve high drug concentrations in alveolar macrophages (AMs), which harbour the *M.tb* bacilli. Ethionamide (ETH) is one of the second- line drugs used to treat MDR-TB. Pulmonary delivery of ETH in a carrier system, capable of being recognized by mannose receptors (abundantly expressed on AM surface) are efficiently endocytosed by AMs. This approach can be promising to improve intracellular chemotherapy compared to the conventional long drawn out (9-12 month oraltherapy). Such an approach can result in lower doses, lesser toxicity and better patient compliance.

Objective:

To assess *in vitro* release profile of mannosylated inhalable nanoliposomal formulation of ETH for AM targeting, which can ensure improved killing of the resident TB bacilli.

Methods

A) Synthesis of mannose conjugated phospholipid**-** Reaction of mannose and long chain amine in the phospholipid by reported N-glycosylation method resulted in formation of a secondary glycosylamine and its characterization was carried out[1].

B) Preparation and characterization of Mannose tagged liposomal DPI systems of ETH - The liposomes were prepared by dry film hydration technique followed by freeze drying. Characterization parameters included: Particle size (Beckman Coulter LS Particle Size Analyzer), Entrapment efficiency(HPLC), TEM, *in vitro* release, *in vitro* lung deposition (Andersen Cascade Impactor), efficacy in terms of *in vitro* macrophage uptake studies in murine macrophage cell line RAW 264.7.

***C) In vitro* release studies** of the developed liposomal systems as well as the free drug, ETH were performed in 100 ml Phosphate buffered saline (pH 7.4) using USP Type IV apparatus at 37°C and 4ml/min flow rate. closed loop system was used. The sample was placed in a dialysis membrane (10-12 kDa) in A4D adaptor of the Flow through cell. The aliquots were withdrawn at periodic intervals for upto 96 hours and ETH content analysed by HPLC.

Results:

Liposomes of 100-300nm size and entrapment > 50% were converted to DPI by freeze drying with lactose as carrier; The particle size and Respirable fraction of the microparticles were found to be 5.34±0.15µ and 26.4% respectively. *In vitro* release studies indicated the sustaining ability of ETH liposomes for up to 96 hours, whereas ETH solution showed a 12 hours release profile. Further, the formulations were found to be non-toxic and the tagged liposomes showed higher uptake as compared to the drug solution in murine macrophage cell line RAW 264.7.

Conclusion:

This study has revealed sustained release of ETH from the developed mannose tagged nanoliposomal DPI formulation, which would ensure reduced dose and frequency of administration of ETH leading to shortened therapy and reduced side effects

Acknowledgments:

Gift sample of ETH (Lupin Ltd). Amrut Mody Research Foundation (AMRF) of Bombay College of Pharmacy, Mumbai, India for financial support.

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P32 - Promising Antiulcer Therapy Using Gastroretentive Floating System Incorporating Chebulinic Acid Solid Dispersions

Sharma Arunim[1], Sharma Rahul[1], Negi Poonam[1*], Lal Ranjan Uma[2] and Gautam Surbhi[1]
School of Pharmaceutical Sciences, Shoolini University, Solan (H.P.)[1]
National Institute of Pharmaceutical Education and Research, Ahmedabad(G.J.)[2]
Email id: arunimsharma245@gmail.com

Key words:

Solvent evaporation, sodium alginate, floating raft system, Eudragit® EPO, alcohol-induced gastric ulcer model.

Background:

Terminalia chebula, a native of India is common medicinal plant used in folk

medicine like Unani, Ayurveda and Homeopathy. It is also employed as co-ingredient in

Ayurvedic formula named 'Triphala' as detoxifying agent in gastrointestinal disorders, purgative in chronicconstipation, and also helps in indigestion. Chebulinic acid (CA) is the stable hydrolyzed

product isolated from *T.chebula* and can serve as a prodrug. It is also reported to have antiulcer activity. However CA has poor aqueous solubility which limits its application as an antiulcer drug.

Objective:

The objective of the current study was to increase the solubility of CA byformulatingsolid dispersion with Eudragit® EPO and develop a Gastroretentive floating system to achieve prolonged gastric residence time to treat gastric ulcers.

Methods:

A) **Formulation development** - Solid dispersions of CA and Eudragit® EPO were prepared by solventevaporation method at different ratios. The optimum ratio of CA and Eudragit® EPO was incorporated into sodium alginate based floating raftforming system.

B) **Characterization** - Solubility of CA solid dispersions was assessed by equilibrium solubility method. The floating ability of sodium alginate raft was then evaluated by determining viscosity, density, and floating lag time. Percent cumulative drug release (%CDR)in 0.1N HCl was determined employing USP 30 rotating paddle dissolution apparatus.Theantiulcer efficacy of CA floating systems was also evaluated in the alcohol-induced gastric ulcer model in Sprague Dawley rats.

Results:

CA solid dispersions demon strated three fold increase in the solubility vis-a-vis their corresponding physical mixtures and CA, in 0.1N HCl (Figure 1A). The release of CA, in 0.1 N HCl was less than 40% in 2hrs, whereas solid dispersion ratio 1:5 showed 95.45% drug release. All the developed floating raft systems had floating lag time of less than 8 seconds, duration of floating of more than 24 hrs, density less than 1 g/mL with more than 80% of sustained drug release in 8hrs (Figure 1B). Further, the CA gastroretentive formulation showed a superior curative effect on the gastric ulcers in terms of the ulcer index compared to the standard drug omeprazole, and CA suspension.

Conclusions:

These studies have illustrated the potential use of a novel raft floating systems for a stomach-specific delivery of a poorly water soluble compound such as CA.

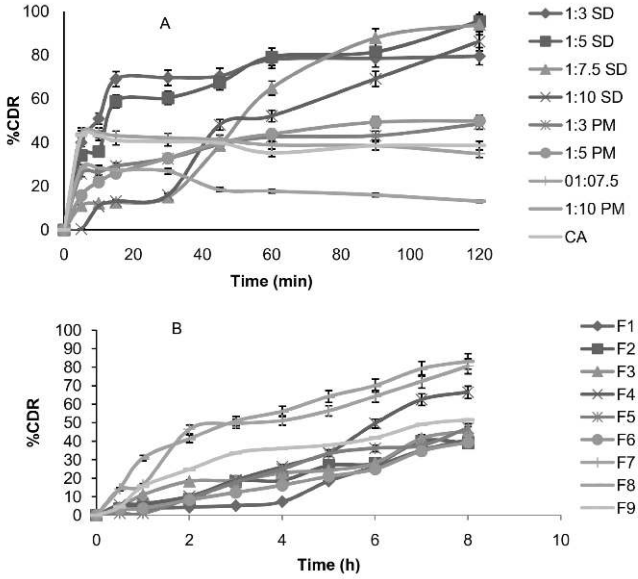

Figure 1:*Dissolution profile in 0.1N HCl A) Chebulinic acid, physical mixture and solid dispersion, B) R*aft forming formulations F1, F2, F3, F4, F5, F6, F7, F8 and F9 incorporating CA solid dispersions

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P33 - Solidification of L-SNEDDS using different methods and carriers and their *in vitro* and *in vivo* performance assessment

Kalyani Desale, Aalhate Mayur, Sameer Katiyar, Rohan Ghadi, Tushar Date, Sanyog Jain*
Center for Pharmaceutical Nanotechnology, National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar (Mohali), Punjab- 160062, India.
Email ID: kalyani.desale4@gmail.com

Keywords:

Self Nano Emulsifying Drug Delivery System, adsorption, lyophilization, solubility, oral bioavailability

Introduction:

Self Nano Emulsifying Drug Delivery Systems (SNEDDS) are helpful to resolve problems of BCS class II and IV drugs[1]. However, liquid SNEDDS (L-SNEDDS) exhibit poor compatibility and stability issues. Current study involves preparation of Solid SNEDDS (S-SNEDDS) from L-SNEDDS which overcome the limitations of L-SNEDDS as they are more stable and convenient during handling.

Methods:

Previously optimized L-SNEDDS formulations of Quercetin(Qt)[2], Tamoxifen (Tmx) and Cyclosporine A (Cyp) were prepared and solidified by adsorption and lyophilization methods with four different solid carriers i.e., Aerosil®200 (Aer), Syloid® 244FP (Syl), Neusilin® US2(Neu), Avicel PH 102 in different ratios. Among the different formulations, some of them were selected based on criteria like particle size, PDI, free flowing ability and further subjected to characterization studies like SEM, TEM, PXRD and *in vitro* release using dialysis tubing of cut off 12 kD in Simulated Gastric fluid (SGF) for initial 2 h followed by Simulated Intestinal fluid (SIF) for 6 h. Additionally *in vivo* pharmacokinetic studies were performed on female SD rat model to determine whether the prepared S-SNEDDS could increase the absorption and thereby enhanced bioavailability after oral administration.

Results:

Aer, Syl, Neu gave free flowing powders at 1:1 ratio and showed maximum loading of L-SNEDDS up to 1:2 ratio. All free flowing formulations were further studied for their reconstitution behaviour in distilled water. These formulations showed lower particle size and PDI with higher L-SNEDDS loading of selected drugs. Release studies showed that total release was comparable with L-SNEDDS, but slower and sustained release was observed in case of S-SNEDDS. Slower desorption of drug from surface and pores of carrier is the main reason behind retarded release of drug but once emulsification was done it showed promising prolonged release. Stability studies showed that formulations were robust to all dilutions and pH conditions. These studies proved better reconstitutional abilities of Aerosil 200 and Syloid S-SNEDDS. Hollow pattern in PXRD was observed indicating that pure drug in amorphous formin the S-SNEDDS may be contributingto improved solubility. SEM results revealed relatively smoother surface with pores filled with SNEDDS particles. Furthermore *in vivo* pharmacokinetic studies on female SD rat model showed increased absorption and thereby increase in bioavailability after oral administration as compared to free drugs.

Conclusion:

Adsorption method is comparable to lyophilization and is less time consuming. The developed S-SNEDDS provide combined benefits of L-SNEDDS and solid dosage form and can be conveniently used as a prototype for the development of various difficult to deliver drugs due to enhanced stability, bioavailability and processability.

Acknowledgement:

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P34 - Palmitoylated Arabinogalactan Anchored Nanostructured Lipid Carrier for Treatment of Malaria: Formulation and Characterization

Deepa U. Warrier, Dr. Ujwala A. Shinde
Department of Pharmaceutics, Bombay College of Pharmacy, Kalina, Santacruz (E),
Mumbai - 98, Maharashtra, India.
Email ID: deepawarr90@yahoo.com

Key words:

Asialoglycoprotein receptor; Palmitoylated Arabinogalactan; Molecular docking; Nanostructured lipid carriers; Box-Behnken design

Introduction:

Malaria is a complex parasitic infection caused by *Plasmodium* species. In *P. vivax* and *P. ovale* induced malaria, hypnozoites harbour in liver and skillfully remain dormant in hepatocytes resulting in relapse of Malaria which could be fatal. Asialoglycoprotein receptors (ASGPR) are primarily expressed on hepatocytes which can be exploited for targeting and internalization of Primaquine (PQ) to treat liver stage Malaria. Objective of present project is to apply QbD approach for formulation development of nanostructured lipid carriers (NLCs) and evaluate release profile using various *in vitro* release techniques.

Methodology:

Lipid conjugated ligand for hepatocyte targeting was selected by molecular docking studies by means of Maestro Schrodinger software 2014-2. Palmitoylated arabinogalactan [PAG] was synthesized and characterized for physical spectroscopic techniques. PQ was selected as model drug and solid lipids, liquid lipids and surfactants were screened for solubility of PQ. PQ loaded NLC dispersions were prepared by melt homogenization technique followed by high pressure homogenization. Risk assessment approach was applied to screen various formulation parameters. Using Box-Behnken experiment design optimized NLC dispersions were obtained. The optimized NLCs were evaluated for particle size, polydispersity index, zeta potential, drug loading and percent entrapment efficiency. The *in vitro* release profiles were investigated using dialysis sac, sample and separate and USP Type 4 method.

Results and discussion:

Docking score of Arabinogalactan (AG) and PAG were -7.17 and -6.3 respectively indicating no significant conformational changes in AG after conjugation with palmitoyl chloride (PC). In FTIR spectrum of PAG, bands at 1745.26 cm^{-1} and 1160.94 cm^{-1} indicate formation of ester bond between the hydroxyl group of monosaccharide unit of AG and carboxyl group of PC. ^{1}H NMR and ^{13}C NMR spectroscopy confirmed intact nature of carbohydrate backbone of AG. PQ showed maximum solubility in oleic acid and Precirol ATO 5. Tween 20 was selected as surfactant. Particle size of optimized formulation was found to be 145.68 nm with zeta potential of -34 mV, PDI 0.25. The formulations exhibited 3.4% drug loading and 79% entrapment efficiency. *In vitro* drug release was achieved for upto 72 h with 88.74% drug release by the dialysis sac method. The sample-separate method was not able to discriminate the dissolution profile of the formulations.

Conclusion:

Thus, within the scope of experimental design the PAG anchored NLCs were developed using Box-Behnken design. Applicability of developed formulation will be further proved with *ex vivo* uptake and toxicity studies, *in vitro* and *in vivo* anti-malarial efficacy and pharmacokinetic studies.

Acknowledgments:

We express our sincere thanks to Mr. Anantha Krishnan and Dr. K. Gunasekaran, at Centre of Advance study in crystallography and biophysics at University of Madras for helping in molecular docking studies. We would like to thank Gattefosse India Pvt. Ltd. and Ipca Lab. Pvt. Ltd. for providing the gift samples of Precirol ATO 5 and Primaquine Phosphate respectively. We thank Punjab University for NMR spectroscopy analysis and MKR Lab. Mumbai for providing FTIR analysis.

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P35 - Improved Dissolution of Amorphous Solid Dispersion of Celecoxib by preparing Barrier Coated Drug Layered Particles

Kavya Reddy. A, Amanpreet Kaur, Vibha Puri, Ajay K Dantuluri, Arvind Kumar Bansal
Department of Pharmaceutics, NIPER, Sector-67, S.A.S Nagar, Mohali, 160062, India
Email ID : kavyaadullareddy@gmail.com

Key words:

Amorphous solid dispersion, celecoxib, Wurster process, devitrification.

Introduction:

Amorphous Solid Dispersion (ASDs) has been used to enhance stability, aqueous solubility and dissolution of amorphous APIs. High polymer content, solid phase transformation, compositional changes during dissolution lead to poor dispersibility and compromised drug release. Higher molecular mobility at the free surface is one of the reasons for devitrification. We thus proposed barrier coated ASDs (or amorphous drug layered particles; ADLPs as shown in fig. 1) for improving dispersibility, dissolution and inhibiting surface crystallization of ASDs.

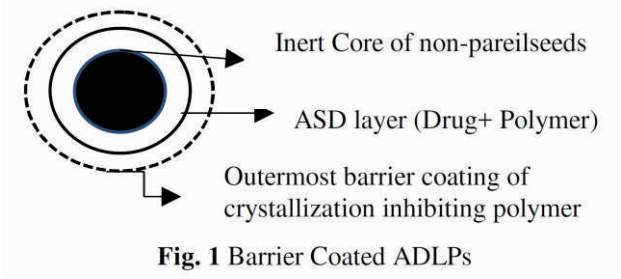

Fig. 1 Barrier Coated ADLPs

Materials and Methods:

Celecoxib (CEL; BCS Class II drug), polyvinyl pyrrolidine (PVP-K 29/32), meglumine (MEG), Microcrystalline Cellulose particles (200-350µm), Polyvinyl Alcohol (PVA), polyvinyl acetate phthalate (PVAP) and inulin for barrier coating and Methanol as spray solvent. ADLPs were prepared by Wurster process with loading efficiency of 31% w/w, bed temperature-30°C-32°C, spray nozzle diameter-0.3mm, atomization air pressure-0.8bar, feed rate-0.5ml/min and air flow-0.1bar. PXRD and DSC were used to check solid state of CEL in ADLPs, drug-polymer interactions (outer coat) were simulated *in situ* in DSC by quench cooling Amorphous Celecoxib Solid Dispersion (ACSD; uncoated particles) followed by spreading uniform layer of polymer and check for change in T_g using mDSC. Dissolution was carried out for uncoated particles and ADLPs using USP type-II apparatus operated at 50rpm, in 1000 mL of water (non-sink) and pH 12 (0.04 M tribasic sodium phosphate; sink media) buffer, at 37±0.5°C.

Results:

Uncoated and barrier coated ADLPs exhibited halo pattern in PXRD, confirmed by single Tg at 69.9°C in DSC. In uncoated particles, hydrophobic intermolecular interactions between CEL and PVP reduced their diffusivity into dissolution media and rather formed crosslinked plug due to partial interactions of PVP with water and CEL. Thus, their dissolution behavior was closely related to crystalline form. In ADLPs barrier coating showed greater affinity towards water and exhibited rapid dispersibility, increased effective surface area and faster dissolution (Fig. 2). The mechanism involved was drug-polymer mixing at the interface. In DSC, in situ, ACSD showed Tg of 65.4°C, but spreading of polymer layer onto it, led to significant increase in Tg in the order of Inulin:70.5°C<PVA:68°C=PVAP:68.3°C.

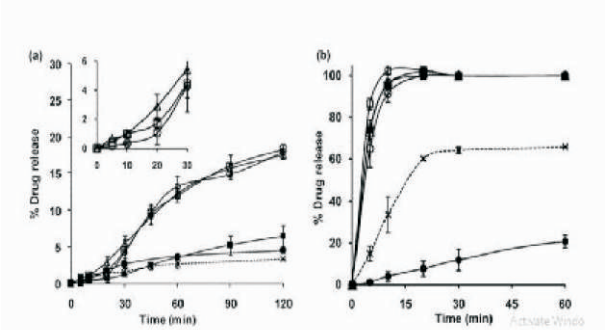

Fig. 2 Difference in the drug release profiles of both uncoated and coated forms of ASD usingdifferentpolymers

Conclusion:

Barrier coating successfully prevented surface recrystallization of ACSD of CEL and yielded high dispersing and faster dissolving ADLPs.

Acknowledgement:

Authors would like to thank 'NIPER, S.A.S Nagar' and 'ICMR' for providing necessary infrastructure and financial support.

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P36 - Application of Physiologically Based Pharmacokinetic (PBPK) modeling to understand the effect of Particle Size Distribution (PSD) on biopharmaceutical performance of Fenofibrate (FNT) nanosuspensions

Vaibhav Punjabi, Divisha Jain, Poonam Singh Thakur, Samarth D Thakore, Arvind K. Bansal.
Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar, Punjab.

Keywords:

Fenofibrate, Biorelevant dissolution method(s), Nanosuspension, Media milling, GastroPlus™

Introduction:

In the recent past, a triad of *in-vitro*, *in-vivo* and, *in-silico* studies have emerged as the centerpiece of pharmaceutical drug development.[1] The utility of this triad has also been explored for understanding *in-vivo* dissolution behavior of various solid forms of active pharmaceutical ingredient like cocrystals, and amorphous form.[2] The current study was aimed to assess the utility of PBPK modeling to understand the impact of PSD on biopharmaceutical performance of FNT nanosuspensions.[3]

Method:

The nanosuspensions with three different PSD (i.e. B1, B2, and B3) were generated using media milling. Micronized-FNT (MFNT) and Tricor® (control) were used for the study. Samples were characterized for PSD using Zetasizer®. Kinetic solubility of FNT was determined in Fasted-state simulated intestinal fluid v2 (FaSSIF v2) using shake-flask method. Dissolution studies of the samples (equivalent to 148 mg of FNT) were performed using USP II apparatus with 500 mL of FaSSIF v2. Permeability and cellular uptake studies (% absorption and desorption)were performed using CaCo-2 cell lines, which were the part of nanosuspensions and Tricor®. Surfactants (viz. sodium lauryl sulfate and dioctyl sulfosuccinate) were used with MFNT during CaCo-2 studies. Oral bioavailability studies were performed in Sprague-Dawley rats, at a dose of 15 mg/kg. Simulations studies were carried out using GastroPlus™, where experimental data was incorporated and absorption rate constant for FNT was optimized to obtain the best fit to the observed plasma concentration-time profile (PCTP) for MFNT. The optimized model was used for prediction of PCTP of nanosuspensions and Tricor®.

Results:

Particle size (Z_{avg}) was found to be 215±12nm, 537±53 nm, and 838±72 nm for B1, B2, and B3, respectively. Kinetic solubility (t=240 min) was 0.25, 0.28, 0.28, 1.25, 1.30 µg/mL for MFNT, B3, B2, Tricor® and B1, respectively. B1 and Tricor® showed statistically significant % dissolution as compared with MFNT, B2, and B3. Surfactants improved the permeability of MFNT due to enhanced dissolution, as a result of wetting. B1 showed the lowest permeability due to high initial concentration in the donor compartment. B1 demonstrated the lowest % desorption amongst the studied samples, which could be due to cellular localization of FNT. The optimized model successfully predicted PCTP for B2 and B3, while the predictions were not consistent with the observed PCTP for B1 and Tricor®. The latter could be due to mucoadhesion and cellular entrapment of FNT.[4]

Conclusion:

FNT nanosuspensions demonstrated superior biopharmaceutical performance as compared with MFNT, while B1 was comparable with Tricor®. PBPK model coupled with cellular uptake studies suggested the presence of additional absorption mechanisms for nanosuspensions with size below 500 nm.

Acknowledgment:

We would like to thank Director, NIPER, S.A.S. Nagar for providing facilities to perform the study.

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P37 - Wettability and Surface chemistry of Crystalline and Amorphous forms of a Poorly Water Soluble Drug

Prakruti Shah, Prashant kumar K. Parmar, Vibha Puri, Arvind K. Bansal*
Department of Pharmaceutics, NIPER, S.A.S. Nagar, India
Email ID: prakruti260gmail.com

Key words:

Celecoxib, wettability, surface free energy, water vapour sorption, surface chemistry

Introduction:

Particle wetting is a preconditioning phenomenon for processes such as dispersion, disintegration, solubilization and dissolution of poorly water-soluble drugs and is primarily dependent on powder surface energetics. The purpose of the present study was to compare energetics of wetting behaviour of amorphous and crystalline forms of Celecoxib (CEL) and correlate it to their surface molecular environment.

Method:

Amorphous CEL was prepared by spray drying and stored in desiccator at 25 ℃ and 0% RH. Various techniques such as sessile drop contact angle measurement, was used for wettability; and surface free energy measurements, specific surface area, isothermal nanocalorimetry were used for water vapor sorption energetic; and x-ray photoelectron spectroscopy (XPS) was used for determination of surface chemistry.

Results and discussion:

Significant differential wetting values were observed for amorphous and crystalline CEL, with various probe liquids and dissolution media. Further, amorphous CEL showed an improved wetting with dissolution media in order of phosphate buffer pH 12 >FSSGF (Fasted state stimulated gastric fluid) +SLS> FSSGF+TXR (Triton X 100®) in comparison to crystalline CEL. Thus, above results bring forward the impact of exposed surface groups, their density, molecular orientation and interfacial interactions at the surface. The crystalline CEL surface primarily showed dispersive surface energy, while the amorphous CEL showed slightly reduced dispersive surface energy and a small additional polar surface energy (4.8 mJ/m^2). Water vapour sorption studies showed that amorphous CEL has high differential heat of absorption of water (155.04 kJ/mol) indicating hydrogen bond interactions with polar energetic sites and water molecules, while crystalline CEL gave no measurable heat of absorption which indicates inertness to water sorption. The surface chemistry determination by XPS revealed that higher surface polarity of amorphous CEL could be linked to its greater oxygen-to-fluorine surface concentration ratio 1.27. The crystallographic studies of the preferred cleavage plane (0 2 0) of crystalline CEL further supported its higher hydrophobicity.

Conclusion:

The amorphous and crystalline CEL exhibited disparate surface properties which attributed towards different degree of interaction with water molecules, wettability with polar liquids, heat of sorption and additionally govern their interaction with different dissolution media which could consequently impact their biopharmaceutical performance.

Acknowledgement:

Authors would like to thank 'NIPER, S.A.S Nagar' and ICMR for providing necessary infrastructure and financial support.

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P38 - Melt granulation: An approach to increase the Dissolution properties of a poorly soluble diuretic, Furosemide

Ketki P. Bhurkunde, Pooja B. Rathod and Namita D. Desai
C.U. Shah College of Pharmacy, SNDT Women's University, Santacruz (W), Mumbai 400049
Email ID : bketki1992@gmail.com

Keywords:

Furosemide, melt granulation, PEG 4000, Syloid 3150 XDP, *in vitro* dissolution

Introduction:

Melt granulation is a solid dispersion technique for enhancing the solubility and bioavailability of poorly water soluble drugs. The technique involves solubilization of drugs using molten carriers which also function as meltable binders. The drug dissolves in the molten binder during processing and the solid carrier acts as an adsorbent for the melt providing high surface area for dissolution and thus enhancing the dissolution rate.[1,2] Furosemide, a BCS Class IV drug shows dissolution rate limited absorption requiring variable doses, clinically. The objective of the present investigation is to enhance the dissolution properties of Furosemide (20 mg) using the technique of melt granulation.

Methodology:

Ultraviolet spectrophotometric method for Furosemide in Methanol AR and phosphate buffer, pH 5.8 was developed and validated for determination of drug content and *in vitro* release studies respectively. Various meltable carriers such as PEG 4000, Glyceryl monostearate, Gelucires, etc were screened for their solubilizing capacity of Furosemide by microscopic evaluation. Various solid carriers such as Syloid 244 FP, Syloid XDP 3150, Sylysia 770 FCP were screened for their adsorbing capacity of drug lipid melt by determining angle of slide. The selected meltable carrier was heated to 5^0 C above its melting point and Furosemide was incorporated to obtain a molten mass. The solid carrier was incorporated and the blend was passed through sieve 30 # to obtain granules that were filled into hard gelatin capsules (Size 4). The developed capsules were evaluated for *in vitro* drug release and other quality control parameters. The *in vitro* drug release was determined using Electrolab TD-06L, USP standard dissolution tester, apparatus II, 50 rpm at 37 ± 0.5^0 in 900 ml of phosphate buffer, pH 5.8. Aliquots were withdrawn at specified time intervals and the amount of drug released at each time point was measured using UV spectroscopy.

Results and Discussions

PEG 4000 was selected as meltable carrier amongst screened carriers for maximum solubility of Furosemide when confirmed for absence of drug crystals by optical microscopy. Syloid 3150 XDP was selected as solid carrier amongst all carriers as it exhibited improved flow properties when angle of slide was determined. The *in vitro* dissolution studies showed enhancement in dissolution rate of Furosemide due to solubilization of the drug in PEG 4000 melt which was confirmed by DSC. At the end of 60 minutes, in *in vitro* dissolution study, 63% of plain Furosemide dissolved while 93% of Furosemide dissolved from the melt granulated formulations.

Conclusions:

Thus, capsules containing Furosemide were successfully prepared by melt granulation technique with PEG 4000 as the meltable binder and Syloid 3150 XDP as solid carrier and showed improved dissolution in *in vitro* release studies. This can be promising, industrially feasible approach to improve oral bioavailability of poorly soluble drugs.

Acknowledgements:

Intas Pharmaceuticals, Gattefosse India (P) Ltd, Grace Materials Ltd., ACG Associated Capsules Ltd.

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P39 - Topical Microspheres for Sustained Release of Norfloxacin in the treatment of Wounds

Hetal B. Karvir., Rutuja S. Kalokhe and Namita D. Desai
C. U. Shah College of Pharmacy, SNDT Women's University, Mumbai 400 049
Email ID: hetalkarvir20@gmail.com

Keywords:

Wounds, Norfloxacin, topical microspheres, quasi-emulsion solvent diffusion, sustained release

Introduction:

Delayed wound healing is one of the major therapeutic challenges and there is a need to explore novel therapies for wound healing. Norfloxacin due to its proven antibacterial activity can act as an adjunct in wound healing process. Microspheres of Norfloxacin (1% w/w) for topical delivery can enhance its wound healing potential.

Methodology:

Analytical methods for Norfloxacin were developed by UV-visible Spectrophotometry and validated. Norfloxacin microspheres were prepared by quasi-emulsion solvent diffusion method using Ethocel (4 cps); Eudragit RLPO as polymers, Ethanol: Dichloromethane as solvents and polyvinyl alcohol as stabilizer. Norfloxacin microspheres were incorporated into Carbopol Ultrez 10 NF as gel base. The developed topical gel was evaluated for quality control parameters, *in vitro* drug release, *ex vivo* permeation and deposition studies in rat abdominal skin. *In vitro* antibacterial activity of the developed gel was evaluated using *Staphylococcus aureus* and *in vivo* wound healing efficacy of the gel was evaluated in Wistar rats. (Protocol No. CUSCP/IAEC/10/2018)

Results and Discussion:

Norfloxacin microspheres were observed to be spherical with 84.88 % drug entrapment with particle size of 25 – 100 µm. The *in vitro* release study of Norfloxacin microspheres through dialysis membrane using 100 mL Simulated Wound Fluid, pH 7.4 at 50 rpm showed release of 53.31 ± 2.87 % while developed topical gel showed release of 42.70 ± 2.00 % at the end of 8 hours indicating sustained drug release from developed formulations that can be proposed to be useful in healing of infected wounds. The particle size, drug content and spreadability of developed topical gel was found to be 35 – 100 µm, 98.85 ± 0.020% and 1495 ± 2.961g.cm/sec respectively. *Ex vivo* permeation and deposition studies through rat abdominal skin using Franz Diffusion cells with 20 ml of Simulated Wound Fluid, pH 7.4 showed slower permeation and twice the drug deposition from the developed gel when compared to the conventional gel at the end of 8 hours suggesting suitability in treating infected wounds due to slow localized drug delivery. In the *in vitro* antibacterial study using Staphylococcus aureus, Norfloxacin microspheres showed smaller zone of inhibition than pure drug, indicating sustained drug release. Animal studies showed absence of oedema and erythema after topical application and the developed microspheres based topical gel had greater efficacy to contract open wounds (100% at the end of 12 days) than Norfloxacin conventional gel (77.77% at the end of 12 days) and blank formulation (62.99% at the end of 12 days).

Conclusions:

The developed Norfloxacin topical gel can provide sustained and localized drug release due to enhanced skin deposition, thereby improving healing efficacy especially in infected wounds.

Acknowledgements:

Macleods Pharmaceuticals Ltd., India, Colorcon Asia Pvt. Ltd., Evonik India Pvt. Ltd, Lubrizol India.

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P40 - Solubility Enhancement by Multicomponent Crystal Engineering

Sanjay S. Pekamwar, Deepak A. Kulkarni, Balaji W. Matore
School of Pharmacy, S.R.T.M. University, Vishnupuri, Nanded- 431606, India.
Email ID: deepakkulkarni68@gmail.com

Keywords:

Solubility, Cocrystal, Bioavailability, Aceclofenac, Cocrystal former (CCF)

Introduction:

Solubility is the key parameter for the development of any pharmaceutical dosage form. Poor water solubility of BCS class-II and BCS class-IV drugs is a challenge for the development of pharmaceutical dosage forms. Bioavailability limitation is also the problem with poorly water soluble drugs.[1] An attempt was made to enhance the solubility of Aceclofenac with multicomponent crystal engineering. Aceclofenac (ACF) is a BCS Class-II nonsteroidal anti-inflammatory drug (NSAID) which is slightly soluble in water.

Objective:

Objective of this study was to improve aqueous solubility of ACF by cocrystallization and thereby enhance its bioavailability; further it was also desired to improve the flow and compressibility index.

Method:

Cocrystals were prepared by neat grinding method using ACF and different conformers in 1:1 stoichiometric ratio using ten different conformers. The drug and cocrystal formers were blended together and subjected to grinding in mortar and pestle for 20 minutes to prepare cocrystals.[2] Prepared cocrystals were screened for their solubility in water at 25^0C by saturated solubility determination method. Differential Scanning Colorimetry (DSC), X-ray diffraction (XRD) and Raman spectroscopic analysis of ACF and ACF-salicylic acid cocrystal was carried to interpret the formation of cocrystal.[3]

Results and Discussions:

After screening of all ACF cocrystals prepared with 10 different coformers, which was confirmed by the Raman spectroscopic, XRD and DSC evaluation. Further, solubility enhancement was evident (Fig 1); cocrystals prepared with salicylic acid exhibited maximum solubility of ACF in water was 309.23 µg/ml and solubility of ACF-salicylic acid cocrystal was found to be increased by seven folds, i.e. 2424.61 µg/ml. ACF-benzoic acid cocrystals also showed marked improvement in solubility, which was four-fold, i.e. 1478.46 µg/ml.

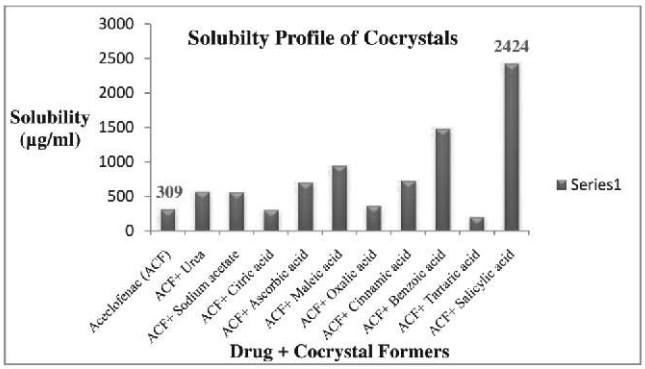

Fig. 1: Solubility profile of different cocrystals.

Conclusion:

Cocrystallization is a promising technique for solubility enhancement of poorly water soluble drugs without any interference in chemical properties and biological activity of drug. Improvement of flow and compressibility is an additional advantage of implementing cocrystallization for solubility improvement. The solubility of ACF was significantly increased after cocrystallization with salicylic acid which can further achieve improvement in bioavailability.

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P41 - Suitable Release Media Design and Application for Novel Formulation of Gefitinib

Purva N. Churi, Sharayu R. Govardhane, Namita D. Desai, Prachi C. Mehendale
C. U. Shah College of Pharmacy, SNDT Women's University, Mumbai - 49, Maharashtra, India
Email ID: purva.churi31@gmail.com

Keywords:

Dry Powder Inhaler, Gefitinib, liposomes, anti-cancer

Introduction:

Lung cancer being most fatal type of cancer needs urgent attention towards targeting the drug via localized drug delivery system. Liposome being safest of all drug delivery systems due to its composition was chosen for targeting locally as a dry powder inhalation (DPI) system. It is very important to determine amount of drug released from the system using a suitable dissolution media. Gefitinib, an EGFR tyrosine kinase inhibitor is sparingly soluble in aqueous buffers and soluble in organic solvents. Hence, to determine amount of gefitinib released from the developed formulation, suitable release media need to be designed by modification of the generally used aqueous buffers; phosphate buffer pH 7.2 and lung simulated fluid pH 5.2. Approaches used to modify the buffer includes incorporation of surfactants, water miscible organic solvent such as alcohol and use of water immiscible organic solvent and choice of approach depends on the maintenance of sink conditions. In the present work release media was modified with the use of surfactant and/ or addition of water miscible organic solvent. UV spectrophotometric method for quantification of amount of gefitinib released was developed in the modified release media and applied to determine the amount of gefitinib released in modified dissolution media.

Methodology:

Liposomes of gefitinib were formulated using ethanol injection method and were converted into DPI using lactose as carrier by spray drying method. For *in-vitro* release study two different media viz. phosphate buffer pH 7.2 and lung simulated fluid pH 5.2were modified to obtain the desired solubility with the maintenance of sink conditions. Modification was done based on the solubility of gefitinib in various organic solvents as well as in the chosen media. Gefitinib was found to show desired solubility in alcoholic media and hence method was developed and validated in alcoholic phosphate buffer 50:50% v/v (pH 7.2) and alcoholic lung simulated fluid 40:60% v/v (pH 5.2). The release study in both the media was performed for Gefitinib-loaded liposomes, Gefitinib DPI as well as for Gefitinib liposomal DPI using dialysis bag (molecularwt cut off 12- 14 kDa) and volume of media 100 ml.

Results and discussion:

The analytical method developed using both mediawas found to be linear in the concentration range 2- 12 mcg/ml at $\lambda_{max}$of 333.5 nmwith linearity equation Y= 0.0446X + 0.0761for alcoholic phosphate buffer pH 7.2 and Y= 0.0513X + 0.0169for alcoholic lung simulated fluid pH 5.2. Both the methods were found to be precise and accurate with % recovery of about 98- 102%.The % gefitinib released from Gefitinib-loaded liposomes, Gefitinib DPI and Gefitinib liposomal DPI was found to be 76.26±1.2%, 75.25±1.2% and 69.58±0.5% respectively in alcoholic phosphate buffer 50:50% v/v pH 7.2, (which mimics lung fluid pH),whereas in alcoholic simulated lung fluid 40:60% v/v pH 5.2 (mimicking alveolar pH)the release was found to be 69.56±0.9%, 74.85±0.2% and 65.65±0.8% respectively. Gefitinib liposomal DPI showed prolonged release for upto 24 hrs, as compared to that of conventional DPI, where thedrug releasedfor upto 3 hrs only.This reveals that developed method as well as modified media are appropriate for determining the release profile for each formulation.

Conclusion:

Gefitinib liposomal DPI has shown controlled release of drug and prolonged duration in modified dissolution media which indicate that the release of drug may occur at surface of lung as well as when drug enters into the alveoli.

Acknowledgements:

Naprod Life Sciences Pvt. Ltd. (Mumbai).

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P42 - Systematic Development of Oral Solid Lipid Nanoparticles for Delivery of Raloxifene with Enhanced Biopharmaceutical Attributes

Atul Jain[1], Teenu Sharma[2], Rajendra Kumar[1], O P Katare[2], Bhupinder Singh[1,2*]
[1]National UGC Centre of Excellence in Application of Nanomaterials, Nanoparticles, and Nanocomposites (Biomedical Sciences), Panjab University, Chandigarh, India
[2]University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Studies, Panjab University, Chandigarh, India
atuljaindops@gmail.com; bsbhoop@yahoo.com

Keywords:

Breast cancer, Lipid nanoparticles, Design of Experiments (DoE), Cell culture studies, Biopharmaceutics

INTRODUCTION:

Raloxifene hydrochloride, a second-generation selective estrogen receptor modulator, has been approved for the management of breast cancer. However, it exhibits poor (~2%) oral and inconsistent bioavailability in humans, ascribable to its low aqueous solubility, extensive first-pass metabolism, P-gp efflux and pre-systemic glucuronide conjugation. Solid lipid nanocarriers (SLNs), with particle size in the range of 50 to 1000nm have demonstrated with high potential to overcome solubility and bioavailability problems of various drug molecules belonging to BCS class II.

Aim:

The present research work encompasses the systematic development and evaluation of SLNs of RLX for its enhanced biopharmaceutical performance to treat breast cancer.

Methods:

Factor screening studies were conducted using Taguchi design, followed by optimization studies employing Box-Behnken design. Preparation of SLNs was carried out using glyceryl monostearate, Compritol® 888 ATO, Phospholipid S-100 and TPGS-1000 employing solvent diffusion method. The optimized formulation was characterized for mean particle size, zeta potential, field emission scanning electron microscope (FESEM), Transmission electron microscopy (TEM). *In vitro* release studies were conducted employing dialysis bag diffusion method using a magnetic stirrer at 50 rpm with 0.1% Tween-80 as dissolution medium. Further, cell cytotoxicity assay, apoptosis assay and cell uptake studies were carried out to evaluate the *in vitro* anticancer activity of the developed optimized formulation. *In vivo* pharmacokinetic studies after oral administration in **Sprague-Dawley** rats and subsequent histopathological examination were also carried out to evaluate the therapeutic and toxic profiles of the developed formulation, respectively.

Results:

The prepared optimized SLNs formulations exhibited an average particle size of 113 nm and zeta potential of 13mV. *In vitro* dissolution profile of the optimized formulation showed Fickian release (n=0.29). The *in vitro* cell line studies like cell cytotoxicity assay (6-folds), apoptosis assay (5.4-folds) and cell uptake (10-folds) indicated quite superior efficacy of RLX-SLNs *vis-a-vis* pure RLX. Besides, the pharmacokinetic studies indicated significantly improved biopharmaceutical performance of RLX-SLNs *vis-a-vis* pure drug, *viz.,* 4.06-folds in $C_{max,}$ 4.39-folds in $AUC_{(0\text{-}72h)}$, 1.53-folds in $K_{a,}$ 2.12-folds in $T_{1/2}$and 1.21-folds in t_{max}.

Conclusions:

Results obtained from the different *in vitro* and *in vivo* studies construe promising anticancer potential of the developed RLX-SLNs, thereby ratifying the lipidic nanocarriers as an efficient drug delivery strategy for improving the biopharmaceutical attributes of RLX.

Acknowledgements:

The authors express their gratitude to UGC, New Delhi, India, for providing necessary financial assistance to the National UGC Centre of Excellence in Nano Biomedical Applications, Panjab University, for pursuing the present research work.

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P43 - Development and Characterization of Nebulised DPPC-Chitosan Nanoparticles of Voriconazole with Modulated Dissolution Profile

Ranjot Kaur[1], Kamalinder K Singh[2], Mandip Sachdeva[3], Anupama Sharma[4], Bhupinder Singh[1,5]*
[1]Univ. Inst. of Pharm. Sciences (UIPS), Panjab University, Chandigarh, India
[2]University of Central Lancashire, Preston, United Kingdom
[3]College of Pharmacy, Tallahasee, Florida A&M, USA
[4]Dr. S. S. Bhatnagar UICET, Panjab University, Chandigarh, India
[5]UGC Centre for Excellence in Nano-Biomedical Applications, Panjab University, Chandigarh
Email ID : ranjotkaur92@gmail.com; bsbhoop@yahoo.com

Keywords:

Phospholipid, Nebulization, Sustained drug release, Aspergillosis, Quality-by-Design.

Introduction:

Pulmonary aspergillosis (PA) represents one of the major lung infections that have raised concern in clinical healthcare [1]. The major limitation associated with conventional therapy of PA is inadequate biodistribution to other vital organs, besides lungs, causing severe adverse effects. Despite the notable potential of inhalation route in delivering drugs directly to lungs it suffers from limitations of rapid clearance from the lungs [2]. The current study, aimed to develop nanostructured systems employing mucoadhesive polymer(s) and a high-transition temperature lipid to sustain drug release and prolong drug retention in lungs. Voriconazole (VRC), a BCS class 2 drug with log P value of 1.8 was used as a model drug used in the study.

Methods:

Dipalmitoylphosphatidylcholine surface-modified chitosan (DCH) nanoparticles (NPs) were prepared by ionic gelation, following by their systematic optimisation. Factor screening studies were performed using fractional factorial design, followed by optimization of the NPs by Box-Behnken design. The NPs were optimized taking particle size, polydispersity index, zeta potential, entrapment efficiency and drug release studies in PBS 7.4 as the pivotal CQAs. *In vitro* drug release studies of VRC and DCH NPs were conducted using dialysis sac method. The NPs (equivalent to 1 mg of VRC) were placed in the dialysis membrane (12 kDa), tethered at both the ends and suspended in 20 mL of the dissolution medium, *i.e.,* phosphate buffered saline (PBS 7.4) containing 0.1% Tween 80, in order to maintain the sink conditions at 37 ± 0.5 °C at 50 rpm.

Results:

The optimized DCH NPs were found to have a particle size of 240-260 nm, PDI of 0.3-0.4, zeta potential of 8-11 and entrapment efficiency of 50-60%. Drug release studies showed negative influence of surfactant, while polymer and crosslinker exert positive influence on controlling the release rate of VRC. Smaller the size of NPs, the faster was the release rate owing to lower diffusion path length travelled by the drug in the former case. More than 90% of VRC was released in 4 h, while developed DCH NPs sustained the drug release, when observed for 48 h (81.1 ± 1.6 %) with initial burst release for 2 h (33.1 ± 2.3 %). Drug release showed best fit into the Korsmeyer-Peppas model (R=0.9883) with the value of diffusional release exponent (0.294) being less than 0.45, indicating drug release to be primarily governed by Fickian mechanism.

Conclusion:

Overall, the study describes the potential of DCH NPs for sustaining the drug release of VRC *in vitro.* Future research will be focused on evaluating its retention time in lungs using validated animal models.

Acknowlegements:

University Grants Commission, India, and Commonwealth Scholarship Commission, UK, are gratefully acknowledged for providing financial grants for the research work.

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P44 - QbD-Enabled Development of Supersaturated LFCS Type III Self-Microemulsifying Oily Formulations of Sorafenib Tosylate with Improved Biopharmaceutical Performance: Imminent Role of Drug Dissolution Kinetics and IVIVC

Teenu Sharma[1], Atul Jain[2], Om Prakash Katare[1], Rajan Swami[1], Bhupinder Singh[1,2]*

[1]University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Studies, Panjab University, Chandigarh, India

[2]National UGC Centre of Excellence in Application of Nanomaterials, Nanoparticles, and Nanocomposites (Biomedical Sciences), Panjab University, Chandigarh, India

Email ID : teenu88sharma@gmail.com; bsbhoop@yahoo.com

Keywords:

Supersaturated SMEDDS, LFCS type-III, Rescigno indices, Cytotoxicity, Drug release kinetics.

Introduction:

Sorafenib tosylate (SFN), a tyrosine kinase inhibitor, is recognized as an important drug for treatment of various cancers, including hepatocellular carcinoma (HCC), renal carcinoma, and thyroid cancer. Lately, it has become the first-line drug for patients with advanced HCC. However, the clinical use of SFN is limited by its low (~8.4%) and inconsistent oral bioavailability, primarily owing to its poor aqueous solubility, and high presystemic hepatic metabolism and efflux by permeability glycoprotein (P-gp).

Aim:

To investigate the potential of lipid formulation classification system (LFCS) Type III self microemulsifying oily formulations (SMEOFs) for SFN in ameliorating its biopharmaceutical performance following oral intake employing the systematic approach of Quality by Design (QbD).

Methods:

Factors creening studies employing Taguchi OA design facilitated the selection of apt lipid, surfactant and cosolventas critical material attributes (CMAs) for the preparation of LFCS Type III SMEOFs. D-optimal mixture design was employed to obtain the optimized formulation, viz., OPT-SMEOFs, which were subsequently supersaturated to obtain Sat-OPT-SMEOFs, employing a blend of HPMC and PVP as polymeric precipitation inhibitors. Dissolution studies were carried out using USP Apparatus 2 employing 5.0%w/v SLS as the dissolution medium. Further, *in situ* perfusion studies and pharmacokinetic studies were carried out in Wistar rats, besides the uptake studies using Caco-2 cell lines.

Results:

Comparison in dissolution profiles of OPT-SMEOFs and Sat-OPT-SMEOFs was made using Rescigno index (1 and 2), with values of nearly 0.022, indicating quite similar mean dissolution profiles. However, the value of 1 and 2 were more than 0.890 when the release profiles of both the developed formulations were compared to pure drug, indicating quite slower and lower drug release at each dissolution time point. Further, the drug release kinetic model fitting reflected Fickian drug release mechanism from both the developed formulations with release exponent (n) of 0.315 and 0.310 for OPT-SMEOFs and Sat-OPT-SMEOFs, respectively. OPT-SMEOFs and S-OPT-Type III also exhibited superior uptake by Caco-2 cells. *In situ* perfusion and *in vivo* pharmacokinetic studies in rats also revealed significant improvement in drug permeability and absorption parameters, as well as in pharmacokinetic parameters from OPT-SMEOFs *vis-à-vis* pure drug suspension. Prevalence of statistically valid level A IVIVC for OPT-SMEOFs, Sat-OPT-SMEOFs and pure drug substantiated high degree of prognostic ability of *in vitro* dissolution conditions (medium, stirring, etc.,) in predicting the *in vivo* biopharmaceutical performance.

Conclusions:

Overall, the current research work reports successful and systematic development of Sat-OPT-Type III SMEOFs of SFN with significantly improved *in vitro* dissolution and *in vivo* biopharmaceutical attributes.

Acknowledgement:

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P45 - Development and Evaluation of Lipocomplex-loaded Self Nanoemulsifying Lipidic Systems of Lumefantrine with Improved Dissolution Profile

Vishav Mohan[1], Ripandeep Kaur[2,3], Ranjot Kaur[1], Varun Gorki[4], Bhupinder Singh[1,2*]
[1]Univ. Inst. of Pharm. Sciences, Panjab University, Chandigarh, India;
[2]UGC Centre for Excellence in NanoBiomedical Applications, Panjab University, Chandigarh, India
[3]University of Salford, Manchester, UK
[4]Department of Zoology, Panjab University, Chandigarh, India
Emai ID: vishavmohan12345@gmail.com; bsbhoop@yahoo.com

Keywords:

Phospholipid, Quality-by-Design, Drug Release, Malaria, SNEDDS.

Introduction:

Lipid-based nano-formulations have been employed to enhance drug absorption from GI tract by facilitating dissolution of drug, bypassing hepatic first-pass effect and P-gp effluxing mechanism, and improving drug permeability [1]. Lumefantrine (LF) is an active antimalarial schizonticide against various *Plasmodium* strains, especially *Plasmodium falciparum*. However, its activity gets impeded owing to very low aqueous solubility (0.02µg/mL) and consequently poor oral bioavailability (12%) in man [2]. The present research, therefore, focuses on developing a lipocomplex of LF, with potential to enhance its solubility and dissolution profile.

Methods:

Three different types of phospholipids were employed for formulation of the complex by rota evaporation and the consequent complex was loaded into the self-nanoemulsifying lipidic formulation, systematically optimized using D-Optimal mixture design. Amounts of lipid, surfactant and cosolvent were taken as critical material attributes, while critical quality attributes were globule size, emulsification time and drug release profile. Drug Dissolution Apparatus II USP (Paddle) was used to carry out the drug release studies on LF and its formulations using simulated gastric fluid (pH 1.2) at 37°C at 100 rpm. The developed complex of LF was evaluated for solid state characteristics through FTIR, X-RD and hot stage microscopy.

Results:

The developed formulation was found to be influential in improving the loading efficiency of LF (1.78-folds) and in inhibiting the *in vitro* precipitation of LF. The drug release showed best fit into the Korsmeyer-Peppas model (R=0.949) and the value of diffusional release exponent was less than 0.45, construing that the drug release is primarily governed by Fickian mechanism. Cumulative drug release from the nanoemulsifying system at 120 min was phenomenally higher (88%) vis-à-vis to the plain drug (14%) with f_1=84 and f_2 =31, which further ratifies dissimilarity among the dissolution profiles.

Conclusion:

Overall, the study describes self-nanoemulsifying lipidic systems of LF with significantly improved dissolution profile and biopharmaceutical potential as compared to the plain drug.

Acknowlegements:

National Centre for Excellence in NanoBiomedical Applications, Panjab University, India, gratefully acknowledges UGC for providing financial assistance.

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P46 - Nano-Lipoidal Gel of Celecoxib To Increase Skin Bioavailability and Effective Management Of Rheumatoid Arthritis

Kamaal Ashraf[1], **Pradip Nirbhavane,**[1] **Gajanand Sharma,1 Bhupinder Singh,**[1,2] **Om Prakash Katare**[1]
1 University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Studies, Panjab University, Chandigarh, 160014, India.
2 UGC-Centre of Excellence in Applications of Nanomaterials, Nanoparticles & Nanocomposites (Biomedical Sciences), Panjab University, Chandigarh, 160014, India
Email ID: drkatare@yahoo.com

INTRODUCTION*:*

Celecoxib (CXB), a COX-2 inhibitor, is primarily indicated for long-term treatment of rheumatoid arthritis (RA). The effective therapeutic ef?cacy of CXB on RA via oral administration shows adverse systemic complications, and therefore, local application of CXB has been recommended. The present study aimed to develop CXB loaded SLN gel and study its skin permeation. (Garg NK et al., 2016).

METHODS:

Celecoxib loaded SLN (CXB-SLNs) were prepared using hot micro-emulsion method, and characterized for Size, zeta potential, % drug entrapment ((PDE). The developed formulation was further incorporated into the Carbopol gel and evaluated for *in vitro* drug release, *ex vivo* skin permeation study, dermatokinetics and stability.

RESULT AND DISCUSSION:

The particle size, polydispersity index (PDI), and percentage drug entrapment (PDE) were found to be 240 nm± 9.67, <0.3, and ~86% respectively. The developed SLNs exhibited sustained release up to 70% at the end of 48 h. Drug permeation was found to be 45% for SLN gel and 31%± 3.25 for conventional gel. In dermatokinetics the drug from CXB-SLN-gel was found to be deposited in much higher concentration compared to conventional gel. At the accelerated conditions only a slight decrease (up to 5% at the end of 3 months) was observed, which demonstrated good physical stability of the formulation (Sharma G et al.,2017).

CONCLUSION:

The developed nano-lipoidal gel of CXB revealed enhanced drug release and permeation characteristics and hence can prove beneficial for the effective management of rheumatoid arthritis.

ACKNOWLEDGEMENT:

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P47 - Lycopene loaded Whey Protein Isolate Nanoparticles To Increase Its Oral Bioavailability.

Nabonita Bhowmik[a], Ashay Jain[a,b], Gargi Ghoshal[b], Bhupinder Singh[a], O. P. Katare[a]
a. University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India
b.Dr S.S Bhatnagar University Institute of Chemical Engineering & Technology,
Panjab University, Chandigarh 160014, India
Email ID: nabonitabgp@gmail.com / drkatare@yahoo.com

INTROUCTION:

Lycopene (LYC) has been recognized as a potential antioxidant, anti-carcinogenic agentthrough minimizing lipidoxidation. However, its poor aqueous solubility and bioavailability are challenges for clinical utility of lycopene. LYC-Whey Protein Isolate nanoparticles (LYC-WPI-NP) deals with the limitations *viz* poor solubility, dose associated toxicity, non-specificity, small half-life, drug resistance development by target cells etc.The present work entails a novel strategy of formulating LYC-WPI-NP and evaluating its biopharmaceutical performance (Garg *et al*., 2016) (Jain *et al*., 2010)

METHOD:

LYC-WPI-NP were preparedby using rational blend of biomacromolecule without using equipment-intensive techniques. The LYC-WPI-NP were fabricated byemploying single step ethanol desolvation method with minor modifications.*In vitro* drug release study, stability in simulated gastrointestinal fluid, stability studies, plasma quantification and organ distribution studies were carried out.

RESULTS:

LYC-WPI-NP were obtained as spherical particles in the size range of 100-350nm, as visualized in FE-SEM. The percent lycopene entrapment of prepared LYC-WPI-NP was estimated in the range of 50-65%.*In vitro* cumulative release study demonstrated extended release i.e. approximately 85% in PBS (pH = 7.4), while at acidic pH (pH = 1.2) was only 65% at the end of 24h. The pharmacokinetic study with LYC-WPI-NP showed about 2.6 fold increase in plasma concentration as compared to free drug suspension.

CONCLUSION:

It can be concluded that lycopene loaded protein nanoparticles were able to enhance the oral bioavailability of lycopene.

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P48 - QbD-Enabled Colon-Targeted Oral Controlled Drug Delivery System of Metformin HCl: *In Vitro* Dissolution, *In Vivo* Pharmacokinetics and IVIVC

Ridhima[1], Anil Pareek[2], Anchal Mattu[1], Ranjot Kaur[1], Bhupinder Singh[1,3]*
[1]Univ. Inst. of Pharm. Sciences, Panjab University, Chandigarh, India
[2]Department of Medical Affairs & Clinical Research Dermatology, IPCA Laboratories, Mumbai, India.
[3]UGC Centre for Excellence in Nano-Biomedical Applications, Panjab University, Chandigarh
Email ID : ridhima.singh1993@gmail.com;bsbhoop@yahoo.com

Keywords:

Quality by Design (QbD), Colon targeting, GLP-1, Diabetes, Microspheres.

Introduction:

Metformin HCl (MET), a biguanide, has been a first-line drug for Type II diabetes since many years. However, its prolonged usage has been known to cause serious side effects like lactic acidosis. Various oral novel drug delivery systems of this BCS class III drug have been developed to enhance its bioavailability (~50%), sustainability and reduce dose-related toxicity. The current studies were endeavoured to develop colon-targeted coated monolithic microsphere delivery system of MET to trigger secretion of GLP-1 hormone responsible for enhancing insulin release.

Methods:

After embarking upon factor screening employing Taguchi OA, two influential critical material attributes *viz*., sodium alginate and inulin and one critical process parameter *viz.* swelling time, were selected for optimization studies employing Box Behnken design on various critical quality attributes, *viz.* bead size, entrapment efficiency, % drug loading and % drug release. The optimised formulation was further coated with 5% Eudragit S 100. USP Type II apparatus was employed for conducting *in vitro* dissolution studies using simulated gastric fluid (pH 1.2), simulated intestinal fluid (pH 7.4) and simulated colonic fluid (pH 6.8) as dissolution media at 37 °C at 50 rpm. *In vivo* pharmacokinetic studies on optimized formulation were carried out in Wistar rats vis-à-vis marketed formulation, and IVIVC established between *in vitro* dissolution profile and *in vivo* absorption. *In vivo* pharmacodynamic studies were also carried out on Streptozotocin-induced diabetic rats with regular monitoring of blood glucose and insulin levels, before and after treatment.

Results:

In *vitro* drug release profiles of optimised coated MET formulation exhibited miniscule release in SGF (4%), modest release in SIF (16%), extensive release in SCF (65%), while marketed formulation released extensively (50%) in SGF, relatively modestly in SIF (38%) and negligibly in SCF (<1%). The optimised formulation was found to follow *Korsemeyer Peppas model (n =1.035; R= 0.978), indicating Case-II transport. In vivo* pharmacokinetic studies showed extension in plasma levels of MET from optimised formulation vis-à-vis marketed formulation, with the values of T_{max} and AUC enhanced by 233.3% and 18.6% respectively, while C_{max} got reduced by 52.3%. Prevalence of statistically valid level A IVIVC for optimised formulation substantiated high degree of prognostic ability of *in vitro* dissolution conditions in predicting the *in vivo* biopharmaceutical performance. *In vivo* pharmacodynamic studies revealed similarity of the optimised monolithic microsphere formulation with marketed formulation ($p > 0.05$) in increasing the insulin levels over naive group even at half the dose of the former.

Conclusions:

The present research work successfully demonstrated the systematic development of MET formulation, leading eventually to remarkable augmentation in *in vitro* dissolution, and *in vivo* pharmacokinetic and pharmacodynamic profiles.

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P49 - Systematic Development of Mucoadhesive Microspheres of Quercetin for Nose-to-Brain Delivery in Alzheimer's disease: Imminent Role of Drug Release Attributes

Gagandeep Singh[#1], Sumant Saini[1], Anu Mathur[1], Atul Jain[2], Bhupinder Singh[*1,2]
[1]Univ. Inst. of Pharm. Sciences (UIPS), Panjab University, Chandigarh, India
[2]UGC Centre for Excellence in Nano-Biomedical Applications, Panjab University, Chandigarh
Email ID : [#]sidhu96gagan@gmail.com; [*]bsbhoop@yahoo.com

KEYWORDS:

Nose-to-brain delivery, Alzheimer's Disease, Quercetin, Water maze test

INTRODUCTION:

Alzheimer's disease (AD) is a progressive neurodegenerative disorder, lately gaining alarming proportions amongst the aged population, across the globe. Oxidative stress owing to increased levels of reactive oxygen species (ROS), constitutes the major factor in the pathogenesis of AD. Quercetin, a natural phenolic flavonoid, has been postulated as a novel neuroprotectant by mitigating oxidative stress. However, its possible effects get diminished owing to its limited penetration into the brain tissue. Besides, bypassing the rigours of blood-brain barrier and first-pass metabolism, delivery of drugs to brain via nasal route is marked with large nasal surface area, porous endothelial membrane, high perfusion rate and improved patient compliance.

METHODS:

The present research, therefore, encompasses the development of polymeric microspheres of quercetin via nasal route. Using Carbopol 934P and ethyl cellulose as the chosen polymers, the formulation was systematically optimised using Central Composite Design. The *in vitro* dissolution was conducted using dialysis bag method in solvent mixture of phosphate-buffered saline (pH 7.4) and methanol (80:20, v/v), stirred at 100 rpm. Model fitting was accomplished using Korsemeyer Peppas model for swellable matrices. Critical quality attributes were Q_{12h}, $t_{50\%}$, entrapment efficiency and bioadhesive strength. Pharmacodynamic investigations on microsphere formulation on AD *vis-a-vis* pure drug was conducted using water maze behavioural studies in rats, and biochemical estimations (GSH, MDA and nitrite) in its brain homogenates.

RESULTS:

The optimised formulation had attributes as T50% of 7.17 h, entrapment efficiency (EE%) of 80.73%, bioadhesive strength of 84.87 g, particle size of 7.6 µm and Q12 of 59.74%. Drug release showed best fit in Korsemeyer–Peppas model with Fickian diffusion constant (K1) as 3.14 and polymer relaxation constant (K2) as 0.85. Microspheres were found to be stable during accelerated stability testing at 40±2°C and 75±5% RH for 6 months. Significant improvement in the locomotor activity of rats and the levels of brain biomarkers construed notable anti-Alzheimer potential of optimized microsphere formulation of quercetin

CONCLUSION:

In conclusion, studies report the promising anti-Alzheimer potential of formulated microspheres of quercetin, primarily by regulating their drug release performance.

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P50 - Nanostructured Lipidic Carriers (NLCs) with Enhanced and Extended Dissolution Profiles: Exploring Drug Release Kinetics using Mathematical Modeling

Sumant Saini[#1], Teenu Sharma[1], O. P. Katare[1], S. K. Tripathi[2], Bhupinder Singh*[1,3]
[1]Univ. Inst. of Pharm. Sciences (UIPS), Panjab University, Chandigarh, India
[2]Department of Physics, Panjab University, Chandigarh
[3]UGC Centre for Excellence in Nano-Biomedical Applications, Panjab University, Chandigarh
Email ID : #sumantarya15@gmail.com; *bsbhoop@yahoo.com

KEYWORDS:

Lipidic carriers, Extended-release, Dissolution enhancement, Ferulic acid, Drug release kinetics

INTRODUCTION:

Dissolution is considered as a pivotal tool in the development of oral drug products or novel drug delivery systems, be it innovator's or generics. Drug release kinetic modeling tends to unravel scientific miniature underlying the mechanistics of drug release from the corresponding devices. The current studies, therefore, were undertaken to demonstrate the application of drug release kinetic modeling in the development of nanostructured lipid carriers (NLCs) of ferulic acid (FA), a BCS Class IV bioactive reported to exhibit poor and variable oral drug absorption.

METHODS:

NLCs were systematically prepared using hot homogenisation technique employing QbD paradigms. Homogenisation speed, surfactant concentration and amount of lipid were prioritized as CMAs, while particle size, cumulative drug release and zeta potential were earmarked as CQAs. *In vitro* drug release studies were carried out employing dialysis membrane method in phosphate-buffered saline pH 7.4 at 37ºC at 50 rpm. The dissolution profiles of pure FA and NLC formulations were analysed for drug release mechanics using first-order, zero-order, Hixon-Crowell cube-root, Weibull, Baker-Lonsdale and Korsmeyer-Peppas models.

RESULTS:

The optimized NLCs were found to have a particle size ranging between 328.6 to 342.3 nm, PDI of 0.36±0.12, zeta potential of -13.5±1.7 mV. The dissolution profiles of NLCs exhibited distinct superiority with enhanced and extended drug release characteristics (81.4±1.2%) vis-à-vis pure drug (20.3±2.4%) at 24 h. Varying degrees of fitness was obtained while fitting different mathematical models to the *in vitro* drug dissolution data, indicating the corresponding outcomes. Data fitting using Korsemeyer-Peppas model indicated non-Fickian drug release with value of n as 0.786.

CONCLUSION:

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

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P51 - Preparation and Characterization of Aceclofenac Polymorphs for Enhanced Solubility.

Ujwala A. Shinde[1], Suhas Yewale[2], Heta S. Vasani[1], Pankaj Sontakke[1], Vivek Dhawan[1].
[1]Bombay College of Pharmacy, Kalina, Santacruz East, Mumbai 98.
[2]SOTAX India Pvt. Ltd., Goregaon East, Mumbai 63.
Email Id: ujwala29@gmail.com

Keywords:

Aceclofenac (ACE); Polymorphism; *In vitro* release; USP Type IV Dissolution Apparatus, Microscopy.

Introduction:

Most of the active pharmaceutical ingredients (APIs) exist in various solid-state forms such as, polymorphs, solvates, hydrates, salts, co-crystals and amorphous solids. Polymorphs are crystalline forms of such APIs that exhibit different conformations and arrangements in the crystal lattice. Crystallization is often used for manufacturing drug substances. Advances of crystallization have achieved control over drug identity and purity, but control over the physical form remains poor. The aim of the present study was to investigate the influence of different solvents used in crystallization process on crystal habit and agglomeration of ACE crystals with potential implication on its dissolution profile and other aspects. ACE is a widely prescribed Non-Steroidal Anti-inflammatory Drug (NSAID), belongs to Class II under BCS system and exhibits low and variable oral bioavailability due to its poor aqueous solubility. Hence, such a drug requires modifications to enhance its solubility which enables us to explore its polymorphs[1].

Methods:

Supersaturated solutions of ACE in organic solvents, such as isopropyl alcohol, acetonitrile, were prepared and solvents were evaporated by air drying to obtain different polymorphs i.e Form I and II respectively [1]. These were then subjected to optical microscopy and the crystals were analyzed for their surface morphology and D10, D50 and D90 particle size distribution values using ipvPClass 2.2 software (ImageProvision). Further studies on their *in vitro* release were performed using Powder cell assembly in USP Type IV Apparatus (SOTAX) [open loop; medium- phosphate buffer solution pH 6.8] and ACE release was quantified using UV Spectrophotometer.

Results and Discussions:

Two different polymorphs of ACE were obtained and confirmed by optical microscopy and ipvPClass 2.2 software. The particle size of the pure drug was found to be 30µm whereas ACE crystals obtained using acetonitrile (Form I) had particle size 12µm and with isopropyl alcohol (Form II) the particle size obtained was 22µm. Different release (mg/mL) patterns were obtained where, received sample of ACE gave release of 1.22 mg/mL; Form I- 1.926 mg/mL; Form II- 2.446 mg/mL respectively. The enhanced solubility of ACE Form II is attributed to reduction in particle size during crystallization.

Conclusion:

The forgoing results indicate that the solvent of crystallization have impact on particle size and hence dissolution of API[2].

Acknowledgements:

Mr. Sandeep Kulkarni, ImageProvision; Dr. Ramaswamy, MD, SOTAX India Pvt. Ltd.; IPCA Laboratories Limited for providing gift sample of Acelofenac.

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P52 - Development and Evaluation of Long Acting Injectable Microspheres of Olanzapine

Ziaul Hoda, Simrandeep Kaur* and Vivek Ranjan Sinha
University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India;
E-mail: simrandeepkaur120@gmail.com; vr_sinha@yahoo.com

KEYWORDS:

Parentral Depot Formulation, Polycaprolactone, Drug Release, Schizophrenia

INTRODUCTION:

Parentral Depot formulations was developed to study thesustain release of olanzapine from its long acting injectable microspheres. Olanzapine, thienoben zodiazepine derivative, is one such novel antipsychotic drug and is used in treatment of schizophrenia and bipolar disorder[1]. However, with oral administration of drug, poor patient compliance was observed along with spitting of the tablet at the time of administration[2]. The olanzapine polycaprolactone microsphere is an effective strategy for the prolonged release of the drug (3-4 weeks) and increase medication adherence which is very important in the treatment of shizophrenia.

METHODS:

Polycaprolactone was used to prepare the microspheres of the olanzapine by solvent evaporation method, which when administered subcutaneously would release the drug for an extended period. The prepared microspheres were optimised through various process parameters such as drug:polymer ratio, polymer concentration in organic phase, stirring speed and surfactant concentration and characterised by determining entrapment efficiency, drug release and particle size. *In-vitro* release study was performed in phosphate buffer saline(PBS) pH 7.4, PBS with Tween 80 (0.5%w/v), PBS with SLS (0.5%w/v) in water bath shaker maintained at 37±2°C rotating at 50 rpm for 30 days

RESULTS:

The release study was performed in PBS (pH 7.4), PBS (pH 7.4) with SLS & PBS (pH 7.4) with Tween 80 to understand the release profile of the drug in dissolution media with varying level of drug solubility. The drug release from PBS (pH 7.4) with SLS was very fast, about 50% of drug was released in 16h and over 95% drug was released in 4 days only. However, drug release in PBS (pH 7.4) and PBS (pH 7.4) with Tween 80 was very slow from the start and drug release was about 41% and 45% respectively on 30th day. *In-vitro drug release* from microspheres in PBS (pH 7.4) and PBS (pH 7.4) with Tween 80 shows zero order kinetics as best fit model having r^2 values of 0.994 and 0.997 respectively, whereas in PBS with SLS follows Korsemeyer-Peppas kinetic model with r^2 value of 0.984.

CONCLUSION:

The developed olanzapine microsphere can sustain the release of the drug for 3-4 weeks, thereby eliminating the daily administration of the drug and would be able to avoid the problem of non-adherence and can manage the schizophrenic patients in a better way.

ACKNOWLEGEMENTS:

University Institute of Pharmaceutical Sciences, Panjab University, India, gratefully acknowledges AICTE for providing financial assistance.

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P53 - Nanostructured Lipid Carrier Mediates Effective Delivery of Methotrexate to Induce Apoptosis of Rheumatoid Arthritis Via NF-κB And FOXO1

Baljinder Singh[1],**Neeraj K. Garg**[1],**Pradip Nirbhavane**[1],**Gajanand Sharma**[1],**Bhupinder Singh**[1,2],**Om Prakash Katare**[1,3]
1 Drug Delivery Research Group, University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Studies, Panjab University, Chandigarh 160014, India
2 UGC-Centre of Excellence in Applications of Nanomaterials, Nanoparticles and Nanocomposites (Biomedical Sciences), Panjab University, Chandigarh 160014, India
Email ID: drkatare@yahoo.com

INTRODUCTION:

Methotrexate (MTX) is a folate anti-metabolite widely used for anti-neoplastic and anti-inflammatory effect. Long term usage of MTX results into adverse effects including mucosal ulceration, stomatitis, bone marrow suppression, loss of appetite, drug induced hepatic fibrosis and cirrhosis (frank and Alan, 2004). Present study is an attempt to develop MTX loaded lipid-based nanoformulation for topical delivery to achieve enhanced skin bioavailability of drug and hence reduce systemic side effects.

METHODS:

Novel Nano-structured lipid carriers (NLCs) containing MTX was formulated by hot microemulsion method. The prepared NLCs were characterized for particle size, poly-dispersity index (PDI), entrapment efficiency. The prepared NLC formulation was further incorporated into Carbopol gel and this NLC based gel formulation was evaluated forin vitro release, *ex vivo* permeation, cell line uptake studies.

RESULT AND DISCUSSION:

The particle size, poly-dispersity index (PDI), entrapment efficiency were found to be <200nm ± 11.5, <0.2, ~85% ± 3.2respectively. In vitro release of MTX from the gel formulation showed slow and sustained release of drug (50%) for upto 48h. The NLC-gel formulation showed better permeation (~ 470 µg/cm^2) than MTX-gel (~280 µg/cm^2). In cell uptake study Coumarin 6-NLCs showed greater uptake in human hyper proliferative keratinocyte cell line (HaCaT) as compared to free Coumarin 6 dye.

CONCLUSION:

The developed formulation was found to show enhanced skin permeability, bioavailability and cell uptake compared to the conventional systems and hence can be a suitable alternative to the oral MTX formulation.

ACKNOWLEDGEMENT:

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