DRPI

DRPI.SPDS.WORLD

Dissolution Research Presentations International

IN ASSOCIATION WITH

aaps® American Association of Pharmaceutical Scientists

India | Australia & New Zealand | Japan & South East Asia | United States

2023

SCIENTIFIC ABSTRACT BOOK

World Finals: September 23 & 24, 2023

Organised by: Society for Pharmaceutical Dissolution Science (SPDS)

SOTAX CE 7 smart

USP Apparatus 4

SOTAX CE7 Smart (USP4 Flow Through Cell) Allows you to see differences in your formulations that apparatus 1 and 2 simply do not show. Also widely recommended for poorly soluble, modified / extended release, and low dose products; Also been used for IVIVC studies and a growing range of dosage types

SOTAX India Pvt. Ltd.

Office No. 2-4, 3rd Floor,
Anupam Annapolis, Aarey Road,
Goregaon (East), Mumbai - 400063

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

CONTENTS

DRPI

DRPI.SPDS.WORLD

Dissolution Research Presentations International

IN ASSOCIATION WITH

aaps® American Association of Pharmaceutical Scientists

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

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

:: Vision ::

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

:: Mission ::

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

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

:: Purpose::

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

Objectives:

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

DRPI

Dissolution Research Presentations International

IN ASSOCIATION WITH

aaps® American Association of Pharmaceutical Scientists

An International Dissolution Research Presentations Competition for Young Pharmaceutical Researchers.

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

drpi.spds.world

DRPI
(Disso Research Presentations International)

To meet with its objectives, SPDS has been organizing dissolution themed annual conferences, known as DISSO India. For the first time in 2020, owing to the pandemic, DISSO India was held online with plenary lectures from worldwide experts. The overwhelming success of DISSO India 2020 led to the organization of DISSO America 2020 Online, an event by SPDS US chapter co-sponsored by the American Association of Pharmaceutical Scientists (AAPS).

As research presentations could not be included as a part of the DISSO India event, a special program 'Dissolution Research Presentations India 2020 – Online (DRPI 2020 – Online)' was held as a premier and pan India competition for young researchers across academia as well as industry. Besides being the first indigenous online research competition for pharma fraternity, a key highlight of the event was the joining of hands by SPDS with Association of Pharmaceutical Teachers of India (APTI), as collaborator for the competition. This was a unique platform for researchers from academia and industry to showcase novel dissolution related science, technology and applications. The competition was held among various zones of India, viz., North, East, West, South, & Central. Another key highlight of the event was the unbiased and totally anonymous evaluation process. In 2021 & 2022, DRPI was conducted online, wherein SPDS joined hands with APTI & AAPS, and the same success story was repeated.

Now, in 2023, SPDS is pleased to announce the fourth DRPI event, and this time it is going to be an international competition between researchers from 5 different regions of the world. DRPI now is no longer Dissolution Research Presentations India, but Dissolution Research Presentations International. The DRPI 2023 competition was held among the following four world regions:

India | Australia & New Zealand | Japan & South East Asia | US

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

BIOSKETCH

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

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

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

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

Vinod P. Shah, Ph.D.

11309 Dunleith Place
N. Potomac, MD 20878
USA

Phone: 240-449-9657
E-mail: Dr.VPShah@Comcast.net

VPS Consulting, LLC

September 21, 2023

It is my great honor and pleasure to welcome Dissolution Research Scholars from all over the world to DRPI-World 2023 Grand Finale event. To welcome Dissolution Research Scholars at this event is really a ***"Dream Come True"***. This is a flagship competition event, one of its kind in the world, for young pharmaceutical research students and scholars in the area of dissolution science.

Dissolution Research Presentation India 2020 (DRPI 2020) was started four years ago with an educational aim of encouraging research students to present their work. The genesis of the event dates back to the Disso India 2020 event, where Dr. Saranjit Singh of NIPER, Mohali, India suggested Dr. L. Ramaswamy, General Secretary, SPDS to develop a student program for Dissolution Research presentation from all over India. Dr. Ramaswamy with this inspiration and his creative mind, motivated his able and dedicated team of faculty to organize a student's competitive research presentation program termed Dissolution Research Presentation India (DRPI). The faculty team under the Chairmanship of Dr. Saranjit Singh and guidance of Dr. Ramaswamy together with Dr. Mala Menon, Dr. Krishnapriya, Dr. Hema Nair and Dr. Varsha Pradhan, and with the excellent IT help from Mr. Tarun Soni organized and implemented DRPI 2020 event, first of its kind in India and probably in the world. A unique, innovative and interactive platform was developed by IT specialist, Tarun Soni to evaluate the abstracts and delivery style by team of experts. It is a fine way of training students for their future role and an excellent way to promote and recognize young researchers in the area of dissolution science. Three years of success of DRPI stands as testimony for the importance of this event.

It is a pleasure to see that the DRPI event is cosponsored with American Association of Pharmaceutical Scientists (AAPS) and APTI. The dream of Dr. Ramaswamy of SPDS and DRPI scientific committee was to expand the event globally and to transform "I" of DRPI from India → International, and this has come true. This year we have the participation of dissolution research scholars from around the globe, India, United States, Europe, Australia, Japan and South East Asia. I wish this event to be a great success. I am happy to be part of this worthy event, and I welcome and congratulate all the research participants and winners.

The success of DRPI Global event is due to great enthusiasm, support and hard work of Global chair and vice chair namely Dr Saranjit Singh and Dr Krishnapriya from India; Dr James Polli and Dr Hardeep Saluja from USA; Dr Nikoletta Fotaki and Deirdre D'Arcy from Europe-UK; Dr Matthias Wacker from Singapore and Atsushi Kambayshi from Japan; and Dr Kamal Dua and Dr Lifeng Kang from Australia. All these leaders have played a very vital role in organising the country wise competition. I am hopeful for their continued support for the future growth of DRPI events, 2024 and beyond.

It is important to recognize, and to acknowledge, that DRPI is a unique platform which encourages young researchers to showcase their scientific work and talent in a global competition.

Vinod P. Shah, Ph.D., FAAPS, FFIP.
SPDS-International Chairman and SPDS-US Founder President.

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

Biosketch

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

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

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

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

He is recipient of Professor M.L. Khorana Memorial Lecture Award from Indian Pharmaceutical Association, and Outstanding Analyst and Eminent Analyst awards from Indian Drug Manufacturers Association.

Dr Saranjit Singh,
2817, Phase 7, SAS Nagar (Mohali) 160062 Punjab, India
Global Chair, DRPI Online 2023

I am extremely happy that the ideation of having DRPI student competition at global level has matured this year. There has been good response in regional competitions and this abstract book compiles all the abstracts that were selected by experts for participation in the mega event. It is also heartening that the competition has been tough and well deserving candidates moved forward to regional finals, and then further now we have a select group that is participating in Global Finale on 23rd and 24th September 2023. My congratulations to all the students who came forward to participate in DRPI and to winners of regional finals for their excellent research presentations. All of us are now waiting to know who are going to be crowned in both Masters' and Ph.D. categories in the Global Finale.

The organization of an event at a global scale, spanning into several months and multiple global regions, requires astute planning and sustained efforts of all involved. Without naming anybody personally, I extend my personal gratitude to everyone for their 100% involvement for the success of the event. Of course, SPDS has high aspirations of making DRPI a true global online competition with participation of researchers from as many possible institutions and countries. I am sure it is matter of time that this will become a reality, for which involvement of all scientists working in area of the dissolution science are solicited. Of course, as has been our commitment all through, our promise stands for this competition to be conducted in totally unbiased, fair, and transparent manner.

My best wishes and looking forward to exciting Global Finale.

Saranjit Singh

Vijay Kshirsagar
Founder President, SPDS

BIOSKETCH

Vijay is an accomplished Quality, Regulatory & Analytical professional with more than 38 years of rich experience of working for reputed Indian, MNC Pharma firms & as a Consultant for more than 9 years. His last stint was with Unichem as Executive Vice President responsible for CQA, Regulatory & Analytical Research, based in Mumbai, where he continues to be as Advisor on Quality & Regulatory matters.

Prior to Unichem he worked for Ranbaxy, Sun , Tata-Merind, IPCA, German Remedies, Lupin & Duphar Interfran in various senior positions like Director-Quality , GM-Quality etc . He has successfully represented his company in US and UK courts regarding IP related matters (Para IV filings).

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 including cGMP/ GLP/ PQS/QRM/Validations (Process, AMV, Cleaning, Microbiological) /QbD/ Dissolution/ Stability/ Handling Regulatory Queries/ Investigations/ CAPA/ Auditing/ Documentation/EM etc. He has spoken in number of national and international forums including SPDS/ISPE/CPHI/USP/IDMA/HRDF etc. He has an unique achievement of converting existing Cephalosporin facility to a general product facility & getting it approved by MHRA (first time in India).

He is the founder President of 'Society for Pharmaceutical Dissolution Science' (SPDS) which is now a global platform. He was conferred upon "Leadership Award" by SPDS. He has also worked on the board of Directors of ISPE-India for 12 years. IDMA has conferred upon him an 'Outstanding Analyst Award 2011' for his contribution towards pharmaceutical analysis.

He has published articles on topics like OOS, QbD & cGMP in reputed journals/books. His chapter on 'OOS Investigations' is a reference material being a part of the book for Pharmacy students. Guideline written by him on CAPA is published by IDMA. He is M.Sc. by Research in Organoanalytical Chemistry from Mumbai University. He has a good Microbiological background too having done his graduation with Microbiology. He is a Mentor to two reputed pharmacy colleges in Mumbai.

Post 2013, he has formed his own Pharma Consultancy called TRAC offering specialized services globally, for cGMP Training, Regulatory Filings, Auditing & Compliance. His current clients include reputed Pharma/API companies based in India, China, US, Europe, Turkey, Bangladesh, Malaysia etc. 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.

Contact Details: vukshirsagar@gmail.com M: +91 9867650160, LL +91 22 35631827

TRAC
TRAINING • REGULATORY • AUDITING • COMPLIANCE
PHARMA CONSULTING

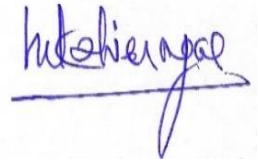
Vijay Kshirsagar
Director
M: +91 9867650160 | L: +91 22 35631827
E: vukshirsagar@gmail.com

Message for DRPI-World 2023

Reaching moon is a big and very proud step for Indian Space Industry. When more and more innovative pharmaceutical products and innovative technology gets developed in India and gets global acceptance, it would be a similar mile stone for Indian Pharmaceutical Industry. For that, original research and its promotion/encouragement & motivation is of paramount importance. Exactly the same job is being done in a very systematic/ organized & scientific manner by DRPI (Dissolution Research Presentations International). Kudos to entire DRPI team including Dr Saranjeet Singh for conceptualizing DRPI & Dr. L. Ramaswamy for taking it further with full devotion to it's present global level starting first with India.

Dissolution Science is the back bone of all these presentations. These young researchers are taking the dissolution science to a very high level for making new products/new delivery systems/new manufacturing & analytical technology that would benefit the patients across the globe for getting safe/efficacious and affordable Quality Formulations. SPDS (Society for Pharmaceutical Dissolution Science) , first such Society in the world dedicated to dissolution Science. SPDS, now more than 10 years old, has shown to the industry, why a good dissolution profile/testing is so important for bioavailability and therapeutic effectiveness. Per say, dissolution test is just one of the tests but it has relevance to lot of allied areas like bioavailability/bioequivalence, in vivo-in vitro correlation, QbD based product and method development, discrimination between a good product and a non-bioequivalent product, sophisticated analytical technology etc. You will get an insight into all these areas through presentations.

Heartiest congratulations to all the finalists and their Guides/Mentors. You all are winners. So enjoy the presentations of global young researchers with lots of take aways. Thank you, all the participants, for your constant support.



Vijay Kshirsagar
Founder President- SPDS
21st Sept 2023.

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

Biosketch

Dr (Ms) Padma V. Devarajan, President Society for Pharmaceutical Dissolution Sciemce (SPDS) is Dean Research and Innovation, Professor in Pharmacy and former Head, Department of Pharmaceutical Sciences and Technology at the Institute of Chemical Technology, Mumbai, India. She is also a member of the Board of Governors and Head of the Incubator at the Institute of Chemical Technology.

She has many granted patents, has licensed technologies to industry and products commercialized in India and Europe. She is author of two books on Targetted Drug Delivery, published by Springer. She was actively associated with Controlled Release Society Inc., USA as Board Member, Member on the Board of Scientific Advisors, Chair of the Young Scientist Mentor Protégé Committee and Chair of the Outstanding Paper Award Committee of the Journal Drug Development and Translational Research. She is a Member on the Editorial board of the Asian Journal of Pharmaceutical Sciences and the European Journal of Drug Metabolism and Pharmacokinetics.

Prof. Devarajan is a nominated Fellow of the Maharashtra Academy of Sciences, and Life Fellow of the Indian Chemical Society. She is a recipient of several awards and recognitions for Research and Innovation, including the American Association of Indian Pharmaceutical Scientists Distinguished Educator and Researcher Award, the VASVIK award for Industrial Research, the APTI Award for Research in Pharmaceutical Sciences, OPPI Scientist Award the Bengaluru Nano Innovation Award and the Outstanding Woman Scientist Award of ICAR, Government of India.

Society for Pharmaceutical Dissolution Science

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

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

From the President's Desk

Dear Delegates,

Greetings and a warm welcome from the Society of Pharmaceutical Dissolution Science (SPDS) to the First Global finals of the Dissolution Research Presentations International (DRPI) 2023. DRPI is an important annual flagship event of SPDS, which focuses on encouraging young researchers and student researchers. We are delighted to have the American Association of Pharmaceutical Scientists (AAPS) as our collaborator in hosting this event. Kudos to the DRPI organising team that has spent hours on looking at minute details to ensure smooth conduct of the programme.

DRPI initiated in 2020 as a national online competition in India, is a classic example of a positive fallout of the most dreaded pandemic the world experienced. When all was at a near stand-still, SPDS came up with this brilliant idea of engaging young students and providing them a platform to showcase their research. Meticulously planned and executed in 2020 DRPI opened up a bright opportunity for researchers across the country to participate from their homes, even during the pandemic peak.

Over the past years DRPI has grown significantly and attracted immense participation across India. After three years of learning the art of running an online competition SPDS in the fourth year (2023) has expanded DRPI globally to benefit young researchers across the globe. WE are delighted that the global finals are finally here with participation from various regions of the globe.

DRPI has some distinct features, for instance the students presentations are in video format. This we understand is a great learning experience for students to upgrade their presentation skills and bring out their best, by overcoming their shortcomings. The judges would be selected from the global platform and would represent many different regions to bring in a wealth of experience to the DRPI stage.

We are extremely thankful to all our collaborators across the globe whose unstinted support has made this dream a reality. Every national finals has been a tough competition, and we look forward to an exciting global finale!!! Special thanks to the Global Chair Prof. Saranjit Singh and Vice-chair Prof. Krishnapriya Mohanraj for planning and overseeing the event. Thanks to all the National Chairs and Co-chairs for their commitment and excellent execution of the national finals.

Best wishes to all the participants who have reached the finals. Competitions are not just for winning but also learning and growing.

A huge thanks to one and all who have contributed to make this event a grand success and Dream-to-Reality!!!

Prof. Padma V. Devarajan

President, SPDS

James Polli
Prof. and Ralph F. Shangraw/Noxell,
Endowed Chair in Industrial Pharmacy and Pharmaceutics,
University of Maryland, School of Pharmacy, USA

Scientific Chair, DRPI-US 2023

BIOSKETCH

UNIVERSITY of MARYLAND BALTIMORE

James E. Polli, Ph.D.
Professor and Ralph F. Shangraw/Noxell Endowed Chair
in Industrial Pharmacy and Pharmaceutics

Department of Pharmaceutical Sciences
20 Penn Street
Baltimore, MD 21201
410-706-8292
jpolli@rx.umaryland.edu

September 20 2023

Dear DRPI Global Chair Dr. Saranjit Singh, and all:

Greetings from USA.

Thank you for involving Late-stage and Early-stage researchers from USA in DRPI. These trainees have benefited from participating in DPRI, in terms of improving their own work and presentation, as well as learning from others.

DRPI-US was successful and benefited greatly from adopting what you have developed and revised over time. As you know, the national competition is rigorous, involving the sequenced phases of abstract, recorded presentation, and live event with questions and answers with judges. But, this rigorous process also highlights the important role of dissolution and release science in drug product development and assessment.

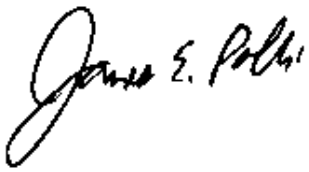
Much thanks to Professor Hardeep Singh Saluja. I very much enjoyed working with you to make DRPI-US happen.

Much thank to the American Association of Pharmaceutical Sciences (AAPS), especially Patrick Sinko and Tina Morris, for promoting DRPI-US.

Much thanks to judge coordinators Dr. Jie Shen and Dr. Sanjay Patel, was well as the AAPS In Vitro Release and Dissolution Community for serving as judges.

Much thanks for Dr Lakshmanan Ramaswamy and Dr Vinod Shah for all your support over the last year in making DRPI-US happen. Much thanks to Tarun Soni and Dana Hammell for great IT and technical support.

Sincerely,



James Polli

Kamal Dua
Senior Lecturer, Discipline of Pharmacy,
Graduate School of Health,
University of Technology Sydney, NSW, Australia
Scientific Chair DRPI-AU&NZ 2023

Biosketch

UTS UNIVERSITY OF TECHNOLOGY SYDNEY

Dr Kamal Dua
Senior Lecturer and Course Coordinator, GMP programs
Discipline of Pharmacy
Graduate School of Health

PO Box 123
Broadway NSW 2007
Australia

23 Sep 2023

It is with great pleasure and anticipation that I extend my warmest thanks to all of you as the Chair of the Dissolution Research Presentations International 2023- Australia & New Zealand Chapter for the Society of Pharmaceutical Dissolution Science (SPDS). This platform serves as a unique platform for scholars, scientists, researchers, and professionals from around the world to come together, exchange ideas, and push the boundaries of knowledge in the area of dissolution sciences.

Our shared commitment to advancing dissolution science and addressing the most pressing challenges of our time is what unites us.

I would like to express my deepest gratitude to the organizing committee, our sponsors, and all the contributors who have made this event possible. Without your unwavering support, this gathering of minds would not be achievable.

I look forward to the insightful final presentations, lively discussions, and fruitful networking opportunities that lie ahead. Let us use this conference as a platform to inspire, learn, and grow, both as individuals and as a collective force for positive change.

Thank you for being a part of this remarkable event, and I wish you all a productive and enriching experience.

Yours Sincerely,

Kamal Dua

Munira Momin
Principal and Professor
SVKM's Dr. Bhanuben Nanavati College of Pharmacy,
Mumbai (bncp.ac.in)

Scientific Chair SPDS

Biosketch

Dr. Munira Momin is currently serving as a Principal and Professor at SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, India. Under her leadership, the institute has received many accolades The college has seen a complete transformation in research and students' professional and societal activities. She has received research funding from several central and state governments of India. Her area of research is targeted nanoparticles-based drug delivery for cancer, wound healing, colon targeted drug delivery systems and inorganic metallic nanoparticles for theranaustic purposes. To mention her academic background, she obtained her B. Pharm and M. Pharm (Pharmaceutics) from L.M. college of Pharmacy, Gujarat University, Ahmedabad, India. She has received F H Jani gold medal for securing the highest marks in Pharmaceutical technology subjects in B. Pharm. She is a recipient of Prof M. L. Khurana Memorial Award for Best Research Paper published during the Year 2008-09 in Pharmaceutics and Bio-Pharmaceutics. She is the recipient of the IDMA-ACG Best Research paper 2019-20 Award, Nehru-Fulbright Academic excellence seminar fellowship award for Higher education administrator in 2019. Dr. Munira has published several research papers in national and international journals. She has four patents granted, nine patents in pipeline and one trademark to her credit. Dr. Momin has four books and 4 book chapters on pharmaceutics, and related subjects

Shri Vile Parle Kelavani Mandal's
DR. BHANUBEN NANAVATI COLLEGE OF PHARMACY
(Affiliated to University of Mumbai, Approved by AICTE, PCI)
DTE Institute Code: PH 3228

Message from Dr. Munira Momin:

Dear Researchers,

Welcome to the grand Finale of DRPI- Global !!

I encourage early and advanced researchers in the field of product development to attend DRPI-Global finale. There will be presentations from the researchers from different labs of academicians and industry across the world. The final selected presentations are of high quality research. There will be a lot of learnings for researchers across the world. This is an opportunity to listen to the stalwarts form the field of Pharmaceutical dissolution. We welcome you to join us on DRPI Global Finale on 23rd and 24th September 2024. Let's learn the science of Pharmaceutical Dissolution. We also encourage you to visit our website https://spds.in/newevents/disso-india-2023/ to learn more about the activities of the Society for Pharmaceutical Dissolution Science.

With Best regards

22/9/23

Prof. Munira Momin

SVKM's Dr. Bhanuben Nanavati College of Pharmacy MUMBAI 400056.

Mala Menon
Adjunct Professor-Pharmaceutics at Bombay College of Pharmacy, Mumbai
Former Vice-chair and member of Core Scientific Committee DRPI

Biosketch

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

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

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

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

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

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

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

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

Bombay College of Pharmacy
Estd 1957 Autonomous

The Indian Pharmaceutical Association - Maharashtra State Branch`s
BOMBAY COLLEGE OF PHARMACY
(Autonomous-Maharashtra State Government Aided Institute)
Kalina, Santacruz (East), Mumbai - 400 098. India. Tel: +91(022) 2667 0871 / 2667 1027 / 2667 0816
E-mail: office@bcp.edu.in/office.bcpindia@gmail.com, Web: www.bcp.edu.in

Vision : To be a leader in Pharmacy Education, Pharmacy Training and Research in Pharmaceutical Sciences
Mission: To educate and train students in the knowledge and practice of pharmaceutical sciences
To contribute to improvement of health of the society through education programs
To contribute to improvement of health of the society through research programs

Date: 23rd Sept, 2023

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

DRPI Online, initiated in 2020 during COVID times generated a lot of enthusiasm in both research students & Faculty of Pharmacy colleges all over India, followed by DRPI 2021 and DRPI 2022 with greater participation. It was a great pleasure and learning while working as part of the Core Scientific Committee for this event and interacting with the scientific committee and stalwarts in the field from all over.

All along the vision was to make DRPI a Global event. This year the DRPI 2023, this has been realized!

All the regional competitions were very interesting, and it was a delight to listen to research scholars from all over the world!

Looking forward to the Global Finals of DRPI 2023!

Wishing the DRPI 2023 World Finals event a great success! All the Best Wishes to the Young Researcher Participants!

Dr Mala Menon

Scientific Committee,

DRPI 2023-Online

Hardeep Saluja
Prof. of Pharmaceutical Sciences,
Bernhardt Scholar,
PharmD./MBA Program Coordinator,
Southwestern Oklahoma State University, USA

Vice-chair DRPI-US 2023

Biosketch

Dr. Hardeep S. Saluja is a distinguished Professor of Pharmaceutical Sciences at Southwestern Oklahoma State University's College of Pharmacy. In addition to his teaching responsibilities, he also coordinates the prestigious Pharm.D./MBA dual degree program. Dr. Saluja holds a Ph.D. in pharmaceutics from MCPHS University in Boston. During his academic career, Dr. Hardeep S. Saluja conducted pioneering research for his master's research thesis at the prestigious Harvard University. His groundbreaking work in the field of total parental admixture has garnered widespread acclaim and has been published in several high-impact journals. Dr. Saluja's diverse educational background also includes a Master of Business Administration (MBA) degree from Southwestern Oklahoma State University. This unique combination of pharmacy and business education has enabled him to apply a multifaceted approach to his research and teaching, and has helped him become a leading figure in the field of pharmaceutical sciences. Dr. Saluja's business acumen and strategic thinking have been instrumental in the success of the prestigious Pharm.D./MBA dual degree program at SWOSU, which he oversees with great skill and dedication.

Dr. Saluja is a renowned academician, and his contributions have been recognized by several prestigious awards, including the 2020 Bernhardt Academic Excellence Award at SWOSU. He is currently serving as the President of American Association of Indian Pharmaceutical Scientist. He has published numerous research articles and book chapters and presented his work at various national and international conferences.

Dr. Saluja's expertise in the field of pharmacy education has also made him a valuable member of the Accreditation Council for Pharmacy Education (ACPE), where he serves as a site team member to review Doctor of Pharmacy programs at universities across the United States. He is an active member of the Weatherford Rotary Club, USA.

Warm greetings to our esteemed guests, participants, and fellow advocates of dissolution research. As Vice Chair of the DRPI US 2023 Scientific Committee and a Professor of Pharmaceutical Sciences at Southwestern Oklahoma State University, I'm both humbled and thrilled to be a part of this transformative journey.

Marie Curie wisely stated, "Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less." The unfolding of the DRPI event demonstrates our shared commitment to understanding and advancing dissolution science. Conceived in 2020 as India's premier online research competition, DRPI today stands not merely as an Indian platform but resonates as a global initiative. Our evolution from "I" for India to "I" for International reflects our expansive vision and commitment to researchers worldwide.

This year marks a significant milestone as we bring DRPI to the US stage. Our global footprint now spans five vibrant regions: India, Australia & New Zealand, Japan & Southeast Asia, Europe, and the US. As we celebrate this expansion, I must extend our deep appreciation to the SPDS, DRPI team and all the reviewers, judges, and organizers for steering the DRPI US and international event with unparalleled expertise.

In the spirit of research, collaboration, and discovery, I thank each one of you for being part of DRPI's international saga. As we engage in fruitful discussions and share insights, may we continue to inspire and be inspired.

With profound gratitude and anticipation,

Prof. Hardeep Saluja.

Lifeng Kang
Senior Lecturer, The University of Sydney School of Pharmacy,
Faculty of Medicine and Health, Australia

Vice-chair DRPI-AU&NZ 2023

Biosketch

Lifeng Kang is a Senior Lecturer at the School of Pharmacy, Faculty of Medicine and Health, University of Sydney. His laboratory is focused on microscale technologies and 3D printing for drug delivery and tissue engineering. Dr. Kang has published 3 books, 5 book chapters, 73 peer-reviewed journal articles (58 as the first/corresponding author), 81 abstracts and filed 7 patent applications (2 granted and licensed). His work has been published in leading journals such as Advanced Drug Delivery Review, Journal of Controlled release, Advanced Functional Materials, Biofabrication, Bioengineering & Translational Medicine. His publications received 3463 citations, with an H-index of 34 (Google Scholar), global top 2% scientists (Stanford University).

He is highly interested in innovation. Three of his patents have been licensed to 3 companies, for drug testing (skinetrate.com) and drug delivery (nusmetics.com), led by his doctorate students and postdoctoral researchers. In addition, another doctorate student also started his own company on pharmaceutical 3D printing (craftheath.me). He is committed in training students. He has supervised 12 postgraduate students, as their primary advisor. He teaches both undergraduate and postgraduate courses.

Dr. Kang obtained his PhD from the National University of Singapore (NUS) in 2006 on drug delivery. Afterwards he was awarded a prestigious NUS-OPF fellowship and travelled to the Massachusetts Institute of Technology (MIT) to study tissue engineering by using microfabricated hydrogel. He returned to NUS in 2009 to work as lecturer for teaching. In 2017, he joined the University of Sydney (USYD) as a lecturer for research and teaching. In 2019, he spent 2 months in Stanford University to study cardiomyocyte biology and was promoted to a senior lecturer. He also studied hydrogel as drug carriers for his MSc degree in China Pharmaceutical University where he completed his undergraduate study as well. More information can be found at his web site: kanglab.net

Dissolution Research Presentations International (DRPI) 2023 is organized by the Society for Pharmaceutical Dissolution Science (SPDS) in association with American Association of Pharmaceutical Scientists (AAPS). The hard work of the organizer and participation of every researcher are very much appreciated. All the best to the DRPI 2023!

Lifeng Kang, PhD

Atsushi Kambayashi
Associate Professor, Faculty of Pharmaceutical Sciences,
Tokyo University of Science

Vice-chair DRPI-JSEA 2023

Biosketch

Dr. Atsushi Kambayashi is an Associate Professor of Faculty of Pharmaceutical Sciences at Tokyo University of Science, Japan. He received his Bachelor of Pharmacy degree from Tokyo University of Science (Tokyo, Japan). He also received his Ph.D. degree of Natural Sciences (Dr. phil. nat.) in the specialty of Pharmacy from Johann Wolfgang Goethe University (Frankfurt am Main, Germany) under the supervision of Prof. Dr. Jennifer Dressman. Prior to his current position at Tokyo University of Science, he worked for Pharmaceutical Research and Technology Labs at Astellas Pharma Inc. for 20 years. His research interests include establishment of physiologically based biopharmaceutics modeling approach to predict drug absorption from various dosage forms in humans.

I am very happy that DRPI 2023 will be held on a grand scale. I think DRPI is a wonderful project that is leading Dissolution Science. Needless to say, Dissolution Science is a research field that forms the basis of formulation development and quality control of drug products, and its importance in drug development has been increasing in recent years. Furthermore, Dissolution Science can be applicable not only to orally administered drugs, such as tablets and capsules, but also to various therapeutic modality drugs. DRPI has also started to be held in Japan and South-East Asia from this year. I sincerely hope that DRPI will continue to contribute to the development of high-quality drugs, the training of young researchers, and the creation of value for patients.

Krishnapriya Mohanraj
Professor of Pharmaceutical Analysis, Bombay College of Pharmacy, Mumbai
Scientific Core Committee member & Vice-chair DRPI-India 2023

Biosketch

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

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

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

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

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

Bombay College of Pharmacy
Estd 1957 Autonomous
The Indian Pharmaceutical Association - Maharashtra State Branch`s
BOMBAY COLLEGE OF PHARMACY
(Autonomous-Maharashtra State Government Aided Institute)
Kalina, Santacruz (East), Mumbai - 400 098. India. Tel: +91(022) 2667 0871 / 2667 1027 / 2667 0816
E-mail: office@bcp.edu.in/office.bcpindia@gmail.com, Web: www.bcp.edu.in

Vision : To be a leader in Pharmacy Education, Pharmacy Training and Research in Pharmaceutical Sciences
Mission: To educate and train students in the knowledge and practice of pharmaceutical sciences
To contribute to improvement of health of the society through education programs
To contribute to improvement of health of the society through research programs

Greetings!

On this occasion of the conduct of the first Disso Research Presentations International (DRPI), it gives me immense pleasure to witness DRPI, blossoming from the online research competition encompassing dissolution related themes, Disso Research Presentations - India, which began in 2020 to Disso Research Presentations - International, now a truly global event.

Am also lucky to be part of the scientific core committee, right from the first Disso Research Presentations India in 2020 to presently becoming Vice Chair of India for the current global competition, encompassing participation from five regions, Australia-New Zealand, Europe, India, Japan and South East Asia and the USA. The journey was a great learning experience with guidance from Prof. Saranjit Singh, the present global Chair, Prof. Mala Menon, former Vice Chair, Prof. Padma Devarajan, SPDS President and the driving force for all events Dr L Ramaswamy, SPDS General Secretary. The stupendous support from Dr Hema Nair and Dr Varsha Pradhan, from the initial DRPI to the present cannot be ignored. The USP of the event is the way how everything is smoothly arranged right from stage one of abstract submission to poster/video presentation, leading to region semifinals/ finals, culminating in global finals, through a software backed program, neatly executed by Mr Tarun Soni of Nic Interactive. Special mention to the judges at each stage. Without their commitment to excellence, the choosing of participants progressing to the next stage would have been a bane.

Each year the presenters have excelled and it is through proper mentorship that we are able to witness so many facets of dissolution focussed research

Saluting the spirit of DRPI-2023 to bring to the fore research on dissolution related sciences and providing an opportunity for industry-academia interactions

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

I wish all the participants the very best for the competition and hoping Disso Research Presentations International will see greater participation from all regions, in the coming years, and will give Dissolution and related studies the platform that it truly deserves.

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

Hema Nair
Professor of Pharmaceutics
Sri Venkateshwara College of Pharmacy, Hyderabad.

Scientific Core Committee member, DRPI 2023.

Biosketch

Dr. Hema A. Nair is presently Professor of Pharmaceutics at Sri Venkateshwara College

of Pharmacy, Hyderabad. She has a B. Pharm and M. Pharm from University of Mumbai, a Ph.D. from the S.N.D.T. Women's University and a Diploma in Patent Law from Nalsar Law University. Professional path prior to the present affiliation, comprises of a brief stint in the formulation development department at FDC, Mumbai, followed by teaching for 15 years at Bombay College of Pharmacy at UG and P.G. levels. She has successfully explored academic pursuits including securing research funding from several granting agencies (UGC, AICTE ICMR, etc.), guiding students towards masters (32) and Ph.D (2), handling industrial projects, delivering invited lectures and so on. Her research contributions include 20 plus articles including original research papers, book chapters and reviews and nearly 50 presentations at various national and international conferences. Several of her research contributions, both published in peer reviewed journals and presented at various conferences have won awards. She is passionate about motivating youngsters to engage in self-development and to understand their science.

Ph : 040-23118528
Sri Venkateshwara College of Pharmacy
(An Institution of Surabhi Educational Society)
Affiliated to Osmania University
86, Hi-Tech City Road, Madhapur, Hyderabad. T.S - 500 081
(Website : www.surabhieducationalsociety.com)

MESSAGE

"You can go as far as you dream, think and imagine." is a quote I once read and DRPI, with its first international edition in the year 2023, is one such dream which has materialized into reality.

DRPI aims to create an avenue for presenting, and thereby encouraging work, in the very relevant topic of dissolution sciences – a niche and important area of pharmaceutical product development and quality control. I applaud SPDS for this tremendous effort. Needless to say, joining hands with prominent bodies such as APTI, provided very good exposure for the local edition. Also, the crown for the competition has been the support from AAPS. The value added by these partners and the sponsors' of the event has raised its reach and stature significantly.

The competition started out primarily as a floor for presenting original academic level research, with the backing of several leading academicians from across India. However, the interest, participation and involvement of members from the industry, whether in the planning stages, or contributing to judging, and as sponsors has been phenomenal. In fact, this year as the competition was opened up to global participants, excellent projects with academia, industry and regulatory bodies partnering in its conception and execution, have been part of the competition.

Having been associated with DRPI since its inception, I feel proud to see it grow to its present level as an International event. It is a matter of great satisfaction that this unique platform is able to reach out to students and researchers across the globe. As part of the core team, I have been witness to the meticulous planning, attention to detail, careful execution and the total focus on creating an unbiased platform that has gone into each edition of DRPI.

I compliment SPDS and all its partners on this very unique and excellent venture and wish DRPI more and greater success in its editions to come.

Dr. Hema A Nair

Professor of Pharmaceutics

Sri Venkateshwara College of Pharmacy, Hyderabad

Varsha Pradhan
Partner – Regulatory Affairs, Roche Products (India) Pvt. Ltd
Scientific Core Committee member, DRPI 2023

BIOSKETCH

She has a professional career spanning 29 years which includes new products registration life cycle management of drugs for India,Sri Lanka, Nepal and Bhutan. She is involved in advocacy related to regulatory Policy and supports projects related to global Pharma education. She has completed her MS in Regulatory Sciences from the University of Maryland Baltimore USA. Prior to that she has completed her B.Pharm from KMK college of Pharmacy Mumbai, M Pharm from ICT Mumbai & a PhD from School of Pharmacy & Technology Management, NMIMS Mumbai. She was the recipient of UNIDO fellowship for Post graduate training in Pharmaceutical Technology at the University of Ghent, Belgium in 1992.

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

In academia she has been a Faculty at MET's Institute of Pharmacy & NMIMS Mumbai. She contributed to bridge the gap between industry and academia & bagged the "Best Faculty Award 'in 2010 at NMIMS Mumbai. She holds an Indian Patent for her PhD formulation work on Nasal drug delivery systems. She has been an invited speaker on various PCI sponsored Faculty Development programs & has also conducted technical refresher programs for industry employees.

She is also General Secretary for Society for Paediatric Medicines & Healthcare Initiative and is working on several collaborative projects with European Paediatric Formulation Initiative.

Dr. Varsha is also an active member in SPDS since its inception and is now a member of the Core Scientific committee for DRPI 2023

SOCIETY FOR PAEDIATRIC MEDICINES AND HEALTHCARE INITIATIVE

MESSAGE

23 September 2023

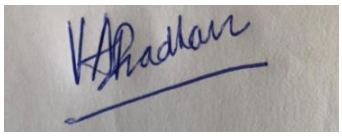
Greetings! A warm welcome to all participants of global DRPI 2023.

It is indeed a privilege and pleasure for me to get associated with DRPI from its inception. Seeing it going global this year was indeed exciting. It fills me with great sense of pride to see DRPI reach Australia, New Zealand, Japan, SEA, Europe and USA . The seamless transition at different levels in various regions across the globe was indeed appreciabe. I am happy to be a part of the Scientific Central core committee & truly appreciate the efforts of entire global organizing committee.

Post Covid we have seen several harmonization initiatives by various regulators across the globe. " One Globe One standard "is indeed a dream state which can be achieved in years to come. This event brought forward research work from international Universities which eventually will lead to harmonization in years to come.

I also take this opportunity to thank AAPS for their support and would eagerly wait for DPRI 2024 to see many more Universities across the globe participating in this excellent knowledge sharing platform.

My best wishes to all the participants in this event!



Dr. Varsha Pradhan

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

Society for Paediatric Medicines and Healthcare Initiative (PMHI)
C/O Institute Of Chemical Technology,
Nathalal Parekh Marg, Matunga, Mumbai 400019, Maharashtra, India.
Email:info@pmhiindia.org

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

BIOSKETCH

Dr. L.Ramaswamy, a graduate in chemistry (1973-78), Double post graduate in management (Marketing & HR from NMIMS, Mumbai) and a doctorate in pharmaceutical Business Administration. A Professional having nearly 4 decades of successful experience in various capacities in Indian Pharmaceutical Industry. He is currently the Managing Director of Sotax India Pvt Ltd, a company head quartered at Switzerland, pioneer Pharmaceutical testing.

Prior to Sotax India he worked for Sarabhai Chemicals as a full time Director and CEO, Managing Director of Stiefel India Pvt Ltd (Which is merged with GSK later), Unichem Laboratories. He represented the Bio Technology Delegation organized by Govt of India to Canada in 2007.

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

He has also been instrumental in conceiving the idea and need for a Society for Pharmaceutical Dissolution Science. and initiated the movement by bringing the Pharma Industry Scientists and Pharmaceutics Faculties from various pharmacy colleges, & Regulators under one roof and registered this Society as SPDS under the Charitable Trust Board at Mumbai.

Nominated as a member in the International Scientific Advisory Board and session chair of 3rd International Symposium on Scientific and Regulatory Advances in Biological and Non-Biological Complex Drugs at Budapest, Hungary.

Society for Pharmaceutical Dissolution Science

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

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

Dear Esteemed DRPI 2023 Chairs, Vice Chairs, Committee Members, Research Students, Guides, Academia, Industry Participants, Regulators, Partners, and Organizers,

As we stand on the precipice of another incredible year for the Dissolution Research Presentation International (DRPI), I am filled with profound joy and gratitude. It is both an honour and a privilege for me to serve as the General Secretary of the Society for Pharmaceutical Dissolution Science (SPDS), and to have been a part of the enduring journey that is DRPI, year after year.

Our journey began with a simple idea, ignited by the visionary Prof. Saranjit Singh, the Global Chair of DRPI, to create a platform for budding research students. This vision was wholeheartedly supported by eminent academic leaders such as Prof. Mala Menon, Dr. Krishnapriya Mohanraj, Dr. Hema Nair, and Dr. Varsha Pradhan, who played pivotal roles in the central committee. Further, we are immensely grateful for the dedication of Dr. Farhan Ahmed, Prof. Biswajit Mukherjee, Prof. Vandana Patravale, Prof. Nayanabhirama Udupa, and Prof. Swarnlata Saraf, who served as Chairs in various zones across India. Behind the scenes, a scientific committee comprising over sixty experienced and esteemed pharmacy educators from diverse institutes and universities in India formed the backbone of this unique program.

At the heart of our endeavour lies a deep commitment to nurturing the next generation of scientists and academics. Under the visionary leadership of Dr. Saranjit Singh, Dr Mala Menon, and Dr. Krishnapriya, we launched the innovative DRPI competition, extending our support to M. Pharm, Ph.D., and young industry researchers. This initiative has gathered tremendous momentum, and this year, we are thrilled to have taken DRPI (Dissolution Research Competition International) to a global stage.

The Society for Pharmaceutical Dissolution Science (SPDS), established as a charitable trust in 2012, has consistently championed the advancement and application of Dissolution Science worldwide. Today, SPDS proudly stands as the sole global society dedicated to this noble objective, contributing significantly to the quality of pharmaceutical products in collaboration with the American Association of Pharmaceutical Scientists (AAPS). We express our deepest gratitude to Dr. Vinod P. Shah from the USA, whose instrumental efforts helped expand SPDS globally and forge this invaluable collaboration with AAPS.

DISSO India, an international conference on Dissolution Science and its applications, held annually in India, and DRPI, a distinguished research presentation competition for Masters and Ph.D. students worldwide, are the flagship scientific events of SPDS. We are also delighted to have partnered with APTI (Association of Pharmaceutical Teachers of India) to conduct DRPI annually.

To all the brilliant research students participating in DRPI 2023, I assure you that your journey through this research presentation competition will be both enriching and enlightening. My heartfelt thanks extend to all the delegates who have registered, joined and participated from all corners of the globe, for it is your collective spirit that fuels this competition. Moreover, I want to acknowledge and appreciate the unwavering support of our partners; this global competition would not have been possible without your invaluable contributions.

I must take a moment to recognize the outstanding commitment of our esteemed office bearers: President Prof. Padma Devarajan, former President Mr. Vijay Kshirsagar, Vice President Dr. Rajiv Desai, Current Scientific Chair Dr. Munira Momin, and former Scientific Chairs Dr. A.K. Bansal, Dr. Padma Devarajan, and Dr. Mangal Nagarsenkar. Special thanks are due to our IT expert, Mr. Tarun Soni of NIC Interactive

As we embark on the exciting journey of DRPI 2023, I extend my warmest congratulations to all participants and winners. I invite you to share this remarkable event with your friends and mentors in other universities, so together, we can inspire even more contestants for DRPI 2024, doubling our impact in the coming year.

In closing, I wish all of you a splendid experience at DRPI 2023 World Finals, filled with learning, inspiration, and camaraderie.

Dr. L. Ramaswamy
General Secretary

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists

INDIA

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

A comparative study of in-vitro dissolution profiles using various formulation approaches of Diroximel fumarate.

Safala Malvankar (safala.s.malvankar@gmail.com)[1], Vaishali Shirsat (vashirsat@gmail.com)[1], Mandar Kodgule[2], Yogita Kodgule[2], Rajendra Gawali[2]

[1]**Bombay College of Pharmacy, Mumbai, Maharashtra** | [2]**IQGEN-X Pharma Pvt.Ltd., Kopar Khairane, Navi Mumbai, Maharashtra**

Background & Rationale: Diroximel fumarate (DRF) is an oral prodrug for use in the treatment of the relapsing-remitting type of multiple sclerosis. It is converted into monomethyl fumarate by the action of esterase which are ubiquitous in the gastrointestinal tract (GIT), blood, and tissues. DRF is known to cause GIT adverse effects such as stomach irritation and diarrhoea. Currently, DRF formulation is available in the market as twice a day formulation. The formulation developed in this study is a single-dose formulation to reduce the pill burden on patients thereby increasing patient compliance. Therefore, the study aims to pharmaceutically design and develop different delayed-release single-dose formulations containing DRF by use of enteric coating polymers and also to evaluate the drug release pattern from different formulation approaches by comparing with the data available from the reported literature.

Methods: A) Formulation development using various strategies: The formulations containing DRF were developed using various strategies like powder blend in a capsule and further enteric coating to the capsule, Tablets in a capsule and further enteric coating to the capsule, Tablets in enteric capsule and further coating to the capsule, Enteric coated tablets in capsule and Enteric coated minitablets in a capsule.

B) *In-vitro* dissolution study for evaluation of drug release: The method used for dissolution is as per USFDA guidelines of *in-vitro* dissolution methods for DRF delayed-release capsules. The studies were performed using USP apparatus II (paddle) with a custom sinker at 75 rpm at 37ºC± 0.5. The drug release was evaluated in the acid stage i.e., 0.1 N HCL followed by the buffer stage i.e., sodium phosphate buffer pH 6.5. Aliquots were withdrawn at sampling intervals and analyzed using high-performance liquid chromatography. Percent drug release was calculated at each sampling interval.

Results & Discussion: In all formulation approaches, the capsules stayed intact in the acid stage with percent (%) drug release NMT 10%, which is the specification criteria for enteric formulations. In the buffer stage, the capsules showed distinguished drug release patterns for different formulation approaches ranging from 70 to 93% at (Q) time point at 60 minutes.

Conclusion: Different formulation strategies were adopted for the development of DRF delayed-release products to protect from the gastric environment. *In-vitro* dissolution profiles of various formulations were studied and found comparable with the literature-based data.

References:

1. Dissolution methods database by U.S. Food & Drug administration.
2. Jonasson, E.; Sejbaek. T. *Diroximel fumarate in the treatment of multiple sclerosis*. Neurodegenerative Disease Management 2020**, 10** (5), 267-276.

Acknowledgements: Bombay College of Pharmacy, Kalina, Mumbai. &-. IQGEN-X Pharma Pvt.Ltd., Navi Mumbai.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: Dissolution & Solubility Modulation

A Novel USP IV Bicarbonate Based Dissolution Method to Predict In Vivo Performance of an Immediate Release Tablet Formulation Containing BCS Class II Drug

Juilee Kulkarni[1] (juileekulkarni@lupin.com), Sajeev Chandran[1] (sajeevchandran@lupin.com)

Advanced Drug Delivery Systems, Pharma Research, Lupin Limited, 46/47A, Nande Village, Mulshi Taluka, Pune, Maharashtra

Background & Rationale: For fast dissolving immediate release (IR) tablet formulations, initial disintegration time and pattern becomes important to make the drug available for dissolution and absorption. An in vitro dissolution method that can discern such differences in formulations arising due to changes in API properties, manufacturing variables, excipient amounts and/grades becomes important tool during formulation development[1]. Here, an attempt was made to develop a dissolution method to discriminate IR tablet formulations in terms of its disintegration behaviour due to changes in the composition and manufacturing process during development. Further, the bio-predictive ability of the method was assessed by establishing a Level-C IVIVC.

Methods: (a) Test formulations – Three IR tablet formulations of a BCS class II drug were manufactured in-house using different processes like dry mix granulation (*T-1*), wet granulation (T-*2)*, and roller compaction (*T-3)* with varying amounts of excipients like microcrystalline cellulose, crosscarmellose sodium, colloidal silicon dioxide, magnesium stearate etc. Further, human bioequivalence studies of the test formulations were carried out to determine their in vivo performance.

(b) Development and *in vivo* predictability of the dissolution method – The disintegration/ dissolution behaviour of the test formulations was studied using a USP IV dissolution apparatus (Sotax, Germany) with pH 4.5 acetate buffer (30 min) followed by pH 5.8 kreb's bicarbonate buffer[2] (120 min) at 8mL/min flow rate. The choice of the media conditions was made to reflect the dissolution under fed state. Samples were collected at predefined time points and analysed using HPLC equipped with RI detector. A Level-C IVIVC was established between the *in vitro* dissolution data obtained from a developed method and the peak plasma concentration data (C_{max}) for the respective formulations obtained from the BE study.

Results and Discussion: Lower *in vivo* C_{max} values were observed for *T-1* and *T-2* compared to *T-3.* In line with the observations, T-3 showed distinct pattern of simultaneous disintegration-de-aggregation yielding fine particles than the other two formulations, which resulted in larger aggregates upon disintegration. This difference also carried forward in the overall dissolution profile of the three formulations. The differences in disintegration behaviour were observed in USP IV apparatus due to its hydrodynamics compared to other conventional apparatus (USP I/II/III). The Level-C IVIVC using dissolution at 60 min time point was found to correlate well with the C_{max} values with prediction error less than 10%, indicating that the method is also bio-predictive.

Conclusions: A suitable discriminatory technique was successfully developed to identify effect of composition and manufacturing process on tablet disintegration behaviour and drug dissolution. The Level-C IVIVC proves the *in vivo* predictive ability of the developed dissolution method for further optimization of the test formulations.

References:

1. Cascone S., *Modeling and comparison of release profiles: Effect of the dissolution method*, European journal of pharmaceutical sciences, 2017, 106: p. 352-361.

2. Silva D., et.al., *Simulated, biorelevant, clinically relevant or physiologically relevant dissolution media: The hidden role of bicarbonate buffer,* European journal of pharmaceutics and biopharmaceutics, 2019, 142: p.8-19.

Acknowledgements: Lupin Research Park

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: Dissolution & Solubility Modulation

A QbD Approach for the Development of Discriminatory Dissolution Method for Vorinostat 5O5[b2] Formulation

Megha Pillai (megha9236@gmail.com)[1], Pinaki Sengupta (pinakis@niperahm.res.in) [1], Ravi Shah[1], Derajram Benival[1], Girish Patil[1], Akhil Perla[1]

[1]National Institute of Pharmaceutical Education and Research Ahmedabad, Gujarat

Background and rationale: Dissolution has evolved into a powerful testing method, progressing from a test to distinguish between different batches of drug products to a tool predicting bioavailability. In addition, supporting biowaivers, reducing clinical studies, and establishing *in vitro-in vivo* correlations (IVIVC). The dissolution method can be used to establish CMA for amorphous polymer dispersion, and CPP attributes of HME process that affect drug release and *in vivo* performance variability. A standardized approach for generating a discriminative dissolution method that predicts *in vivo* performance and helps set CMA and CPP is essential. The aim of the current study is to develop a discriminatory dissolution method using a Quality by Design (QbD) approach for Vorinostat, a BCS class IV drug. Further, application of the method is to establish an IVIVC with the aid of computational tool for mechanistic understanding of each process and compound attributes impacting the dissolution. In a big picture of drug development, a new state-of-the-art strategy using computational method will serve as a foundation for risk analysis and aid in planning future *in vivo* studies.

Methods:

Development of discriminatory dissolution method by using one factor at a time (OFAT) approach

OFAT approach was considered to screen the factors that will impact the dissolution. USP apparatus II (paddle) and USP apparatus I (basket type) were used to explore the impact of basket vs paddle. The design of experiment (DOE) was employed to determine the appropriate surfactant %, rotational speed and pH in each set of trials, when developing a discriminatory dissolution method on USP I apparatus. I-Optimal custom design was used to achieve desired dissolution profile by varying each factor from highest value to lowest value. Utilizing statistical methods, the I-Optimal custom design was assessed for design space adequacy and statistical significance. In order to identify the variables having a substantial impact on response, 2D and 3D surface plots were used. The experimental data was used to validate the projected results.

Results and discussion:

The dissolution rate of Vorinostat was affected by changes in pH, surfactant content, and stirring rate. Thus, all these factors were considered while developing QbD approach to estimate the drug release at 15 min, 45 min, 60 min and 90 min. The software recommended using pH 6.8, rpm 80 and at 3 distinct surfactant concentrations (1.91%, 1.17%, 0.16%) to accomplish the desired dissolution profile of Vorinostat. The predicted design space was validated with experimental data and the R^2 value was greater than 0.9.

Conclusion:

The developed discriminatory dissolution method by QbD approach has aided in the establishment of a suitable space to perform dissolution test for Vorinostat 5O5[b2]. Further, the method can be used to establish an IVIVC with the aid of computational tool for mechanistic understanding of each process and compound attributes impacting the dissolution.

Acknowledgements: We acknowledge NIPER-Ahmedabad for providing the necessary support for this work.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Amphotericin B Nanoformulation Insta-AmB - Tracking Safer Monomeric AmB Release

Pooja Todke (poojatodke34@gmail.com)[1], Padma Devarajan (pvdevarajan@gmail.com) [1], Suhas Yewale[2]

[1]**Institute of Chemical Technology, Mumbai, Mumbai, Maharashtra** | [2]**Sotax India Private Limited**

Background & Rationale: Amphotericin B (AmB) a drug of choice for leishmaniasis exhibits fatal renal toxicity attributed to the aggregated state. This study presents Insta-AmB nanoformulation prepared using revolutionary in-situ nanotechnology, based on instantaneous generation of drug loaded nanoparticles by simple addition of drug-nanocarrier preconcentrates into aqueous media. The aim of the study was design of Insta-AmB preconcentrate to obtain nanosize(~100nm) and high entrapment efficiency(EE), safety and efficacy. A major objective was to confirm safety by evaluation for the super-aggregated state and release of safe monomeric AmB through in vitro release studies.

Methods: ***A) In-silico Prediction of Insta-AmB Excipient:*** Material studio using blend module was employed to determine two miscibility parameters Mixing energy (Emix) and Interaction parameter (χ). Further, molecular docking of AmB-with Lipid and molecular dynamic simulation of lipid with ergosterol and cholesterol were performed using Molecular Operating Environment (MOE).
B) "Insta-AmB" by In-situ Nanotechnology: Insta-AmB preconcentrate was prepared by dissolving drug, lipid and stabilizers in a pharmaceutically acceptable vehicle and sterilizing by filtration(0.22µm). Addition of preconcentrate to sterile dextrose injection resulted in nanosize Insta-AmB with high AmB entrapment in the lipidic NP. Insta-AmB (10µg/mL) was scanned in UV-visible region to confirm the AmB state.
C) In-vitro Dissolution study: Tracking Safer Monomeric Release in Biorelevant Media AmB release was evaluated by direct addition using USP-II and USP-IV, in biorelevant parenteral medium(Krebs-Ringer Buffer pH 7.4 with albumin(4%)[KRB]) and biorelevant artificial lysosomal fluid(pH 4.5). AmB state was determined by scanning dissolution medium in UV-visible region, and absorbance measured at 405nm to quantify AmB monomer, at different time points.
D) Safety of Insta-AmB to human erythrocytes was evaluated by monitoring haemolysis.
E) In-vitro Antileishmanial Efficacy was evaluated using infected leishmania amastigotes in J774A.1 macrophage cell line using miltefosine as control.

Results and discussion: Negative values of Emix and χ, suggested very high miscibility, furthermore, molecular docking study predicted complete wrapping of AmB by novel lipidic excipient(NLE) proposing super-aggregated state of Insta-AmB[1]. Insta-AmB(5mg AmB/mL) using NLE exhibited average particle size ~90 nm, PDI<0.3, EE>95% and spherical shape(TEM). A dominant UV peak at <325nm and 400-410nm reflects safe super-aggregated and monomeric AmB state respectively, while 325-350nm reflects the aggregated(toxic) state. The Insta-AmB dominant peak at 322.5nm confirmed super-aggregated state. Molecular dynamic simulation demonstrated the specificity of Insta-AmB for ergosterol while sparing cholesterol. Hence safety of Insta-AmB is proposed. In vitro dissolution revealed safer monomeric AmB release(405nm) from superaggregated Insta-AmB in both biorelevant media, confirming super-aggregated AmB served as monomer depot enabling continuous monomeric AmB release. USP IV provided higher release than USP II with lower deviation and superior reproducibility. The cholesterol sparing effect and hence lower toxicity proposed by monomeric release was confirmed by the safety study in human RBC which revealed very low hemolysis(<15%). *In-vitro* antileishmaniasis studies revealed a low IC50(0.0499 µg/mL) and high safety as seen from a low selectivity index(SI).

Conclusion: Release of monomeric AmB from Insta-AmB proposes great promise as a safe, efficacious nanosystem for leishmaniasis. Monitoring monomeric AmB in the in vitro release study provides a useful tool to predict AmB toxicity.

Reference: Journal of Controlled Release.2022;349:756-64.

Acknowledgements: Thankful to SOTAX India (Pvt) Limited for Dissolution Testing USP 4 Apparatus.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Cisplatin(IV) Prodrug and Venetoclax Loaded Phenylboronic Acid-modified TPGS-lactide Polymeric Nanoparticles: Targeting Multiple Cellular Pathways in Breast Cancer Management

Oly Katari (katarimoutuli@gmail.com)[1], Sanyog Jain (sanyogjain@niper.ac.in)[1], Tushar Date[1]

[1]**National Institute of Pharmaceutical Education and Research (NIPER)-S.A.S. Nagar, Mohali, Punjab**

Background and Rationale: Cisplatin is a potent anti-cancer agent and is highly effective in difficult-to-treat cancers like triple-negative breast cancer. However, it causes severe systemic side effects and development resistance. Cisplatin(IV) prodrugs have been proven to overcome such drawbacks and therefore in this investigation dual-action prodrug cisplatin-chlorambucil (CP-CBL) was synthesized. The prodrug was further loaded in d-α-tocopheryl polyethylene glycol 1000 succinate-lactide (TPGS-LA) polymeric nanoparticles (TNPs) along with venetoclax (VTX). Further, 4-carboxyphenyl boronic acid (PBA) was conjugated with TPGS which acted as both stabilizer and targeting ligand.

Methods: (A) Design and development of CP-CBL and VTX loaded TNPs: Initially, CP-CBL was synthesized and characterized for successful conjugation. The CP-CBL and VTX loaded TNPs were developed by solvent injection method. Formulation parameters like organic solvent, stabilizer concentration drug loading etc. were optimized and the optimized formulation was lyophilized.

(B) In-vitro and in-vivo characterization of TNPs: The TNPs were evaluated for drug release along with other in-vitro and in-vivo parameters. The drug release study was performed using dialysis bag method in 30 ml release medium (PBS 7.4 pH, containing 0.4% w/v SLS). Samples were withdrawn at predetermined time intervals and were analyzed for the presence of VTX using validated HPLC method and Pt content using ICP-MS. Further, the pharmacokinetic study was conducted by administering treatment samples in the tail vein of female Sprague Dawley rats. At predertermined time intervals blood was collected, centrifuged and the plasma was analyzed for drug content.

Results: The optimised TNPs were spherical particles with 143 nm size and 0.186 polydispersity index. The TNPs showed initial burst release within 2h followed by sustained drug release till 72 h. The results highlighted Higuchi release kinetic model for release of CP-CBL and VTX from TNPs with r2 values 0.95 and 0.98. The TNPs showed better results at cell culture level than the free drugs. The pharmacokinetic study of TNPs revealed remarkable enhancement of AUCtot, t1/2 and MRT compared to free drugs. Ultra-short half-life of Platinum drugs offers unique chemotherapy challenges for cisplatin. Loading of drugs in TNPs can assist in improving half-life and MRT and may show sustained therapeutic action compared to free drugs. Also, the TNPs showed superior results at pharmacodynamic and toxicity levels.

Conclusions: The TNPs possessed improved in-vitro and in-vivo performance with enhanced pharmacokinetic, bio-distribution and safety profiles. Overall, this investigation proved that targeted co-delivery strategy using TNPs could aid in managing breast cancer. Findings from this study could be easily extrapolated to other platinum drugs for designing better cancer therapies using prodrug approach.

References:

1. Wang, X., et al., Phenylboronic acid-mediated tumor targeting of chitosan nanoparticles. Theranostics. 2016. 6(9): p. 1378.
2. Johnstone, TC., et al., The next generation of platinum drugs: targeted Pt (II) agents, nanoparticle delivery, and Pt (IV) prodrugs. Chemical reviews. 2016. 116(5): p. 3436-86.
3. Lee, JB., et al., Venetoclax enhances T cell-mediated anti-leukemic activity by increasing ROS production. Blood. 2021. 138(3): p. 234-45.

Acknowledgements: Director, NIPER S.A.S. Nagar for providing necessary facilities and infrastructure.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: Dissolution & Solubility Modulation

Comparative Analysis of In Vitro Dissolution Profile and In Vivo Pharmacokinetics of Niclosamide from Polymeric Amorphous Solid Dispersion and Coamorphous Delivery System

Amruta Padakanti (padakantiamruta@gmail.com)[1], Naveen Chella (naveen@niperguwahati.in)[1], Amruta Padakanti[1], Prashanth Kolimi[1], Naveen Kolagani[1], Srikanth Ponneganti[1], Radhakrishnanand P[1]

PTF department, NIPER, Guwahati, Assam

Background and Rationale: Supersaturated drug delivery system like amorphous and co-amorphous drug delivery have gained a lot of interest recently due to their ability to enhance dissolution, solubility and bioavailability of poorly soluble drugs. Till now, very many scientists have explored the potential of these delivery systems individually. But very limited data is available on the comparative analysis between amorphous and co-amorphous systems. In the current study we have tried to prepare polymeric amorphous dispersions (PASD) and co-amorphous systems (CAMs) using a repurposed drug niclosamide and compared their *in vitro* dissolution and *in vivo* pharmacokinetics profiles.

Methods: PASD was prepared by hot melt extrusion using PVP K17 as polymer. CAMS were prepared by ball milling using amino acids as coformers. The prepared formulations were characterized for solid state transformation with the help of DSC, PXRD, SEM, hot stage microscopy. In vitro dissolution was performed under non-sink conditions and in vivo pharmacokinetic studies were performed in rats.

Results: Solid state transformation was confirmed by differential scanning calorimetry, powder X-ray diffraction and hydrogen bond interactions were confirmed by FTIR studies. CAMs showed higher drug loading (50%) compared to PASD (30%). *In vitro* dissolution performed under non-sink condition indicated, significantly higher dissolution (approx.10 folds) from PASD over CAMs. But presence of drug in metastable state was retained by CAMs for prolonged periods compared to PASD. *In vivo* studies showed higher C_{max} from PASD (854.11 ± 237.05 ng/mL) over CAMs (335.6 ± 86.2 ng/mL). There was no significant difference in the AUC of niclosamide from both formulations. MRT was higher from CAMs compared to PASD.

Conclusion: More studies should be conducted using different carriers and drug with different properties before concluding the best technology. Similarly, commercial scale up feasibility angle also needs to be checked among the used technologies.

References:

1. Tze Ning Hiew, Dmitry Y. Zemlyanov, Lynne S. Taylor. Balancing Solid-State Stability and Dissolution Performance of Lumefantrine Amorphous Solid Dispersions: The Role of Polymer Choice and Drug–Polymer Interactions. Mol. Pharmaceutics 2022, 19, 2, 392–413.

Acknowledgements: The authors acknowledge the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India, for the support in completing the project and National Institute of Pharmaceutical Education and Research (NIPER) Guwahati for providing facilities to conduct the research work.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: Dissolution & Solubility Modulation

Development and Evaluation of Inclusion Complex of Bedaquiline Fumarate to Improve Biopharmaceutical Performance

Parth Patel (parthrpatel1996@gmail.com)[1], Keerti Jain (keertijain.02@niperraebareli.edu.in)[1], Vishwas Pardhi[1]

[1]**National Institute of Pharmaceutical Education and Research (NIPER) - Raebareli, Lucknow, Uttar Pradesh**

Background and Rationale: Bedaquiline fumarate (BQF) is a BCS class – II drug approved for the treatment of multidrug resistant tuberculosis. Poor solubility and dissolution rate are the limiting factors in drug absorption through gastrointestinal tract, which eventually resulted in compromised bioavailability, reduced efficacy and increase in required active dose [1]. Thus, solubility enhancement *via* formation of inclusion complex with provides cost effective and industrially feasible alternative to such molecules. Further, more than 90% of the cases of tuberculosis found in the medium to lower income countries and treatment duration are comparatively longer, thus such approaches are more appropriate in case of tuberculosis treatment [2]. The main objective of the study was to prepare formation of inclusion complex of BQF with β-cyclodextrin (β-CD) derivatives and evaluate for *in vitro*, *ex vivo* and *in vivo* studies for solubility and permeation enhancement.

Methods: Higuchi and Connors method was used to carry out the phase solubility study. Inclusion complexes were prepared by freeze drying method at 1:1 molar ratio. The dissolution was performed under sink and non-sink conditions using official dissolution media (0.01 N HCl). The *ex vivo* permeability was measured using inverted sac method.

Results: The phase solubility study of BQF versus β-CD and hydroxypropyl-β-cyclodextrin (HP-β-CD) provided A_L type solubility curve. The results of *in vitro* dissolution study of HP-β-CD showed initial burst release of 90.02 ± 6.70% and 100.08 ± 2.04% in sink and non-sink condition, respectively within 5 minutes. Altogether, BQF inclusion complex with β-CD and HP-β-CD showed 2.51-fold and 2.42-fold enhancement in dissolution rate at t_{60} min under sink condition, while, under non-sink condition, it was 20.75 and 41.06-fold, respectively, compared to pure BQF. Permeability of HP-β-CD was found to be 6-fold and 2-fold higher as compared to pure BQF and its physical mixture, respectively. $AUC_{0\text{-}48\ hr}$ under fasted as well as fed conditions were found to be improved for HP-β-CD inclusion complex by 1.23 and 1.12-fold, respectively.

Conclusion: Overall, the current study provides a straightforward and versatile strategy to develop alternative formulation of Sirturo® due to better biopharmaceutical performance of HP-β-CD inclusion complex.

References:

1. Li Y, Sun F, Zhang W. Bedaquiline and delamanid in the treatment of multidrug-resistant tuberculosis: Promising but challenging. Drug development research. 2019 Feb;80(1):98-105.
2. Abou Jaoude GJ, Baena IG, Nguhiu P, Siroka A, Palmer T, Goscé L, Allel K, Sinanovic E, Skordis J, Haghparast-Bidgoli H. National tuberculosis spending efficiency and its associated factors in 121 low-income and middle-income countries, 2010–19: a data envelopment and stochastic frontier analysis. The Lancet Global Health. 2022 May 1;10(5):e649-60.

Acknowledgements: The authors acknowledge Department of Pharmaceuticals (DoP), Ministry of Chemicals and Fertilizers, Government of India for providing facilities for this research work.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development and In Vitro Release Studies of Paliperidone Nanoformulations for Nasal Delivery

Niserga Sawant (nisergasawant@gmail.com) [1], Namita Desai (namitadd@rediffmail.com)[1], Pratima Tatke[1]

[1]**C.U.Shah College of Pharmacy, S.N.D.T.Women's University, Mumbai, Maharashtra**

Background and Rationale: Paliperidone, an atypical antipsychotic BCS class II drug is used in the management of schizophrenia. It has poor oral bioavailability (28%) and also undergoes efflux via P-glycoprotein efflux transporters present on the blood brain barrier thereby limiting its entry into the brain. (1,2) Intranasal delivery, a non-invasive approach would help in improving bioavailability of the drug with potential for direct brain delivery. Hence, an attempt has been made to develop mucoadhesive paliperidone nanoemulsions for nasal delivery wherein the nanoemulsions would help in enhancing drug solubility and permeability across nasal mucosa and presence of mucoadhesive polymers can reduce mucociliary clearance and prolong nasal residence time of the drug.

Methods: UV spectrophotometric method for paliperidone in Methanol AR and Simulated Nasal Fluid (SNF), pH 6.4 was developed for quantification of drug from formulations and during *in vitro* release studies respectively and validated. Development of nanoemulsions involved screening of oils, surfactants and cosurfactants for their solubilizing capacity for paliperidone. Nanoemulsions of paliperidone (1% w/v) were optimized by response surface methodology using Design Expert 13 software and evaluated. Various derivatives and concentrations of chitosan as mucoadhesive polymer (0.1%-0.5% w/v) were included in the nanoemulsions and subsequently characterized for their mucin binding capacity and coating efficiency. *In vitro* release studies of developed nanoformulations were performed using dialysis bag (molecular weight cut off 12,000kDa) in USP Type II apparatus, 100 ml SNF, pH 6.4, 75 rpm, 37 ± 0.5°C for 8 h.

Results and Discussion: The absorbance values of paliperidone in methanol and SNF, pH 6.4 were found to be linear in the range 8 – 16 µg/mL with R^2 = 0.9904 and 0.999 respectively. The composition of optimized nanoemulsions was oleic acid (8.9% w/w) as oil phase, Tween 80 and Transcutol (50% w/w) as S_{mix} (1: 1) and water. (Fig. 1). Chitosan (0.4% w/v) could be incorporated in the nanoemulsions for mucoadhesion while higher concentrations led to gelling in the dispersions. Paliperidone nanoemulsions showed negative zeta potential (-12.7±0.5mV) while mucoadhesive paliperidone nanoemulsions presented positive zeta potential (+31±0.3 mV) which confirmed surface coating of nanoemulsion droplets by chitosan. *In vitro* mucoadhesion study using mucin showed that mucoadhesion of chitosan coated paliperidone nanoemulsions was 2-fold higher than the nanoemulsions. *In vitro* release studies showed that when compared to pure drug, paliperidone nanoemulsions showed improved release while presence of chitosan in the nanoemulsions showed sustaining effect over 8 hours. (Fig. 2)

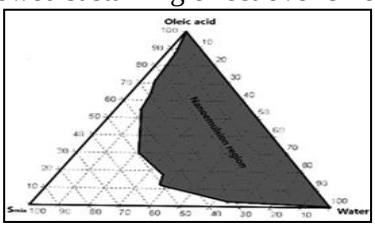


Fig. 1: Paliperidone nanoemulsions

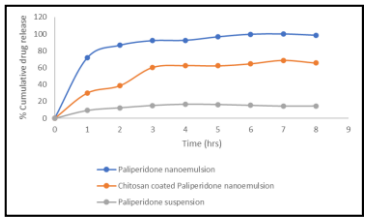


Fig. 2: *In vitro* release studies

Conclusions: Paliperidone nanoemulsions were successfully prepared by ultrasonication method and chitosan could be incorporated in the nanoemulsions for mucoadhesion. *In vitro* release studies showed sustained release of paliperidone from nanoemulsions in the presence of chitosan which can be proposed to increase residence time of developed nanoformulations in the nasal cavity for direct brain delivery.

References:

1. Rehman S, et al., Chemistry and Physics of Lipids. **2021**;234:105005.
2. Spina E, Cavallaro R. Expert Opinion on Drug Safety. **2007**;6(6):651–62.

Acknowledgements: The investigators express sincere thanks to Micro Labs India Pvt. Ltd, Gattefosse India Pvt. Ltd, and Swakit Biotech Pvt. Ltd for the generous help as gift samples of drug and excipients and RGSTC, Govt. of Maharashtra for financial support.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development and Validation of In Vitro Release Testing Method for Dapsone Topical Gel Formulation using Vertical Diffusion Cell Apparatus

Palak Karia (palak.karia@ves.ac.in) [1], Anita Ayre (anita.ayre@ves.ac.in) [1], Mangal Nagarsenkar[1], Supriya Shidhaye[1], Ashvin Patel[2], Harshil Joshi[1]

[1]V. E. S. College of Pharmacy, Chembur, Mumbai, Maharashtra|, [2]Analytical Research and Business development at Teledyne Hanson, Ontario, Canada

Background and Rationale: In-vitro release testing (IVRT) can reflect numerous or combined effects of several physical and chemical parameters of the active and other properties of the delivery system. The method should have the necessary specificity, precision, selectivity, and reproducibility to detect differences in qualitative (Q1) and quantitative (Q2) properties as well as the microstructure and arrangement of matter (Q3) between products. The objective of the project work was to develop an IVRT method to assess the release and diffusion of Dapsone from different strengths of gel formulations intended for local action and to ensure that the method had the requisite discriminatory power to detect significant differences between the formulations.

Methods:
A) Membrane selection: Various synthetic membranes such as Nylon, Polyether sulfone, and polyvinylidene difluoride (PVDF) were screened for dapsone binding and for drug release using 30% alcohol as the receptor medium.
B) Receptor media selection for Dapsone: Different concentrations of isopropyl alcohol, ethyl alcohol, and dimethyl sulfoxide with water were evaluated as receptor media for suitability for use in the IVRT method. The solubility of dapsone in receptor fluid was also determined.
C) IVRT method development and validation: The IVRT method system was developed based on the results of the assessment of membrane inertness, solubility of dapsone in receptor fluid, linearity, specificity, selectivity, and precision parameters. Gels containing 3.75g, 7.5g, and 15g of dapsone were specially formulated for the purposes of testing the release patterns. Generic dapsone gel (7.5%) was used to compare the in-house dapsone gel 7.5%. Dapsone gel (400 mg) was applied to PVDF membranes mounted on each cell. The receptor chamber was filled with 10.0 mL of ethanol/water solution (60/40 v/v) maintained at 32 °C and were continuously stirred at 400 rpm using individual magnetic stirrers in each cell.

Results and Discussion: In accordance with the SUPAC-SS guidance, the resulting release rates for each Vertical Diffusion Cell were calculated using linear regression. The mean release rates (n = 3) from the runs with 3.25%, 7.5%, and 15% Dapsone gels increased with increasing Dapsone concentration. Values of slope for plot of cumulative release per unit area versus under root of time were 2144.3, 3538.4 and 4679.5 $\mu g/cm^2/min^{1/2}$ respectively. The coefficient of variation values were less than 15% confirming precision and reproducibility. Release rate of marketed generic product was lower than that of gel formulated in house with value of slope as 2012.2 $\mu g/cm^2/min^{1/2}$. Difference in release rates could be attributed to differences in polymer matrix and possibly concentration of the cosolvent.

Conclusion: A comprehensive characterization of the operational parameters of an IVRT method was performed and an IVRT method for dapsone Gel 7.5% was developed and partially validated. The results indicate that the IVRT method was very precise and reproducible, thereby confirming its suitability to discriminate differences in release rates of dapsone from topical gel formulations and its value as a useful tool in the formulation development of topical products.

References:*Nonsterile Semisolid Dosage Forms: Scale-Up and Post approval Changes (SUPAC-SS): Chemistry, Manufacturing and Controls; In Vitro Release Testing and In Vivo Bioequivalence Documentation*; Guidance for Industry; U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation Research (CDER), U.S. Government Printing Office: Washington, DC, 1997. DOI: 10.1201/9780824741969.axe.

1. In Vitro Release Test Studies for Topical Drug Products Submitted in ANDAs Guidance for Industry. U.S. Department of Health and Human Services, Food and Drug Administration, Centre for Drug Evaluation Research (CDER), Office of Generic Drugs: Silver Spring, MD, 2022, Oct 2022.
2. USP <1724>, Semi Solid Drug Products-Performance Tests, USP PF 48 (3)

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

*Region: India | Category: PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development of Methotrexate Loaded Long Acting In-situ Gel Formulation for the Treatment of Rheumatoid Arthritis.

Jyotsna Vitore (jyotsna.vitore@niperahm.res.in)[1], Derajram Benival (derajram@niperahm.res.in)[1], Manoj Dhangar[1]

[1]**NIPER-Ahmedabad, Ahmedabad, Gujarat**

Background and Rationale:

Rheumatoid arthritis (RA) is considered a debilitating disease that increases the risk of significant morbidity and premature mortality. Methotrexate (MTX) is the drug of choice for the treatment of RA. The existing delivery of MTX poses limitations including non-linear pharmacokinetics and frequent administration of injection based formulation, which lead to poor patient compliance. There is a substantial need for an enhanced delivery system. Over past decades, considerable progress has been made in designing effective long acting parenteral formulations in both preclinical and clinical settings. The newly emerged 'Eligard' technology for leuprolide acetate has motivated to fabricate the biodegradable, biocompatible PLGA based long acting injectable suspension for the improved pharmacokinetics and patient compliance. In this research, PLGA based in-situ gel depot formulation was developed to obtain sustained release of MTX.

Methods:

A) **Preparation and optimization of in-situ gel:** Various grades of PLGA such as 75:25, 85:15, and 50:50 were screened in the preliminary study to obtain the gel like formulation. Initially, PLGA and MTX was dissolved in NMP and vortexed properly. Further, aqueous phosphate buffer of pH 7.4 was added to organic phase to obtain the gel. Various concentrations of NMP, PLGA and methotrexate were investigated to check the effect on burst release from prepared formulation.

B) **Physicochemical characterization**: The developed formulation was characterized by several techniques including DSC, FT-IR, PXRD, *in vitro* release and syringeability. The *in-vitro* release was performed by using by modified dialysis bag method. Initially, the prepared organic phase was added with 1 mL of PBS in order to mimic the in-situ depot in the dialysis bag (MW 8000). Further, 50 mL phosphate buffer saline (pH 7.4) was used as release media. The study was carried at 37±2°C and 50 rpm. 1 mL of sample was withdrawn and replaced at each time interval. The quantification of released MTX was performed by validated RP-HPLC method. The study was carried out for 7 consecutive days. In addition, sol to gel transition status was observed for morphological changes under optical microscope.

Results and Discussion: In the preliminary screening the PLGA 50:50 was shown in-situ gel depot system and thus used for further characterization. Among all screened factor, NMP and PLGA concentration showed effect on burst release. The observation suggested that with increase in concentration of PLGA, burst release was found to be increased. However, with increase in NMP concentration burst decrease in burst release was observed. However, the change in concentration of methotrexate did not significantly affect the burst release. Out of all prepared batches, the optimized formulation containing 117.5 mg PLGA provided 45 ± 0.494% release up to 7 days. The developed formulation was syringeable when passed through 22G, 23G and 24G.

Conclusions: The present work has potential to develop an improved drug delivery of methotrexate for the treatment of rheumatid arthritis. To the best of our knowledge, so far there are no reports of PLGA based long acting formulation for methotrexate. Thus, an attempt was made to design a formulation with potential to improve pharmacokinetics and avoid frequent injections, which, in turn can lead to improved patient compliance.

References:

1) Madhugiri P.V., et al., *Targeted drug delivery of Methotrexate in situ gels for the treatment of Rheumatoid Arthritis.* Saudi Pharmaceutical Journal, 2020, 28(12): p.1548-57.
2) Tchobaniouk LV., et al., *Once-monthly subcutaneously administered Risperidone in the treatment of schizophrenia: patient compliance*, Dovepress, 2019, 13: p. 2233-41.

Acknowledgements: The authors acknowlege NIPER-Ahmedabad for providing research facility.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Drug Release Studies of Nanoparticulate Drug Delivery System of an Anticancer Drug

Prachitee Ayare (prachitee.ayare@ves.ac.in)[1], Rajashree Hirlekar (rajashree.hirlekar@ves.ac.in)[1], Samiksha Mestry[1]

Vivekanand Education Society's College of Pharmacy, Mumbai, Maharashtra

Background and Rationale: Erlotinib is approved for the treatment of metastatic non-small cell lung cancer. Erlotinib has a low oral bioavailability due to its poor water solubility and presystemic metabolism. It shows side effects after oral administration. Thus, intravenous route can be preferred route of administration which can also reduce the dosing frequency and dose related side effects. Solid lipid nanoparticles (SLNs) can be used as potential delivery systems for Erlotinib. Further, use of cationic lipid in the formulation can increase the chances of passive targeting to tumors. The present study is aimed at development of SLNs of Erlotinib. The formulations were evaluated for particle size, PDI, zeta potential and drug release. The In-vitro drug release studies were carried out by using the dialysis bag method.

Methods: SLNs were prepared using stearylamine, a cationic lipid and tripalmitin as lipid phase. Alcoholic solution of drug was added to molten lipid phase. The aqueous phase was prepared by dissolving surfactant (Tween 80) in water. Both the phases were maintained at the same temperature in hot water bath and then aqueous phase was added to lipid phase to form primary emulsion. After bath sonication, it was subjected to high pressure homogenization at 5000 psi pressure for six cycles. Drug release studies were performed using the dialysis bag method. 2 ml drug solution in Transcutol HP, 2 ml drug dispersion in water and 2 ml SLNs containing 2 mg of drug was filled in the dialysis membrane and subjected to dissolution using buffer pH 1.2 as a medium. The aliquots were withdrawn at specified time intervals of 30min, 1, 2, 3, 4, 5, 6, 7, 8 and 9 hours, filtered and analyzed at 333 nm on UV visible spectrophotometer.

Results and Discussion: Developed SLNs showed particle size of 220.1 nm, PDI of 0.294 and zeta potential of 41.8± 4.138 mv. About 99.61% drug was released at the end of 2 hours from the drug solution in Transcutol HP, whereas only 35% and 20% of drug was released respectively from suspension and SLN in the same time interval. About 83% of drug was released at the end of 3 hours from drug dispersion and 88% of drug was released in 9 hours from SLN formulation. Thus, release of drug from SLN formulation was lesser than that from drug solution and drug dispersion.

The lipid matrix used for preparation of SLN retarded the drug release as compared to drug solution. The release profile of drug loaded SLN showed an initial burst followed by significant and stable release over a prolonged period. An initial burst release may be due to the drug adsorbed on the outer shell of SLN rather than the inner core.

Conclusions: The SLNs were successfully prepared using stearylamine and tripalmitin as a lipid and Tween 80 as surfactant. The dissolution pattern showed retardation of drug release from SLN as compared to drug solution and suspension.

References:

1. Rajani Rampaka, Kusuma Ommi, Naveen Chella, Role of solid lipid nanoparticles as drug delivery vehicles on the pharmacokinetic variability of Erlotinib, Journal of Drug Delivery Science and Technology, Volume 66, 2021, 102886, ISSN 1773-2247.

2. Pandey P, Dua K, Dureja H., Erlotinib loaded chitosan nanoparticles: Formulation, physicochemical characterization and cytotoxic potential. Int J Biol Macromol. 2019 Oct 15;139: 1304-1316.

3. Vrignaud S, Hureaux J, Wack S, Benoit JP, Saulnier P. Design, optimization and in vitro evaluation of reverse micelle-loaded lipid nanocarriers containing Erlotinib. Int J Pharm. 2012 Oct 15;436(1-2):194-200.

Acknowledgements: Authors are thankful to Vivekanand Education Society's College of Pharmacy for providing facilities to carry out research and Neon labs for gift sample of Erlotinib.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: Dissolution & Solubility Modulation

Evaluation of Suitability of USP Type IV Flow-through Apparatus to Examine the Dissolution Behavior of Efavirenz Delivered via Proliposomes

Vaishali Bambal (vaishalibmbl@gmail.com)[1], Vanaja Kenchappa (vanaja_ceutics@yahoo.com)[1], Surya Kovvasu[2], Ruoqiong Cao[3], Vishwanath Venketaraman[3], Guru V Betagiri[2]

College of Pharmaceutical Sciences, Dayananda Sagar University, Bengaluru, Karnataka | [2]College of Pharmacy, Western University of Health Sciences, California, USA,| [3]College of Osteopathic Medicine of the Pacific, Western University of Health Sciences, California, USA

Background & Rationale: Proliposomes are dry, free-flowing granular products, which upon hydration disperse to form multilamellar vesicles (MLVs) and are reported to improve the dissolution of poorly soluble drugs. (1) USP IV flow-through-cell has been reported to be the most suitable for dissolution analysis of drug nanoparticles in powder form in the optimization of poorly soluble drugs. (2) In the present investigation, efavirenz (EFA) which has lower intrinsic dissolution rate used specifically in the treatment of HIV-1 infection was selected for loading into proliposomes.

Methods: Objective of the study was to formulate efavirenz (EFA) proliposomes, characterize and examine its dispersibility upon hydration and measure the rate of drug release using USP type IV apparatus (Sotax CE7 smart with CY 7 piston pump, Sotax, Horsham, PA) of closed loop system with flow-through cells in comparison to conventionally used USP type II apparatus. To confirm the suitability of the method and dissolution profile comparison, studies were performed using water as the discriminatory medium, at different flow rates (4, 8 and 16 mL/min). At a selected flow rate, dissolution profiles were further obtained using 1% SLS (USP compendial method - EFA capsules) and at pH 6.8. Dissolution profiles were compared with marketed product of EFA (Sustiva™ capsules) as per compendia USP dissolution medium. Intracellular delivery of EFA to THP-1 Mo/Mac cells was also evaluated.

Results and Discussion: EFA proliposomes were prepared using either of the lipids - PL-90H (EFA-F1); DMPC (EFA-F2) and DSPC(EFA-F3) along with cholesterol using solvent hydration method. On hydration, all proliposomal formulations formed negatively charged multilamellar vesicles of size > 500nm and PDI > 0.3. At higher agitation (16 mL/min), no clear difference was observed with dissolution profiles between pure EFA, EFA-F1 and EFA-F3 as the cumulative release was 9.47%, 10.89% and 11.10% at the end of 4 h. In case of EFA-F2, dissolution profile increased linearly with increase in flow rate, which was about 18.8 % (4 mL/min), 25.8% (8 mL/min) and 32.14% (16 mL/min) in comparison to pure EFA which was < 9 % at all flow rates. It was observed that the cumulative percent of EFA released from the DMPC lipid formulation system (EFA-F2) exceeded the other lipid systems at all flow rates. Influence of lipid on dissolution of EFA proliposomes was prominent at 8mL/min with USP type IV with similarity factor (f2) < 50; whereas with type II, f2 was >50 when discriminatory media was used. Proliposomes loaded with EFA demonstrated 80% release in compendial media and exhibited 2 to 7.5 fold increase in different pH media in comparison to pure EFA.

Conclusions: Results demonstrated the superior discriminatory power of the USP IV flow through cell, hence could be employed to evaluate dispersion ability and dissolution performance of poorly soluble drugs encapsulated in proliposomes. Intracellular EFA uptake by differentiated macrophages was enhanced by 3.5 fold in comparison to pure EFA, further confirmed by confocal images. Also, proliposomal systems could be used to load ARV drugs for subsequent intracellular delivery to macrophages which harbors infectious HIV.

References:

1. Hiremath, P.S., K.S. Soppimath, and G.V. Betageri, Proliposomes of exemestane for improved oral delivery: formulation and in vitro evaluation using PAMPA, Caco-2 and rat intestine. Int J Pharm, 2009. 380(1-2): p. 96-104.
2. Bhardwaj, U. and D.J. Burgess, A novel USP apparatus 4 based release testing method for dispersed systems. Int J Pharm, 2010. 388(1-2): p. 287-94.

Acknowledgements: We acknowledge the funding received by Dr. V. V. from NIH grand no. RHL143545-01A1.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Formulation and Evaluation of Oral Guggulosomes Loaded with Gold Nanoparticles Synthesized from Hydroalcoholic Extract of *Tinospora cordifolia Miers*

Sheeja Koliyote (sheejakoliyote@gmail.com)[1], Jessy Shaji (jessy.shaji@gmail.com)[1]

[1]**Prin. KMK College of Pharmacy, Mumbai, Maharashtra**

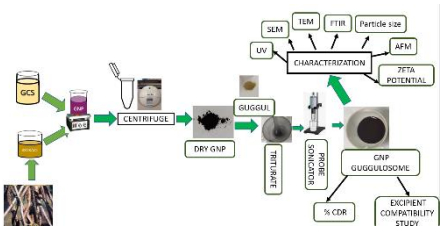
Background and Rationale: Guggulosomes are vesicular drug delivery systems in which the guggul forms drug-entrapped vesicles when it is triturated with the drug solution. Gold nanoparticle (GNP) synthesized from *Tinospora cordifolia Miers* have shown to possess enhanced anti-inflammatory property compared to *Tinospora cordifolia* hydroalcoholic extract. This study includes development, characterization and optimization of oral GNP gugulosomal formulation.

Method: Guggulosomes (GGNP) were prepared by trituration followed by probe sonication method. In total 4 guggulosomal formulations using different concentrations of guggul were processed to determine the optimized formulation amongst all. The prepared GNP loaded guggulosomes were characterized for particle size, zeta potential, polydispersity index and further guggulosomes were tested for % entrapment efficiency, % cumulative drug release, excipient compatibility, FTIR, HPTLC, AFM, TEM, SEM, TGA, DSC studies. Optimized formulation GGNP 3 was filled in hard gelatin capsule. *In vitro* drug release was carried out using USP Dissolution test apparatus II using 900 ml of pH 6.8 Phosphate buffer as release medium maintained at 37 ± 0.5 ºC. Rotational speed was 100 rpm. Aliquot (5 mL) was withdrawn at different time intervals and replenished with an equal volume of fresh medium. The amount of GNP released was determined at a wavelength of 546 nm. The *in-vitro* drug release was carried out in triplicate and further the percentage cumulative drug release (%CDR) was calculated and plotted against time.

Results and Discussion: After evaluating the formulations GGNP 1- GGNP 4, GGNP 3 was considered optimized with an average size of 342.2 ± 6.32 nm, PDI of 0.386 ± 0.02 and zeta potential of -17 mV. The % entrapment efficiency was 85.4 ± 0.732 with good % cumulative drug release of 82.9 ± 1.085 in 4hrs showing a sustained release profile. The guggulosomes showed all the characteristic peaks in FTIR. While the GGNP HPTLC fingerprint shows most of the bands of guggul than GNP, indicating guggul has encapsulated GNP. With the assistance of AFM, it was conceivable to detect that the guggulosome was having smooth surface but uneven shape. TEM reveals that GNP retains its shape and size even after being encapsulated by guggul, while SEM reveals a spherical surface morphology having diameter > 200nm. TGA analysis demonstrates that GNP had more thermal stability compared to Guggul as well as GGNP. The overlay graph of DSC shows that the GGNP graph is very similar to Guggul indicating that in GGNP, GNP is encapsulated in guggul. The FTIR spectra of GGNP with starch and lactose confirmed the absence of any chemical interaction with GGNP. GGNP showed good physical properties with acceptable stability.

Conclusion: In the present study potential of guggul in oral drug delivery of GNP synthesized from *Tinospora cordifolia* was investigated for the first time. This study suggested that guggul could serve as a sustained release carrier for GNP and GNP guggulosome can be used for oral delivery to treat chronic ailments such as rheumatoid arthritis.

Reference: 1. Dave V, Yadav RB, Gupta S, Sharma S. Guggulosomes: A herbal approach for enhanced topical delivery of Phenylbutazone. Future J Pharm Sci. 2017;3(1):23-32.



Acknowledgements: The authors would like to thank KMKCOP and MET IOP for all the facilities provided for the study.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Formulation Development and In-vitro Studies of Novel Micro-emulgel for Candidiasis

Jueeli Shiriskar (jueeli.shiriskar@ves.ac.in)[1], Ganga Srinivasan (ganga.srinivasan@ves.ac.in)[1], Ruchika Satam[2], Neha Chhabra[1], Vinay Saini[3]

[1]**Vivekanand Education Society's College of Pharmacy, Mumbai, Maharashtra** | [2]**Cipla Ltd, Mumbai** | [3]**Ostic Pharma Pvt. Ltd**

Background and Rationale: Candida species is the leading cause of a wide range of infections and during the pandemic, a surge in fungal infections was observed due to compromised immunity, nosocomial and iatrogenic transmissions which enhanced the demand for innovative therapies for candidiasis. This study focuses on formulating an Itraconazole-Diclofenac sodium combination therapy to achieve an antifungal activity with a release pattern above minimum inhibitory concentration at lower doses of both components to reduce fungal resistance. The micro-emulgel was the formulation of choice due to enhanced hydration of the stratum corneum and improved rate of skin absorption.

Methods:

A) Formulation development: Pre-formulation studies and quantitative analysis of both drugs were performed. The microemulsion was prepared by the phase titration method. The formulation was optimized by the Quality by Design approach using Design Expert software. A stable micro-emulgel was formulated after screening various gelling agents and was then evaluated for appearance, particle size, PDI, spreadability, viscosity, syneresis measurement, extrudability, pH, drug content, and antifungal activity. Stability studies of the formulation were carried out as per ICH guidelines.

B) *In vitro* release studies: The study was performed using Franz diffusion cell fitted with a dialysis membrane. The receptor compartment was filled with phosphate buffer pH 7.4: ethanol system in the ratio of 7:3 to maintain sink condition. The diffusion medium was continuously stirred with a magnetic bead at a constant rate. The temperature was controlled at 32°C by a circulating water bath. Both the drugs are poorly soluble and belong to BCS class II hence the challenge was to select a discriminating media for dissolution studies. UV Spectrophotometric method was developed and validated for analysis as per ICH Q2 guidelines using the simultaneous equation method and the % cumulative release of the drug was calculated.

Results and Discussion: The *in vitro* drug release of optimized micro-emulgel showed that 45% of the Itraconazole and 48.65% of Diclofenac sodium were released from the formulation throughout 8 hours which was above the Minimum Inhibitory Concentration.

Conclusions: The optimized formulation had adequate particle size and PDI. The *in vitro* drug release performed in phosphate buffer 7.4: ethanol (7:3) showed drug release from the formulation above MIC throughout 8 hrs. The antifungal activity showed a greater inhibiting area for optimized micro-emulgel. The formulation was stable over one month at 40±5ºC /75% RH and 30±5ºC /65% RH.

References:

1. Brilhante, R. S. N., et al., *Diclofenac exhibits synergism with azoles against planktonic cells and biofilms of Candida tropicalis.* Biofouling, 2020. *36*(5), 528-536.
2. Mohit, R., et al., *Development of simultaneous spectrophotometric method of mesalazine and prednisolone in same dosage form*. Int J Appl Pharm, 2010, *2*, 8-11.
3. Patel, M. R., et al., *Investigating the effect of vehicle on in vitro skin permeation of ketoconazole applied in O/W microemulsions.* Acta Pharmaceutica Sciencia, 2010, *52*(1).

Acknowledgements: We would like to express our deep and sincere gratitude to Ostic Pharma Pvt. Ltd. for providing the required facilities and constant guidance and motivation to reach the goal.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Four-Dimensional (4D) Printed Construct from Thermo-Responsive Self-Folding Feedstock for Pharmaceutical Applications

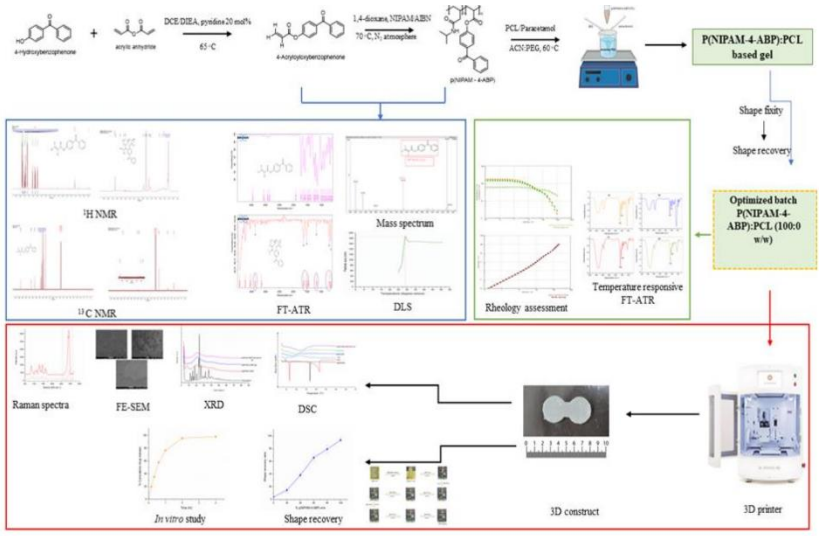
Purushottam Suryavanshi (suryavanshipurushottam1@gmail.com)[1], Subham Banerjee (subham.banerjee@niperguwahati.ac.in)[1]

[1]**Department of Pharmaceutics, NIPER Guwahati, Guwahati, Assam**

Background and rationale: Four-dimensional (4D) printing, is a newly evolving technology to formulate drug delivery devices, displays distinctive advantages that can autonomously monitor drug release according to the actual physiological circumstances. The aim of this study as to assess the potential use of a 4D printed construct for the effective drug delivery application using a novel temperature-responsive shape memory polymer named p(NIPAM-4-ABP) taking paracetamol (PCM) as a model drug.

Methodology: The semi-solid feedstock was prepared from the synthesized novel shape memory polymer i.e., (NIPAM-4-ABP) with different concentrations of PCL and PCM for the semi-solid extrusion-mediated 3D printer INVIVO Rokit Healthcare, Seoul, Korea). Physical, mechanical, and solid-state characterization of the prepared gel was performed using shape recovery analysis. Further, drug content and *in vitro* drug release with respect to shape recovery was investigated systematically.

Results and Discussion: The synthesized novel shape memory polymer i.e., p(NIPAM-4-ABP) and its corresponding hydrogel were evaluated and validated by 1H NMR, 13C NMR, mass spectrometry, FT-ATR, and Raman spectroscopy. The prepared gel was evaluated for rheological assessment and similar rheological properties were found for placebo and drug-loaded gel. The 3D printing parameters were optimized to print the 3D construct, and the 3D construct was printed with high resolution. Further, the formed prototype was evaluated for the shape fixity and recovery ratio. The performed study shows that PCL alone does not have any shape recovery property, while pure p(NIPAM-4-ABP) shows the highest shape fixity and shape recovery ratio of 90.07 and 93.64, respectively. DSC and P-XRD spectra show uniform mixing of polymer and drug at a molecular level. FE-SEM analysis confirms the morphological changes in the polymer network at different temperatures. Finally, the *in vitro* release of PCM from the programmed construct showed a biphasic pattern i.e., immediate release of around 75% within 1 hr, followed by a sustained release pattern attaining 100% release within 4.0 hr, suggesting a suitable drug delivery system for both fast and fed state conditions, with first-order release kinetics and classical Fickian diffusion as a PCM release mechanism.



Conclusion: The present work successfully explored the pharmaceutical application of novel 4D printing technology and its drug-release capabilities. The temperature-responsive, self-folding, p(NIPAM-4-ABP) based shape memory polymer was synthesized and evaluated. The p(NIPAM-4-ABP):PCL: Paracetamol-based hydrogel was prepared and meticulously screened for its 3D printability. The 3D construct shows excellent shape recovery properties from its temporary state to its original state at body temperature. Finally, *in vitro* studies suggest a biphasic release of PCM from 4D construct i.e., immediate release of around 75% within 1 hr, followed by a sustained release pattern attaining 100% release within 4.0 hr.

Acknowledgements: Financial support received from the Science and Engineering Research Board (SERB), Ministry of Science and Technology, Government of India, through SERB-SIRE fellowship, vide File No: SIR/2022/000111.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

High Permeation Vesicle-mediated Localized Delivery of Fulvestrant for Treating Breast Cancer

Junia Akhtar (juniaakhtar8@gmail.com)[1], Sanyog Jain (sanyogjain@niper.ac.in)[1]

[1]**Department of Pharmaceutics, NIPER-S. A. S. Nagar, Mohali, Punjab**

Background and Rationale: Breast cancer is a commonly diagnosed cancer in women, but the use of conventional chemotherapeutics causes serious systemic side effects. An alternative transdermal approach can aid in overcoming these challenges due to the distinct anatomical features of human breasts (1). However, the skin poses a major barrier for the permeation of drug molecules and therefore, we developed high permeation vesicles (HPVs) consisting of synergistic combination of permeation enhancers (SCOPE) to increase permeability of the system and provide a localized transdermal delivery of fulvestrant in breast cancer.

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

B) In vitro release study: The in vitro release of prepared formulations was conducted via dialysis bag method (MWCO 12kDa) in phosphate buffer pH 5.8 (to mimic skin pH) with 0.5% tween 80 to maintain the sink conditions and compared with free drug, SCOPE mixture and liposomal formulation.

C) Ex vivo skin permeation study: The permeation efficiency of prepared formulation across pig ear skin was evaluated using a Franz diffusion cell.

D) Cell culture Studies: Cellular uptake analysis of the formulation was analysed in MCF-7 and MDA-MB-231 cell lines. The in vitro cell cytotoxicity study was evaluated in the MDA-MB-231 cell line.

Results and Discussion: The optimized formulation of HPVs resulted in spherical vesicles of size 80.64±2.32 nm, PDI 0.214±0.014, zeta potential -35.2±3.1 mV and 76.45±3.54 % entrapment efficiency. The free drug and SCOPE showed a rapid release profile. The encapsulation of fulvestrant in HPV helped in attaining sustained drug release. HPV and liposomal formulation exhibited 80% and 70% drug release, respectively at 48 h. The incorporation of HPVs in the gel matrix further assisted in sustaining the drug release pattern and showed 60% drug release in 48 h. The skin permeation and deposition study were performed to determine the transdermal fulvestrant permeation and amount of fulvestrant present in skin layers. Out of all groups, HPVs showed the highest percent of skin permeation with ~17% fulvestrant permeation. The free drug gel showed negligible permeation of fulvestrant across the skin, highlighting the role of the SCOPE combination and nanocarriers in improving fulvestrant permeation. The cell-line-based studies showed superior results for HPVs compared to that of free drug and liposomes assuring the enhanced therapeutic activity of HPV.

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

References:

1. Lee, O., et al., Novel routes for administering chemoprevention: local transdermal therapy to the breasts. Seminars in Oncolog, 2016. 43(1): p. 107-115.
2. Jain, S., et al., Mechanistic insights into high permeation vesicle-mediated synergistic enhancement of transdermal drug permeation. Nanomedicine, 2019. 14(16): p.2227-2241.

Acknowledgements: The authors would like to acknowledge Director, NIPER S.A.S. Nagar for providing the necessary facilities and infrastructure.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Investigation of Co-crystal Formation as a Strategy to Improve the Stability and Solubility of Antispasmodic drug in Immediate Release Tablets

Sanika Kole (kolesanika5@gmail.com)[1], Ashwin Kuchekar (ashwin.kuchekar@mitwpu.edu.in)[1], Rutuja Vinchurkar[1], Ashwini Gawade[1]

[1]**School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra**

Background and Rationale: Different API degrades differently under different stress conditions like acid hydrolysis, base hydrolysis and oxidative, thermal and photolytic exposures. To overcome the problem of degradation and to make the API more stable, different novel technologies have to be applied. Cocrystallization of pharmaceuticals is an innovative strategy that aims to modify the physicochemical properties of active pharmaceutical ingredients to enhance their stability and solid-state characteristics. The objective was to select an appropriate co-former and investigate its impact on the formation of co-crystals with API and to prepare, characterize and evaluate immediate release tablets of the co-crystals.

Methods: A. Molecular Docking and selection of Co-formers for development of co-crystals by kneading method: A molecular docking study using AutoDock V4.2.6 software was performed on selected five co-formers namely Fumaric acid, Tartaric acid, Citric acid, Oxalic acid, Succinic acid. Further application of the docking score of selected co-former as Fumaric acid and utilizing the kneading approach, co-crystals in the ratio of (1:1, 1:2, and 1:3) were prepared (1).

B. Direct compression method for preparation of Immediate Release Tablets: Microcrystalline Cellulose was combined with co-crystals, and the mixture was prepared for direct compression by adding starch, talc, and magnesium stearate as excipients. The blend was compressed using a 6 mm punch in a tableting machine.

C. In-vitro drug release study: Utilizing a USP II dissolution test (Paddle Apparatus), invitro dissolution experiments for IR tablets of prepared co-crystals were performed. The test was conducted in 900 ml of pH 1.2 medium at a temperature of 37°C and 50 RPM to determine drug release (2).

Results and Discussion: API: co-former co-crystals and IR tablets of resultant co-crystals were prepared successfully. The stability, solubility, and dissolution rate were improved by successfully preparing, screening, and optimizing co-crystals and co-crystal IR tablets. The selected batch exhibited the highest drug release rate of 95.5% within a 60-minute timeframe and remained stable for 12 months.

Conclusions: This type of delivery system will aid in enhancing the stability, dissolution, disintegration, drug content of API, with potential to improve its ex-vivo antispasmodic activity as well as create a future platform for targeted drug delivery systems.

References:

1. Wasim M, Mannan A, Asad MHH Bin, Amirzada MI, Shafique M, Hussain I. Fabrication of Carbamazepine Cocrystals: Characterization, in Vitro and Comparative in Vivo Evaluation. Biomed Res Int. Published online 2021. doi:10.1155/2021/6685806
2. Gawade A, Kuchekar A, Boldhane S, Baheti A. Improvement of Physicochemical and Solubility of Dipyridamole by Cocrystallization Technology. J Drug Deliv Ther. Published online 2021. doi:10.22270/jddt.v11i1-s.4696.

Acknowledgements: Authors express gratitude to the School of Health Sciences and Technology, Dr. Vishwanath Karad MIT WPU, Pune for providing all resources.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Mucoadhesive Lecithin-Chitosan Hybrid Nanoparticles for Augmented Oral Delivery, In Vitro Efficacy and Safety of Dasatinib

Srushti Mahajan (srushtimahajan7@gmail.com)[1], Pankaj Kumar Singh (pankajksingh3@gmail.com)[1]

[1]**National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad, Telangana**

Background and Rationale: Triple-negative breast cancer (TNBC) is an aggressive form of breast cancer with low survival rates. Dasatinib (DAS) is a tyrosine kinase inhibitor with established antiproliferative activity in TNBC. However, its efficacy is significantly reduced due to poor solubility in the small intestinal and low oral bioavailability (14-34%) [1]. A suitable carrier system can improve the delivery efficiency of DAS. Chitosan, a cationic biocompatible mucoadhesive polymer, widely applied in drug delivery. It can prolong the residence time by interacting with the mucin layer and reversibly open the intracellular tight junction [2]. Thus, this research aimed to improve DAS's oral delivery and efficacy in TNBC by fabricating mucoadhesive lecithin-chitosan hybrid nanoparticles (DAS-L/CS-NPs).

Methods: A) Preparation, optimization and characterization of DAS-L/CS-NPs: The DAS-L/CS-NPs were prepared by nanoprecipitation technique and optimized by the Box– Behnken design using Design Expert® software. The optimized NPs were characterized for mean particle size, polydispersity index (PDI), zeta potential and entrapment efficiency. SEM, TEM, PXRD, DSC and FTIR analysis were also conducted.

B) **In-vitro, ex-vivo and in-vivo evaluation of DAS-L/CS-NPs:** In-vitro drug release was performed in SGF (pH 1.2), acetate buffer (pH 4), SIF (pH 6.8) and PBS (pH 7.4). Ex-vivo drug permeation study using a non-everted gut sac method was done to estimate DAS's apparent permeability and flux from DAS-L/CS-NPs. Ex-vivo mucoadhesion, in-vitro mucin particle method and turbidimetric method were used to assess the mucoadhesive absorption. In-vitro cell-culture assays in MDA-MB-231 cells were conducted to appraise efficacy against TNBC. In-vivo intestinal absorption study was executed in female Balb/c mice using FITCloaded L/CS-NPs. Further, the in-vivo safety of DAS-L/CS-NPs was evaluated by histological examination and measuring plasma levels of toxicity markers.

Results and Discussion: The optimized DAS-L/CS-NPs exhibited nano-ranged size with a 33.4 ± 0.985 mV zeta potential. Physicochemical characterization revealed spherical NPs with an entrapped amorphous form. DAS-L/CS-NPs showed sustained release at different pH conditions, with 79% and 53% release in pH 4 acetate buffer and SIF (pH 6.8) upto 48 h respectively, owing to slow diffusion of DAS from lecithin matrix and chitosan shell. DAS's apparent permeability coefficient and flux were found to be 10 times higher from NPs than free DAS due to the opening of tight junctions between enterocytes by chitosan. Further, the NPs showed significantly higher ($P<0.01$) mucoadhesion than free DAS in the ex-vivo study, which is attributed to the interaction between chitosan and mucin. In the turbidimetric study, the absorbance difference of DAS-L/CS-NPs between water and mucin was significantly high, demonstrating increased interaction between chitosan and mucin. Cell culture studies revealed a 3.8 times decrease in IC50 and significantly higher cellular uptake of NPs in MDA-MB-231 cells. Confocal images of jejunum sections of the FITC-loaded L/CS-NPs treated mice group showed higher fluorescence than the free FITC group, displaying higher uptake and absorption characteristics. Histological examination and plasma marker analysis indicated an improved safety profile of the DAS-L/CS-NPs.

Conclusion: The developed mucoadhesive DAS-L/CS-NPs showed promising carrier properties in enhancing DAS's oral delivery and anticancer effect in TNBC.

References:

1. Y. Tsume, S. Takeuchi, K. Matsui, G.E. Amidon, G.L. Amidon, In vitro dissolution methodology, mini-Gastrointestinal Simulator (mGIS), predicts better in vivo dissolution of a weak base drug, dasatinib, European Journal of Pharmaceutical Sciences 76 (2015) 203-212.
2. H. Cheng, Z. Cui, S. Guo, X. Zhang, Y. Huo, S. Mao, Mucoadhesive versus mucopenetrating nanoparticles for oral delivery of insulin, Acta Biomaterialia 135 (2021) 506-519.

Acknowledgements: The authors acknowledge the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Govt. of India.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: Dissolution & Solubility Modulation

Novel Bio-Predictive High Shear Based Dissolution Method for In Vitro Evaluation of Prolong Release Erodible Formulation

Vishal Bagul (vishalbagul@lupin.com)[1], Sajeev Chandran (sajeevchandran@lupin.com)[1]

[1]**Advanced Drug Delivery Systems, Pharma Research, Lupin Limited, 46/47A, Nande Village, Mulshi Taluka, Pune, Maharashtra**

Background and Rationale: In vitro dissolution tests play a crucial role in formulation development and optimization. The current study describes the development of a novel, bio-predictive, high shear based dissolution method as a formulation optimization tool for a generic prolong release erodible formulation of a BCS Class-II molecule. The formulations are based on a hydrophobic matrix formed by talc and cellulose polymer, exhibiting diffusion and erosion-controlled drug release mechanism. To achieve a discriminatory method, we have carried out mechanistic studies to assess the impact of parameters such as agitation speed, buffer species, concentration and type of surfactant etc. Bio-predictiveness of the developed dissolution method was assessed by comparing the in vitro dissolution of the formulations with the in vivo performance observed in human BE studies.

Methods: A) Formulation of prolong release tablets: The formulation design constitutes a core-coat system with the core containing the API in a matrix of extended release polymer and other excipients, coated with rate controlling polymer and other excipients. Three lots of the formulation with different API PSD *viz.*, 26, 60 and 99 µm D_{90} were manufactured. Further, human bioequivalence studies of the batches were carried out to determine their in vivo performance.

B) Development of discriminatory dissolution method: Studies were performed in 250 mL of simulated intestinal fluids (pH 6.5) with 0.05% Tween 80, maintained at 37±0.5°C and agitated at 30 DPM using USP-III reciprocating cylinder apparatus[1]. Attempt to establish multiple level-C *in-vitro–in-vivo* correlation[2] (IVIVC) was made to determine the bio-predictiveness of dissolution method.

Results and Discussion: Among the three lots with different PSD of API, the optimised formulation with API PSD of 60 µm was found to be bioequivalent to RLD. The bioavailability of drug was in line with the API PSD viz., lots with smaller particle size showing faster and higher bioavailability. The formulation is designed for drug release in the high shear environment of the GIT. Based on this, it would be easier to emulate such high shear conditions using USP III dissolution apparatus. The dissolution method was able to discriminate the formulations in accordance with their *in vivo* performance. A multiple Level-C IVIVC showed an average prediction error of less than 10% for C_{max} T/R values, indicating a good fit of the *in-vitro* and *in-vivo* data.

Conclusion: Implementation of high shear using USP type III dissolution apparatus was found to correlate well with the *in-vivo* stress and hydrodynamics exerted on the formulation during GI transit. The established multiple level-C IVIVC was able to predict *in-vivo* bioavailability from prolong release erodible matrix system of BCS class II drug candidate.

References

1. Rohrs, B. R., et al., USP Dissolution Apparatus 3 (Reciprocating cylinder): Instrument Parameter Effects on Drug Release from Sustained Release Formulations. *J. Pharm. Sci.*, 1995, *84* (8), p. 922–926.
2. Kaur, P., et al., Applications of In Vitro–In Vivo Correlations in Generic Drug Development: Case Studies. *The AAPS Journal*, 2015, 17 (4), p. 1035-1039.

Acknowledgements: Lupin Research Park

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Optimization and Cytotoxic Evaluation of a Novel Andrographis Extract and Sesame Oil Emulgel through QbD Approach.

N V L Sirisha (sirisha.mulukuri@nitte.edu.in)[1], Kusum Devi V (drvkusum.devi@nitte.edu.in)[1], Pankaj Kumar[1], Moumitha Dhara[1]

[1]**Nitte College of Pharmaceutical Sciences, Bangalore, Karnataka**

Background and Rationale: Epidermoid carcinoma is a type of non-melanoma skin cancer originating from the outer layer of squamous cells in the skin. Previous research has demonstrated the inhibitory effects of *Andrographis* extract and Andrographolide on the growth and proliferation of epidermoid carcinoma cells, as well as their ability to induce cell cycle arrest and apoptosis[1]. This study aimed to enhance the anticancer efficacy of Andrographolide-rich extract by formulating it into a Nano-emulgel.

Methods: The emulgel formulation was prepared using sonication and homogenization techniques, incorporating sesame oil as the oil phase instead of synthetic oils to minimize potential side effects. Triethanolamine was added to adjust the pH within the range of 5.85-6.35. The optimized gels were subjected to various preliminary evaluations along with SEM studies, drug release, anti-cancer activity.

A. *Invitro* release studies: The experimental emulgels were applied to a dialysis membrane and placed in a Franz diffusion cell. Buffer solution (pH 7.4) was added to the bottom compartment of the cell to simulate medicament release. The setup was stirred continuously at 37°C on a magnetic stirrer. Blank readings were taken for comparison, and every 30 minutes, 1 ml of release medium was withdrawn and replaced with fresh medium to maintain sink conditions. The experiment lasted for 8 hours, and the collected samples were diluted and analyzed using UV-spectrophotometry at 223 nm. Cumulative percentage drug release values were calculated based on a standard plot.

B. Anticancer studies: A-431 cells (2 x 104) were seeded into each well of a 96-well tissue culture plate containing 100 µL of DMEM medium and incubated at 37°C with 5% CO_2 for one day. The cells were treated with the emulgel formulations; a 5 mg/mL MTT solution in PBS was added (20 µL) to each well and incubated for 4 hours at 37°C. The optical densities were measured at 570 nm using an ELISA reader (Bio-Rad, CA, USA). The cell cycle studies were performed to know the further mechanisms involved in the cell death.

Results and Discussion: The optimized emulgel displayed well-defined spherical morphology as observed through SEM analysis, with a droplet size of 226 ± 1.8 nm, a negative surface charge of -30.1 ± 1.6 mV, and a low PDI (Polydispersity Index) value of 0.157. The drug release study revealed the sustained release of 92.8% of active over time at pH 7.4. The release followed zero-order and Hixson–Crowell kinetics, which explains the sustained release observed with the emulgels. In cellular studies, the selected emulgel showed a significant reduction in the viability of A431 cells, with an IC50 value of 16.56 µg/ml, by MTT assay, which is higher compared to cells treated with a placebo or the extract alone.

Conclusions: Based on the results, the enhanced anticancer efficacy of Nano-emulgel formulations observed in A431 cells highlights the potential of this formulation strategy for addressing skin cancer.

References:

1. Liu, G. & Chu, H. Andrographolide inhibits proliferation and induces cell cycle arrest and apoptosis in human melanoma cells. *Oncol. Lett.* **15**, 5301–5305 (2018).

Acknowledgements: N V Satheesh Madhav, Head R & D, Vital Therapeutics & Formulations Pvt Ltd, Hyderabad.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Phospholipid - coated Biomimetic Membranes for Permeability Studies - Preparation and Evaluation

Pankaj Sontakke (sontakkepankajmumbai@gmai.com)[1], Mala Menon (maladmbcp@yahoo.co.in)[1], Ujwala Shinde[1]

[1]**Bombay College of Pharmacy, Mumbai, Maharashtra**

Background & Rationale: *In vitro* permeability studies employing and barrier membranes are important tools in drug discovery and development. Barrier membranes include animal intestine models, artificial membranes and cell culture models. Cell culture models, though ideal, are labor intensive, time consuming and expensive. Artificial membranes are preferred for quicker screenings. Use of phospholipids in developing biomimetic membranes are reported. Objective of the present work was to prepare and evaluate biomimetic phospholipid membranes (BPM) for passive drug permeability studies.

Methods: A. Preparation and characterization of BPMs -Phospholipid (LIPOID S 100, Lipoid GmbH, Germany) and cholesterol (Sigma-Aldrich.) in the ratio of (2:1) were dissolved in chloroform, and poured to form a thin layer on following artificial membranes- a) Polyvinylidene fluoride (PVDF) hydrophilic filter membrane-PHP (Axiva Sichem), b) PVDF hydrophobic filter membrane- PHB (Merck Life Sciences) and c) Dialysis membrane (DM) – (50, LA387-5MT, 12000-14000 Dalton, Himedia). Organic solvent was allowed to evaporate at RT to obtain PBMs, viz. Lipid coated Dialysis membrane (LC-DM), Lipid coated PVDF hydrophilic (LC-PHP) & Lipid coated PVDF hydrophobic (LC-PHB). The membranes were characterized for colour, odour, thickness, visual appearance, tackiness and surface area.

B) *In vitro* permeation study - Diltiazem HCl (DIL- BCS class-I) and Metformin HCl (MET- BCS class-III) were selected for assessment of the prepared BPM. The permeation study was carried out using vertical diffusion cells (Hanson, Germany) for up to 4 hours**;** donor cell contained drug solution in pH 6.8 buffer (5 mL -1000 µg/mL); receptor medium - pH 7.4 Kreb's Ringer buffer (7 ml)**;** 37 ± 0.5°C**.** Aliquots (1 mL) withdrawn were analysed by validated HPLC method. Flux, permeability coefficient, diffusivity, lag time and resistance were calculated.

Results and Discussion: The prepared BPM were translucent/opaque with slightly tacky surface on the coated side. The various calculated parameters: **a)** for DIL- Flux (µg/ sec*cm): DM-0.0371, LC-DM -0.0049, PHP- 0.0271, LC-PHP- 5.22, PHB- 0.0033 and LC-PHB -0.0047. Permeability (x 10^{-6} cm/sec) for DM- 39.1, LC-DM -5.22, PHP- 65.19, LC-PHP- 6.5, PHB- 3.26 and LC-PHB - 4.56. **b)** For MET- Flux (µg/ sec*cm): DM- 0.0271, LC-DM – 0.0021, PHP-0.0589, LC-PHP- 0.0027, PHB- 0.0019 and LC-PHB - 0.0011. Permeability (x 10^{-6} cm/sec) for DM- 28.22, LC-DM - 2.24, PHP- 65.19 , LC-PHP- 6.5, PHB- 3.26 and LC-PHB - 4.56. Thus, in case of all three prepared BPM barriers, flux and permeability values were found to decrease for both drugs, in comparison to uncoated membranes. Further, lag time and diffusivity were decreased for both drugs in lipid coated membranes, except LC-PHB for DIL. This reflected a lower lipid layer resistance for DIL compared to MET. Lipid layer permeability (P_{lip}) was calculated, which also corroborated this fact.

Conclusions: This study depicts feasibility of preparing simple biomimetic barrier membranes by phospholipid coating, and their usefulness in permeability testing of oral drugs. Further refinement and validation are essential to commercialize this approach.

References:

1. Brandl, M., Flaten, G.E., Bauer-Brandl, A., 2009. Passive diffusion across membrane. *Wiley Encyclopedia Chem. Biol*. 2009,3, pp.541-500.
2. Di Cagno, M., Bibi H. A., Bauer-Brandl, A. New biomimetic barrier Permeapad™ for efficient investigation of passive permeability of drugs. *European Journal of Pharmaceutical Sciences*, 2015, 73, pp. 29–34.

Acknowledgements: Authors are grateful to IPCA Lab. Mumbai for providing gift samples of Diltiazem HCl and Metformin HCl drugs., and Lipoid GmbH, Germany for Phospholipid LIPOID S 100 for research work.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: Pharmacokinetics & IVIVC Studies

Selection of Phytoconstituents for Targeting PPARs in NAFLD: an In-silico and Molecular Docking based Pharmacokinetic Study

Shweta Padher (padhersarita68@gmail.com)[1], Varsha Pokharkar (varsha.pokharkar@bharatividyapeeth.edu)[1],

[1]**Bharati Vidyapeeth Poona College of Pharmacy, Pune, Maharashtra**

Background and Rationale: Non-alcoholic fatty liver disease (NAFLD) is becoming one of the most common liver diseases with a high global occurrence, but treatment strategies are lacking. Herbal medicines are considered "nature's pharmacy" and form a major component in all indigenous traditional medicines. A number of herbal preparations are available in the market, but limited bioavailability and scarce information on their ADME properties restrict their use. Experimental and computational approaches are now being employed, which have paved the way to successful drug repurposing and minimizing the cost, time, and risk of de *novo* drug discovery. In this study, we have identified the target proteins of NAFLD as reference materials i.e PPAR-α & PPAR-μ,which are the best-known anti-obesity transcription factor in the adipose tissue and liver, and performed in-silico analysis, followed by molecular docking to select the appropriate phytoconstituents for further formulation and evaluation. A reverse pharmacology based approach to identify phytoconstituents, analyse their in-silico ADME properties, binding actions on the peroxisome proliferator-activated receptors and pharmacokinetic parameters post formulation, was therefore applied for the study.

Methods: Canonical SMILES data from Pubchem followed by the collection of disease genes related to NAFLD from GeneCards (http://www.gengcards.org/), OMIM (http:// omim.org/), and DisGeNET (http://disgenet.org/home/) were collected.The selected phytoconstituents were further subjected to in-silico screening using softwares like SWISS ADME, pkcsm and ADMET lab. Computational docking analysis was performed using AutoDock Vina based on scoring functions to finally narrow down to selection of the best phytoconstituents for use in formulation development for NAFLD. Phytoconstituents thereby selected (Glycrrhizic acid, Ellagic acid) were formulated as lipid-based phospholipid complex with phosphatidylcholine (Lipoid S100) by rotary evaporation method. Pharmacokinetic evaluation was carried out in male wistar rats (Dose:100 mg/kg for both). Time intervals used for blood collection were 0,2,4,6,8,10,12 and 24 hours.

Results and Data Analysis: For this, 40 phytoconstituents were initially subjected to ADMET screening by Swiss ADME and other platforms,through which 29 were further used as ligands for studying molecular interaction with the target proteins of NAFLD.Out of the selected phytoconstituents,ellagic and glycrrhizic acid when formulated as phospholipid complexes and evaluated for pharmacokinetic parameters,showed a two-fold increase in the Cmax for both the drugs.

Conclusions: These results indicated that certain phytoconstituents displayed both good drug-like characteristics and ADME properties and also showed good binding affinity energies with the ligands.Pharmacokinetic studies also proved to enhance the bioavailability of the selected phytoconstituents by virtue of their complex with the phospholipid.These could hence be the potential leads to be used in NAFLD for preclinical and clinical evaluation by virtue of further formulation and optimisation.

References:

1. Tang Z, Li L, Xia Z. Exploring Anti-Nonalcoholic Fatty Liver Disease Mechanism of Gardeniae Fructus by Network Pharmacology, Molecular Docking, and Experiment Validation. ACS Omega. 2022 Jul 12;7(29):25521-25531.
2. Venkatesh Murugan, Kakali Mukherjee, Kuntal Maiti, And Pulok K. Mukherjee.Enhanced Oral Bioavailability and Antioxidant Profile of Ellagic Acid by Phospholipids. J. Agric. Food Chem. 2009, 57, 4559–4565 45.

Acknowledgements: Bharati Vidyapeeth, Poona College of Pharmacy

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Solid Self Nano-emulsifying Drug Delivery System (SNEDDS) Improves Dissolution, Endows in-vitro Efficacy and Pharmacokinetic Profile of Dasatinib

Mayur Aalhate (mbalhate44@gmail.com)[1], Pankaj Kumar Singh (pankajksingh3@gmail.com)[1],

[1]**National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad, Telangana**

Background and Rationale: Dasatinib (DST) is a multi-targeted oral tyrosine kinase inhibitor with poor aqueous solubility and high permeability [1]. The low bioavailability of DST is mainly related to its susceptibility to first-pass metabolism and incomplete absorption owing to its low solubility in the small intestine [2, 3]. To outwit the issue of poor oral bioavailability, we have formulated and optimized a solid self-nano emulsifying drug delivery system (S-SNEDDS) of DST.

Methods: I-optimal extreme vertices mixture design was used for exhaustive optimization of SNEDDS using Linalool, Cremophor RH40 and Transcutol P. The final dosage form was lyophilized DST-SSNEDDS with Aerosil® 200 as a carrier. Formulation was characterized by SEM, TEM, DSC, PXRD. Further, in-vitro dissolution studies were performed in Apparatus I at pH 6.8 phosphate buffer, dialysis release in SIF (pH 6.8) and ex-vivo gut permeation studies were performed on goat duodenum. Moreover, cell based cytotoxicity, cell uptake and apoptotic potential was evaluated in MDA-MB-231 cells to evaluate the anticancer potential. Acute toxicity studies and plasma pharmacokinetic study was performed to assess the safety and bioavailability of S-SNEDDS respectively.

Results and Discussion: Size of optimized DST-S-SNEDDS was observed below 200 nm. DSC and PXRD studies revealed that DST is present in the amorphous state in the formulation. Developed DST-S-SNEDDS demonstrated significantly higher drug dissolution with >70% DST released from SNEDDS in 6 h which could be attributed to nano-sized emulsion droplets and the higher solubilizing capacity of the SNEDDS components. Gut permeation data showed 1.51-fold increment in flux of DST-SSNEDDS (21.161 µg/cm2 /h) as compared to free DST (15.979 µg/cm2 /h). Cell cytotoxicity experiments in MDA-MB-231 cells revealed an IC50 value of 1.825 µg/mL for DST-S-SNEDDS, significantly lower than the free DST (7.298 µg/mL). Acute toxicity studies demonstrated no-significant rise in toxicity markers such as ALT and AST as compared to control. In in-vivo pharmacokinetic studies, a 1.94-fold increment in AUC0-t and a 3.78-fold increase in Cmax was observed for the DST-S-SNEDDS treated group compared to the free DST.

Conclusion: In a pursuit to enhance the oral bioavailability and anticancer activity of DST-S-SNEDDS, the formulation was extensively optimized with the aid of DoE. The resultant formulation was highly robust and demonstrated excellent dissolution. MTT assay and apoptosis studies also corroborated the effectiveness of DST-S-SNEDDS as compared with naked DST. Moreover, 1.94-fold increase in bioavailability makes DST-S-SNEDDS an attractive drug delivery approach with possible options of industrial scalability.

References:

1. Zhang, Y., et al., Dasatinib self-assembled nanoparticles decorated with hyaluronic acid for targeted treatment of tumors to overcome multidrug resistance. Drug Delivery, 2021. 28(1): p. 670-679.
2. Mikus, G. and K.I. Foerster, Role of CYP3A4 in kinase inhibitor metabolism and assessment of CYP3A4 activity. Transl Cancer Res, 2017. 6(Suppl 10): p. S1592-S1599.
3. He, S., et al., Therapeutic drug monitoring and individualized medicine of dasatinib: focus on clinical pharmacokinetics and pharmacodynamics. Frontiers in Pharmacology, 2021: p 3439.

Acknowledgements: The authors would like to acknowledge the Department of Pharmaceuticals (DoP), Ministry of Chemicals and Fertilizers, Govt. of India.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Unveiling the Potency of Nano Cream-Gel formulated with Alpha Hydroxy Acid in Skin Rejuvenation: A Comprehensive Investigation Bridging In Vitro and Animal Studies

Rutuja Vinchurkar (1102220263@mitwpu.edu.in)[1], Ashwin Kuchekar (ashwin.kuchekar@mitwpu.edu.in)[1], Sanika Kole[1], Ashwini Gawade[1]

[1]**School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune, Maharashtra**

Background and Rationale: In today's era, people prioritize maintaining healthy, radiant skin and feeling confident in their appearance. Skin rejuvenation treatments offer a solution to enhance the overall look of the skin. However, existing invasive treatments often result in irritation, inflammation, and high costs. To overcome these drawbacks, a non-invasive formulation is needed, specifically targeting the basal cell layer responsible for skin regeneration. The Nano Cream Gel (NCG) has demonstrated exceptional potential in precisely stimulating the basal cell layer, promoting natural cell renewal processes. This capability facilitates skin rejuvenation and effectively addresses concerns related to aging and skin damage. NCG represents a promising advancement in skincare, providing a targeted and effective approach to achieving youthful skin.

Methods: A) Preparation of NCG: In the preparation of NCG, a combination of novel acryl block polymers and alpha hydroxy acid was utilized. The formulation process involved magnetic stirring and homogenization methods to ensure proper dispersion and uniformity. To achieve an optimized batch, a 3^2 factorial design was employed, wherein different grades of polymers were incorporated at various concentrations.

B) *In Vitro* study and Acute Dermal Toxicity Study: A Franz diffusion cell with a phosphate buffer of pH 6.8 was used to withdraw samples at specific intervals from 0 to 60 minutes. Each sample was replaced with an equal volume of fresh release media. Female Wistar rats were subjected to an acute dermal toxicity study, where doses of 200, 1000, and 2000 mg/kg were applied to 10% of their shaved dorsal section area. The rats were monitored daily for 14 days to assess signs of irritation or inflammation resulting from the application. This study aimed to evaluate the test substance's safety profile.

Results and Discussion: In the 3^2 Factorial designs, 0.5% and 0.75% A and B polymers were identified as suitable for NCG formulation. The NCG exhibited a pH of 6.2, viscosity of 12,500 cps, particle size of 405.5 nm, and zeta potential of -71.9 mV, displaying pseudoplastic flow. It remained stable for 16 months. With a cumulative drug release of 91.52% and a drug content of 90.6% ± 0.52%, the NCG demonstrated faster absorption than the placebo, without causing skin irritancy or inflammation. Histopathology reports indicated increased new cell formation, including collagen and elastin, specifically in the basal cell layer. These findings confirm the NCG's effectiveness in promoting skin rejuvenation and facilitating cellular regeneration.

References:

1. Zerbinati N, Sommatis S, Maccario C, Di Francesco S, Capillo MC, Rauso R, Herrera M, Bencini PL, Guida S, Mocchi R. The anti-ageing and whitening potential of a cosmetic serum containing 3-o-ethyl-l-ascorbic acid. Life. 2021 Apr 29;11(5):406.
2. Campione E, Cosio T, Lanna C, Mazzilli S, Dika E, Bianchi L. Clinical efficacy and reflectance confocal microscopy monitoring in moderate-severe skin aging treated with a polyvinyl gel containing retinoic and glycolic acid: An assessor-blinded 1-month study proof-of-concept trial. Journal of Cosmetic Dermatology. 2021 Jan;20(1):310-5.

Acknowledgements: The authors would like to thank the School of Health Sciences and Technology, Dr. Vishwanath Karad MIT World Peace University, Pune for providing all of the resources.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

A Systematic Approach to Study Influence of Coating Composition of Carboxymethyl Ethyl Cellulose on In Vitro Release of Extended-release Formulations of a Highly Soluble Drug

Ankita Thorat (ankitathorat426@gmail.com) [1], Madhur Kulkarni (madhur.kulkarni@indiraicp.edu.in)[1], Rahul Aware[2], Prashant Pisal[2]

[1]SCEs Indira College of Pharmacy, Pune, Maharashtra | [2]ACG Engineering Pharmatechnology

Background and Rationale: Carboxymethyl ethyl cellulose (CMEC) is a pH-sensitive, hydrophobic, non-gelling, novel polymer that is official in Japanese Pharmacopoeia. It is slower to disintegrate in a lower pH (< 5) but faster at a higher pH. Lower concentration of CMEC (< 10%) shows delayed release potential while 10-30% concentrations exhibit extended release (ER) behavior. It has been reported to have excellent film forming properties. However, CMEC has been seldom explored in drug delivery field. The current work aimed at studying the release retarding potential of CMEC using a water soluble, poorly compressible model drug, metformin hydrochloride (Met). Objectives of present work was 1. Development of ER granules and tablets of Met using CMEC as a release retardant and to study the effect of hydroxypropyl methyl cellulose 5 Cps (HPMC E5) as a pore former on drug release.

Methods: A) Preparation of ER Met granules: Appropriate quantity of Met was weighed and blended in high shear mixer with HPMC K100LV and lactose. Granules were prepared with water and dried using fluid bed dryer at inlet temp of 35-400C for 10 mins. Met granules were coated with the coating composition of CMEC and HPMC E5 in the ratios of 97:3, 95:5, 93:7 up to the weight gain of 2%, 3%, 4% in case of each ratio. Fluid bed processor was used for the coating operation. **B) Preparation of ER Met tablet formulation:** Uncoated Met granules were compressed into tablets using suitable quantity of magnesium stearate and colloidal silicon dioxide. Met tablets were coated with the coating composition of CMEC and HPMC E5 in the ratios 97:3, 95:5, 93:7 up to the weight gain of 2%, 3%, 4% in case of each ratio. Fluid bed processor was used for the coating operation. **C) Characterization of ER granules and tablets:** The ER Met granules were evaluated for particle size distribution, flow properties, drug content, and in-vitro drug release studies. The ER tablet formulations were evaluated for weight variation, hardness, thickness, drug content. and in-vitro drug release studies. The release studies were performed as follows

Apparatus	Dissolution medium	Temp.	Stirring speed	Aliquot withdrawal	Wavelength
USP type II	Phosphate buffer (pH 6.8) 1000 ml	37±5°C	100 rpm	0.5, 1, 2, 4, 6, 8 and 10 h	232 nm

The dissolution studies results were subjected to different kinetic models to study the mechanism of drug release. The dissolution profiles of the trial formulations were compared with that of marketed product (Okamet SR 500) to determine the similarity factor.

Results and Discussion: The in-vitro drug release profiles of Met ER granules of various coating compositions did not match with the dissolution profile of the marketed formulation. The tablet formulation consisting of 97% CMEC and 3% HPMC E5, when coated to achieve a weight gain of 4%, exhibited drug release of 90.20±0.69% within 8 hours. The average weight, thickness and hardness was found to be 805.7 ±1.1 mg, 6.359±0.01 mm and 13.1±0.94 Kg/cm2 resp. The calculated value of "n" in the Korsmeyer-Peppas model was found to be 0.47, indicating anomalous transport. This suggests that the drug release is not solely governed by Fickian diffusion but involves additional mechanism such as erosion. Similarity factor f2 of 60.38 indicated the similarity of the drug release profile of the developed formulation with the marketed formulation.

Conclusion: CMEC demonstrated its efficacy as a rate-controlling agent in Met ER formulations The drug release rate was found to enhance as the pore former conc. increased from 3 to7%. Tablet formulation with 4% coating of CMEC and HPMC E5 in 97:3 ratio exhibited desired drug release profile. The formulations of Met coated granules need to be optimized further to obtain desired drug release characteristics.

References:

1. Parthasaradhi Reddy, Bandi, Khadgapathi, Podili, Ramesh, Kappala. Extended-release compositions of quetiapine., PCT patent; PCT/IN2012/000282, 2012
2. Meiyan Yang, Si Xie, Qiu Li, Yuli Wang, Xinyi Chang, Li Shan, Lei Sun, Xiaoli Huang, Chunsheng Gao. Effects of polyvinylpyrrolidone both as a binder and pore-former on the release of sparingly water-soluble topiramate from ethyl cellulose coated pellets. 465 (2014) 187–196.

Acknowledgements: The presenting author is grateful to the mentors and defence committee, who generously provided knowledge and expertise. Additionally, this endeavor would not have been possible without the generous support from the ACG engineering pharmatechnology, who permitted completion of the research work in the firm.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Assessment of In Vitro Release behavior of Injectable Gel loaded with Polymeric Micelles for management of Volumetric Muscle Loss

Khushali Nathani (khushali.nathani.2930@gmail.com)[1], Sujata Sawarkar (sujata.sawarkar@bncp.ac.in)[1]

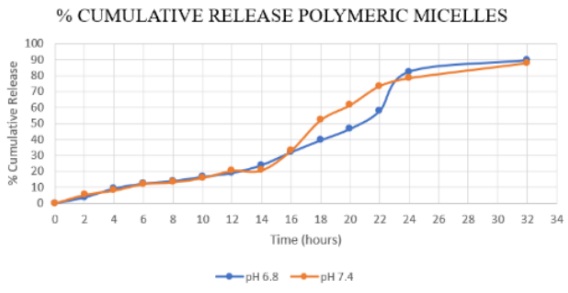
[1]SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra

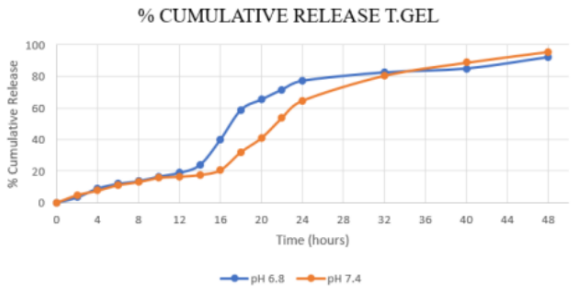
Background and Rationale: Volumetric muscle loss is a catastrophic skeletal muscle injury involving the loss of functional and regenerative capacity of skeletal muscle fibers. This leads to further tissue damage due to accumulation of reactive oxygen species followed by oxidative stress and cell death delaying the regenerative process. Quercetin a BCS Class IV polyphenol flavonoid drug prevents cells from undergoing oxidative stress by scavenging free radicals. In order to overcome the issue of limited bioavailability due to poor solubility and permeability of quercetin, polymeric micelles were selected as carrier system. In the present project we have incorporated drug loaded polymeric micelles into *in situ* injectable gel to enable localized sustained effect of the drug thereby enhancing its bioavailability and efficacy.

Methodology:

A) Preparation of Quercetin loaded Polymeric Micelles in situ injectable gel- Polymeric micelles were prepared using solvent co-evaporation method using Soluplus and Poloxamer 407. The prepared polymeric micelles were included in *in situ* gelling comprising of HPMC K4M and combination of Poloxamer 188 and 407. The developed formulation was further evaluated for the particle size, entrapment efficiency, pH, *in vitro* diffusion, gelling temperature and duration of *in situ* gel. **B) In Vitro Release Profile-** The release study was carried out at Phosphate buffer pH 6.8 and pH 7.4 for polymeric micelles and gel loaded with polymeric micelles. The diffusion studies were carried out in dialysis bag using Franz diffusion apparatus at 37^0C. The release media comprising total volume of 22ml is the combination of PBS : Ethanol in ratio (1:1) for both buffer system pH 6.8 and pH 7.4.

Results and Discussion: The particle size of optimized polymeric micelle batch was found to be 50 nm by TEM analysis. The entrapment efficiency of the quercetin loaded polymeric micelles was found to be 88.3%. Zero order drug release was observed *in vitro* for both polymeric micelles as well as *in situ* injectable gel at pH 6.8 as well as pH 7.4. At pH 6.8, 89.5% of drug was released from polymeric micelles within 32hrs whereas, *in situ* injectable gel showing sustained release with 90.7% drug release within 48hrs. A similar trend was found at pH 7.4 where 87.9% drug was released from polymeric micelles within 32hrs and 95.6% was released from *in situ* injectable gel.





Conclusion: The present study showed sustained drug release of Quercetin from polymeric micelle loaded *in situ* injectable gel. Further proof of concept studies should be undertaken to determine the therapeutic efficacy of the developed formulation.

References:

1. Wang Y, Wei X, Wang L, Qian Z, Liu H, Fan Y. Quercetin-based composite hydrogel promotes muscle tissue regeneration through macrophage polarization and oxidative stress attenuation. Compos B Eng. 2022;247(110311):110311.
2. Qiu Y, Hamilton SK, Temenoff J. Improving mechanical properties of injectable polymers and composites. In: Vernon B, editor. Injectable Biomaterials. Elsevier; 2011. p. 61–91.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Bioinspired labrum Shaped Stereolithography Assisted 3D Printed Hollow Microneedles (HMNs) for Effectual Delivery of Ceftriaxone Sodium

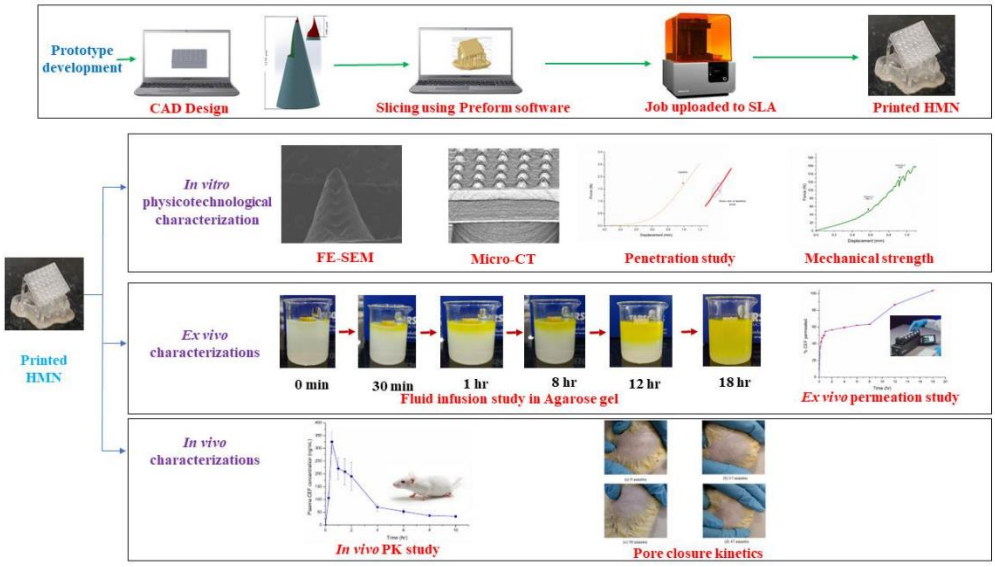
Shubham Kawre (shubhamkawre59@gmail.com) [1], Subham Banerjee (subham@niperguwahati.in)[1], Purushottam Survayanshi[1]

[1]**National Institute of Pharmaceutical Education and Research, Guwahati, Guwahati, Assam**

Background and Rationale: Ceftriaxone sodium, a broad-spectrum antibiotic from Cephalosporin class which belongs to BCS Class III having high solubility and less permeability thus commercially available only as injectables. For instance, through alteration of delivery route to transdermal and thereby improving diffusion profile along with enhancement of patient compliance by getting rid of the side effects of injectables like pain, requirement of skill person etc. In present work, we proposed HMNs which are labrum shaped for easy insertion into the skin with minimal pain. The HMNs were fabricated by Stereolithography 3D printing technology using biocompatible, USP Class VI Biomed amber resin which never used earlier thus the novelty is about the material.

Methods: The CAD design of labrum shaped HMNs was created using SolidWorks software and printed using SLA 3D printer. Physicotechnological characterizations were performed using FE-SEM, X-ray Computed Tomography (µCT), Texture Analyzer, Mechanical strength. Diffusion studies were performed using Agarose gel (skin model) and *ex vivo* permeation study through porcine skin. Lastly, *in vivo* pharmacokinetic study was performed on SD rats (approval number: NIPS/AH/23/04) and analyzed using LC-MS/MS.

Results and discussion: The printed HMNs were characterized using FE-SEM and Micro CT, suggesting formation of proper labrum shape with no microchannel blockage. The penetration efficiency into porcine skin was evaluated using Texture Analyzer and was found to be 1.54 N which is even lesser than one's hand press. To avoid the fracture of HMNs during insertion into the skin it's mechanical strength was evaluated using Universal Testing Machine. Safety margin of printed HMNs was found to be 32.4 which is far better than available literature which shows HMNs are safely inserted into the skin without any fracture and damage to the skin. The diffusion studies were performed into Agarose gel (1.5%) and through the porcine skin. Interestingly, both showed similar diffusion pattern. The *ex vivo* diffusion study through porcine reveals that almost 100% drug is releasing in 18 hrs following the Korsemeyer-Peppas diffusion model with R_2 value of 0.9632. *In vivo* pharmacokinetic study was performed on SD rats and plasma samples were analyzed using LC-MS/MS technique. Cmax was found to be 325.51±44.60 ng/mL, and the time taken to reach Cmax was found to be 0.5 hr. The AUC_{0-t} was found to be 952.74±68.04 ng h/mL which suggested that bioavailability of CEF was improved. Further, the plasma CEF vs time profile conveys that CEF was detectable upto 10 hr. The overall obtained results suggests that the HMNs array was able to release the CEF beyond 6 hr, indicating more sustainable CEF action. Additionally, pore closure kinetics was determined which showed 45 minutes are required for complete disappearing of pore created by HMNs skin surface.



Conclusion: The presented work successfully demonstrated that HMNs is good alternate for effectual delivery of Ceftriaxone sodium with its drug release capabilities. The physicotechnological characterization of HMNs like FE-SEM, µCT, Texture Analyzer, Mechanical strength were performed. *Ex vivo* permeation study shows triphasic release pattern of CEF through porcine skin and releases around 56% in first hour and 100% in 18 hours. Finally, *in vivo* pharmacokinetics study reveals C_{max}, T_{max}, AUC_{0-t}, $T_{1/2}$, Ke were found to be 325.51±44.60 ng/mL, 0.5 hr, 952.74±68.04 ng h/mL, 4.87±3.49 hr, 0.10 h-1 respectively.

References:

1. Economidou SN, Uddin MJ, Marques MJ, Douroumis D, Sow WT, Li H, Reid A, Windmill JF, Podoleanu A. A novel 3D printed hollow microneedle microelectromechanical system for controlled, personalized transdermal drug delivery. Additive Manufacturing. 2021 Feb 1;38:101815.

Acknowledgements: Department of Pharmaceuticals, Government of India

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

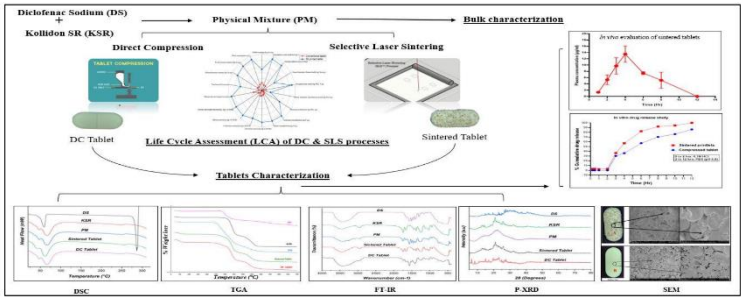
Comparative In Vitro Physicochemical Assessment of both Conventionally and Additively Manufactured Sustained Release Tablets

Twinkle Gharate (twinklegharate1@gmail.com)[1], Subham Banerjee (subham.331@gmail.com)[1]

[1]**National Institute of Pharmaceutical Education and Research, Guwahati, Assam**

Background & Rationale: Approximately, 70% of drugs are administered as tablets because of accurate dosing, high stability, and patient compliance. Tablets can be manufactured by different conventional techniques like wet or dry granulation and direct compression (DC) but these techniques have many limitations like confined tablet shapes, multistep manufacturing processes, use of multiple excipients, and use of solvent which may cause risk of toxicity. Among all 3D printing technologies, selective laser sintering (SLS) is green AM technology that enables to fabrication of complex geometrical, high-dose loaded solid oral dosage form in bulk quantities with a tuneable drug release pattern, utilizing single-step approach [1]. Diclofenac sodium (DS) sustained-release tablets are fabricated using DS as a model drug and Kollidon SR (KSR) as a sustained-release polymer [2]. This study aimed to comparative assessments of *in vitro* physicochemical evaluation of Conventionally (DC process) and Additively (SLS-mediated) manufactured tablets. Along with in-vivo evaluation and one-month short-term stability of sintered tablets.

Methods: A) Fabrication of DS sustained-release tablets using an SLS 3DP printer and tablet compression machine: In SLS, tablets are printed by partial melting of a physical mixture (PM) of DS (15%) and KSR (85%) which is present on feed and print bed whose temperatures were optimized to 30°C and 40°C. Similarly, tablets were compressed by a direct compression (DC) machine utilising tablet thickness to 4N/m (DB tooling) by using same ratios PM. First, comparative life cycle assessment (CLCA) of DC and SLS process were done, using OpenLCA software. Afterward, all in vitro-physicochemical characterizations were done. In further steps, *in vivo* evaluation and short-term one-month stability testing at 40°C/75%RH were done for sintered printlets. **B) *In vitro* release of SLS 3DP and compressed tablets**: For both formulations, study was performed in 0.1N HCL (pH 1.2) for initial 2 hr followed by PBS (pH 6.8) for next 10 hr by using USP type-I apparatus (rpm- 100; temperature 37±2°C). Aliquots were withdrawn at different time intervals and filtered using a 0.22µm membrane filter and were assessed for DS release using RP-HPLC. **C) *In vivo* release of SLS 3DP tablets:** Six sintered tablets containing 14 mg/kg of DS were orally administered to six individual rabbits. The concentration of DS in rabbits' plasma samples was determined by the developed RP-HPLC bioanalytical method. Pharmacokinetics (Pk) parameters were evaluated.



Result and Discussions: CLCA study represent high impact of sintering process on the environment, owing to high energy consumption. The weight variation, hardness, and dimensional analysis were found in acceptance limits according to IP. DSC, TGA, and FTIR results were reveals compatibility of excipients with each other. SEM of surface morphology were indicating differentiation of the void present in DC and sintered tablets. Sintered tablets have a more void than DC tablets. Prepared DC and sintered tablets were introduced dissolution media, Owing to water solubility of polyvinylpyrrolidone it oozes out from tiny pores through which the API slowly diffuses out in a controlled and pre-determined pattern. Based on obtained results, we found that tablets fabricated using a sintering released **100 %** DS within 12 hr. but when compared with release from DC tablets, it showed approximately **87%** DS release within 12 hr**.** Dissolution followed Korsmeyer-Peppas release model. Where n is 0.5 < n < 1 indicating **Fickian diffusion mechanism**. *In vivo* performance of sintered tablets was evaluated in rabbits after the oral administration at different time intervals, The C_{max}, T_{max}, $T_{1/2}$, AUC_{0-t}, $AUC_{0-\infty}$, K_{el} was found to be **13.48 ± 2.6 (µg/ml), 4 ± 0.1 hr, 1.2 ± 0.03 hr, 66.17 µg/ml, 66.17 µg/ml, 0.5634 hr**$^{-1}$ respectively.

Conclusion: The *in vitro* release profile and mathematical models indicate that release of DS can be effectively sustained from both DC and sintered release tablets using Kollidon SR as a matrix-forming agent.

References: 1. Giri BR, Maniruzzaman M. Fabrication of Sustained-Release Dosages Using Powder-Based Three-Dimensional (3D) Printing Technology. AAPS PharmSciTech. 2022 Nov 29;24(1):4.

2. Lekurwale S, Karanwad T, Banerjee S. Selective laser sintering (SLS) of 3D printlets using a 3D printer comprised of IR/reddiode laser. Annals of 3D Printed Medicine. 2022 Jun 1;6:100054.

Acknowledgements: The authors would like to acknowledge the Department of Pharmaceuticals

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Comparitive In vitro Study Between Conventional and Novel Formulation for Rheumatoid Arthritis

Amogh Bhanushali (amoghbhanushali2@gmail.com)[1], Meenal Rane (meenal.rane@bncp.ac.in)[1]

SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra

Background and Rationale: Rheumatoid Arthritis (RA) is an autoimmune disease characterized by chronic synovial inflammation, osteoporosis and cartilage damage. Primary causes include auto-citrullination leading to antigenicity and failure of tolerance pathway of immune system. Conventional drugs used for RA such as glucocorticoids and NSAIDs cause adverse effects like osteoporosis, GI bleeding and ulcers. Anise oil is GRAS approved herbal drug which have shown anti inflammatory, osteoprotectant and anesthetic properties combating drawback of convention therapy. Anise oil itself act as penetration enhancer and show burst and immediate release effect. Use of biphasic nano emulsion system adds a barrier for immediate drug release, further incorporation in nanoemulgel formulation aid to subtle burst release effect and show sustained release ideal for patients suffering from RA. Nanoemulgel formulation offers superior properties like higher thermodynamic, higher loading capacity and low cost of production

Methods: (A) Spontaneous emulsification method is used for formation of nanoemulsion. With S-mix of Tween 80 and transcutol, 4% of anise oil concentration, 1% carbopol gel was formed and both solution were mixed to give nanoemulgel formulation (B) In vitro release -These studies were performed in pH 7.4 phosphate buffer and ethanol in 1:1 ratio using Franz diffusion apparatus [22 ml volume, with magnetic stirring 80- 100 rpm] at 37±2º C using dialysis membrane as diffusion medium and 1 gram of formulation was loaded on donor compartment. Studies were carried out for 8 hrs .Aliquotes were withdrawn at periodic interval ,with suitable dilution with 7.4 buffer and assessed using UV-Visible spectrophotometer.

Results and Discussion: Stable nanoemulgel was successfully prepared with a pH of 7-7.4, droplet size below 50 nm, zeta potential of 1-5mv with transparent nature and pleasant odour. Nanoemulgel formulation showed sustained release of 75% at 8 hrs compared to conventional formulation ideal for RA patient suffering from morning stiffiness.

Conclusion: Anise oil after in corporation in nanoemulgel system showed sustained release effect, which prolong the duration of action and decrease frequency of application compared to conventional oil system.

References: 1. Ritter, A. M. V., Hernandes, L., da Rocha, B. A., Estevão-Silva, C. F., WisniewskiRebecca, E. S., Cezar, J. dos S., Bersani-Amado, C. A. (2017). Anethole reduces inflammation and joint damage in rats with adjuvant-induced arthritis. Inflammation Research, 66(8), 725–737. doi:10.1007/s00011-017-1053-3

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

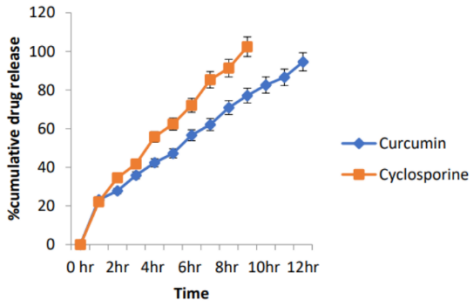
Design and Evaluation of Novel Topical Delivery System for Enhancing Penetration of Poorly Soluble Anti-Arthritic Agents

Madhura Mulkutkar (madhura.mulkutkar@gmail.com)[1], Sujata Sawarkar (sujata.sawarkar@bncp.ac.in)[1], Shriya Karmarkar[1], Sankalp Gharat[1]

[1]**SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and rationale: Rheumatoid arthritis (RA) is a systemic autoimmune disease that causes persistent joint inflammation and results in significant disability and eventual mortality. Conventional non-invasive treatments are accompanied with off-target effects and eventually drug resistance. Combination of curcumin (antiinflammatory) and cyclosporine (immunosuppressant) have the potential to reduce RA associated inflammation. Topical delivery of these poorly soluble drugs can overcome the challenges of low oral bioavailability and drug associated side effects. The objective of this research project was to formulate a topical curcumin and cyclosporin loaded lipomer in gel product. Curcumin and cyclosporine have poor solubility and permeability. Lipomer is a hybrid of liposome and polymeric nanoparticle. In this study we aim to improve penetration by the lipid coat of the lipomer and provide pH dependent drug release by the polymeric core of the lipomer. Additionally, administration of the prepared lipomer as topical gel would eliminate the systemic drug losses and provide high concentration of the drug at target site.

Methods: Lipomers were prepared by nanoprecipitation technique using soy lecithin as the lipid and Eudragit L100 as the polymer. Cyclosporine: Curcumin were taken in the ratio of 1:2. Further, Carbopol Ultrez 10F was added to get the final gel formulation. The formulation was evaluated for particle size, zeta potential, drug content, viscosity and spreadability. *In vitro* release study and *ex vivo* permeation study was performed on Franz diffusion apparatus using PVDF membrane and porcine ear skin respectively. A combination of phosphate buffer (pH 7.4): ethanol (7:3) was used as the diffusion media. 22mL of diffusion media was maintained at 32 ± 0.5°C and constantly stirred at 100 RPM throughout the experiment.



Results and Discussion: The particle size and zeta potential were found to be 105nm and -30.9mV respectively. The drug content was found to be >70% for both drugs. The formulation exhibited zero order drug release *in vitro* where 91.29% of cyclosporine and 70.88% of curcumin was released at the end of 8h. Approximately 100% release within 24hr was observed for both the drugs in *Ex vivo* study. Permeation coefficient for cyclosporine and curcumin was found to be 0.0128cm/hr and 0.0135cm/hr respectively.

Conclusion: Besides sustaining drug release, Lipomer based gel formulation was found to enhance the drug penetration across the skin; significantly improving the tissue bioavailability of the encapsulated drug. Hence, this approach can be leveraged for managing rheumatoid arthritis.

1. **References:**

Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. Bone Res. 2018 Apr 27;6:15. doi: 10.1038/s41413-018-0016-9. PMID: 29736302; PMCID: PMC5920070.

2. Zhang, L., Chan, J. M., Gu, F. X., Rhee, J. W., Wang, A. Z., Radovic-Moreno, A. F., Alexis, F., Langer, R., & Farokhzad, O. C. (2008). Self-assembled lipid--polymer hybrid nanoparticles: a robust drug delivery platform. ACS nano, 2(8), 1696–1702. https://doi.org/10.1021/nn800275r.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

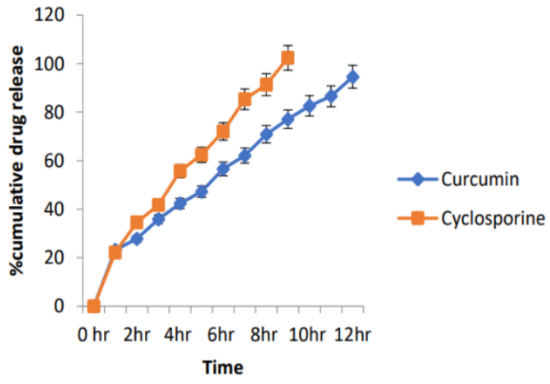
Development and Evaluation of Curcumin and Cyclosporine Loaded Nanoemulgel for Management of Psoriasis

Taufique Siddiquee (siddiqueetaufique57@gmail.com)[1], Sujata Sawarkar (sujata.sawarkar@bncp.ac.in)[1], Shreyas Salgaonkar[1], Sankalp Gharat[1]

[1]**SVKM's Dr. Bhanuben Nanavati College Of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Psoriasis is an autoimmune chronic disorder with hyper-proliferation as well as poor differentiation of keratinocytes in skin epidermis characterized by red scaly and itchy patches on skin. Conventional topical corticosteroids used for treatment are associated with side effects. A combination of curcumin (anti-inflammatory) and cyclosporine (immunosuppressant) has the potential therapeutic activity against psoriasis but its poor biopharmaceutical (low aqueous solubility and skin penetrability) attributes hamper the therapeutic efficacy for skin applications. Hence, novel formulation of these poorly soluble drugs can overcome the challenges of low solubility and permeability and associated side effects. The objective of this research project was to formulate a topical curcumin and cyclosporine loaded nanoemulsion based gel. Nanoemulgel exhibited thixotropic rheological behavior and a significant ($p < 0.05$) increase in skin penetrability characteristics compared to curcumin dispersed in conventional topical system and enhance bioavailability. It showed that the formulation was capable of reducing the symptoms associated with psoriasis. Additionally, direct application of developed nanoemulgel at targeted site would eliminate its systemic drug losses and enhance its biovailability at targeted site.

Methods: Nanoemulgel system was prepared by high-energy ultrasonication technique. Curcumin: Cyclosporin were taken in the ratio of 2:1. Further, Carbopol aqua SF, Carbopol 974P, Carbopol Ultrez 10NF, was added in 1%, 2% 1.5% respectively to get the final gel and formulation was neutralized with 10% meglumine in order to achieve viscosity. The formulation was evaluated for drug content, appearance, viscosity, pH, globule size, zeta potential, and spreadability. In vitro release of drug was studied by using Franz diffusion apparatus and ex vivo drug release was determined using porcine ear skin. Ethanol and phosphate buffer pH (6.8) was used as diffusion media in the ratio of (6:4). The temperature of cell was maintained at 37°C ± 0.5°C with constant stirring speed at 100rpm.



Results and Discussion: The particle size, zeta potential and pH of developed nanoemulgel were found to be 80.20nm, -28.8Mv and 5.2 ± 0.2 respectively. The drug content was found to be >95% for both drugs. At the end of 11 hrs in vitro drug release of curcumin and cyclosporine was found 89.45% and 99.36% respectively. Ex vivo drug release profile demonstrated the release of above 50% for both the drugs at end of 24h.

Conclusion: Nanoemulgel based formulation can enhance the drug penetration across the skin and showed prolonged release with desired skin retention hence enhance the bioavailability of drug. Hence, this approach has potential advantages for the formulation development for managing psoriasis.

References:

1. Algahtani MS, Ahmad MZ, Nourein IH, Albarqi HA, Alyami HS, Alyami MH, Alqahtani AA, Alasiri A, Algahtani TS, Mohammed AA, Ahmad J. Preparation and Characterization of Curcumin Nanoemulgel Utilizing Ultrasonication Technique for Wound Healing: In Vitro, Ex Vivo, and In Vivo Evaluation. Gels. 2021 Nov 14;7(4):213. doi: 10.3390/gels7040213. PMID: 34842698; PMCID: PMC8628781.
2. Naz Z, Ahmad FJ. Curcumin-loaded colloidal carrier system: formulation optimization, mechanistic insight, ex vivo and in vivo evaluation. Int J Nanomedicine. 2015 Jul 3; 10:4293-307. doi: 10.2147/IJN.S82788. PMID: 26170665; PMCID: PMC4498720.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development and In Vitro Release Studies of Starch based Tinidazole Microparticles for Colonic Delivery

Jayashri Chavan (jayashree121997@gmail.com)[1], Namita Desai (namitadd@rediffmail.com)[1]

[1]**C.U Shah College of Pharmacy, S.N.D.T Women's University, Mumbai, Maharashtra**

Background and Rationale: Tinidazole, an anti-ameobic drug, is available as 300 mg and 500 mg conventional tablets administered in 2 g strength as single dose for 3 days. This high dose is required to compensate the drug lost due to release in the stomach and small intestine before reaching the site of action namely colon. Colonic delivery helps to improve treatment of diseases affecting the colon, while minimizing systemic side effects. Polysaccharide-based delivery systems have several advantages including availability, safety, stability, ease of modification and degradability. The present research involves development and *in vitro* release studies of starch based microparticles of Tinidazole.

Methods:

a) **Analytical method**: UV spectrophotometric method was developed and validated for the quantification of Tinidazole in Methanol AR, pH 1.2 HCl buffer, pH 6.8 phosphate buffer, pH 7.4 phosphate buffer. The developed method was applied for drug analysis in formulations and during *in vitro* release studies respectively.

***b)* Development of starch based Tinidazole microparticles**: Emulsion cross-linking method was selected for developing starch based microparticles of Tinidazole. The product and processing parameters such as type and amount of starch, ratio of aqueous to organic phases, ratios of surfactants and epichlorohydrin, temperature, stirring time, stirring speed were optimized. Emulsion of presoaked starch in excess of water with methylene chloride containing drug and mixture of surfactants was prepared and further cross-linked.

c) ***In vitro* drug release**: The study was performed in USP type II apparatus, 37°C, 75 rpm using pH gradient dissolution media. Microparticles were placed in dialysis membrane (molecular weight cut-off 12000 kDa) in 500 ml pH 1.2 HCl buffer for 2 hours followed by addition of 0.5N sodium hydroxide and 160 ml pH 6.8 buffer for further 3 hours. Suitable aliquots were withdrawn at specified time intervals and analyzed by UV-visible spectrophotometer (Jasco V-630) at 312nm and 315nm respectively.

Results and discussion: Starch based microparticles of tinidazole were developed by optimizing processing parameters. The emulsion composition was 55%w/v aqueous phase containing 5% w/v starch, methylene chloride phase containing drug and 17.5%w/v of Tween 20 and Tween 60 (4:3), further cross-linked with epichlorohydrin to form drug microparticles. The formed microparticles were filtered, washed and dried at 40°C. The microparticles exhibited spherical morphology (Fig.1) and particle size of 40-100 microns. *In vitro* release of developed microparticles showed less than 10% release at the end of 5 hours in pH 1.2 and pH 6.8 buffers. (Fig.2).

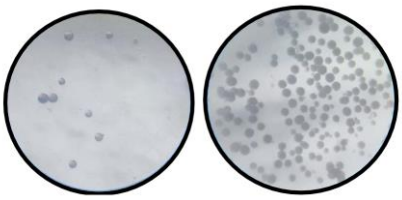


Fig.1 Microscopy of Tinidazole microparticles (10X)

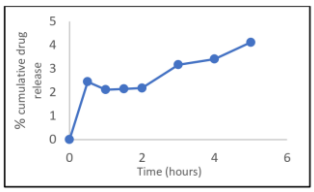


Fig.2 *In vitro* release of Tinidazole microparticles

Conclusions: Starch based microparticles of Tinidazole were developed using emulsion cross linking method and *in vitro* release studies in pH 1.2 and pH 6.8 buffers indicate potential for colon specific drug delivery. The developed microparticles will be further evaluated in release medium simulating colonic conditions for determining site specific drug release.

References:

1) Builders, P. F., et al, (2016), *Starch/Stärke*, 68(9-10), 864-873.
2) Prajapati, V. D., et al, (2015), *Expert Opinion on Drug Delivery*, 12(8), 1283-1299.

Acknowledgements: The investigators express sincere thanks to Aarti Drugs Ltd. for the gift sample of drugs.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development and Permeation Studies of Fluocinolone Acetonide Microneedles for Posterior Uveitis

Imtiyaz Khan (1208imtiyazii@gmail.com)[1], Munira Momin (munira.momin@bncp.ac.in)[1], Bharti Gupta[1]

[1]**Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Posterior uveitis is the inflammation of uvea that is choroid, retina and optic nerve which may lead to permanent vision loss. Due in part to the barrier established by the corneal epithelium, ocular medication bioavailability is relatively poor when pharmaceuticals are applied topically [1]. The invasive techniques, such as intra-vitreal injections and implants, are used to deliver drugs to the posterior region of the eye. Microneedle is emerging technology in delivering the fluocinolone acetonide to the posterior segment for the treatment of posterior uveitis [2]. Microneedles were fabricated through the micro-moulding technique by using Hyaluronic acid (HA), Polyvinyl alcohol (PVA) for the baking layer and Eudragit RS 100, Eudragit RL 100 for array of microneedles and evaluated for other effects of various parameters such as vacuum, type of polymer and solvent, ratio of polymer etc. The patches were evaluated for drug content, dissolution, in-vitro and ex-vivo release.

Methods:

A. Development of Bilayered Drug Loaded Microneedle: Hyaluronic acid, dextran sulphate and PVA was dissolved in water. Drug was first dissolved in ethanol, Eudragit RS 100 and Eudragit RL 100 was added in above solution and stirred for 30 mins. 30 microliters of it was poured onto a mold and vaccum was applied.

B. In-vitro permeation study: Modified Franz diffusion cell was used for the study. PVDF membrane of 0.4nm was used. Temperature was maintained 37^0C with 100 rpm stirring speed. 2 Patches were placed in each donor compartment. C. Ex-vivo permeation study: Whole eyeballs of goat was procured and goat sclera was used to perform the study using Franz diffusion cell. Experimental conditions were same as in-vitro release studies.

Results and Discussion: Ocular microneedle for posterior uveitis were successfully fabricated and able to deliver the drug to the posterior region. In-vitro drug release showed 18±2.1% drug was released in 24 hr. At 6 hours 10.31% drug was released. Ex-vivo drug release was found to be 67.457% after 24 hours. Conclusion In this study we developed an ocular Fluocinolone acetonide loaded microneedle which delivers the drug directly to posterior segment of the eye for the treatment of posterior uveitis. The in-vivo and ex-vivo studies showed good diffusion across PVDF and goat sclera membrane respectively.

References:

1. Ibrahim, M., & Nguyen, Q. D. (2009). Treatment of posterior uveitis with a fluocinolone acetonide implant. EvidenceBased https://doi.org/10.1097/IEB.0b013e3181b95d92 Ophthalmology, 10(4), 224-226.
2. Lee, J. W., & Prausnitz, M. R. (2018). Drug delivery using microneedle patches: not just for skin. Expert Opinion on Drug https://doi.org/10.1080/17425247.2018.1471059 Delivery, 15(6), 541-543.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development and Release Studies of Lipid Microparticles of Carbamazepine for Nasal Delivery.

Asfiya Khan (asfiyanajmunalikhan@gmail.com)[1], Namita Desai (namitadd@rediffmail.com)[1]

[1]**C.U Shah College of Pharmacy, S.N.D.T Women's University., Mumbai, Maharashtra**

Background and Rationale: Solid lipid microparticles (SLMs) are micron sized drug carriers with large surface area, high drug loading and sustaining capacity for lipophilic drugs. Carbamazepine is a drug widely used as antiepileptic agent in the therapy of psychomotor seizures. It is a highly lipophilic molecule, a BCS class II drug, available in the form of oral suspensions, tablets, capsules, etc. The major limitation with oral formulations of carbamazepine is slow and irregular gastrointestinal absorption due to poor water solubility. Nasal delivery is a non-invasive and patient friendly approach that can provide ease of delivery, direct entry into the blood stream with potential of brain targeting. Hence the present work aims to develop and evaluate solid lipid microparticles of carbamazepine for nasal delivery to overcome limitations of oral delivery.

Methodology: Analytical method for carbamazepine was developed in Methanol AR and Simulated Nasal Fluid, pH 6.4 by UV-Vis Spectrophotometry and validated. Various methods such as solvent evaporation, melt dispersion and solvent diffusion were evaluated for preparation of microparticles. Solid lipids such as Compritol 888 ATO, Compritol HD5 ATO, Precirol ATO 5 and cetyl palmitate and surfactants such as Tween 20, Tween 80, Span 20, Span 80, Gelucire 43/01 and Poloxamer 188 were screened at varying concentrations for formation of microparticles. The microparticles were characterized for size, entrapment efficiency and *in vitro* drug release. *In vitro* release of carbamazepine was investigated using USP type II apparatus, 100 ml Simulated Nasal Fluid, pH 6.4, 37 ± 0.5 ° C, 100 rpm. Aliquots were withdrawn at predetermined time intervals and analysed using UV-Visible Spectrophotometer (Jasco V-630) at 286 nm.

Results and Discussion: UV spectrophotometric method for Carbamazepine in Methanol AR and Simulated Nasal Fluid, pH 6.4 at λ_{max} of 285 nm and 286 nm respectively was found to be linear over 4-16ppm, R^2 of 0.9997 and were found to be precise and accurate. Carbamazepine microspheres were prepared by melt dispersion method using cetyl palmitate as solid lipid (15% w/w) and Tween 80, Span 20 and Poloxamer 188 (5.2% w/v, 10:1:2) as surfactants. 1% w/v gelatin was used in aqueous phase to prevent drug precipitation. The microparticles were observed to be spherical with particle size 50-200 µm and showed 60% drug entrapment. *In vitro* release of Carbamazepine microspheres showed sustained release of 60 % after 8 hours

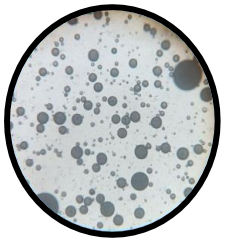


Fig.1 Microscopy of Carbamazepine microparticles (10X)

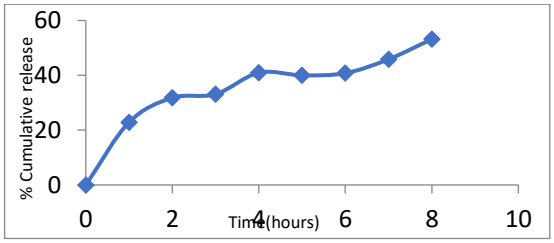


Fig.2 *In vitro* release of Carbamazepine microparticles

Conclusions: Carbamazepine lipid microparticles were found to be spherical with sustained *in vitro* release for 8 h. The lipid microspheres will be further developed into *in situ* nasal gelling systems with potential for brain delivery.

References:

1. Scalia S, Young PM, Traini D.(2015), Solid lipid microparticles as an approach to drug delivery. *Expert Opin Drug Deliv.*; 12(4): 583-99.
2. Acharya S, et al. (2013), Preparation and evaluation of Transnasal microemulsion of Carbamazepine. *Asian J Pharm Sciences*. 8:64-70.

Acknowledgements: The investigators express sincere thanks to Bajaj Healthcare Ltd. and Gattefosse India Pvt. Ltd. for the gift samples of drugs and excipients and to AICTE for providing Junior Research fellowship.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development and Release Studies of Norfloxacin Microspheres for Topical Delivery

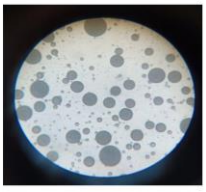
Aruna Murugan (arunammurugan@gmail.com)[1], Namita Desai (namitadd@rediffmail.com)[1]

[1]**C.U Shah College of Pharmacy, S.N.D.T Women's University., Mumbai, Maharashtra**

Background and Rationale: Burn wounds pose a significant challenge in clinical practice due to their susceptibility to infections and slow healing. A moist, thermally coagulated burn wound, with its constantly replenished supply of diffusing serum nutrients and warm surface temperature, provides an environment suitable for rapid microbial growth. Localized therapy with sustained drug release can greatly enhance the efficacy of treatment in burn wound. Norfloxacin (NOR), an antibacterial agent, has demonstrated potential for the management of burn wounds. However, conventional topical formulations lack sustained release and prolonged effects. Lipid microspheres provide sustained release of entrapped drugs, promoting prolonged antibacterial activity and wound healing at burn sites. This study aims to optimize formulation parameters and investigate the release of Norfloxacin from lipid microspheres.

Methods: A. UV spectrophotometric method was developed and validated for the quantification of Norfloxacin in 0.1N HCL and Simulated Wound Fluid (SWF) pH 7.4. The method was applied for drug analysis in formulations and during in vitro release studies respectively. B. Different methods like solvent evaporation and melt dispersion were evaluated for lipid microspheres preparation using lipids such as Stearic acid, Compritol HD5 ATO and Precirol ATO5. Surfactant concentrations of Span 80, Tween 80 and Tween 20 were studied. Stabilizers like polyethylene glycols, polyvinylacetate, and Trancutol P were evaluated to enhance stability and drug loading. Melt dispersion technique was used for Norfloxacin-loaded microspheres. The formed microspheres were evaluated for appearance, size, drug loading, drug content, and in vitro release. C. In vitro release of Norfloxacin from the microspheres was investigated using a dialysis membrane (molecular weight Cut off 12,000 kDa) in USP type II apparatus, 100 mL SWF, pH 7.4, 37±0.5°C, 50 rpm. Aliquots were withdrawn at predetermined time intervals and analysed using a UV-Visible Spectrophotometer (Jasco V-630) at wavelength 273 nm.

Results and Discussion: Among the various lipids, stearic acid and Compritol HD5 ATO as lipids (5% w/v), Tween 20 as surfactant (0.5 % w/v) and Transcutol P as stabilizer (1.5% v/v) were selected for preparing the microspheres containing Norfloxacin (0.8 % w/v) by melt dispersion technique. The developed microspheres exhibited spherical morphology (Fig.1) and particle size ranging from 50-100 microns. The drug loading was 80±5% and the drug content was within limits. In vitro studies in SWF pH 7.4 demonstrated sustained drug release over 8 h in SWF pH 7.4 (Fig. 2).



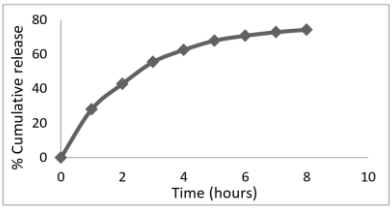


Fig.1: Microscopy of NOR microspheres (10X) **Fig.2: In vitro release of NOR microspheres**

Conclusions: The Norfloxacin microspheres exhibited spherical shape and sustained drug release for 8 hours in in vitro release studies and will be incorporated into topical gels to enhance wound healing. The sustained release from microspheres indicates promising potential in prolonged drug action at the site of burn wounds.

References:

1. Kamal Dua, et al (2016), Interv Med Appl Sci. Jun 1; 8(2): 68–76
2. Scalia S, et al, (2015), Expert Opin Drug Deliv.;12 (4): 583-99.

Acknowledgements: The investigators express sincere thanks to Aarti Drugs Ltd. and Gattefosse India Pvt. Ltd. for the gift samples of drugs and excipients.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development of Nanostructured Lipid Carriers for Enhancing Oral Bioavailability of Ursolic Acid

Hiral Joshi (hiraljoshi787821@gmail.com)[1], Sanyog Jain (sanyogjain@niper.ac.in)[1]

[1]**NIPER S.A.S Nagar, Mohali, Punjab**

Background and Rationale: The aim of this study was to develop nanostructured lipid carriers (NLCs) for enhancing the oral bioavailability of ursolic acid. This phytoconstituent belongs to BCS IV, exhibits poor bioavailability due to its low solubility, low permeability and rapid first pass metabolism. NLCs tend to improve its oral bioavailability by overcoming these challenges and enabling the lymphatic drug uptake, thus, by-passing their first pass metabolism.

Methods: A) Preparation and optimization: Solid lipids and liquid lipids were screened based on the drug solubility. The NLCs were prepared using emulsification-sonication method and optimized using the Box-Behnken design. Further, the formulation was characterized for size, PDI and entrapment efficiency (%EE).

B) In vitro release studies: In vitro release studies were performed using dialysis bag method (MWCO 12 kD). The release of UA-NLC and free UA solution was carried out for 2h in SGF (pH 1.2) followed by 6h in SIF (pH 6.8) (both containing 1% tween 80 w/v) to simulate the GIT environment. The release assembly was kept in shaker water bath maintained at 37°C and 100 strokes/min[1] . At different time intervals the samples were withdrawn and replaced with equal volume of media to maintain the sink conditions. The HPLC method was used to determine the drug release.

C) In vitro lipolysis: In vitro lipolysis study was carried out using a pH-stat titrator. The pH of the digestion medium was maintained at 6.5 using 0.2M NaOH. At different time points samples were collected and analysed using HPLC to evaluate the rate and extent of lipid digestion. D) In vivo studies: To assess the oral bioavailability, free UA suspension and UA-NLCs were orally administered to Sprague-Dawley rats at a dosage of 10mg/kg/day, and subsequently analyzed for various pharmacokinetic parameters.

Results and Discussion: NLCs were prepared using glyceryl monostearate, geranic acid and tween 80 as solid lipid, liquid lipid and surfactant respectively. The optimized formulation was found to possess the particle size, PDI, and %EE of 247±12nm, 0.226±0.05, 63.15±2.24% respectively. The release study showed biphasic release pattern with an initial burst release of 22.17±4.67% in 2h followed by sustained drug release of 56±5.25% in 8h and followed Weibull release kinetic model with β as 1.461 which indicates the initial burst release. The lipolysis study demonstrated that the aqueous phase of the digestion media contained 45.26% solubilized drug fraction whereas 49.02% drug was found in the sediment. The pharmacokinetic study revealed 3.33-, 2.93- and 6.07-fold increase in Cmax, T1/2 and AUC0-∞ respectively as compared to free UA suspension.

Conclusions: The study findings demonstrated successful development of NLCs, leading to a significant enhancement in bioavailability. The findings underscore the potential of NLCs as a promising approach for improving the oral absorption of drugs with low bioavailability.

References:

1. P. Patel and M. Patel, 'Enhanced oral bioavailability of nintedanib esylate with nanostructured lipid carriers by lymphatic targeting: In vitro, cell line and in vivo evaluation', Eur. J. Pharm. Sci., vol. 159, p. 105715, Apr. 2021, doi: 10.1016/j.ejps.2021.105715.

Acknowledgements: Author would like to acknowledge Director, NIPER S.A.S. Nagar for providing necessary facilities and infrastructure.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development of Tinidazole and Pantoprazole Sodium Sesquihydrate Loaded Bio Adhesive Pellets for Management Of Helicobacter Pylori Infection

Aditi Dubey (dubeyaditi65@gmail.com)[1], Munira Momin (Munira.Momin@bncp.ac.in)[1], Raj Katri[1]

[1]**Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: The spiral-shaped bacteria *H. pylori* grow in the mucus that covers the stomach's interior lining. It generates ammonia, which reduces the stomach's acidity and provides a friendly habitat for the bacterium. In some instances, it can also lead to peptic ulcers, which are uncomfortable lesions in the upper digestive tract. The present formulation contains pantoprazole and tinidazole, agents commonly prescribed for peptic ulcer prepared as pellets. Pantoprazole belongs to the class of proton pump inhibitors. Tinidazole belongs to the group of drugs known as nitroimidazole antimicrobials and functions by eradicating the infection-causing microorganisms.

Method: Using the extrusion spherization technique, bio adhesive pellets containing a proton pump inhibitor and antibiotic are created. These pellets are then included in a ready-to-dispense sachet formulation.

a) In vitro release of tinidazole: Dissolution medium for tinidazole was 0.1N HCl and USP Type apparatus was Type – II (Paddle type), the aliquot was withdrawn for 1to 8 hours.
b) In vitro release of pantoprazole: Pantoprazole dissolution media was 0.1N HCl and 6.8 pH Phosphate buffer and Type – I (Basket Type) apparatus was used. Withdrawal time points were 1 and 2 hr for one medium then the dissolution medium was replaced and reading was taken for next 4 hrs.

Results And Discussion: The in-vitro release of tinidazole and pantoprazole sodium sesquihydrate from the respective pellets was observed to follow sustained release with almost more than 95% release at the end of 8 hours. Tinidazole pellets follow Korsemeyer-Peppas as well as Higuchi model for release kinetics whereas pantoprazole pellets follow Higuchi model for release kinetics majorly as compared to other release patterns.

Conclusion: Formulation development studies suggests that Noveon AA being bioadhesive polymer and HPMC K polymers being the swellable matrix forming polymer imparted good swellability, adhesion and followed an optimum sustained release pattern at the target site. Further drug-excipient compatibility studies have stated that the drug and excipients are stable at conditions specified by ICH guidelines.

Reference

1. Samantha Flores-Treviño, Soraya Mendoza-Olazarán, Paola BocanegraIbarias, Héctor Jesús Maldonado-Garza & Elvira Garza-González (2020) *Helicobacter pylori* drug resistance: therapy changes and challenges, Expert Review of Gastroenterology & Hepatology, DOI:10.1080/17474124.2018.1496017

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Dissolution and Diffusion from Lecithin Based Solid Dispersion: Mechanism and Role of Polymer in Release Enhancement

Sadhana Patil (sadhanap13499@gmail.com)[1], Abhay Sangamwar (abhays@niper.ac.in)[1], Ajay Lale[1], Arvind Sirvi[1]

[1]**National Institute of Pharmaceutical Education and Research (NIPER) S.A.S. Nagar, Mohali, Punjab**

Background and Rationale: With increasing number of poorly water-soluble drug candidates, it is crucial to develop formulations that enhance their bioavailability for oral administration.1 Lecithinbased solid dispersion (LBSD) is a promising formulation approach to tackle the limitations and maneuvers the overall biopharmaceutical performance of such drugs. 2 The present study aims to investigate the use of Lecithin and Hydroxypropyl methylcellulose acetate succinate (HPMCAS) in dissolution and diffusion of a brick dust molecule-Aprepitant (APT) from LBSD in biorelevant conditions.

Methods: A) Fabrication of binary (BD) and ternary dispersions (TD): APT- dispersions were prepared by co-solvent evaporation technique. Further characterisation was performed using PXRD, SEM, FTIR and NMR to study the solid-state properties and molecular-level interactions.

B) In vitro evaluation of BDs and TDs: Dissolution studies were conducted in simulated fasted- and fed-state using USP Type II apparatus containing 500 mL media (FaSSIF v2 and FeSSIF v2) set at 37±0.5 °C for all BDs and TDs. Following the experiments, TEM and particle size analysis was performed to examine the changes in the particulate structure of dispersion. Furthermore, diffusion of APT from BDs and TDs were measured using Franz diffusion cells in reverse dialysis setup at biomimetic conditions using cellophane membrane model.

C) In vivo evaluation of BDs and TDs: Oral pharmacokinetic study was performed on Sprague Dawley rats. Pharmacokinetic parameters, including Cmax, Tmax, AUC0-t were calculated and compared with aqueous APT suspension. Results and Discussion: Dissolution of APT was found to be 6.7 times higher in FeSSIF than FaSSIF, indicating a significant positive food effect. However, this food effect was overcome in both BDs and TDs. Dissolution of APT in BDs increased with increasing lecithin content. Similarly, for TDs, it has been observed that the food effect reduced with higher phospholipid and polymer content, while the percentage of drug dissolved increased. TEM analysis revealed the formation of nano-sized vesicles in TD within FaSSIF medium, indicating structural changes in the outer layers of particles. This leads to increased dissolution, thereby enhancing diffusion in the unstirred water layer and ultimately improving the overall bioavailability of the formulation. FTIR and NMR, analysis showed significant molecular level interactions in components of TD. In vivo oral pharmacokinetic study demonstrated significantly higher AUC(0-t) (p value < 0.05) for TD and BD formulations of APT (2.27-fold and 1.58- fold) compared to the pure drug suspension, respectively.

Conclusions: Polymeric LBSD formulation successfully improved the oral bioavailability of APT by enhancing dissolution profiles and diffusion compared to free drug suspension and lecithin dispersion. These findings support the idea of formulating LBSD to enhance dissolution and diffusion of poorly water-soluble drugs.

References:

1. Shono Y, et.al., Forecasting in vivo oral absorption and food effect of micronized and nanosized aprepitant formulations in humans. European Journal of Pharmaceutics and Biopharmaceutics, 2010;76(1):95-104.
2. Fong SYK, et.al. Solid Phospholipid Dispersions for Oral Delivery of Poorly Soluble Drugs: Investigation into Celecoxib Incorporation and Solubility-In Vitro Permeability Enhancement. Journal of Pharmaceutical Science, 2016;105(3):1113-1123.

Acknowledgements: All the authors are thankful to Director, NIPER, S.A.S. Nagar for providing facilities.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Dissolution Studies of Solid Dispersions of Antihyperuricemic drug

Ankita Kanade (kanade.ankita@ves.ac.in)[1], Rajashree Hirlekar (rajashree.hirlekar@ves.ac.in)[1]

[1]**Vivekanand Education Society's College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Xanthine oxidoreductase inhibitors (XORI) are used for the management of hyperuricemia in patients with or without gout. The selected novel XORI has advantages over the current treatment, such as a low dose of drug and fewer side effects. It is a BCS class II drug showing poor solubility, responsible for low bioavailability. Aim of this project is to prepare its Solid Dispersions (SD) using water-soluble carriers to increase its aqueous solubility.

Methods: A) Preparation of SD: Binary SDs were prepared using PEG 4000, PEG 6000, Soluplus in 1:1,1:2,1:3,1:4,1:9 ratio and PVP K30 in 1:1, 1:2 ratio and ternary SDs were prepared using drug, PVP K30, PEG 6000 and drug, PEG 6000, Soluplus in ratio (1:1:1).The fusion method involved adding drug to the molten carrier with continuous stirring until a homogeneous dispersion was formed which was sieved after solidification (1). In the solvent evaporation method, the drug and carrier (PVP K30) were solubilized in alcoholic mixture of 0.1N HCl, followed by evaporation under continuous magnetic stirring (1)(2).

B) Evaluation: SDs were characterized and evaluated for assay, solubility and dissolution. Dissolution studies were conducted using 900 ml of either water or buffer pH 1.2 as dissolution medium at 50 rpm at 37°C using paddle apparatus. At specific time intervals, aliquots were withdrawn and analyzed spectrophotometrically (3).

Results and Discussion: Instrumental characterization indicated no chemical changes in the drug. Binary SD containing Soluplus showed highest solubility in water compared to other systems. In water as a dissolution medium, plain drug showed 12.37 % and 15.98% release at the end of 5 and 15 minutes respectively. All binary SDs containing drug and polymers, PEG 4000, PEG 6000 and Soluplus in the ratio 1:9 showed maximum drug release of 80% within 15 minutes as compared to lower ratios. In the case of ternary systems containing drug, PVP K30, PEG 6000 and drug, PEG 6000, Soluplus in ratio (1:1:1), showed 36.08% and 39.73% drug release respectively at the end of 15 minutes. With buffer pH 1.2 as dissolution medium, Binary SDs containing PEG 4000, PEG 6000 and Soluplus in the ratio 1:3, showed 94 %, 100% and 91% release at the end of 5 minutes. In the same time interval both the ternary systems showed only about 68% of drug release.

Conclusions: The characterization studies showed no chemical changes in the drug. Solid dispersion containing PEG 6000 showed 1.29 times increase in solubility with better dissolution, both in water and buffer pH 1.2. Thus SD containing PEG 6000 (1:3) prepared by fusion method improved solubility and dissolution of the drug.

References:

1. Josimar Oliveira Eloy, Juliana Maldonado Marchetti Solid dispersions containing ursolic acid in Poloxamer 407 and PEG 6000: A comparative study of fusion and solvent ethodshttps://doi.org/10.1016/j.powtec.2013.11.017
2. S.Sethia, E. Squillante, Solid dispersion of carbamazepine in PVP K30 by conventional solvent evaporation and supertical methods,doi:10.1016/j.ijpharm.2003.11.025
3. Kogermann K, Penkina A, Predbannikova K, Jeeger K, Veski P, Rantanen J, Naelapää K. Dissolution testing of amorphous solid dispersions doi:10.1016/j.ijpharm.2013.01.042.

Acknowledgements: Authors would like to thank Precise Chemipharma for the gift sample of drug and BASF for the gift sample of polymer Soluplus.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Effect of surfactant on the drug release behaviour from amorphous solid dispersions

Prachi Shrivastav (shrivastavprachi21@gmail.com)[1], Arvind Bansal (akbansal@niper.ac.in)[1], Soumalya Chakraborty[1]

[1]**National Institute of Pharmaceutical Education and Research, S.A.S. Nagar, Mohali, Punjab**

Background and Rationale: Amorphous solid dispersion (ASD) is a solubility-enhancing enabling technology, consisting of API and polymer(s). Often, surfactants are included in ASDs, which reduce surface tension and can facilitate their dissolution kinetics. Nonetheless, the plasticizing capacity of surfactants can reduce wet Tg and increase molecular mobility[1]. Hence, it is important to understand the impact of surfactants on the dissolution mechanism of ASD, to harness optimum drug release performance.

Methods: A) Preparation of ASDs: Binary and ternary ASDs of efavirenz (EFV) and hydroxypropyl methylcellulose acetate succinate (HPMCAS-LF) at various drug loadings (5%, 10%. 20%, 30%, 40%, and 50% w/w) were prepared with spray drying. In ternary ASDs, sodium dodecyl sulphate (SDS) (5% of ASD weight) was included, maintaining its concentration below critical micellar concentration (CMC).

B) Non-sink powder dissolution: In vitro powder dissolution studies were performed using inhouse micro-dissolution set-up at 37±0.5 ℃ and 300 rpm in 50 mL 100 mM pH 6.8 phosphate buffer for 2 h. EFV and HPMCAS-LF concentrations were determined using HPLC and colorimetry, respectively.

C) Mechanistic understanding of dissolution behaviour: a) Residue analysis: Solid form of the undissolved particles was monitored using optical microscopy, PXRD, and SEM. b) Solution state behaviour: Hydrodynamic radius of the in situ formed colloidal nanodroplets was monitored using DLS. c) ASD film hydration: Spin-coated ASD films containing prodan and rhodamine 6G as fluorescent dyes were stored at 97% R.H. for 48 h and the phase morphology was observed under CLSM. Spray-dried ASDs were exposed to similar storage conditions and were analyzed using DSC.

Results and Discussion: Drastic decline in drug release was observed upon increasing drug loading from 20% to 30% in EFV-HPMCAS ASDs. ASDs with lower DLs (5%, 10%, and 20%) demonstrated rapid and simultaneous release of EFV and HPMCAS-LF, generating visibly turbid solutions owing to LLPS while at higher drug loadings (30%, 40%, and 50%), undissolved ASD particles were evident. DLS study showed that the size of nanodroplets was approximately 180–400 nm in diameter. Realtime residue analysis revealed the contribution of matrix crystallization at higher drug loading behind the poor dissolution of high DL ASDs. In ternary ASDs, no significant drop-off with DL was observed. They dissolved rapidly and generated highly supersaturated solutions in 45 min, along with LLPS and nanodroplet generation (for low DL ASDs), followed by a sharp drug concentration decline. Real-time residue analysis indicated SDSinduced accelerated matrix crystallization and subsequent precipitation of needle-shaped crystals of EFV behind the decline in drug concentration. CLSM and DSC-based phase behaviour studies indicated the absence of phase separation as a kinetic trigger of matrix crystallization.

Conclusions: The presence of SDS significantly affected the dissolution mechanism of ternary ASD systems. Although an overall higher extent of drug release was observed for ternary ASDs, SDS promoted matrix crystallization and bulk precipitation at the later phase.

References:

1. Indulkar et al., Role of Surfactants on Release Performance of Amorphous Solid Dispersions of Ritonavir and Copovidone. Pharmaceutical Research, 2022. 39(2): p. 381–397.

Acknowledgements: We would like to thank NIPER S.A.S. Nagar for providing the infrastructure and the research fellowship awarded by NIPER is greatly acknowledged.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Efficacy Study of Nanosilver Based Amorphous Hydrogel for Wound Healing.

Rajeshwari Bale (rvybale2000@gmail.com)[1], Munira Momin (Munira.Momin@bncp.ac.in)[1], Iqraa Shaikh[1], Amrita Bajaj[1], Diksha Kanojiya[1]

[1]**Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: The wound care market is growing at a CAGR of 5.0% from 2016 to 2022 and comprises all the products available to enhance or support wound healing. Amorphous hydrogels form a type of dressing which can incorporate most of the ideal properties of wound dressing for deep and necrotic wounds. Silver in the form of nanoparticles (AgNPs) is an excellent microbicide. Several mechanism have been proposed for its action: e.g. AgNPs release Ag + ions which act as antimicrobial agents by their interaction with sulphur and phosphorus groups in the structure of proteins of the cell wall and plasma membrane of bacteria that lead to dysfunction of this protein which leads to cell death [1]. The objective of the present study was to develop and characterize the novel hydrogel containing nanosilver stabilized by biofunctional excipient sodium hyaluronate offering delayed and sustained release to treat low-exuding wounds and assisting regeneration [2].

Methods: A) Preparation of nanohydrogels: Nanosilver particles were developed using the wet chemical method. Silver nitrate was added in millipore water then reagent sodium hyaluronate and sodium borohydride were added slowly, stirred solution vigorously. Nanosilver dispersion was transferred to soaked carbopol base with propylene glycol and the gel was made with a drop of triethanolamine.

B) Comparative in vitro diffusion study with marketed formulation: The in vitro diffusion study was performed on the Franz diffusion cell apparatus. Silver nanoparticle dispersion based amorphous hydrogel and marketed hydrogel was subjected to diffusion studies in release media 7.4 pH buffer by simulated wound environment for 7 hours. The results of in vitro drug diffusion studies of formulation were fitted in various kinetic models and r^2 values were calculated.

C) In vivo study for determining wound healing efficacy: Wistar rats were randomly divided into 8 groups. Dorsal hair was shaved under anesthesia and made aseptic then a wound of 1 cm diameter was created. All groups, except normal control and negative control, were treated with optimized formulation treatment for 16 days and then sacrificed for histopathological analysis.

Results: The diffusion test showed a delayed and sustained release as compared to the marketed hydrogel. Release kinetic study was found to follow zero order with r^2 of 0.9078. In-vivo wound healing efficacy was studied in Wistar rats and showed the promising effect of promoting wound healing with the lowest strength of nanosilver (16 microgram/ml).

Conclusions: The formulations of hydrogel dispersions containing nanosilver along with sodium hyaluronate provide controlled release of silver hence avoiding the cytotoxic effect of silver and also enabling the enhancement of wound healing while overcoming the limitations of the current commercial stabilizers.

Reference:

1. M. Zakia et al., “Development of silver nanoparticle-based hydrogel composites for antimicrobial activity,” Green Chem. Lett. Rev., vol. 13, no. 1, pp. 34–40, 2020, doi: 10.1080/17518253.2020.1725149.
2. V. Pechová and J. Gajdziok, “[Possibilities of using sodium hyaluronate in pharmaceutical and medical fields].,” Ces. a Slov. Farm. Cas. Ces. Farm. Spol. a Slov. Farm. Spol., vol. 66, no. 4, pp. 154–159, 2017.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Evaluating Bile Salt based Co-Amorphous System of Sorafenib using In-Vitro Dissolution and In-Vivo Pharmacokinetic Studies

Manasi Pawar (manasipawar631@gmail.com)[1], Abhay Sangamwar (abhay@niper.ac.in)[1]

[1]**National Institute of Pharmaceutical Education and Research, S.A.S. Nagar, Mohali, Punjab**

Background and Rationale - Co-amorphous system (CAMS) is a single-phase homogenous system of drug and low molecular weight excipient in amorphous state, stabilized via intermolecular interaction that add benefit of thermodynamic stability. It falls under the category of supersaturating drug delivery system, providing high drug loading and enhanced dissolution rate compared to neat drug. Sorafenib is BCS class II molecule exhibiting precipitation linked absorption. To tackle this challenge, binary and ternary co-amorphous system of sorafenib with bile salt (sodium taurocholate) and HPMC were prepared to enhance the solubility and dissolution rate, leading to its augmentation in pharmacokinetic effect.

Methods:

A) Preparation method: Spray drying was employed as a preparative method to fabricate the binary and ternary CAMS.
B) In-vitro dissolution studies: Powder dissolution was carried out under the sink condition in pH 6.8 phosphate buffer with 0.5% SLS for 2 hr. Before testing, 500 mL media was preheated to 37± 0.5°C and rpm was set at 150. At predetermined time points, aliquots of 2 mL were withdrawn, filtered and then suitably diluted. The drug content in samples was analysed by validated HPLC method.

C) In-vivo pharmacokinetic studies: Pure drug and formulations were administered to SD rats (n=5) by oral gavage at dose equivalent to 20 mg/kg of sorafenib. About 300 µL blood was withdrawn at predetermined time points and subjected to centrifugation to separate plasma. Plasma was further processed and then analysed by bioanalytical HPLC method.

Results and Discussion: Neat drug had less than 5% drug release at the end of 120 min. Binary CAMS of sorafenib-sodium taurocholate (1:2 molar ratio) showed the initial boost in release (50% release) but after that dissolution profile drastically dropped. Sorafenib-Sodium taurocholate (1:2)-HPMC (7.5% w/w of total wt.) ternary CAMS exhibited slow and sustain release reaching to 52% release at 45 min and at 120 min, 30% drug release was observed. Invitro dissolution advantage of CAMS also reflected into in vivo oral bioavailability benefit. In ternary formulation, as HPMC maintained the supersaturation for longer time, so 7 and 3-folds improvement in Cmax and AUC was observed, while in binary formulation only 5.6- and 2.35- folds improvement in Cmax and AUC was achieved respectively.

Conclusion: The present approach suggests that co-amorphous system is a promising alternative to the conventional formulations for brick dust molecules like sorafenib. HPMC used in the formulation maintained the supersaturation for prolong time which resulted in augmentation of biopharmaceutical properties of sorafenib.

References:

1. Lalge R, Suryanarayanan R., et.al., Dual Functionality of Bile Acid: Physical Stabilization of Drugs in the Amorphous Form and Solubility Enhancement in Solution. Mol Pharmaceutics. 2022;19(7):2595-260
2. Wang Y, Grohganz H, Rades T. Effects of polymer addition on the non-strongly interacting binary co-amorphous system carvedilol-tryptophan. International Journal of Pharmaceutics. 2022;617:121625

Acknowledgements: Authors are thankful to Director, NIPER, S.A.S. Nagar for providing facilities.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Evaluation of Permeability Enhancement Potential of Terbinafine Hydrochloride using Microemulsion based Shampoo Hair Gel for *Tinea capitis*

Kailash Patil (patilkailash438@gmail.com)[1], Sujata Sawarkar (Sujata.Sawarkar@bncp.ac.in)[1], Ishra Khatri[1]

[1]**Dr. Bhanuben Nanavati College Of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: A serious fungal infection of the scalp known as *Tinea capitis* manifests as thickened, scaly, and occasionally bogging swellings or as rising, elevated red rings. There is a direct need to develop topical antifungal formulations since oral formulations manifest serious hepatotoxicity. In the present study, a microemulsion-based hair gel containing Terbinafine Hydrochloride was developed to facilitate rapid skin penetration in a shorter application period of 2 hours for the effective therapy of *Tinea Capitis*.

Methods: (A) Preparation of Terbinafine Hydrochloride loaded Microemulsion based gel: Microemulsion of terbinafine hydrochloride was developed using mixture of oil (Capryol 90 and Lemon oil) and S_{mix} (Tween 80 as surfactant and Transcutol P as co-surfactant). The gel formulation was prepared by incorporating the prepared microemulsion into gel base comprising of Carbopol 980 and Polaxamer 407.

(B) *In vitro* and *ex vivo* drug diffusion study of developed formulation: *In vitro* diffusion studies were performed in medium comprising of phosphate buffer, pH 5.5 in combination with ethanol in the ratio of 1:1 using Franz diffusion apparatus and nylon as artificial diffusion membrane maintained at 32 ± 2°C and stirred at 50 RPM for a period of two hours. For *ex vivo* studies, mice skin was used as diffusion membrane. The developed formulation was compared with marketed cream.

Results and Discussion: Microemulsion based shampoo hair gel showed drug permeation of 10.47 % at the end of 5 minutes whereas marketed product showed 2.68% in ex vivo drug diffusion study. The enhanced permeation attributed by microemulsion approach helped in attaining effective inhibitory concentration of terbinafine hydrochloride by topical route within 5 minutes. At the end of 2 hours microemulsion based shampoo hair gel and marketed cream exhibited % drug diffusion of 88.54% and 40.77% respectively. The flux and diffusion rate constant were increased by 2.28 and 3.95 folds respectively compared to the marketed cream.

Conclusion: The microemulsion-based shampoo hair gel technology demonstrated encouraging results for improving drug permeability for poorly soluble terbinafine hydrochloride. However future clinical trials are required to be conducted to confirm proof of concept.

References:

1. Zhu W. Microemulsion-based hydrogel formulation of penciclovir for topical delivery. Int J Pharm. 2009;378(1-2):152-158.
2. Chauhan Lalit (2013). Design, development, and evaluation of topical microemulsion. International Journal of Pharmacy and Pharmaceutical Sciences, 5(2),605-610.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Evaluation of Skin Penetration Potential of Microemulsion Based Gel Of Quercetin for Treatment of Psoriasis.

Sahil Gaikar (gaikarsahil06@gmail.com)[1], Sujata Savarkar (Sujata.Savarkar@bncp.ac.in)[1], Vijay Yadav[1], Tejaswini Desai[1]

[1]**Dr. Bhanuben Nanavati College Of Pharmacy, Mumbai, Maharashtra**

Background & Rationale: Psoriasis is a chronic autoimmune disease characterized by the excessive proliferation of skin cells, leading to the development of thick, scaly plaques. Conventional therapy using synthetic drugs have drawbacks like poor drug solubility, poor drug permeability, high drug toxicity and short half-life. Quercetin inhibits the accumulation of exudates and mobilization of leukocytes that may represent a novel strategy for the modulation of inflammatory response in psoriasis. In this study, quercetin microemulsion is incorporated to prolong skin retention and enhance its skin permeation.

Methods:

A. **Preparation of Quercetin loaded microemulsion gel:** Microemulsion of quercetin was developed by using mixture of oil (sesame oil: oleic acid) and Smix (Labrasol+ Kolliphor HS 15+Tween80 as surfactant and Transcutol P as co-surfactant), then formulated microemulsion was incorporated in gel base composed of Carbopol ETD2020, water, propylene glycol and Aloe Vera pulp.
B. **Preparation of Quercetin loaded conventional gel:** Quercetin was incorporated in base comprised of Carbopol ETD 2020, water and propylene glycol.
C. ***In vitro* and *ex vivo* drug diffusion and skin retention study of developed formulation:** *In vitro* studies was performed using Franz diffusion apparatus with nylon membrane of 0.45 µm as diffusion membrane. A combination of phosphate buffer pH 6.8 and ethanol in 65:35 ratio was used as the diffusion medium and was maintained at 32±2ºC, at 100 RPM for 24hrs. *Ex vivo* investigations was done on mice skin and skin retention and permeation was recorded. The results of the formulated microemulsion based gel was compared with the conventional gel for the effect on skin permeation and retention.

Results and Discussion: Microemulsion based gel showed a higher drug release of 61.38% as compared to conventional gel which showed 11.72% release at the end of 8 hrs in *in vitro* studies. An improvement in skin permeation of the drug was observed in *ex vivo* studies wherein 58.17% drug permeating from microemulsion based gel whereas only 12.11% of drug was found to permeate from microemulsion based gel; which was five-fold greater than that observed for conventional gel (4.36%). The flux and permeability coefficient for *ex vivo* was increased by 811 and 945 folds respectively as compared to the conventional gel.

Conclusion:

Quercetin loaded microemulsion based gel showed improvement in the solubility, skin retention and permeability of quercetin. Further studies on animal models may serve as a proof of concept for this formulation.

References:

1. Azar Kajbafvala, Alireza Salabat, Anayatollah Salimi, Formulation, characterization and in-vitro/ex-vivo evaluation of quercetin loaded microemulsion for topical application, Pharmaceutical Development and Technology, Nov 2016.
2. T. Hatahet et al., Quercetin topical application from conventional dosage form to nano dosage forms, Eur.J. Pharm. Biopharm.2016; 108: 41-53.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Exploring the Potential of Nanofiber Technology to Enhance Bioavailability of Azilsartan Medoximil

Gaurav Pandey (2000gaurav.a.pandey@gmail.com)[1], Sujata Sawarkar (Sujata.Sawarkar@bncp.ac.in)[1], Priyanka Gavali[1], Pranav Shah[2]

[1]**SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra** | [2]**Maliba Pharmacy College, Surat, Gujarat**

Background and Rationale: Poorly soluble drugs exhibit limited dissolution, bioavailability, and therapeutic efficacy. Therefore, there is a dire need to improve the solubility profile of the drug without altering its chemical nature and activity. Azilsartan medoximil a BCS class IV drug with low solubility and high permeability is used to treat the condition of Hypertension. The poor solubility hinders its therapeutic effect and creates difficulties in the manufacturing process. Drug-loaded nanofibers offer benefits like increased surface-to-volume ratio, enhanced porosity, amorphization leading to enhanced solubility and dissolution rate. The objective of this study is to improve the solubility of a BCS class IV drug by integrating it into nanofibers and assessing its dissolution characteristics. In the present research project formulated nanofibers were converted into capsule, tablet and solid dispersion and further compared with the marketed product.

Methods: A) Preparation of Electrospun Azilsartan medoximil loaded nanofibers: The electrospinning of nanofibers were prepared by E-SPIN NANOTECH SUPER ES2 using drug Azilsartan medoximil in combination with Eudragit E 100, PVP K30, stearic acid.

B) Incorporation of developed nanofibers into solid dosage forms: The nanofiber was combined with suitable diluents and converted into capsule, tablet, and solid dispersion.

C) In vitro release study of developed nanofibers-based formulation: Multimedia dissolution studies were performed in pH1.2, pH4.5, pH6.8 and OGD recommended medium at pH 7.8 with an RPM of 50 at 37 ±2°C for one hour in each medium using USP Apparatus Type II for tablet, capsule, solid dispersion, marketed tablet and pure API. The samples were withdrawn at periodic interval as per the protocol and analysed for percent drug release.

Results and Discussion: The drug release of nanofibers-based capsules, tablets were compared to marketed tablet, API solid dispersion prepared using same excipient in same proportion and pure API.

Drug release (%) from all formulations in various media at the end of one hour				
Formulation/ pH	**1.2**	**4.5**	**6.8**	7.8 (OGD)
NF-Capsules	97.07	90.04	79.85	96.52
NF-Tablets	87.35	82.97	76.39	87.17
API-Solid Dispersion	51.70	43.25	29.85	36.45
Marketed Product	59.25	55.12	37.58	51.54
Pure API	15.88	28.01	7.61	11.31

The enhanced dissolution profile in case of nanofiber-based capsules and tablets was attributed to the drug being changed into its amorphous form and enhancement of surface area using electrospun nanofiber technology.

Conclusion – Azilsartan medoximil loaded nanofiber blend incorporated in the capsule formulation can be used as a promising approach for solubility enhancement of drugs with poor solubility. However, as a future potential of this study, the biocompatibility and efficacy of the developed system should be tested by performing preclinical and clinical experiments to ascertain enhancement in bioavailability.

1. **References** –
Alghoraibi I, Alomari S. *Different Methods for Nanofiber Design and Fabrication.* Handbook of Nanofibers, 2018: 1-46.
2. Ainurofiq A, Putro DS, et al., *A review on solubility enhancement methods for poorly water soluble drugs.* J Reports Pharm Sci, 2021, 10(1): 137-147.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Fabrication of Binary and Ternary ASDS of Pretomanid: Improved Dissolution and Biopharmaceutical Performance

Krishna Mehtre (krishnamehtre65@gmail.com)[1], Abhay T. Sangamwar (abhays@niper.ac.in)[1], Mehak Juneja[1]

[1]**National Institute of Pharmaceutical Education and Research (NIPER) S.A.S. Nagar, Sector 67, S.A.S. Nagar (Mohali), Punjab**

Background and Rationale: Amorphous solid dispersions (ASDs) have been extensively exploited as a strategy for improving the solubility and dissolution performance of poorly water-soluble drugs. 1,2 Besides the benefits of ASDs, which have some limitations such as drug loading (DL) and stability, in many cases, one polymer alone is not able to maintain supersaturation for prolong time at higher drug loading, which raises a need for reasonable combination of either polymer with surfactant or polymer-polymer. Unfortunately, combination of polymer with surfactant, results in a negative impact on stability of supersaturated system. The aim of this study is to develop binary and ternary ASDs of poorly water-soluble drug with sustained drug release at higher drug loading.

Methods: A) Fabrication of Binary and Ternary ASDs: The binary and ternary ASD formulations were prepared by solvent evaporation method using a spray dryer.

B) In vitro drug release: The drug release study was performed in 500mL phosphate pH-6.8 buffer media with 0.5% SLS, the drug and formulations equivalent to 100 mg of drug was added in dissolution media, 2ml of aliquot sample were taken at different time intervals up to 12 hrs, with replenishing 2ml fresh media to maintain sink condition. Samples further filtered and analysed by validated HPLC method.

C) In vivo Pharmacokinetic Study: The prepared formulations were evaluated for in-vivo behaviour of both binary and ternary ASDs in SD Rats.

Results and Discussion: In binary ASDs, 80% HPMCAS-HF was required to stabilize the amorphous form of Pretomanid, whereas in ternary ASDs containing combination of HPMCAS-HF and PVP-K30, 30% DL was obtained. The crystalline drug showed only 10% drug release. While the ternary ASDs with 20% and 30%DL demonstrated a higher and sustained drug release (65% and 47% respectively) for 12 hrs, in comparison to binary ASD which showed 50% drug release. The higher drug release obtained, which could be due to more hydrophobic interactions involved between hydrophobic groups of pretomanid and polymers in ternary ASD, than the interactions between drug and HPMCAS-HF in binary ASD as confirmed by FTIR and NMR. The generated ASDs was stable for 3 months at room temperature. In in vivo study, ternary ASD showed 4-6-fold improvement in Cmax and AUC respectively compared to crystalline drug.

Conclusion: As a combination of two polymers, HPMCAS-HF and PVP K-30 was effective in inhibiting recrystallization and maintaining sustained drug release even at higher drug loading of highly re-crystallizing, GFA class-I drug. The combination strategy in ternary ASDs, also shows a synergistic effect over binary ASDs.

References:

1. Xie T., et al., Improved Release of Celecoxib from High Drug Loading Amorphous Solid Dispersions Formulated with Polyacrylic Acid and Cellulose Derivatives. Molecular Pharmaceutics 2016. 13, 873−884.
2. Monschke M., et al., Impact of HPMCAS on the Dissolution Performance of Polyvinyl Alcohol Celecoxib Amorphous Solid Dispersions. Pharmaceutics 2020, 12, 541.

Acknowledgements: All the authors are thankful to Director, NIPER, S.A.S. Nagar for providing facilities.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Favipiravir Solid Lipid Nanoparticles- In vitro dissolution using USP II with Novel dialysis adaptor.

Shubham Thete (shubhamthete273@gmail.com)[1], Padma Devarajan (pvdevarajan@gmail.com) [1], Esha Attar[1], Suhas Yewale[2]

[1]**Institute of Chemical Technology, Mumbai, Maharashtra** | [2]**Sotax India Private Limited**

Background and Rationale: Favipiravir an antiviral was approved by some countries, including India, for COVID-19 treatment. In this study we present favipiravir Solid Lipid Nanoparticles (FPV-SLN) for lung targetted delivery. The rationale is based on lymph mediated uptake of SLN through intestinal Peyer's patches which will enable bypass of first pass metabolism and thereby facilitate lung targeting[1]. The aim of the work was development of FPV-SLN of desired physico-chemical properties. Drug release from the FPV-SLN following administration is a critical requirement. Hence the objective of the present study was development of a robust method for in vitro release testing from the FPV-SLN using the novel Dialysis adaptor.

Methods: A). Development and physico-chemical characterization of FPV-SLN: FPV-SLN were prepared by melt-homogenization method and optimized for particle size and entrapment efficiency by using OVAT approach. Zeta potential, SEM, TEM, FTIR, DSC, XRD were recorded.

B) In vitro release study: This was carried out using USP II with dialysis bag/ Novel dialysis adaptor and USP IV apparatus with dialysis(A4D) adaptor: FPV-SLN were evaluated for release by varying formulation parameters and media. Three physiological pH conditions studied were gastric pH 1.2, duodenal/lysosomal pH 4.5 and intestinal pH 6.8. In USP IV effect of flow rate on release was also evaluated. Mathematical models were applied to understand release kinetics and mechanism of drug release from the nanoparticles.

C) Ex vivo permeation study: Permeability study was carried out using Franz diffusion cell. Chicken intestinal mucosa was mounted with the epithelium facing the donor side and equilibrated for 30 minutes with the receptor compartment containing 10 mL PBS 7.4 at 37 ± 0.5ºC, and the donor compartment PBS pH 7.4 (1 mL). For the confirmation of intact nanoparticle translocation TEM analysis was performed.

Results and Discussion: FPV-SLN of average particle size of ~400 nm, PDI < 0.3 and entrapment efficiency >70% was developed. TEM and SEM revealed spherical FPV-SLN of size (~400 nm). XRD/DSC revealed partial amorphization. In vitro release study using dialysis bag method showed lower percentage release with high standard deviation while Novel dialysis adaptor and USP IV apparatus showed very low standard deviation and high reproducibility. In general, higher release was seen with plain FPV compared to FPV-SLN. Furthermore, FPV release was higher in pH 6.8 and pH 4.5 compared to pH 1.2. Good discrimination was observed with all methods at different pH. Increased flow rate in USP IV revealed increase in release rate. Maximum drug release was observed in intestinal pH as compare to gastric and lysosomal. Increase in lipid ratio resulted in slower release due to the lipidic barrier. Change in lipid composition revealed no effect in release profile. Formulations exhibited Korsemeyer Peppas release kinetics. USP IV demonstrated slower release and better discrimination. FPV-SLN showed 2.56-fold permeation enhancement through chicken intestinal mucosa compared to FPV solution. Intact FPV-SLN nanoparticles in the acceptor medium proposes lymph mediated transport.

Conclusion: In vitro release study revealed good discrimination. Importantly the novel dialysis adaptor with USP II, provided high reproducibility with low standard deviation and was comparable with USP IV, proposing great advantage.

Reference: Bachhav SS, et al. Mol Pharm. 2018;15(10):4434-45.

Acknowledgements: Authors are thankful to Sotax India Private Limited for USP IV apparatus; Avra Laboratories PVT LTD. & Gattefosse for gift samples of Favipiravir & Glyceryl Monostearate respectively. Shubham is thankful to AICTE, GOI for Research Fellowship

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Formulation and Development of Microsponges for Acne Vulgaris giving Controlled and Targeted Release

Jill Nanavati (jillnanavati1408@gmail.com)[1], Prachi Pimple (Prachi.pimple@bncp.ac.in)[1], Prabha Singh[1], Shruti Dudhat[1], Raj Kapadia[1]

[1]**Dr Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Acne vulgaris is a chronic skin condition causing inflammatory and/or non inflammatory lesions. There are various factors responsible like dysregulated hormones, bacteria, and increased sebum production. Salicylic acid has keratolytic, comedolytic with some anti-inflammatory and bacteriostatic activities. Polyphenols are antioxidants and play a role in preventing oxidative damage caused by the reactive oxygen species and possess anti-inflammatory property, can reduce sebum production, and has antibacterial activity. Polyphenols are found in green tea and are responsible for activity being catechins. Epigallocatechin gallate is the most found catechin in green tea. Microsponges are polymeric delivery systems consisting of porous microspheres. The aim of this study is to formulate microsponges of salicylic acid in order to provide targeted effect, decreased irritation potential and providing synergistic mechanism of action against acne vulgaris.

Methods: A) Formulation: Salicylic acid was loaded into the microsponges and green tea extract was directly loaded in the gel base. Ethyl cellulose was selected as the polymer for microsponge production. The internal phase contained the solvent (DCM), ethyl cellulose and NaCl solution. The external phase consisted of PVA and/or Tween-80 (stabilizer) and distilled water. The internal phase added dropwise to the external phase with continuous stirring resulted in formation of small globules and upon evaporation of the solvent resulting in insoluble microparticles.

B) In vitro drug release studies and Ex vivo skin permeation and retention studies: For In vitro drug release studies diffusion of the gel was performed on PVDF hydrophilic, cellulose acetate phthalate and, dialysis membrane. Dialysis membrane was selected as it gave the best release profile. Diffusion study was done by using Franz Diffusion Cell, Diffusion membrane: Dialysis membrane, Release medium: 22 mL of phosphate buffer pH 5.5 + ethanol (1:1), Temperature: 37°C ± 2 °C, Stirring speed: 100 rpm. Ex vivo studies were done using Franz Diffusion Cell: Diffusion membrane: Porcine ear skin, Release medium: 22 mL of phosphate buffer 5.5 + ethanol (1:1), Temperature: 37°C ± 2 °C, Stirred speed: 100 rpm

Results and Discussion: The marketed gel (Zitcare S) gave a 83.063% release by 5th hour whereas the microsponge gel gave a controlled release of 72.776% by 8th for salicylic acid and 85.316% for green tea extract. The ex-vivo skin permeation showed that the salicylic acid microsponge loaded green tea gel exhibited better permeation and was retained for prolonged time compared to the marketed gel. Low flux values were obtained indicating controlled release effect. The flux values for salicylic acid, green tea extract and marketed gel are 0.481, 0.576 and 0.852 respectively.

Conclusions: The results indicated that salicylic acid microsponges loaded in green tea gel was found to have controlled and targeted release.

References:

1. Garg T. Current nanotechnological approaches for an effective delivery of bio-active drug molecules in the treatment of acne. Artif Cells Nanomedicine Biotechnol. 2016;44(1):98-105.
2. Kanlayavattanakul M, Lourith N. Therapeutic agents and herbs in topical application for acne treatment. int J Cosmet Sci. 2011;33 (4):289-97.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Formulation and Evaluation of Modified Release Oxybutynin Hydrochloride Matrix Tablet

Nirmiti Prabhu (nirmiti.prabhump2021@ves.ac.in)[1], Pradnya Shinde-Korlekar (pradnya.korlekar@ves.ac.in)[1], Sameer Padhye[2], Shivali Tank[1]

[1]**VES College of Pharmacy, Chembur, Mumbai, Maharashtra**; [2] **Arihant Innochem Pvt. Ltd, Mumbai, Maharashtra**

Background and Rationale: The marketed SR oral formulation for oxybutynin is an osmotic controlled release system (OROS), which permits once-daily administration, and improves the tolerance of oxybutynin compared to the formulation for immediate release. However, specialized technology is required for OROS manufacturing. To treat urinary incontinence, an attempt was undertaken to design oxybutynin SR matrix tablets.

Methods: A) Formulation: Matrix tablets were formulated with different grades of Carbopol (Carbopol 71 G, and Carbopol 971 P), HPMC (K100M, K50M, and K4M) as release retarding polymers. Carbopol 71 G were prepared by direct compression and 971 P and HPMC, alone and in combination were prepared using wet granulation.

B) Release study: Dissolution study was conducted using USP apparatus 1 in simulated gastric (pH 1.2) and intestinal fluid (pH 6.8) (SGF and SIF respectively) at 37°C ± 2°C at 100 rpm. The tablet was exposed to SGF for 2 hours and later to SIF for 24 hours. Aliquots were withdrawn every two hours and then analyzed on HPLC. The matrix is intended to release the drug via diffusion and matrix relaxation later.

Results and Discussion: Combination batches of Carbopol 971 and HPMC gave a good sustained release when compared to Carbopol alone. It is observed that HPMC retards the drug release in the initial SGF phase and Carbopol in later SIF.

Conclusion: Sustained-release matrix tablets have the potential to replace the expensive and sophisticated OROS technology.

References:

1. Naik, S., Venkateswarlu, K., & Chandrasekhar, K. B. (2016). Formulation and evaluation of Oxybutynin chloride extended-release matrix tablets. Indo Am J Pharm Res, 6(1), 4179-84.
2. Zambito, Y., Baggiani, A., Carelli, V., Serafini, M. F., & Di Colo, G. (2005). Design and in vitro evaluation of an extended-release matrix tablet for once-daily oral administration of oxybutynin. Journal of drug delivery science and technology, 15(5), 397-402.

Acknowledgements: We thank M/s Arihant Innochem) for providing us with gift samples of Polymers and guidance. We are grateful to Prof. Mangal Nagarsenkar for her valuable guidance.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Formulation and Permeability Enhancement of Bromocriptine Loaded Bilosomal Nasal In-Situ Gel.

Surabhi Sureshan (surabhisureshan10@gmail.com)[1], Gowtham Menon (gowthamm1984@gmail.com)[1], Rohit Choure[1], Vishnu A S[1]

[1]**Sanjivani College of Pharmaceutical Education & Research, Kopargaon, Maharashtra**

Background and Rationale: Parkinson's disease is the second most prevalent progressive central nervous system disorder and the major challenge for brain-targeting drugs is efficiently delivering the drug across the blood-brain barrier to the targeted sites. The nasal route takes the drug straight to the brain avoiding hepatic first pass metabolism and bypassing the BBB, but for this many hurdles have to be overcome with respect to solubility and permeability of the drug. Bromocriptine is a class II drug with low oral bioavailability. The aim of this study was to create a bromocriptine loaded bilosomal in situ gel for the treatment of Parkinson's disease via the nasal route to overcome the drawbacks associated with oral administration in terms of its solubility, permeability and bioavailability. The entrapment efficiency and drug release of the fifteen formulations were investigated along with other elements of evaluation.

Methods: A. Formulation of bromocriptine-loaded Bilosomes: The formulation was done using three factor, three-level Box-Behnken design and thin film hydration method and the bilosomes were loaded into in situ gel consisting of gellan gum and hydroxypropyl methylcellulose using cold method.

B. In vitro drug release study: A Franz diffusion cell with a capacity of 10 ml was used to conduct in-vitro drug diffusion experiments of the formulation. Before the experiment, pieces of dialysis membrane were soaked in phosphate buffer pH 6.4 for 24 hours. The dialysis membrane was placed on the diffusion cell, which was filled with phosphate buffer pH 6.4 and a water bath was used to keep the temperature at 37°C. The contents of the receptor fluid were constantly stirred at 250 rpm. At 60,120,180, 240, 300, 360, 420 and 480 minutes, samples were withdrawn and replaced with an equivalent amount of new buffer solution. A UV-visible spectrophotometer (Shimadzu 1900) set to 303 nm was used to measure the amount of drug in withdrawal samples.

Results and Discussion: Out of formulations developed by three-factor, three-level Box-Behnken design, maximum release after 8 hours was found for the F12 formulation. This indicates a release of 77.6% drug availability. The obtained results of formulation have shown significant prolongation of drug release across biological membrane considering an 8 hours release pattern. The quantitative analysis of the values obtained in dissolution/release was subjected to mathematical modeling which can ultimately help to optimize the design of a therapeutic device to yield information on the efficacy of various release models.

Conclusion: The study's aim was to transport drugs on a nanoscale to the brain for targeted treatment for neuro-degenerative disorders such as Parkinson's disease. In situ gel has the potential to maintain a constant plasma drug levels in the body by sustaining drug release and it is known to extend the drug's life in mucosa. This optimized formulation containing bilosomes of bromocriptine mesylate proved to have good mucoadhesive property with potential for improved availability of the drug at the target site, post nasal administration, for treatment of Parkinson’s disease.

References:

1. Agrawal M, Saraf S, Saraf S, Antimisiaris SG, Chougule MB, Shoyele SA, Alexander A (2018) Noseto-brain drug delivery: An update on clinical challenges and progress towards approval of anti- Alzheimer drugs. Journal of controlled release : official journal of the Controlled Release Society281:139–177.
2. Alexander A, Agrawal M, Bhupal Chougule M, Saraf S, Saraf S (2020) Nose-to-brain drug delivery: an alternative approach for effective brain drug targeting. Nanopharmaceuticals: Volume 1: Expectations and Realities of Multifunctional Drug Delivery Systems 175–200.
3. Kaur P, Garg T, Vaidya B, Prakash A, Rath G, Goyal AK (2015) Brain delivery of intranasal in situgel of nanoparticulated polymeric carriers containing antidepressant drug: behavioral and biochemical assessment. Journal of drug targeting 23:275–286.

Acknowledgements: We express our sincere gratitude towards the Management of Sanjivani Groups of Institutes for supporting us to complete this work successfully.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Formulation Development and In-Vitro Characterization of Hot-Melt Extruded Cyclosporine Ocular Inserts for Dry Eye Disease

Bharathi K (ahariharan0102@gmail.com)[1], Derajram Benival (derajram@niperahm.res.in)[1], Sahil Shaikh[1], Amit Sharma[1], Sagar Salave[1], Nitish Sharma[1]

[1]**National Institute of Pharmaceutical Education and Research, Gandhinagar, Gujarat**

Rationale: The currently approved topical solutions and emulsions of cyclosporine, for the treatment of dry eye disease, are associated with a high frequency of administration. The presence of surfactants and preservatives in such formulations causes discomfort to the patient on prolonged use. Our study aimed to develop and characterize preservative-free, sustained-release ocular inserts containing cyclosporine, that are capable of increasing the retention time at the ocular surface, that would enhance patient compliance.

Methods:A) Fabrication of cyclosporine-loaded ocular inserts: The inserts loaded with 1% w/w of drug, were fabricated using the polymer, hydroxypropyl cellulose. The CaliCut™ post-extrusion system was utilized for precise cutting of the extrudes. Optimization of the process parameters such as pre-mixing step, barrel temperature, screw speed, and housing temperature were carried out, to study its effect on the drug content, extrudability, drug release and the sharpness of insert edges, respectively.

B) Development of an *in-vitro* discriminatory dissolution method: Since there is no compendial dissolution method available for ocular inserts, an in-house method was developed, to assess the real-time dissolution behaviour of the inserts. The novel method involved the use of a 10 mL glass vial, in which the inserts were placed in between the bottom of the glass vial and a stainless-steel mesh, with a magnetic bead being rotated above the mesh. The discriminatory power of the developed method was established by its ability to differentiate the dissolution behaviour of inserts prepared with different molecular weights of the polymer. The dissolution medium composed of 0.25% SLS in 5 mL PBS was used to maintain sink conditions. Cyclosporine was quantified using RP-HPLC. The developed inserts were characterized for weight, thickness, surface pH, drug-excipient compatibility, in-vitro release profile, in-vitro degradation profile, swelling index and stability at RT and at 40ºC/75% RH.

Results: Cyclosporine-loaded ocular inserts with an average weight of approximately 5 mg, and dimensions of around 3.5 mm x 1.27 mm (length x diameter) were fabricated using hot-melt extrusion. The in-vitro release profile, indicated that, among the various molecular weight grades of hydroxypropyl cellulose, the inserts fabricated using the grade MXF (850,000 Da) provided a sustained release of the drug over a period of 24 hours, making it an ideal choice for daily administration. The % drug release at the end of 24 hours was found to be approximately 90%. The % weight remaining of the inserts at the end of 24 hours was found to be < 10%, as demonstrated by the in-vitro degradation profile. The formulation was found to be stable with no significant changes in the drug content and release profile, at the end of three months of storage.

Conclusion: The developed formulation enables the attainment of sustained drug release over a period of one day, that in turn would enhance patient compliance by reducing the frequency of administration.

References:

1. Cequa™: Highlights of prescribing information, Sun Pharmaceutical Industries Inc, NJ.

2. Restasis®: Highlights of prescribing information, Allergan Inc, U.S.A.

Acknowledgements: We would like to acknowledge National Institute of Pharmaceutical Education and Research- Ahmedabad and the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers for the funding and providing facilities for the successful completion of the project

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Formulation Development and In-Vitro Evaluation of a Novel Formulation of Acyclovir- Loaded Cubosomes Dispersed In Olopatadine HCl In-Situ Gel.

Nipun Panchal (nipunppanchal@gmail.com)[1], Prabha Singh (prabha.singh@bncp.ac.in)[1], Himanshu Sharma[1]

[1]**Department of Pharmaceutics, SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Herpes keratitis is a serious disease condition caused by herpes simplex virus, that can progress through cornea perforation, causes inflammation, and might lead to blindness. Acyclovir an antiviral drug used in treatment alone is not effective in the inflammatory stage and hence, Olopatadine Hydrochloride an antihistaminic acting as an H1 antagonist employed in combination is effective for treatment. The study aims to formulate less permeable, acyclovir loaded in liquid crystalline nanoparticle cubosomes that is incorporated into in-situ gel dispersed with Olopatadine HCl, optimize it, and evaluate for its in-vitro permeation, release kinetics, irritation, and stability studies

Methods: A) Formulation: Cubosomes of acyclovir were prepared using mono-olein as polymer and Poloxamer 407 as a surfactants using a Top-down technique and was further incorporated into a dispersion of Gellan gum, HPMC, and Olopatadine HCl and pH adjusted to 6.5 using 0.1N HCl

B) In-vitro evaluation: Permeation studies were conducted using Franz diffusion cell having dialysis membrane of 150 Daltons, 22mL of receptor compartment comprising of prepared Simulated tear fluid (STF) at pH 7.4, the temperature of 37±0.5°C and 100 rpm, aliquots withdrawn at an interval of an hour for 10 hours and analysed using UVspectroscopy. The absorption correction method was used for the simultaneous analysis of Acyclovir and Olopatadine HCl in STF pH 7.4. Ocular irritation study was performed by HET-CAM study on hen's eggs for positive controlled, negative controlled, Acyclovir cubosomes, conventional solution, olopatadine gel, and cubosomal in-situ gel.

Results and Discussion: The release study of the cubosomal in-situ gel showed sustained release with release kinetics of zero-order for both drugs in prepared formulation (93±0.5% at 10hrs and 95±0.5% at 7hrs for acyclovir and olopatadine respectively, as well as individual only acyclovir-loaded cubosomes and only olopatadine HCl in-situ gel, also showed zero order kinetics for release. The prepared formulation showed the highest flux (of 0.7674 µg/cm^2 /hr for acyclovir and 1.0263 µg/cm^2 /hr for olopatadine HCl) and permeability coefficient (0.2258 cm/hr for acyclovir and 0.3421 cm/hr for olopatadine HCl) as compared to marketed formulations (2.193 µg/cm2 /hr and 0.7312 cm/hr for acyclovir and 3.424 µg/cm^2 /hr and 1.14 cm/hr for olopatadine HCl respectively). No irritation was observed in the HET-CAM ocular irritation study with the prepared formulation. Conclusion: The developed acyclovir-loaded cubosomes in-situ gel with olopatadine HCl has great potential as a viable substitute as compared to conventional eye drops.

References:

1. Eldeeb A. et al. Formulation and evaluation of cubosomes drug delivery system for treatment of glaucoma: Ex-vivo permeation and in-vivo pharmacodynamic study. Journal of Drug Delivery Science and Technology, August 2019. p 236-247.
2. Ranch K. et al. Optimization of a novel in situ gel for sustained ocular drug delivery using Box-Behnken design: In vitro, ex vivo, in vivo and human studies, International Journal of Pharmaceutics, January 2019. p 264-75.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Formulation, Development and Evaluation of Novel Drug Delivery System for Management of HIV Latency

Divya Dubey (dsdubey22111998@gmail.com)[1] Prabha Singh (prabha.singh@bncp.ac.in)[1]

[1]**SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: HIV-1 is a causative agent for acquired immunodeficiency syndrome (AIDS) representing one of the deadliest worldwide epidemics. Despite the progress in available treatments, eradication of HIV infection has not been accomplished. HIV latency is a reversible state in which a pathogenic virus goes dormant in particular cells and the latent reservoirs are established at the early phase of the viral life cycle and accumulate overtime. A well-known natural phytoalexin called resveratrol (3, 4, 5′-trihydroxystilbene) was successful in reactivating latent HIV without widespread T cell activation. The protease inhibitor (PI), atazanavir sulphate, prevents the cleavage of the nascent viral proteins required for final assembly into new virions by inhibiting the protease enzyme. Nanostructured lipid carrier (NLC) can solve issues related to solubility, efflux, poor oral bioavailability of both the drugs.

Methods: NLC was made using the melt emulsification technique. The solid and liquid lipid were chosen as a consequence of the screening process. Sesame oil, Migliyol, a liquid lipid, and glyceryl monostearate (GMS), a solid lipid, were chosen. The ratio of solid and liquid lipid was optimized. Poloxamer-188, a surfactant, was added to the aqueous phase after which it was heated to 65 °C. Transcutol-HP, a co-surfactant, and lipids should be melted at the same temperature before the drugs are dissolved in the lipidic phase. The lipid drug mixture was added drop by drop into the aqueous phase under agitation and the agitation by an overhead stirrer was continued for one hour at 500 rpm. After that, a dispersion is created, which is subsequently exposed to 20–25 cycles of High Pressure Homogenization (HPH) at 1000 psi. The size, zeta potential, entrapment effectiveness, in vitro and ex vivo release etc. of the resultant NLC were characterized.

Results And Discussion: The optimized formulation exhibited particle size of 34 nm and 17 nm for Atazanavir sulfate and resveratrol respectively, and PDI of 0.2, zeta potential of -24 mV and -29 mV, entrapment efficiency of 98 and 99.6%. In-vitro release of NLC was found to be 98% and 99% at the end of 24 hrs and of NLC gel was found to be 95% and 97% at the end of 24 hrs . Ex vivo study showed release of NLC was found to be 92% and 94% at the end of 24 hrs and of NLC gel was found to be 90% and 93% at the end of 24 hrs. The animal studies are still ongoing.

Conclusion: The results indicated that Atazanavir sulfate and Resveratrol with good drug loading efficiencies could be prepared and the drug loaded NLCs showed controlled release.

References:

1. Xu X, Lin Y, Zeng X, Yang C, Duan S, Ding L, et al. PARP1 Might Substitute HSF1 to Reactivate Latent HIV-1 by Binding to Heat Shock Element. Cells. 2022 Jul;11(15).
2. Costa CP, Moreira JN, Sousa Lobo JM, Silva AC. Intranasal delivery of nanostructured lipid carriers, solid lipid nanoparticles and nanoemulsions: A current overview of in vivo studies. Acta Pharm Sin B. 2021;11(4):925–40.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

High-throughput Screening Protocol for In-Vitro Release Testing for Atrigel Drug Delivery System: An Unconventional Dissolution

Gegal Shah (shahgegal832@gmail.com) [1], Ravi Shah (ravi.shah@niperahm.res.in)[1], Feniben Kapadiya[2], Prerana Gangawane[3], Habeeba Saleha[4], Neeraj Kulkarni[5], Bichismita Sahu[5]

[1]Department of Pharmaceutical Analysis, NIPER Ahmedabad, Gujarat, Gandhinagar, Gujarat | [2]Sandoz Development Center, Genome valley, Hyderabad, Telangana | [3]Novartis Healthcare Pvt. Ltd., HITEC City, Hyderabad, Telangana | [4]Dr. Reddy's Laboratories Ltd., Bachupally, Hyd | [5]Department of Medicinal Chemistry, NIPER Ahmedabad, Gujarat

Background & Rationale: Atrigel® drug delivery system is one such widely accepted formulation technology used for developing an in-situ forming implant, which uses a liquid polymeric matrix formulation consisting of drug and water-insoluble biodegradable polymer(s) dissolved/suspended in biocompatible organic solvents[1]. But the path to develop an appropriate in vitro release testing method is difficult since there has been no guidance till date on such types of formulation as well as conventional apparatus are not fit for the purpose. Therefore, due to lack of guidance and research focus towards this arena, a very few generic manufacturers could crack the innovation and get approval for generic product. The major reason is non-comparable drug release profile due to specific grade of polymer (in terms of molecular weight and specific chemistry like LA:GA ratio for PLGA), process of making the product and IP limitation. The present study describes the workflow for selection of formulation components and monitoring drug release.

Methods:

A) Formulation science: Many compounds [excipient selection compounds: ESC] were selected based on their capability to form hydrogen bonding and π- π interaction with PLGA. Matrices composed of PLGA and ESC were utilized as vehicles for modifying release kinetics of model drug diclofenac sodium. A procedure for fabricating these polymeric delivery systems involved mixing the polymer and ESC with drug solution was optimized.

B) *In vitro* drug release: A simple and reliable assembly to conduct a 168-hour release study was designed in such a way that it mimics the biological environment, maintains the sink condition, while making it easier to collect the control release samples with negligible error during sampling every 24 hours following the collection of the initial burst release of the formulation. Further, the collected samples were evaluated using HPLC to find out the drug release.

Results and Discussion: The in-vitro dissolution tests were performed for 72 DoE runs designed by Design Expert v13 software using formulation variables including 17 different ESCs, 6 different grades of PLGA with varying ratios of PLGA:ESC combination in NMP/DMSO/DMA solvent for formulation preparation. The comparative in-vitro release data shows that the PLGA-ESC combination had modified the release kinetics with reduced burst release for the drug diclofenac sodium compared to Atrigel formed with alone PLGA.

Conclusions: The endeavor of the present work is to provide a systematic and reliable platform for the generic players to accelerate their development cycle for such long-acting injectable formulations.

References:

1. Wang, X. & Burgess, D. J. Drug release from in situ forming implants and advances in release testing. *Adv Drug Deliv Rev* 178, 113912 (2021).

Acknowledgements: The authors are grateful to the Ministry of chemical and fertilizer for funding and support to carry out this research work.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Impact of Test Parameters On In Vitro Release Of An Antirheumatic Drug From Microemulgel

Nikita Mashilkar (nikita.mashilkarmp2021@ves.ac.in)[1], Supriya Shidhaye (supriya.shidhaye@ves.ac.in) [1], Shivali Tank[1], Mangal Nagarsenker[1]

[1]**Vivekanand Education Society's College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Rheumatoid arthritis (RA), an autoimmune disorder is characterized by chronic inflammation of synovial tissues and infiltration of the affected joints by blood-derived cells. Leflunomide, one of the disease-modifying antirheumatic drug acts primarily by inhibition of de novo pyrimidine synthesis by its active metabolite. The drug is associated with gastrointestinal side effects, such as diarrhoea, nausea and dyspepsia, and the potential to cause liver toxicity when administered orally limits its long-term use in RA management. In the present study topical microemulsion based gel was developed and impact of the parameters on in vitro release of poorly water-soluble drug leflunomide was studied using vertical diffusion cell (VDC).

Methods: The microemulsion, a clear, thermodynamically stable system containing leflunomide was prepared using propylene glycol dilaurate as oil phase, a combination of surfactants and solvent and was formulated into a gel. The formulation was analyzed for particle size, poly dispersibility index, zeta potential with the help of Malvern Zetasizer. The in vitro release of the formulation was methodically evaluated using VDC. The effect of various parameters such as stirring speed (400rpm ,600rpm, 800rpm), release media composition (35,40,45% methanol/buffer v/v), media volume (10ml and 15ml) and type of artificial membrane (Polyether Sulfone 0.45µm, Cellulose acetate 12kDa molecular weight cut-off and Polyvinylidene fluoride 0.45µm) on release profile of drug were studied.

Results and Discussion: The average particle size, poly dispersibility and zeta potential values of the microemulgel were 46.93 ± 2.17 nm, 0.397 and -18.6mV, respectively. For topical delivery system, monitoring the drug release rate from the formulation across the membrane is considered as an important quality control parameter to ensure reproducibility of the product. With increase in stirring speed from 400 to 800 rpm the % cumulative amount release increased from 13.13% to 34% respectively. When methanol concentration was 45% in the media, highest release of 21.2% was observed. With change in volume of release media there was less significant change in the release pattern however the type of membrane had a major effect on the release profile where cellulose acetate membrane showed a release of 5.5 % and Polyether sulfone of 19.7% in medium containing buffer: methanol containing 55:45% at a speed of 600 rpm.

Conclusion: The current investigation focused on systematic evaluation of major factors influencing the rate of drug release from microemulgel. The experiments establish that changes in the stirring speed, receptor fluid composition, the type of membrane have a significant effect on the release of the API. Based on the results of the study, the IVRT method for leflunomide semisolid dosage forms can be developed which can be guide in formulation and a quality control tool.

References:

1. Naik, P., Shah, S.M., Heaney, J.A., Hanson, R., & Nagarsenker, M.S. (2016). Influence of Test Parameters on Release Rate of Hydrocortisone from Cream: Study Using Vertical Diffusion Cell. Dissolution Technologies, 23, 14-20.
2. Vinod P. Shah, Jerome Elkins, Steve Shaw, Royal Hanson. (2003) In Vitro Release: Comparative Evaluation of Vertical Diffusion Cell System and Automated Procedure. Pharmaceutical Development and Technology 8:1, pages 97-102

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

In Vitro and Ex Vivo Skin Permeation Studies of Novel Topical Gel for Cutaneous Lupus Erythematosus

Sweety Chheda (sweety.chheda99@gmail.com), Meenal Rane (meenal.rane@bncp.ac.in)[1]

[1]**SVKMs Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Lupus is a chronic, inflammatory, autoimmune disorder mainly prevalent in women of age between 15-44. Cutaneous Lupus Erythematosus (CLE) is a type of lupus that can present as an isolated skin disease or as a manifestation within the spectrum of systemic lupus erythematosus. CLE specific cutaneous manifestations are characterized mainly by butterfly rash and UV light induced skin lesions. CLE can be a source of disability and poor health related quality of life because rashes are often visible to the public as it tends to occur on sun exposed areas like a patient's face, chest, and arms. Currently there is no CLE specific FDA approved medications and the established standard treatment of CLE includes topical corticosteroids and calcineurin inhibitors, antimalarials, immunosuppressants all of which are known to have severe side effects. Our research aimed to formulate green tea extract loaded microsponge based gel as a suitable alternative herbal treatment. The drug would provide antiinflammatory effect along with photoprotection and formulation would prevent the drug from permeating systemically and give localized sustained drug release all of which is required for CLE treatment.

Methods: A) Formulation Development: Microsponges were prepared using quasi emulsion solvent diffusion method. Batch which gave maximum yield and entrapment, size below 300 micron and in vitro release of microsponge loaded gel more than 75 % in 12 hrs was taken ahead for further evaluation.

B) Evaluation of in vitro and ex vivo drug release: Comparative in vitro and ex-vivo release studies between the prepared formulation and conventional formulation was carried out by using Franz diffusion cell. The diffusion media used were phosphate buffer (pH 5.5): Ethanol in 1:1 ratio. Aliquots were withdrawn at 1hr interval and after suitable dilution drug release was determined using UV spectrophotometer. For in vitro studies dialysis membrane was mounted between the compartments of Franz diffusion cell while for ex vivo studies properly excised porcine ear skin was used.

C) Evaluation of skin deposition: At the end of 12hr the excised skin was washed with distilled water and wiped with cotton swab to remove the excess formulation. Tape stripping method was used to evaluate the amount of drug deposited in stratum corneum (SC).

Results and Discussion: The optimized batch had drug: polymer ratio 1:12 and 1% PVA. The conventional formulation released 99% of drug in 5hrs while prepared formulation showed sustained drug release for more than 12hrs. The ex-vivo diffusion studies confirmed that the drug from the prepared formulation did not penetrate transdermally. The amount of drug retained on SC from conventional formulation was 30.29µg/cm2 while for prepared formulation it was 45.72µg/cm2 .

Conclusions: The prepared formulation shows sustained drug release and better drug retention compared to conventional. Hence it might prove to be an alternative therapy for CLE.

References:

1. Tiwari A, Tiwari V, Palaria B, Kumar M, Kaushik D. Microsponges: a breakthrough tool in pharmaceutical research. Futur J Pharm Sci [Internet]. 2022;8(1). Available from: https://doi.org/10.1186/s43094-022-00421-9.

Acknowledgements: SVKMs Dr. Bhanuben Nanavati College of Pharmacy

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

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

Rameshwar Khillare (ramkhillare31@gmail.com)[1], Derajram Benival (derajram@niperahm.res.in)[1]

[1]**National Institute of Pharmaceutical Education and Research, Ahmedabad, Gujarat**

Background: Aqueous solubility of a drug substance is one of the key properties required for successful pharmaceutical formulation development. For immediate release drug products, it is essential to have faster rate of dissolution to produce rapid onset of effect. In addition, faster rate of dissolution is also required to enhance the extent of drug absorption and bioavailability. Amorphous solid dispersion (ASD) that are formulated using immediate release polymer, releases the drug in stomach and gets precipitated over time. We aim to prepare an ASD using enteric polymer that prevents release of the drug in stomach and maintains supersaturation in intestine where absorption is not rate limited and hence maximum bioavailability is achieved. This is based on the concept of spring and parachute effect. Interestingly, it has been observed in few marketed products such as Tolsura®, Xtandi® that enteric polymers when used to prepare solid dispersion/solution enhances the oral bioavailability significantly in comparison to solid dispersion/solution of drugs prepared using pH independent hydrophilic polymers and surfactants.

Methods:

a) **Formulation development of amorphous solid dispersion:** Enteric polymers were screened based on physicochemical properties and miscibility of the drug and polymer. The process parameters of HME, such as temperature and screw speed, were optimized to achieve good extrudability.
b) **In-vitro dissolution studies:** To evaluate the role of polymers in enhancing the dissolution rate, a discriminative dissolution method was developed. USP Type II dissolution apparatus was used. The release was studied in acidic pH 1.2 and basic pH 6.8. 0.25% SLS was incorporated in the dissolution media to maintain sink condition. An RP-HPLC method was developed to analyze the amount of drug released from the solid dispersions.

Results: The prepared amorphous solid dispersion using enteric polymer HPMC phthalate was found to significantly enhance the dissolution rate. It is significant to note that the milled extrudes were able to resist the release of fenofibrate to less than 10% at pH 1.2, thereby meeting the USP dissolution criteria in acidic media. On the other hand, at pH 6.8, greater than 85% fenofibrate was found to dissolve within 30 mins. Drug content in the milled extrudes was found to be in between 85% and 115%.

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

References:

1. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208901s000lbl.pdf
2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213674s000lbl.pdf
3. Simoes, Marta., Pinto, Rui, S imoes, Sergio. HME in the pharmaceutical industry: toward filing a new drug application.

Acknowledgements: We would like to thank NIPER A and the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, for the funding and for providing facilities for successful completion of the project.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

In-vitro Permeation Studies using Phytoconstituents as Potential Skin Penetration Enhancers for a Model Drug Aceclofenac

Shubham Munde (shubhamvmunde@gmail.com)[1], Norma Rebello (normar@sjipr.edu.in)[1]

[1]**AET's St. John Institute of Pharmacy and Research, Palghar, Maharashtra**

Background and Rationale: Aceclofenac is a Non-Steroidal Anti-inflammatory Drug (NSAIDS) widely used to treat local, analgesic, and inflammatory disorders. Topical drug delivery systems avoid many side effects of oral administration of NSAIDS, like gastric intolerance, nausea, dyspepsia, abdominal pain, etc. Regarding topical application, poor skin permeation of the drug affects its biopotential. Synthetic permeation enhancers are associated with skin irritation and toxic effects; hence there is a need to investigate novel, safe, and effective skin penetration enhancers. The herbal extract possessing secondary metabolites can act as permeation enhancers and possess anti-inflammatory activity. Hence the present study aims to assess the influence of herbal extract on the permeation of Aceclofenac carbopol gel in a topical formulation and prediction of anti-inflammatory activity with help of in- silico screening.

Methods: Successive solvent extraction method was used to extract plant material using n-hexane, chloroform, ethanol, and ethyl acetate. Respective extracts were subjected to qualitative phytochemical screening and Thin layer Chromatography (TLC) to confirm the presence of eugenol and lupeol. Molecular docking of eugenol and lupeol was performed with target proteins responsible for inflammation with the help of PyRx and evaluated with the help of Biovia Discovery Studio. Various batches of carbopol gel containing aceclofenac (1% w/w) and selected concentrations of synthetic penetration enhancer and herbal extracts were formulated. These formulations were subjected to appearance, pH, viscosity, and spreadability characterization tests. Formulations were subjected to in-vitro permeation using Franz diffusion cells. The herbal extracts' permeation was compared with a synthetic penetration enhancer (Coco caprylate).

Results and Discussion: The formulation containing ethanolic and n-hexane possessing eugenol and lupeol shows better % cumulative release (54.55% and 57.85%) when compared to synthetic penetration enhancer (48.99%) and gel devoid of penetration enhancer (46.98%). According to a molecular docking study, lupeol has a better binding affinity with target proteins.

Conclusion: Incorporating the herbal extract can be a safer and better alternative for increasing the permeation of Aceclofenac with additional synergistic effects for treating inflammatory disorders.

References:

1. Singh V, Chaubey N. Design and Evaluation of Topical Hydrogel Formulation of Aceclofenac for Improved Therapy. Journal of Drug Delivery and Therapeutics. 2019 Sep 15;9(5):118–22.
2. Biondo NE, Argenta DF, Rauber GS, Vitali L, Caon T. Enhancing the skin permeation of testosterone with natural terpenes. Journal of Drug Delivery Science and Technology. 2022 Nov 1;77:103911.

Acknowledgements: We sincerely thank the Management and Teaching Faculty of St. John Institute of Pharmacy and Research for their support. We would like to thank Invochem laboratory, Vasai Road (E) for providing the gift sample of the drug

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

IVRT Study of a Topical Delivery System for Local Anesthesia in Dental Treatments

Tanvi Mondkar (tanvi.mondkarmp2021@ves.ac.in)[1], Harsha Kathpalia (harsha.kathpalia@ves.ac.in)[1]

[1]**Vivekanand Education Society's College of Pharmacy, Chembur, Mumbai, Maharashtra**

Background and Rationale: Oral surgery, periodontal, endodontic, prosthetic and restorative dental procedures include mechanical, thermal, or chemical stimulation that cause pain in the patient. During such surgeries, local anesthesia aids in the management of discomfort. Currently available local anesthetics have certain limitations like use of needles which arouse fear and pain in patient, high dental anxieties, missed or delayed appointments, side effects like gingivitis, mouth ulcers, bleeding, etc. In situ gel is a novel approach that overcomes these limitations. This system also meets the requirements of both low viscosity that allows for easy instillation into the periodontal pockets, and would undergo a rapid sol to gel transition and have a high viscosity in order to provide superior adhesiveness that helps to maintain high levels of the drug in the gingival crevicular fluid for long periods to gain the desired clinical benefits. To study the performance attributes of the product in vitro release studies play a very important role.

Methods: The in-situ gel was prepared using articaine hydrochloride and poloxamers along with other excipients. The gel was analyzed for physicochemical tests, and comparative invitro release study was performed for prepared gel and drug solution in distilled water. For release study two different approaches were opted i.e., Franz diffusion cell method using Teledyne-Hanson apparatus and diffusion bag method using USP dissolution apparatus-1. For both type of release study phosphate buffer pH 6.8 medium was used and temperature was maintained at 37°C. In Franz diffusion cell method two different types of artificial semipermeable membranes (Supor and Dialysis) were analyzed with rpm speed of 600. On other hand for diffusion bag method only dialysis membrane was used with stirring speed of 50 rpm. The studies were carried out for a period of 4 h. Aliquots were removed at periodic time intervals and after suitable dilutions were assessed for drug release.

Results and Discussion: The release rate of gel was slower as compared to drug solution. The formulation showed 60% drug release through dialysis membrane, whereas from Supor membrane, the formulation showed more than 80% of the drug release, indicating more suitability of Supor membrane for release study than dialysis membrane. The release pattern followed Korsemeyer-Peppas equation of release kinetics with n value of 0.7229 indicating diffusion and erosion mechanism of drug release from polymer system.

Conclusion: The articaine Hydrochloride in-situ gel has the potential to serve as an alternative for topical local anesthesia in minor dental ailments or treatment procedures as it overcomes the drawbacks of present injectable and topical anesthetics by providing pain free and site-specific action.

References:

1. Singh, P. (2012). An emphasis on the wide usage and important role of local anesthesia in dentistry: A strategic review. In Dental Research Journal (Vol. 2). www.drj.ir
2. Li, T., Bao, Q., Shen, J., Lalla, R. v., & Burgess, D. J. (2020). Mucoadhesive in situ forming gel for oral mucositis pain control. International Journal of Pharmaceutics, 580. https://doi.org/10.1016/j.ijpharm.2020.119238.

Acknowledgements: Authors would like to extend their sincere thanks to IQGenx Pharma for providing API and other required excipients.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Microparticulate Nasal Drug Delivery System for Treatment of Parkinson's Disease – Development and In Vitro Release Studies

Pradnya Jadhav (praddnya1234@gmail.com)[1], Namita Desai (namitadd@rediffmail.com)[1]

[1]**C.U.Shah College of Pharmacy, S.N.D.T. Women's University, Mumbai, Maharashtra**

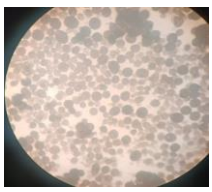
Background and Rationale: Rasagiline mesylate is a highly effective, irreversible MAO-B inhibitor that mitigates dopamine catabolism. Oral administration of the drug faces hurdles in crossing blood-brain barrier, has undesirable gastrointestinal side effects and rapid hepatic first-pass metabolism, resulting in low oral bioavailability (36%). To address these challenges, nasal route is a promising and noninvasive approach with potential for direct brain delivery. Starch microparticles are promising for nasal administration due to their biocompatible, biodegradable and non-toxic nature. The present work proposes to develop and evaluate starch microparticles of rasagiline mesylate for nasal delivery.

Methods: **A) Analytical method:** Ultraviolet spectroscopic method for rasagiline mesylate in distilled water and Simulated Nasal Fluid (SNF), pH 6.4 respectively were developed for quantification of drug.

B) Starch microparticles of Rasagiline mesylate: The development of starch microparticles involved screening of various methods such as emulsion gelation, solvent evaporation for preparation and excipients such as oils, surfactants, starch from different sources such as maize starch, rice starch etc. for formation of microparticles. To obtain the organic phase, various solvents, including methanol, ethanol, chloroform, light liquid paraffin, cyclohexane, acetone and dichloromethane were screened individually and in combination to form emulsions. For a typical batch, the aqueous phase was prepared by heating starch solution to 80°C and forming emulsion with oil phase and surfactant, finally crosslinking the formed microparticles. The formed starch microparticles were stirred, washed, filtered and evaluated for appearance, particle size, drug loading and *in vitro* drug release.

C)*In vitro* release: *In vitro* release of Rasagiline mesylate microsparticles was carried out in USP type II dissolution apparatus using dialysis membrane (molecular weight cutoff 12000kDa) in SNF, pH 6.4 at 37±0.5°C for 7 hours. Suitable aliquots were withdrawn and drug release quantified using UV spectrophotometer (Jasco V-630) at 265 nm.

Results and Discussion: Among the various starches, ex-potato starch (30 %w/v) were selected, Tween 20 and Tween 60 (6% w/v,2 :1) as surfactant and epichlorhydrin as crosslinking agent were selected for preparing the starch microparticles by solvent evaporation method. (Fig. 1)The formed microparticles were maintained under stirring for 5 hours at 40°C and then washed with ethyl acetate. The developed microparticles were spherical and showed particle size 30-60 microns. *In vitro*s tudies in SNF, pH 6.4 demonstrated sustained drug release over 7 hours. (Fig. 2)



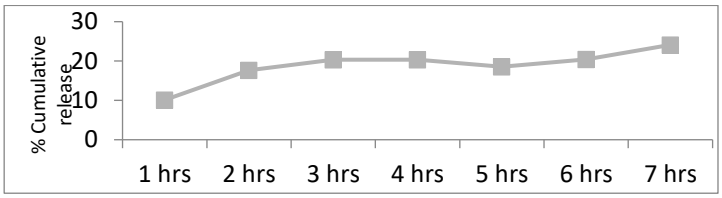


Fig. 1: Microscopy of RM microparticles(10X) **Fig. 2: *In vitro* dissolution profile of RM microparticles.**

Conclusion: The developed rasagiline microparticles showed sustained *in vitro* release for 7 h during and will be further optimized for release and permeation. The microparticles will be developed into *in situ* nasal gelling system with potential for brain delivery.

References: 1. Illum, L., Jorgensen, et al.(1987), *Int. J. Pharm*. 39, 189–199.

2. Shirui Mao1,Jianming Chen,et al. (2004),*Int. J. Pharm*,37-43.

Acknowledgements: The investigators express sincere thanks to Micro Labs Ltd for the gift sample of drug and AICTE for providing Junior Research fellowship.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Novel Nanofiber Insert for Management of Dry Eye Disease

Mayur Mhase (mayurmhase1839@gmail.com)[1], Munira Momin (munira.momin@bncp.ac.in)[1], Mayur Chandwani[1], Shailesh Rathod[1], Darshana Sakpal[1]

[1]**SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: India has higher prevalence rates of dry eye (DE) illness than the rest of the globe, with prevalence rates ranging from 18.4% to 54.3%. Dry eye disease is a condition arises when your tears are unable to effectively moisten eyes. Untreated dry eye can increase the risk of ocular infection, corneal ulcer, and blindness. In order to address issues with low bioavailability and patient compliance linked to eye drops, we created a multilayer sandwich-type nanofiber insert in this study for the treatment of DE illness.

Method:

A) Nanofiber membrane preparation - Nanofiber based ocular insert containing 100 µg of drug (dexamethasone sodium phosphate) was successfully formulated using chitosan (CS) (1%w/v)/PVA (10%w/v)/Drug (0.1%w/w) (core layer) and Eudragit RL 100(25%w/v)/HPMC E 15(4%w/v) (Blank layers).

B) In vitro testing – The optimized formulation was subjected to diffusion study to quantify the amount of drug release through dialysis membrane (molecular weight of 150 Dalton's). Study was conducted in a vial containing 5 ml of STF of pH 7.4. The formulation was enclosed into the dialysis membrane and tide to the clamp such that the surface of membrane touches the STF in vial.

Results and Discussion: Nanofiber based ocular insert containing 100 µg of drug was successfully formulated. The average nanofiber diameter was 125±30 nm observed under SEM. It was found that the entrapment efficiency was more than 90%. According to in-vitro release study, 70% of the drug was released after 24 hours.

Conclusion: The developed formulation would be able to offer benefits such as increased residence time, prolonged drug release, reduction in the frequency of administration, and thereby definitely prove to improve patient compliance.

References:

1. Agarwal, P.; Craig, J.P.; Rupenthal, I.D. Formulation Considerations for the Management of Dry Eye Disease. Pharmaceutics 2021, 13, 207. https://doi.org/10.3390/pharmaceutics13020207
2. Shahla Mirzaeei et al., Polyvinyl Alcohol/Chitosan Single-Layered and Polyvinyl Alcohol/Chitosan/Eudragit RL100 Multi-layered Electrospun Nanofibers as an Ocular Matrix for the Controlled Release of Ofloxacin: an In Vitro and In Vivo Evaluation. AAPS PharmSciTech (2021) 22: 170

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Optimization and Evaluation of Herbal Drug-Loaded Phytosomal Powder for Weight Loss

Bhakti Kambli (bhaktikambli99@gmail.com)[1], Meenal Rane (meenal.rane@bncp.ac.in)[1], Sweety Chheda[1], Urvashi Parmar[1]

[1]**Department of Pharmaceutics SVKM's Dr Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: Obesity is a serious problem caused by sedentary lifestyles and reduced physical activity. Synthetic appetite suppressants have side effects and can lead to weight gain when discontinued. The research aims to find an herbal alternative for weight loss and management. Green tea and piperine are two herbs that can promote weight loss through thermogenesis which aids the fat-burning process. The study focuses on developing and evaluating an efficient phytosomal powder formulation for these herbs to enhance their effects on weight loss.

Methods: A) Formulation development: Herbals selected were green tea and piperine. Placket Burman was used as a screening design for pre-optimization. The 3^2 factorial design was adopted for optimization. Drug: lipid ratio, RPM, and time were selected as independent variables, and % entrapment efficiency of green tea, % entrapment efficiency of piperine, in-vitro drug release and particle size were selected as the dependent variables. The optimized formulation was prepared using ethanol: DCM (1:1) as a solvent with the drug: lipid ratio of 1:1 in RBF by a rotary evaporator (Roteva). Invitro dissolution studies for the prepared formulation were carried out by dialysis sac method using the USP apparatus- I (paddle) for 6 hours. Comparative in-vitro dissolution studies of the marketed formulation (capsule) and the prepared formulation were carried out by dialysis sac method using the USP apparatus- II (basket) for 6 hours. The dissolution media used were HCl buffer 1.2 and phosphate buffer 6.8, 7.4 with a volume of 900 ml at 37 0± 2°C and a stirring speed of 100 rpm. Aliquots were withdrawn at periodic time intervals and after suitable dilution release of green tea and piperine was determined.

Results and Discussion: The formulation with the drug: lipid content 1:1 showed a better release profile compared to the rest of the formulations, with 87% of drug release in 3 hours and hence was selected for comparative studies with the marketed formulation. The marketed formulation required 3 hours to exhibit 77% drug release, whereas the developed formulation exhibited 97% drug release indicating better dissolution of the developed formulation. The in vitro dissolution study and kinetic study indicated that the release followed the Higuchi model (diffusion) with R^2= 0.9633.

Conclusion: From the optimization studies and comparative in vitro studies of the developed phytosomal formulation and marketed phytosomal formulation, the developed formulation showed more rapid dissolution. The prepared phytosomal dry powder for reconstitution might prove to be a promising therapy for weight loss and weight management.

References:

1. Barani M, Sangiovanni E, Angarano M, Rajizadeh MA, Mehrabani M, Piazza S, et al. Phytosomes as innovative delivery systems for phytochemicals: A comprehensive review of the literature. Vol. 16, International Journal of Nanomedicine. 2021. 6983–7022 p.
2. Sharma T, Kanwar SS. Phytomolecules for Obesity and Body Weight Management. J Biochem Cell Biol. 2018;1(1):1–8.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Oral Fast Dissolving Film of Rivaroxaban with Improved Solubility and Dissolution

Poorna Chandra (chandrapoorna39480@gmail.com)[1], Preeti Sudheer (preetisudheer@gmail.com)[1]

[1]**Krupanidhi College of Pharmacy, Bangalore, Karnataka**

Background and rationale: Anticoagulant therapy is widely used to prevent and treat venous and arterial thromboembolism. The study focuses on delivering the anticoagulant agent, rivaroxaban, a factor Xa inhibitor, as an oral film for better patient compliance. However, Rivaroxaban being a BCS Class II drug faces low solubility issues. The study aims to prepare nano cocrystal of Rivaroxaban to avoid the problem of solubility mentioned above and present the formulation as a nanococrystals combined oral film to achieve a faster onset of action.

Methods: The solubility issues of the drug were tackled by converting the drug into nano cocrystals using gallic acid as a co former, utilizing the anti-solvent method, which was then followed by drying and incorporating the drug precipitate into an oral film formulation. The "Custom Design" was selected to optimize the formulations, generating 12 experimental runs. Based on the responses, the optimum formula was selected, and the formulation was subsequently prepared and evaluated. The optimum nano-crystal formulation was converted into an oral disintegrating film using hydroxy propyl methyl cellulose (HPMC E 5) as a film forming polymer and various additives such as plasticizers PEG 400, Saliva stimulating agents, citric acid, flavouring agents and sweeteners. The oral films were evaluated for various physical parameters, drug content, disintegration time and *in vitro* release profile.

Results and Discussion: The saturation solubility of the resulting co-crystals ranged from 0.149 mg/ml to 1.83 mg/ml. The dissolution ranged between 63.2±0.26% to 98.7±0.36% for 1h. FTIR spectra show no chemical interaction between rivaroxaban and the excipients used. The in vitro release studies showed a drug release of 30±0.14% to 58.2±0.26% at 10 min. 49.3±0.18 to 98.7±0.36% at 120 minutes, The optimum formulation's solubility and dissolution rate, were found to be 1.61 mg/ml and 90 %±0.25 at 60 minutes. The X-ray diffraction pattern of optimum formulation indicated a change in the crystalline nature of Rivaroxaban, which was evident from the reduction of the number and intensity of peaks and was greatly supported by the results of DSC. The formulation's particle size ranged from 50 to 200nm, and the average particle size was 67.2 nm. The physical properties of the films were found to be satisfactory. The selected film (6.2cm^2 areas contained 4mg drug) was disintegrated in 47 s± 0.5 s, and 98.1±0.25% of the drug was released in 60 min. A twofold increment in drug release (%) was observed compared to the pure drug release profile.

Conclusion: The nano-cocrystal incorporated oral film could be an alternative for addressing the solubility issue of rivaroxaban and attaining faster drug action and patient compliance.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: India | **Category:** MPharm
Theme: Dissolution & Solubility Modulation

SNEDDS Based Oral Film: A Promising Drug Delivery Strategy for Solubility Enhancement Of BCS-II Drug

Ram Gingine (gingine.ram@gmail.com)[1], Meenal Rane (Meenal.rane@bncp.ac.in)[1], Shubham Tonape[1]

[1]**SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai, Maharashtra**

Background and Rationale: More than 10 million cases of migraine are recorded each year in India. Headaches and a heightened sensitivity to light and sound are some of these disease's symptoms. To overcome the limitations of the synthetic drugs used in the treatment of migraine, an endeavour was made to formulate and evaluate an herbal (anise oil) based SNEDDS (Self-Nano-Emulsifying Drug Delivery System) incorporated into an oral film. Given that anise oil is a BCS-II medication with substantial lipophilicity and unfavorable aqueous solubility, this novel and promising approach has been adapted, in order to enhance the solubility and bioavailability of the oil. The present research work aims at evaluating the therapeutic potency along with its in-vitro drug performance, disintegration time, drug content, and physicochemical parameters of developed formulation.

Methods: A) Formulation development: The SNEDDS were prepared by plotting pseudo ternary phase diagram to optimize the ratios of surfactants, co surfactants and water for identifying the efficient self emulsification region. Blending is done by the help of water titration method. And, anise oil loaded SNEDDS assimilated oral disintegrating film was formulated by solvent casting method.

B) In-Vitro andd In-Vivo evaluation: In-vitro release of the formulation was studied using USP dissolution apparatus 1. The dissolution medium comprising phosphate buffer (pH 6.8) and ethanol in the ratio of (7:3) with volume of 900 ml at 37±1°C and stirring speed of 50 rpm. Aliquots were withdrawn at periodic time intervals and drug concentration was determined spectrophotometrically, at lambda max of 258nm. The albino rat model was used to conduct in vivo studies. To induce a migraine, nitroglycerine was given intraperitoneally. Behavioral parameters were studied using the elevated plus maze and hot plate models.

Results and Discussion: Both the In-Vitro and In-Vivo study results reflected the enhanced solubility with better bioavailaibility of selected herbal drug. The film formulation demonstrated rapid disintegration time i.e. 6- 11 secs along with 100% dissolution within 1 min. And the drug content was found to be nearby 97%. The release behavior of current formulation exhibited the Korsemeyer peppas model. In addition, the films also have distinctive mechanical characteristics, which was advantageous for stability during storage. Here behavioral parameters from in vivo studies illustrated that SNEDDS based oral film significantly decreased migraine in migraine induced Albino rats.

Conclusion: The research established that SNEDDS based oral film formulation strategy could resolve anise oil's solubility and low bioavailability problems, which are biopharmaceutical challenges. Formulation with such safety profile is not available in the market and hence it can be commercialized.

References:

1. Nagendra, Ertsey C. Combination of Ayurveda and Yoga therapy reduces pain and improves quality of life in patients with migraine headache. Complementary therapies in clinical practice. 2018 Aug 1; 32:85-91.
2. Banarjee T, Akhtar J. A review on fast dissolving films for buccal delivery of low dose drugs. Int. J. Life Sci. Rev. 2015; 1:117-23.

Acknowledgements: SVKM's Dr. Bhanuben Nanavati College of Pharmacy

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Dissolution & Solubility Modulation

Studies of Influence Of Excipients on Dissolution Profile of Selective Estrogen Receptor Modulator (SERM) loaded Supersaturated Silica-Lipid hybrid (super-SLH) Oral Drug Delivery System.

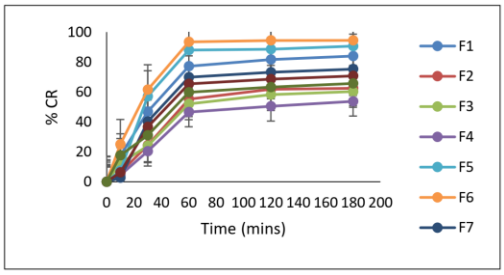
Shweta Chaurasia (shwetachaurasia511@gmail.com)[1], Varsha Pokharkar (varsha.pokharkar@bharatividyapeeth.edu)[1], Rashi Bajaj[2]

[1]Poona College of Pharmacy, Pune, Maharashtra | [2]Sanofi

Background and Rationale: Silica-lipid hybrid (SLH) microparticles are a solidified lipid-based drug delivery system to improve drug loading and to enhance the oral bioavailability of poorly water insoluble drugs. For the model SERM drug, belonging to BCS class 2, frequently prescribed in postmenopausal women, this approach was explored in the present study. The therapeutic efficacy of the selected drug is constrained by its low oral bioavailability (2%) and restricted water solubility (0.000512 mg/ml), thus super-SLH RLX showed a significant advantage over plain drug. To study the influence of excipients on solubility and dissolution kinetics the approach of Qbd was applied.

Methodology: Since the system contains lipid and silica, lipid selection was done on the basis of equilibrium solubility of SERM in lipid at different temperatures, Parteck SLC 500 was selected as silica because of its high surface area of 500 m2/g and a small 6 nm pores. 3^2 factorial design was employed for selecting the right composition of the super-SLH with desired solubility and in vitro drug dissolution. Solid state characterization (FTIR, DSC, XRPD) and surface morphology (SEM) were conducted. Further, saturation solubilities in different medias, in vitro drug release and in vivo pharmacokinetic studies were performed.

Results and Discussion: A 11-fold increase in solubility was observed and solid state characterization confirmed the amorphization of SERM by lipid and silica. The drug release of optimized super-SLH SERM at 30 mins and 1 hr was found to be 61.52% and 93.44% respectively which was greater than pure drug fig. (1). It was observed that when the amount of lipid and amount of silica is increased the drug release and solubility also increased significantly. Plasma-concentration time curve indicates 2.33 folds increase in bioavailability than pure drug.



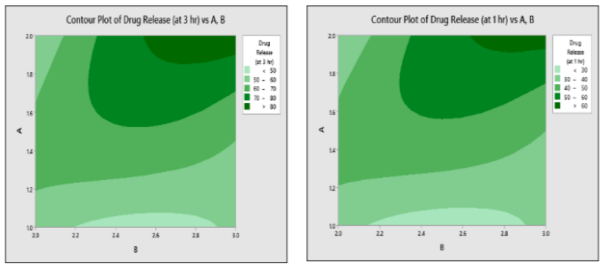


Fig. 1 *In vitro* drug release of pure drug and from super-SLH **Fig. 2 Contour plots showing the effects of conc of lipid and silica**

Conclusions: The use of Parteck SLC 500 and Phosal 50 PG in a supersaturated silica-lipid hybrid is a potential method for improving drug loads, solubility, and bioavailability. The DoE approach was effectively used to understand that lipid and silica had significant effect on solubility and dissolution of the active.

References:

1. H. B. Schultz, P. Joyce, N. Thomas, and C. A. Prestidge, "Supersaturated-Silica Lipid Hybrids Improve in Vitro Solubilization of Abiraterone Acetate," Pharm. Res., vol. 37, no. 4, 2020.
2. Tan, S. Simovic, A. K. Davey, T. Rades, B. J. Boyd, and C. A. Prestidge, "Silica nanoparticles to control the lipase-mediated digestion of lipid-based oral delivery systems," Mol. Pharm., vol. 7, no. 2, pp. 522–532, 2010.

Acknowledgements: Authors are grateful to All India Council for Technical Education (AICTE), Government of India for providing fellowship and Cipla for providing gift sample of drug.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Supersaturable Bio-Self-Nanoemulsifying Drug Delivery System for Improving Oral Bioavailability of Dasatinib

Dharshini M (m.dharshini123@gmail.com)[1], Sanyog Jain (sanyogjain@niper.ac.in)[1]

[1]**NIPER S.A.S.Nagar, S.A.S.Nagar, Punjab**

Background and Rationale: Oral drug delivery continues to be the most convenient and route of administration. However, poorly water-soluble drugs fail to exploit the full advantage of oral delivery due to their physicochemical properties. Incorporating such drugs into lipidic formulations will make their oral delivery feasible and efficient. In the present investigation, we have explored the potential of a Supersaturable bioactive self-nano-emulsifying drug delivery system (su-Bio-SNEDDS) to enhance the solubility and bioavailability of Dasatinib (DAS), which is a BCS Class II drug. The conventional dissolution studies are inappropriate for predicting drug release from lipid-based formulations (LBFs). Hence, we have examined the relevance and correlation of an alternative simultaneous lipolysis-permeation strategy.

Methods: A) Preparation, optimization and characterization of su-Bio-SNEDDS: DAS Bio-SNEDDS containing Oleic acid, Chamomile oil, Cremophor RH 40 and Transcutol HP was optimized through Design of Experiments (DOE). Various polymeric precipitation inhibitors (PIs) were screened based on their ability to maintain drug supersaturation on lipolytic breakdown and concentration was optimized. The optimized formulation was characterized for its droplet size, polydispersity index, stability in gastrointestinal fluids, and robustness to dilution.

B) Simultaneous In vitro lipolysis and permeation: Conventional dissolution studies will not provide proper insights into the fate of LBFs. Hence, we used a simultaneous lipolysis permeation method which was more relevant in mimicking the digestion and absorption of su-Bio-SNEDDS. It was performed by combining the in-vitro lipolysis model to a consecutive drug permeation step across dialysis membrane barriers in Franz diffusion cells. The extent of digestion and permeation in the presence and absence of precipitation inhibitor was quantified and compared.

C) In vivo pharmacokinetics: In vivo pharmacokinetic parameters were evaluated after oral administration of free drug and formulation to Sprague Dawley rats and compared with the in vitro results.

Results and Discussion: Composition of su-Bio-SNEDDS was optimized using DesignExpert® and 2.5% PVP K30 which was efficient in maintaining drug supersaturation for a longer period without precipitation was chosen as the PI. The optimized su-BioSNEDDS with droplet size and PDI of 52.82±0.35 nm and 0.314±0.006, were stable in GI fluids and robust to dilutions. On lipolysis, su-Bio-SNEDDS was able to maintain ~1.4 fold higher concentration of Dasatinib in aqueous phase and exhibited greater permeation in comparison to Bio-SNEDDS without PI. This is attributed to the precipitation inhibitory potential of PVP K30 through retardation of crystal growth and achieving a parachute effect. These in vitro results were corroborated by the in vivo pharmacokinetic data where, su-BioSNEDDS revealed ~1.2 fold and ~1.9 fold increase in Cmax and AUC in comparison with Bio-SNEDDS without PI and ~1.8 fold and ~2.7 fold increase in Cmax and AUC in comparison with drug suspension. The in vitro and in vivo results were correlated.

Conclusion: su-Bio-SNEDDS can potentially be used in delivering Dasatinib, which shows poor oral bioavailability. The evaluated lipolysis-permeation method was found to be a promising tool for estimating the in vivo performance of SNEDDS, but more studies are needed to evaluate the method further.

Acknowledgements: Authors would like to acknowledge the Director of NIPER S.A.S.Nagar for providing us with the necessary facilities and infrastructure

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: India | **Category:** MPharm

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Topical Semisolid Formulations of Celecoxib: Evaluation and Comparison using IVRT and IVPT

Priyanka Mundankar (mundankarp@gmail.com)[1], Madhur Kulkarni (madhur.kulkarni@indiraicp.edu.in)[1]

[1]**Indira College of Pharmacy, Pune, Maharashtra**

Background and Rationale: Recently, celecoxib (CXB) has been shown to exhibit broad-spectrum antimicrobial activity in addition to its anti-inflammatory activity. Therefore, it holds significant potential for the treatment of skin infections. The present study aimed to develop and compare topical semisolid formulations of CXB using optimized IVRT and IVPT methods. The objectives of the study were i.) Development of various topical formulations of celecoxib. ii.) IVRT and IVPT method development and optimization for the evaluation and comparison of the formulations.

Methods: A) Preparation of CXB topical formulations: CXB was dissolved in PEG 400 and added to various semisolid bases prepared by standard methods. The gel formulation was prepared using Carbopol 934P. The o/w cream formulation was prepared using suitable oil and aqueous phase. Two types of ointments viz. water-soluble ointment comprising PEG 4000 and hydrophobic ointment were prepared using formulae reported in literature. All formulations contained 3%w/w CXB. The formulations were evaluated for appearance, viscosity, spreadability, and drug content.
B) IVRT studies: Drug release from the formulations was studied using USP type-II dissolution apparatus with immersion cell as well as vertical diffusion cell. In immersion cells, different barrier membranes such as Ultipore, Durapore, and Fluropore were used. Different dissolution media (150ml) like phosphate buffer pH 7.4 (PB) PB with 0.5% Tween 80, and PB-ethanol mixture (1:1) were used. The studies were conducted at 32±0.5°C under constant stirring at different RPMs (100, 150, 200). In vertical diffusion cells, studies were conducted at 32±0.5°C under constant stirring at 200rpm, using an Ultipore membrane with the same dissolution media (25ml) as used in immersion cells. Aliquots were withdrawn at 0.5, 1, 2, 3, 4, 5, and 6 hours and replaced with fresh medium. The aliquots were suitably diluted, and UV spectroscopic analysis was performed at 270 nm.
C) IVPT studies: Pig skin was placed as a barrier membrane on vertical diffusion cells. The receptor medium consisted of 25 ml PB or PB with 0.5% Tween 80 or PB-ethanol mixture (1:1). The system was maintained at different temperatures (32±0.5°C and 37±0.5°C) under constant stirring at 200rpm. Formulations were applied to the skin in the donor compartment, and aliquots were withdrawn from the receptor at 0.5, 1, 2, 3, 4, 5, and 6 hours. UV spectroscopic analysis was performed at 270 nm.
D) Skin retention studies: were performed using the tape-stripping method. The skin was washed, and the stratum corneum (SC) layer was stripped off using 8 tapes, each applied 20 times. Tapes containing the SC and remaining skin were cut were sonicated in PB - ethanol mixture (1:1). UVspectroscopic analysis was conducted at 270 nm.

Results and Discussion: The CXB topical formulations had an acceptable appearance, viscosity, and spreadability. and drug content. Optimized IVRT method using immersion cells included Ultipore as a barrier membrane, 100 rpm stirring speed, 150mL of PB-ethanol mixture (1:1). Maximum drug release was observed from PEG ointment (753.35±105.78 µg/cm^2.hr) in 6 hr followed by gel (404.81±47.68 µg/cm^2.hr), cream (368.52 ± 97.90 µg/cm^2.hr), and lastly paraffin ointment (90.09 ± 13.5 µg/cm^2.hr). In vitro release studies using vertical diffusion cells also exhibited similar results. IVPT studies when conducted at 32°C, both gel (17.45 ± 3.75 µg/cm^2.hr) and PEG ointment (16.71 ± 1.2 µg/cm^2.hr) showed good permeation in 6 hr, whereas at 37°C, PEG ointment (20.13 ± 1.4 µg/cm^2.hr) showed higher permeation followed by gel (14.58 ± 6.9 µg/cm^2.hr), cream(14.56 ± 3.8µg/cm^2.hr), and paraffin ointment (10.36 ± 4.6 µg/cm^2.hr). PEG ointment (582.9 µg/cm^2) showed higher skin retention compared to gel (424.05µg/cm^2) followed by paraffin ointment (396.2 µg/cm^2) and cream (390 µg/cm^2). Antimicrobial studies of the formulations are in progress.

Conclusions: Both IVRT and IVPT methods reflected highest release and permeation of CXB from PEG ointment and gel formulations indicating their promising potential as vehicles for topical delivery of CXB. The outcome of the currently undergoing antimicrobial studies of these formulations will confirm their repurposing potential as topical anti-infective preparations.

References:

1. Thangamani S., Younis W., Seleem MN., Repurposing celecoxibas atopicalantimicrobial agent. Frontiers in microbiology, 2015. 750(6): p. 1-12.
2. Marto J., Duarte A., Simoes S., Goncalves L., Starch-Based Pickering Emulsions as PlatformsforTopical Antibiotic Delivery: In Vitro and In Vivo Studies. Polymers. 2019. 11(1): p. 1-16.

Acknowledgements: Authors are grateful to Indira College of Pharmacy for providing the necessary resources, facilities, and infrastructure to conduct this research.

Japan &
South East Asia

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: JSEA | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Ageing as a Stabilising Process for Sustainable Dissolution Enhancement in a Carrier Tailored Atovaquone Electrospun

Xin Yi Teoh (txy1807@gmail.com)[1], | Siok Yee Chan (sychan@usm.my)[1]

[1]**Universiti Sains Malaysia, Minden, Malaysia, Penang**

This study intends to investigate the performance of supersaturated atovaquone (ATQ) amorphous solid dispersion (ASD) electrospun systems after the ageing process, particularly the sustainable dissolution enhancement attained in the optimised freshly prepared electrospun samples.

Electrospun samples were maintained under accelerated condition (75% RH, 40°C) for 3 months and dry and temperate condition (0% RH, 25°C) and 12 months. Aged electrospun samples were analysed with polarised light microscopy, Attenuated Total Reflectance-Fourier Transform Infrared and Differential Scanning Calorimetry. Drug stability after the ageing process was determined via drug content assay using HPLC analysis. A non-sink condition was employed to study the dissolution performance of aged electrospun samples.

Electrospun samples aged under accelerated condition recrystallised and completely reversed the advantage of ASD formulation in achieving supersaturation level, resulting in resembling raw ATQ in the drug release profile. In contrast, the electrospun sample aged under dry and temperate condition successfully preserved the sample amorphicity and exerted a positive effect in sustaining the dissolution enhancement. It was proposed that a dry storage condition avoided the moisture-induced recrystallisation, consequently allowing the amorphous content to structurally relax to its equilibrium glassy state through ageing. A more pronounced stabilising effect through ageing under dry and temperate condition was reported in the formulation with only hydrophilic components as carrier matrix (ES ATQ/K90) comparing the rest with hydrophobic components. This serves as an alternative method for stabilising the supersaturation achieved by ASD systems which was not previously achieved through the optimisation of the hydrophilic-hydrophobic balance of the polymeric carrier system.

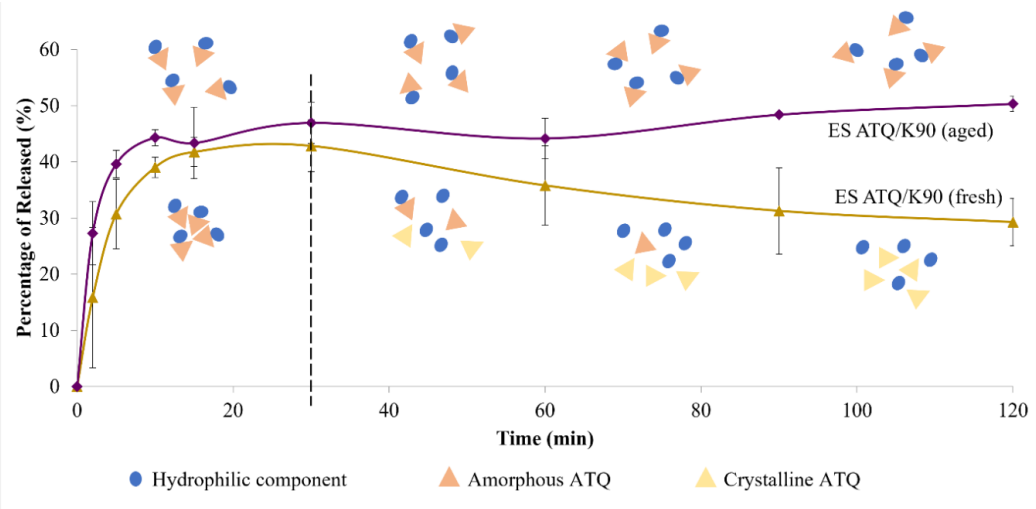


Fig. 1: Proposed mechanism of the maintenance of ATQ supersaturation by the annealing effect in the aged electrospun sample during the dissolution process

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: JSEA | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Mechanistic Exploration of the Drug Release Properties of Advanced Semisolid Dosage Forms Using the Dispersion Releaser

Namrata Dhakal (e0670838@u.nus.edu)[1], Matthias Wacker (matthias.g.wacker@nus.edu.sg)[1], Ern Ern Saw[1]

[1]**National University of Singapore, Singapore.**

In the rapidly growing global healthcare market, topical nano-formulations have emerged as a promising approach for efficient drug delivery [1]. These formulations offer significant advantages, but there is a lack of standardized procedures and testing methods to evaluate their in vitro performance. The Dispersion Releaser (DR), a dialysis-based technique commonly used for testing nanocarrier delivery systems, has recently been explored for assessing semisolid dosage forms [2, 3]. However, there is a limited understanding of how the physicochemical properties of these formulations and the operational parameters of the DR influence drug release. To address this gap, our study aims to investigate the impact of different stirring rates in the DR on the release behavior of liposomal berberine incorporated into hydroxypropyl methylcellulose hydrogel, forming a lipogel. We synthesized berberine chloride lipogel with different liposomal and gel attributes. By employing the DR with varying stirring rates, we aimed to distinguish the contributions of different components in the drug release process. Here, we showed that, at the lower stirring rate (25 rpm), the discrimination of drug diffusion and release behavior from the hydrogel were detected more sensitively. At the higher stirring rate (75 rpm), disruption of the hydrogel led to a release behavior that was largely influenced by the dispersed phase (liposomes). Our experimental results shed light on the release mechanism and identified the individual components of the dosage form responsible for their behavior. These findings are valuable for quality control and early screening of advanced topical formulations, especially in observing material interactions under non-physiological conditions.

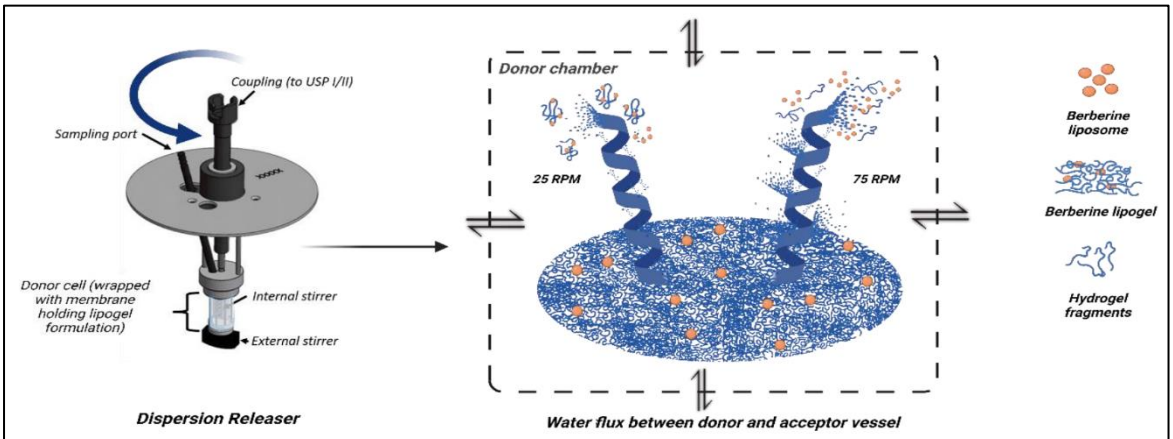


Figure: Release studies of berberine lipogel using the dispersion releaser under various agitation conditions

References:

1. Raszewska-Famielec, M. and J. Flieger, *Nanoparticles for Topical Application in the Treatment of Skin Dysfunctions;An Overview of Dermo-Cosmetic and Dermatological Products.* International Journal of Molecular Sciences, 2022. **23**(24): p. 15980.
2. Mast, M.-P., et al., *An Update to Dialysis-Based Drug Release Testing & Data Analysis and Validation Using the Pharma Test Dispersion Releaser.* Pharmaceutics, 2021. **13**(12): p. 2007.
3. Wallenwein, C.M., et al., *Pharmaceutical Development of Nanostructured Vesicular Hydrogel Formulations of Rifampicin for Wound Healing.* International Journal of Molecular Sciences, 2022. **23**(24): p. 16207.

Acknowledgements: The presenting author would like to express her sincere gratitude to the Ministry of Education, Singapore (MoE) for granting the SINGA scholarship to support her studies in the Department of Pharmacy at NUS.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists

Region: JSEA | **Category:** PhD

Theme: Pharmacokinetics & IVIVC Studies

Role of Cell Interactions of PLG Nanoparticles in the Drug Delivery Lifecycle

Julia Malinovskaya (j.malinowskaya@gmail.com)[1], Svetlana Gelperina (svetlana.gelperina@gmail.com)[1], Tatyana Kovshova[1], Pavel Melnikov[2], Zhuoxuan Li[3], Matthias Wacker[3]

[1]Mendeleev University of Chemical Technology of Russia, Moscow, Russia | [2]V. Serbsky Federal Medical Research Centre of Psychiatry and Narcology of the Ministry of Health of the Russian Federation, Moscow, Russia | [3]National University of Singapore, Singapore

The pharmacokinetics of nano-delivery systems is mostly evaluated by their plasma concentration-time profiles. At the same time, the blood partitioning behavior of the widely used PLG nanoparticles (PLG NP) indicates that a significant fraction is bound to the blood cells, resulting in misinterpretation of the nanoformulation pharmacokinetics (1). In the present study the NP – blood cell interactions over time and the role of immune cells in the PLG NP extravasation and tumor delivery was investigated using the intravital microscopy (IVM).

The doxorubicin-loaded PLG NP (PLG-Dox NP) with different drug release rates (fast-medium- and slow-releasing formulations) were prepared by a homogenization – solvent evaporation technique. The fluorescent label (Cy5) was covalently attached to the polymer allowing visualization of both NP and Dox. Visualization of the NP delivery to the subcutaneous 4T1 tumor in mice was performed by IVM (Nikon A1R MP). The NP uptake by subpopulations of immune cells was further investigated by flow cytometry.

The extravasation through the tumor vessel wall via the macro- and microleakages were detected for all NP types, enabling Dox delivery to the cell nuclei. The unspecific adsorption of the NP to the blood cells followed by their redistribution to the monocytes and neutrophiles was observed starting from 15 min after injection and was increasing with time (uptake by neutrophils was 1.5% to 25% after 15 and 30 min, respectively). Thus, the NP uptake by immune cells appears to be an additional phase in the nanoparticle drug delivery lifecycle.

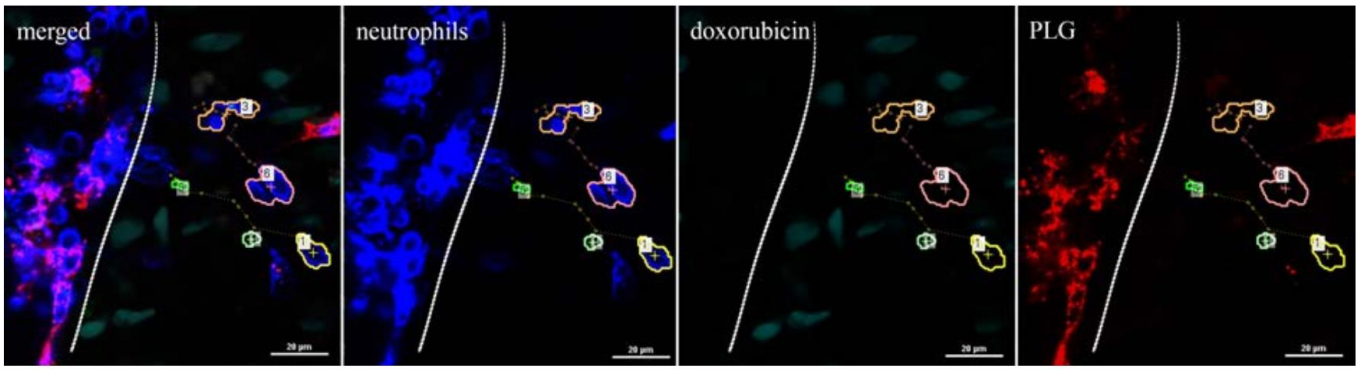


Fig.1: Neutrophil-mediated transport of PLGA-Cy5-Dox NP across the vessel wall. Neutrophil tracing.

Reference:

1. Kovshova T, et al. Exploring the Interplay between Drug Release and Targeting of LipidLike Polymer Nanoparticles Loaded with Doxorubicin. Molecules 2021; 26(4): 831. doi.org/10.3390/molecules26040831

Acknowledgements: This work was funded by the Ministry of Science and Higher Education of the Russian Federation (project FSSM-2022-0003).

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: JSEA | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Understanding the Structure-Release Relationships of Sepineo

Ayca Altay Benetti (ayca.ben@nus.edu.sg)[1], Giorgia Pastorin (phapg@nus.edu.sg)[1] Harshvardhan Modh[1], Abu Zayed Badruddoza[2], Jaymin Shah[2] , Thean Yeoh[2], Matthias Gerhard Wacker[1]

[1]National University of Singapore, Department of Pharmacy, Singapore, 117544, Singapore | [2]Pfizer, Drug Product Design, Worldwide Research, Development and Medical, Pfizer Inc., Groton, Connecticut 06340, USA.

The physical and mechanical characteristics of gel samples are of utmost importance in the development and manufacture of a wide variety of products. This work aims to provide a thorough examination of the impact of pH changes and ionization status of an API (diclofenac sodium) loaded in Sepineo**TM** gels on the rheological behaviour, surface tension, *in vitro* release properties and *ex vivo* skin permeation profiles of the dosage form. Moreover, a comprehensive study on molecular dynamic simulations has been conducted to understand the relationship between drug molecules and SepineoTM at different pH ranges, considering the pKa value of diclofenac sodium.

To evaluate the impact of pH changes and diclofenac ionization, four different SepineoTM (3%) gels loaded with diclofenac sodium (0%, 0.1% or 1%) were prepared at different pH conditions; 2.55, 5.55, 7.4 and 11.56, respectively. As pH shifted from acidic to basic conditions, a change in the stiffness of Sepineo was observed with and without diclofenac loading. However, the elasticity behaviour wasn't affected by the changes of pH. On the other hand, the static contact angle measurement proved that the blank and 0.1% formulations had a pHdependent behaviour ($p<0.02$, ANOVA test). *In vitro* release studies using Dispersion Releaser technology were performed at 25 RPM to understand the release mechanism from the SepineoTM gels loaded with 0.1% of diclofenac, whereby release profiles confirmed that ionized diclofenac had a quick release compared to the one with unionized formulation. The *ex vivo* permeation analysis of 0.1% gel formulations across pig ear skin was performed, with the expectation that fully ionized diclofenac would have permeated more. Surprisingly, the formulations at pH 11.56 showed lower release of drug and permeation through the skin. Overall, we found that the pH of the formulation, rather than the rheological properties, could significantly affect drug release and permeation profiles. Through these in-depth characterizations, it will be possible to optimize drug release and permeation of other APIs from gel formulations to achieve maximum efficacy.

Acknowledgements: This work was supported by the PIPS grant (A-8000240-00-00), Singapore.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: JSEA | **Category:** PhD

Theme: Computational Tools, PBPK Modelling

Use of PBPK modelling for predicting absorption and systemic exposure of compounds with complex absorption kinetics: a case study on stevioside and its metabolites

Hor Cheng Koh (Koh_Hor_Cheng_from.tp@sifbi.a-star.edu.sg)[1], James Chan (James_Chan@sifbi.a-star.edu.sg)[1,2,3], Shili Yang[2,3]

[1]Singapore Institute of Food and Biotechnology Innovation, Agency for Science Technology and Research, Singapore | [2]Innovations in Food and Chemical Safety Programme, Agency for Science Technology and Research, Singapore | [3]A*STAR Skin Research Labs, Agency for Science Technology and Research, Singapore

Characterizing absorption profiles typically focuses on defining aqueous solubility, dissolution profile and membrane permeability. However, this neglects the role of the gut microbiome in modulating the bioavailability of orally ingested compounds, which includes pharmaceutical agents and food ingredients. This may occur directly via gut microbiome-mediated metabolism, or indirectly through alterations of transporter kinetics by microbial metabolites[1]. Here we report how physiologically-based pharmacokinetic (PBPK) modelling can be utilised to investigate and predict the *in* vivo performance of a compound with a complex absorption profile using the natural sweetener stevioside as a case study. While not a drug, stevioside exhibits interesting characteristics such as (1) microbially-controlled, pre-systemic metabolism of stevioside to steviol resulting in "flip-flop" absorption kinetics and (2) saturable, dose-dependent intestinal permeability of steviol, resulting in non-linear systemic pharmacokinetics. A middle-out PBPK model was developed by integrating *in vitro* pharmacokinetic data of stevioside and its metabolites steviol and stevioside glucuronide (SVG), with human physiological data to predict the plasma concentration-time profiles of both metabolites. In particular, the kinetics of microbial hydrolysis of stevioside to steviol measured using human stool samples were incorporated into the model. The time-courses simulated by our model were successfully validated against published human *in vivo* clinical data for low and high dose scenarios[2,3]. Importantly, we demonstrate that stevioside systemic kinetics can be modulated by adjusting the degree of microbial metabolism. Our work exemplifies how PBPK modelling can be extended to simulate the systemic exposure of compounds whose absorption profiles are influenced by microbial biotransformation.

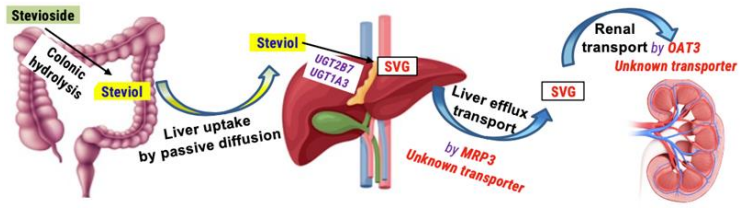


Fig 1. Description of the processes involved in stevioside disposition in humans.

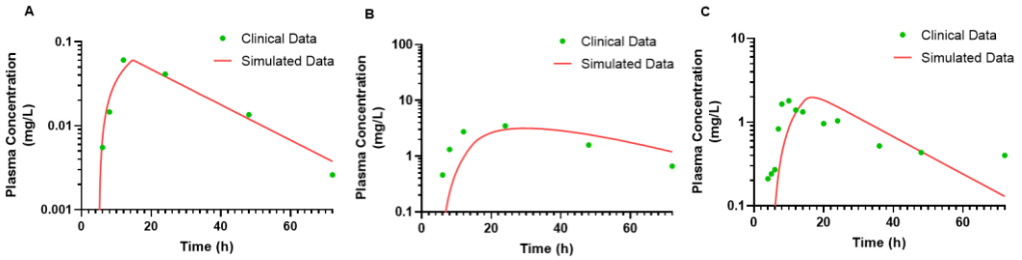


Fig 2.Simulated versus clinical plasma concentration-time profiles of (A) steviol (B) SVG at high dose and (C) SVG at low dose in model.

References:

1. Tsunoda, S. M., Gonzales, C., Jarmusch, A. K., Momper, J. D., & Ma, J. D. (2021). Contribution of the gut microbiome to drug disposition, pharmacokinetic and pharmacodynamic variability. *Clinical pharmacokinetics*, 60, 971-984. doi: 10.1007/s40262-021-01032-y
2. Roberts, A., Renwick, A. G. (2008). Comparative pharmacokinetics and metabolism of rebaudioside A, stevioside, and steviol in rats. *Food Chem Toxicol 46*, S31-39. doi: 10.1016/j.fct.2008.05.006
3. Wheeler, A., Boileau, A. C., Winkler, P. C. et al. (2008). Pharmacokinetics of rebaudioside A and stevioside after single oral doses in healthy men. *Food Chem Toxicol 46*, S54-60. doi: 10.1016/j.fct.2008.04.041

Acknowledgements: This work was supported by a joint grant between Agency for Science, Technology and Research (A*STAR) Singapore and DP Beverages Limited [Grant number ASTAR-DP-2019-012]. J.C.Y.C. conceived and directed the study. S.L.Y performed the experiments, while H.C.K built the models and conducted the simulations. H.C.K, S.L.Y and J.C.Y.C wrote the manuscript.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: JSEA | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Drug release from a biodegradable Chemo-Radioembolization agent loaded with Sm-153 Radionuclide and Doxorubicin

Asseel Alregib (asseelhisham.i@gmail.com)[1], Chai Hong Yeong (chaihong.yeong@taylors.edu.my)[1,3], Yin How Wong[1,3], Azahari Kasbollah[2]

Eng Hwa Wong[1,3]

[1]School of Medicine, Faculty of Health and Medical Sciences, Taylor's University, 47500 Subang Jaya, Selangor, Malaysia | [2]Medical Technology Division, Malaysian Nuclear Agency, 43000 Bangi, Selangor, Malaysia | [3]Medical Advancement for Better Quality of Life Impact Lab, Taylor's University, 47500 Subang Jaya, Malaysia

Background: Liver cancer is the fifth most common cause of cancer death among males, and 7th among females. Transarterial chemoembolization (TACE) and transarterial radioembolization (TARE) are both promising treatments for intermediate stage liver cancer, however the treatments are currently administered separately at different procedures This study aimed to develop a biodegradable microsphere loaded with both chemotherapy drug, Doxorubicin (Dox) and radioactive agent, Samarium-153 (^{153}Sm).

Methods: The microspheres were synthesized using a water-in-oil-in-water solvent evaporation method and then irradiated via neutron activation to produce the radioactive Dox-^{153}Sm-PHBV microspheres. The physiochemical properties, ^{153}Sm radioactivity, Dox loading content, ^{153}Sm retention efficiency, and in-vitro drug release in phosphate buffer solution (PBS) were analyzed. The microspheres cytotoxicity was tested on Hepg2 cell line at 72 h.

Results and Discussion: The microspheres were spherical with a diameter of 24-36 micrometers and a density of 1.438 g/cm3. The specific activity of the Dox-^{153}Sm-PHBV microspheres was 8.68 GBq/g. The microspheres were thermally stable up to 155.23°C and had an encapsulation efficiency of 98.41%. In vitro release studies showed that the microspheres released 65.21% of Dox in PBS solution of pH 7.4, and 29.96% of Dox in PBS solution of pH 5.0 after 984 hours. In vitro cytotoxicity tests showed that the Dox-^{153}Sm-PHBV microspheres were more cytotoxic to HepG2 cells than ^{153}Sm-PHBV or Dox-PHBV microspheres.

Conclusion: The Dox-^{153}Sm-PHBV microspheres developed in this study fulfilled all the desirable physicochemical properties for a chemo-radioembolization agent. Further studies are needed to compare the synergistic effect of radio-chemoembolization with the conventional approaches (TACE and TARE).

Acknowledgements: This study was funded by the Fundamental Research Grant Scheme (FRGS/1/2019/SKK06/ TAYLOR/02/3), sanctioned to C.H.Y. by the Ministry of Higher Education, Malaysia. A.H.A is scholarly funded by the Taylor's Research Scholarship Programme.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: JSEA | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Particle Size and In Vitro Correlation of Transdermal Patch Development Based on Nanophytosomes of Leaf Ethanol Extract of Kenikir (*Cosmos caudatus*) as Prevention Efforts Complication Dislipid

Putri Antika Yusniasari (putri.antika.yusniasari-2020@ff.unair.ac.id)[1], Retno Widyowati (rr-retno-w@ff.unair.ac.id)[2], Putri Antika Yusniasari[1], Mochamad Radika Tory Alifiansyah[1], Qiara Amelia Putri Priyono[1], Retno Widyowati[1], Andang Miatmoko[2]

[1]Undergraduate Program Faculty of Pharmacy, Universitas Airlangga | [2]Department of Pharmaceutical Science, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

Background: According to WHO (2022) estimates, non-communicable illnesses will be the leading cause of mortality and the biggest obstacle to sustainable development in 2045. It contributes 74% and dominates by cardiovascular disease (17.9 million people each year). The innovation is kenikir (*Cosmos caudatus*) patch based on nanophytosome as an antidyslipidemia. Leaf ethanol extract of kenikir at 200 mg/kg BW reduced levels of triglycerides, total cholesterols, and LDL in the blood (1). However, compounds that prevent dyslipidemia have low bioavailability, so a modification of the delivery system is needed, namely a transdermal patch based on nanophytosome (2). The use of nanophytosome based transdermal patches can increase bioavailability and permeability of the compounds present in kenikir leaf extract to penetrate biological membranes (3).

Method: This research used a quantitative-experimental method and determined the relationship between particle size and the in vitro drug release. This patch development compared particle size reduction using a magnetic stirrer and ultra-turrax. As a result, in-vitro drug release studies were carried out by observing the release profile using a dissolution apparatus I (basket method).

Results: The result showed that particle size reduction by ultra-turrax was smaller (900 nm). Based on in-vitro drug release results, smaller particles by ultra turrax have higher dissolution and faster drug release.

Conclusion: The development of transdermal patch based nanophytosome as an antidyslipidemia increased bioavailability and permeability. Keywords: kenikir, patch, nanophytosome, particle size, in vitro.

References:

1. Perumal V, Hamid AA, Ismail A, Saari K, Abas F, Ismail IS, Lajis NH, Khatib A. Effect of *Cosmos caudatus* Kunth leaves on the lipid profile of a hyperlipidemia-induced animal model. Journal of Food Chemistry and Nutrition. 2014, 2(1), 43-51.
2. Miatmoko A, Cahyani DM, Widyowati R. Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems Part II: Liposomes for Herbal Drug Delivery. Bentham Science Publishers Pte. Ltd. Singapore. 2022, 227-252.
3. Widyowati R, Miatmoko A. Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems Part II: Pharmaceutical Nanosciences and their Application in the Delivery of Various Phytoconstituents. Bentham Science Publishers Pvt. Ltd. Singapore. 2022, 1-24.

Acknowledgements: We are grateful to the Dean of the Faculty of Pharmacy, Universitas Airlangga for giving us the resources necessary to conduct this research efficiently.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: JSEA | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Developing and optimising an in vitro gel-based release assay for subcutaneously administered insulins with the USP dissolution apparatus IV

Chen Liang Teng (cl.teng@yahoo.com.sg)[1], Matthias G. Wacker (phamgw@nus.edu.sg)[1], David Li[1]

[1]**National University of Singapore, Singapore, Singapore**

A more prevalent use of biologics (which mostly cannot be orally administered) together with improved patient compliance (compared to intravenous injections) led to an increase in drug products administered subcutaneously [1]. Hence, an *in vitro* assay that can quantify the release of such drug products will be of great appeal in formulation development and quality control. Agarose hydrogels have been postulated to mimic certain characteristics of the subcutaneous tissue by creating a diffusion barrier [2]. This study aims at the development and optimisation of a biopredictive *in vitro* gel-based release assay by customization of the USP dissolution apparatus 4. Our "gel-in-cell" model employs an agarose gel in a modified flow-through cell, and was used to assess the release of insulin and the preservative m-cresol, which served as a small-molecular standard, from commercial insulin formulations, Actrapid® and Apidra®, across the agarose gel layer. Our results indicate that the model was capable of quantifying the release of insulin and m-cresol. The release of insulin from Apidra® was faster than that of Actrapid® which reflected the relative *in vivo* performances of the two insulin formulations [3]. The release of m-cresol was similar for both insulin formulations which was expected. The difference factors ($f1$) and similarity factors ($f2$) of insulin and m-cresol were also calculated to give some insight into the discriminatory ability of the assay. This model is in its early development stage and further modifications are expected to reflect more characteristics of the physiological environment and cater for subcutaneous drug products with different release mechanisms.

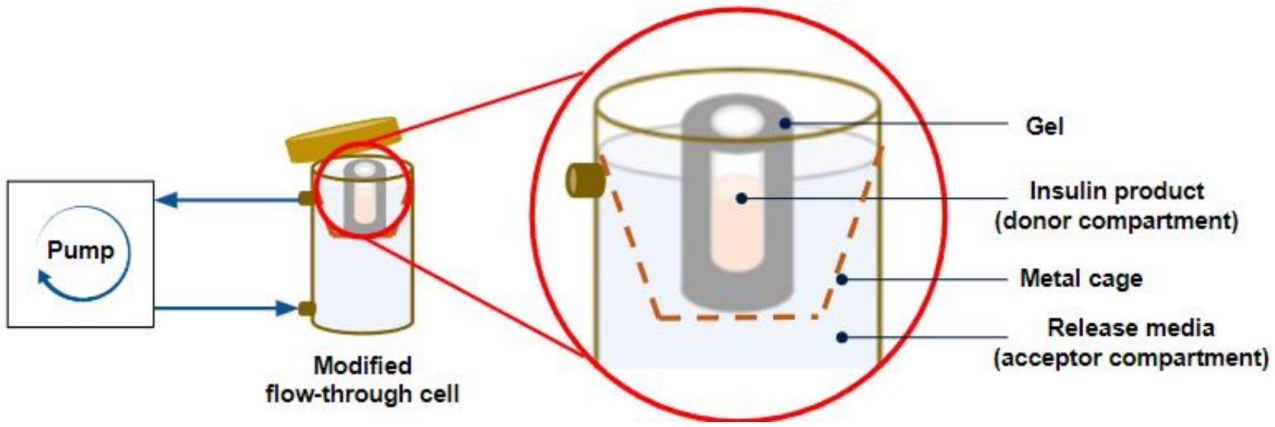


Fig. 1: Illustration of the setup used for the gel-based release assay. Arrows indicate direction of media flow

References:

1. Bittner, B., W. Richter, and J. Schmidt, Subcutaneous Administration of Biotherapeutics: An Overviewof Current Challenges and Opportunities. BioDrugs, 2018. 32(5): p. 425-440.
2. Leung, D.H., et al., Development of a Convenient In Vitro Gel Diffusion Model for Predicting the InVivo Performance of Subcutaneous Parenteral Formulations of Large and Small Molecules. AAPSPharmSciTech, 2017. 18(6): p. 2203-2213.
3. Soeborg, T., et al., Absorption kinetics of insulin after subcutaneous administration. Eur J PharmSci, 2009. 36(1): p. 78-90.

Acknowledgements: The authors acknowledge that SOTAX provided the SOTAX CE7smart Offline, encompassing the SOTAX Fraction Collector, SOTAX Dissolution Testing Unit and SOTAX Piston Pump, and the associated accessories.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: JSEA | **Category:** MPharm
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Development of Autoclave Stable Cationic Polymer Eluting Antifungal Contact Lenses for Fusarium Keratitis

Junietta Lim (e0325911@u.nus.edu)[1], Rajamani Lakshminarayanan (pharal@nus.edu.sg)[1,2]

[1]**Department of Pharmacy, Faculty of Science, National University of Singapore, Singapore** | [2]**Singapore Eye Research Institute**

Fungal keratitis is a significant cause of fungal corneal infection and blindness. Among the causative species, *Fusarium solani* is especially prevalent in tropical and subtropical climates and is particularly difficult to manage. Presently, only one ophthalmic antifungal eye drop formulation is approved; but due to low bioavailability, frequent administration is needed over a long period of time. In contrast, contact lens (CL) acts as a physical barrier, forming a post-lens tear film that prolongs drug contact with the cornea for maximum penetration, making it ~35 times more effective, and a promising ocular drug delivery device. Nonetheless, conventional antifungal drugs may not possess sufficient thermal stability to withstand autoclave conditions during CL manufacturing. The overall objectives of this work are to determine the autoclave stability of three cationic polymers, their uptake and release characteristics from a soft CL, as well as the antifungal and optical properties of the polymer-loaded CL.

We determined the antifungal properties of these cationic polymers before and after autoclaving and all three polymers displayed fungicidal activity against the tested *Fusarium* strains, which was retained after autoclaving. Additionally, more than 50% uptake into CL was recorded and polymer release was sustained over 24 hours. Therapeutic (minimum fungicidal concentration) amounts of branched polyethylenimine and poly-L-homoarginine were released within 30 minutes. All the polymer-loaded CLs were visually clear, with more than 95% light transmittance recorded at 600nm. These results highlight the prospect of polymer-eluting CL as a more efficient alternative treatment that may improve clinical outcomes from *Fusarium* keratitis.

References:

1. Brown, L., Leck, A. K., Gichangi, M., Burton, M. J., & Denning, D. W. (2021). The global incidence and diagnosis of fungal keratitis. The Lancet Infectious Diseases, 21(3).
2. Patton, T. F., & Francoeur, M. (1978). Ocular bioavailability and systemic loss of topically applied ophthalmic drugs. American Journal of Ophthalmology, 85(2), 225- 229.

USA

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Lipid Dissolution: Introducing a Novel Dissolution Model to Investigate the Lymphatic Uptake of Oral Drug Products

Malaz Yousef (malaz@ualberta.ca1)[1], Raimar Loebenberg (raimar@ualberta.ca)[2], Neal Davies[2]

[1]University of Maryland, Baltimore, Maryland | [2]University of Alberta

Background and Rationale: Intestinal lymphatic delivery of xenobiotics is currently not considered in terms of its contribution to the overall pharmacokinetics or therapeutic effect. However, there is a growing interest in developing lymphotropic formulations that are specifically designed for selective uptake by the intestinal lymphatic [1]. Traditional dissolution tests, although important for evaluating drug quality and performance, cannot measure or predict whether absorption occurs through the portal pathway or via lymphatic circulation. To bridge this crucial gap, our research aimed to develop a novel dissolution model which focusses on assessing lipid dissolution as surrogate for lymphatic uptake. Our model has shown the potential to differentiate between lymphotropic behavior of drugs and formulations. This novel lipid dissolution system can serve as a valuable tool for investigating the lymphotropic properties of drugs or formulations. This is particularly important for lipid based formulations and the assessment of their *in-vivo* performance.

Methods: Dissolution tests were conducted on three commercially available lymphotropic drug products: Terbinafina, Apo-Terbinafine, and Lamisil. These tests were performed using modified USP Apparatus II and IV that included a lymphatic compartment to simulate lymphatic uptake. To create the lymphatic space, a dialysis bag with a molecular weight cut-off (MWCO) of 12-14kD and a width of 45 mm- was used and filled with 5 ml of Intralipid®. Intralipid® serves as an artificial chylomicron, mimicking lymph-carrying lipoproteins produced by enterocytes, which aid in drug transport through the lymphatics [2]. Standard dissolution conditions were applied to assess drug release in different media. Samples were collected at various time intervals, up to 60 minutes, and then filtered using 0.2µ nylon filters before being injected into HPLC vials for analysis. Prior to filtration and HPLC analysis, drug samples from the lymphatic compartment were treated with acetonitrile.

Results: Our approach provided a comprehensive analysis of release profiles over time. By utilizing the described experimental setup, we were able to simultaneously evaluate the rate and extent of drug release into the aqueous and lipid compartments. The uptake into the artificial chylomicrons was impacted by the excipients used in the formulations. Noteworthy variations in the percentage of dissolved drug were observed at different time points among the three products, as shown in Table 1. Apoterbinafine exhibited the lowest release in both models, and the modified USP IV method proved more effective in distinguishing between the products. These differences in performance were attributed to the specific excipients used in the tested products. Overall, the lymphatic uptake profile of the products closely mirrored

Table 1. Performance Results of Three Terbinafine Products in a Modified Dissolution Apparatus for Lymphotropic Performance Testing their release profile into the portal circulation (vessel release).

	Modified USP Apparatus II (media: simulated gastric fluid (pH =1.9))			Modified USP Apparatus IV (media: simulated gastric fluid (pH =1.9) and phosphate buffer (pH =6.8))		
% absorbed of the 250-mg dose from the different products	Terbinafina	APO-TERBINAFIINE	Lamisil	Terbinafina	APO-TERBINAFIINE	Lamisil
Absorption into blood circulation (% of drug in Vessel)	83.17	71.69	87.90	101.93	11.49	83.93
Lymphatic Uptake (% of drug in Intralipid®)	2.58	1.71	2.32	2.14	0.21	1.16
Total amount absorbed	85.75	73.40	90.22	103.107	11.70	85.09

Conclusions: Our research results underscore the potential of the developed lipid dissolution models in evaluating formulations and identifying factors that impact chylomicron uptake. It is crucial to establish reliable pharmaceutical lymphotropic performance testing methods that can accommodate the increasing complexity of pharmaceutical products. The presented model provides valuable insights for assessing formulation and manufacturing processes, and holds the potential to contribute to in-vitro bioequivalence guidelines specifically tailored for lymphotropic formulations.

References:

1. Trevaskis N, Kaminskas L, et al., From Sewer to Saviour—Targeting the Lymphatic System to Promote Drug Exposure and Activity. Nature Reviews Drug Discovery, 2015. 14(11): p. 781-803.
2. Yousef M, Park C, et al., Simulated Lymphatic Fluid for In-vitro Assessment in Pharmaceutical Development. Dissolution Technologies, 2022. 29(2): p. 86-93

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Novel Adapter Designs for In Vitro Release Testing of Long-Acting Injectable Suspensions

Nileshkumar Malavia (nilesh.malavia@uconn.edu)[1], Diane Burgess (d.burgess@uconn.edu)[1], Quanying Bao[2]

[1]**University of Connecticut, Storrs, Connecticut** | [2]Boehringer Ingelheim

Purpose: Long-acting injectable (LAI) suspensions are drug products containing highly lipophilic active pharmaceutical ingredients (APIs) that form a depot at the site of injection and undergo controlled drug release over a prolonged duration (up to three months). Unfortunately, the currently reported *in vitro* dissolution methods do not provide an accurate representation of the clinical performance of LAIs which makes product development challenging. For example, the US FDA-recommended *in vitro* release methods are short (45 mins to two days) and require dispersing the suspension in the release media. Dispersion is not ideal since a larger drug surface area is exposed for dissolution when compared to the *in vivo* depots. The other reported methods (semi-solid adapters with USP-IV apparatus and enhancer cells with USP-II apparatus) extend the release duration to some extent. However, these methods do not form a desirable depot. In semi-solid adapters, the suspension is often smeared when loaded onto the adapter surface. In the enhancer cells, the suspension is placed between the wetted filter membrane and the cells which often causes sample leakage and/or smearing. Smearing and leakage result in uneven sample distribution causing high variability, undermining the reliability of these methods. To overcome the shortfalls of the existing methods, novel adapter (sample holder) designs were developed which can maintain the integrity of the suspension samples, maintain depot shape, and provide a longer duration of drug release. The dissolution data obtained using the novel adapters were validated with *in vivo* data to establish *in vitro* and *in vivo* correlations (IVIVCs).

Methods: Various shaped designs were considered and two different designs with a shallow conical cavity, one for USP-II apparatus and one for USP-IV apparatus were selected, fabricated and tested. To assess the reproducibility and discriminatory ability of the adapters, three Q1Q2 medroxyprogesterone acetate LAI formulations (F1, F2 & F3) of the reference listed drug (RLD) Depo SubQ 104 Provera® were prepared, considering the PEG source and particle size as critical material and quality attributes. Formulations F1 and F3 were prepared using PEG3350 obtained from different sources. An antisolvent method was utilized to change the particle size of formulation F2 (achieving larger particle size and size distribution). All formulations along with the RLD were tested for particle size, size distribution, morphology, sedimentation volume (F-value), and drug release. A rabbit model was used to obtain drug plasma concentration-time profiles. IVIVC analysis was performed using WinNonlin® software.

Results: Design optimization suggested that the geometry and dimensions of the sample holder cavity of the adapter play a crucial role in obtaining robust dissolution profiles. Different shapes have different ramifications. For example, a square-shaped and deep conical cavity has sharp edges where media flow is poor, resulting in incomplete dissolution. Whereas a shallow cone-shaped cavity maintains depot formation and results in complete and consistent dissolution profiles.

Using the optimized adapters with USP-II and USP-IV apparatus, the dissolution profiles of Depo SubQ 104 Provera® (n=6) were highly reproducible (Fig 2D). In addition, the adapters showed good discriminatory ability and captured minor formulation differences between F1, F2 and F3. Although formulations F1 and F3 have similar particle size (Dv50 ~ 13.5µm), F3 showed faster drug dissolution (Fig 2C). This is due to F3 forming a looser agglomerate as indicated by its higher sedimentation volume. Although the particle size of the RLD (Dv50~ 20.0µm) and F1 (Dv50~ 13.5µm) were significantly different, they showed comparable dissolution profiles. Similar to F3, the RLD showed a higher sedimentation volume explaining its faster than expected drug dissolution profile. Formulation F2, which had large particle size (Dv50~ 20.0µm) and the highest span value, showed the slowest drug release. This was attributed to the lower overall surface area of the large particles and the close particle packing due to the broad size distribution. Formulation F2 had the lowest sedimentation volume. Furthermore, the dissolution profiles of all the formulations were extended to ~ two weeks using the optimized novel adapters with USP-IV apparatus, and ~ four weeks with USP-II apparatus. The longer duration of dissolution proved advantageous in developing IVIVCs for the LAIs. Linear regression analysis performed between the *in vivo* and *in vitro* release resulted in R-square values of 0.99, suggesting excellent correlation when the novel adapter method is used.

Conclusions/Impact: The novel adapter designs were excellent in terms of reproducibility and discriminatory ability when used with USP-II and USP-IV apparatus for *in vitro* dissolution testing of the medroxyprogesterone acetate LAI formulations. These adapters significantly improve the dissolution method by maintaining depot integrity, achieving more clinically relevant (longer) drug release profiles, and establishing robust IVIVCs. Dissolution methods using the adapters can be applied in formulation development and quality control and may aid in prediction of *in vivo* performance through *in vitro* approaches. Furthermore, the

novel adapters may be utilized with USP-II and USP-IV apparatus for *in vitro* release testing of other long-acting injectable drug products.

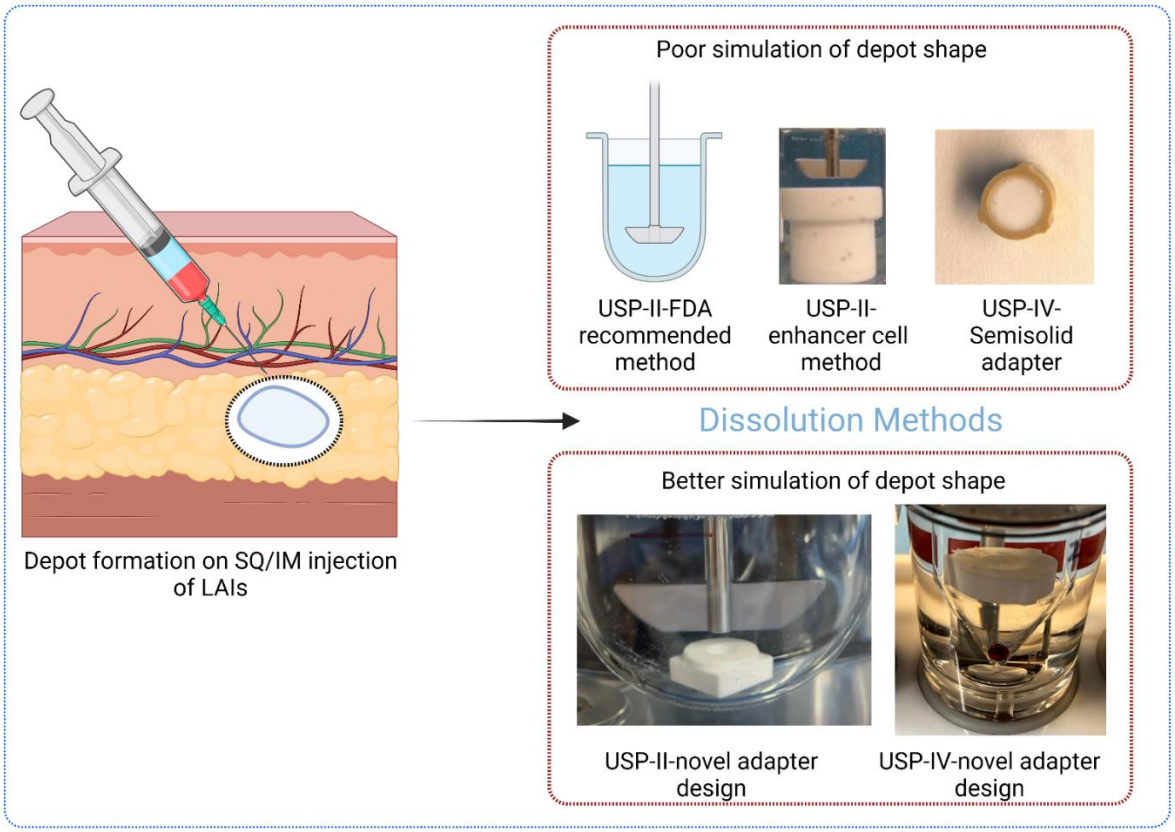


Figure 1: Pictorial representation of *in vivo* depot formation at the subcutaneous or intramuscular site and comparison of novel adapter dissolution methods with the methods reported in the literature in terms of maintaining depot integrity

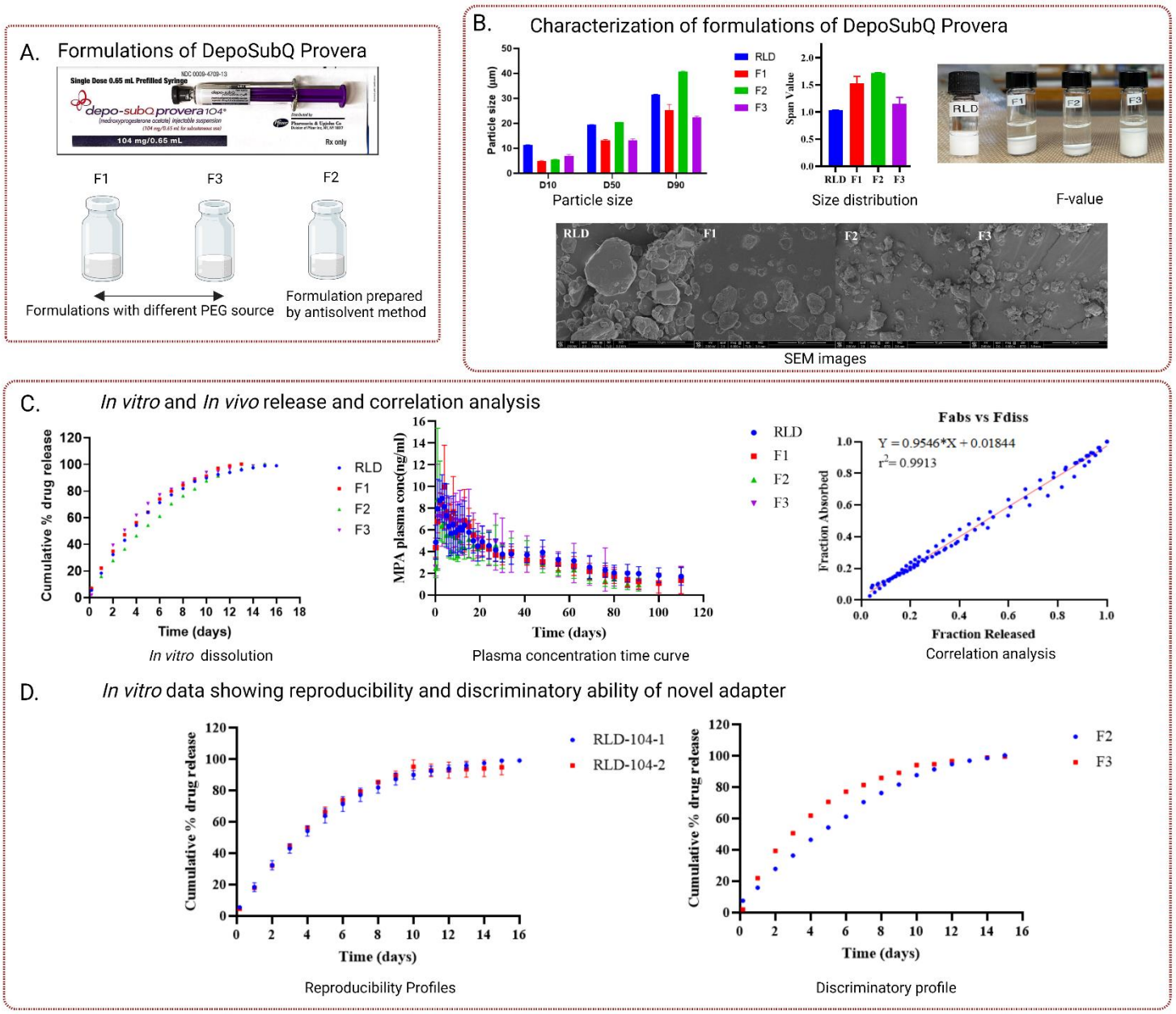


Figure 2: Schematic representation of A) Preparation of Q1/Q2 formulations of Depo SubQ Provera 104®; B) Physicochemical characterization of Q1/Q2 formulations and Depo SubQ Provera 104®; C) *In vitro* release, *In vivo* absorption profiles of Q1/Q2 formulations and Depo SubQ Provera 104® and correlation analysis performed between *in vitro* and *in vivo* data; D) *In vitro* release profiles showing reproducibility and discriminatory ability of novel adapter.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: Pharmacokinetics & IVIVC Studies

A novel 2-method Accelerated In Vitro Release Testing Strategy using USP Apparatus 2 to Predict the In Vivo Release Profiles of Combination Long-acting Injectable Suspensions

Krutika Harish Jain (krutika.harishjain@gilead.com)[1], Tien Ho[1], Anumeha Muthal[1], Bo Wan[1], Chris Foti[1]

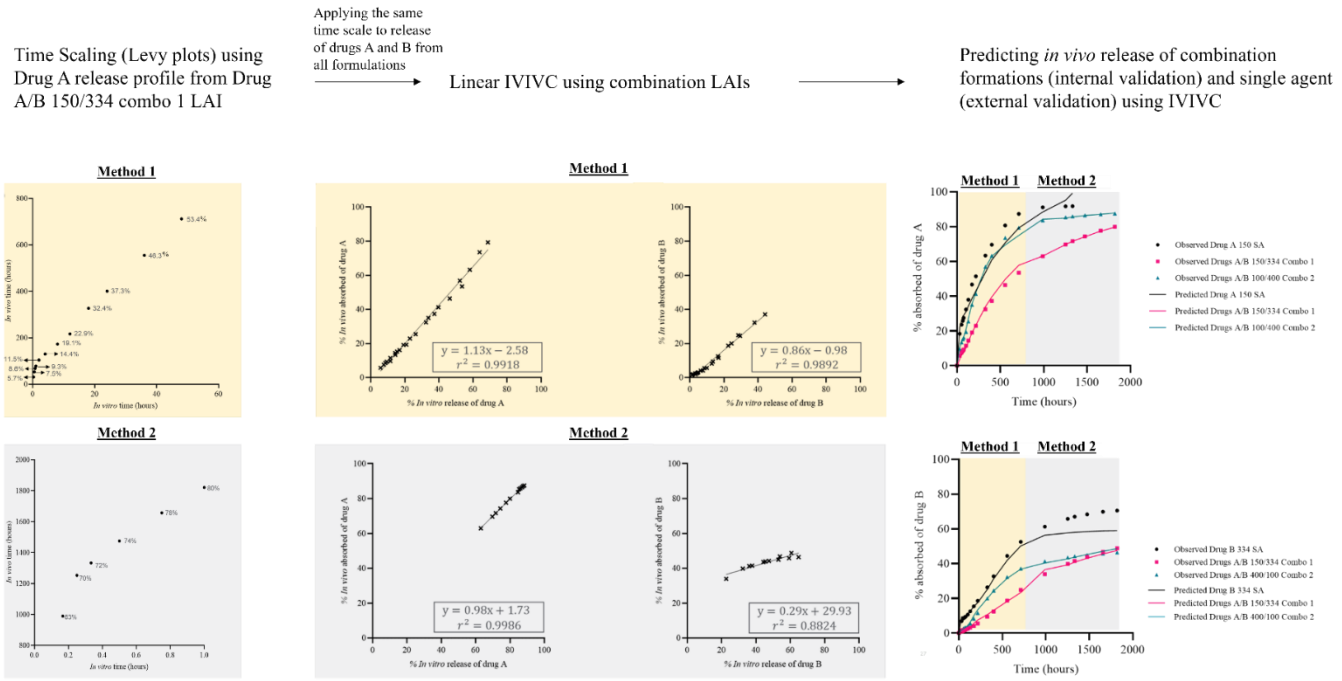
[1]**Analytical Development and Operations, Gilead Sciences, Foster City, California**

Purpose: Long acting injectables (LAIs) are complex formulations designed to release one or more active pharmaceutical ingredients (APIs) over extended durations and achieve a prolonged therapeutic exposure. It is critical to understand the factors influencing the *in vivo* performance of LAIs to facilitate formulation development. *In vivo* studies to assess LAI product performance are resource and time-intensive, ranging from weeks to months. Therefore, the objective of this study was to develop an accelerated and biopredictive 2-method *in vitro* release testing (IVRT) strategy using USP apparatus 2 (paddle) to predict the complete preclinical PK profile of intramuscular (IM) LAI suspension formulations consisting of two APIs.

Methods:

A. Formulations: APIs A and B were compounded into four LAI formulations of varying composition. Single agent (SA) LAIs of drug A aqueous solution (150 mg/mL, Drug A 150 SA) and drug B microsuspension (334 mg/mL, Drug B 150 SA) were formulated. For combination LAIs, micronized drug B was suspended in pre-dissolved drug A solution, resulting in 150/334 mg/ml or 100/400 mg/ml doses of drugs A and B, respectively. All LAI formulations were designed to form a depot at IM injection site and release gradually over a period of three months.
B. Rat PK Study: A rat *in vivo* PK study was conducted with these formulations and the plasma concentration-time profiles were deconvoluted in GastroPlus® to obtain *in vivo* absorption profiles.
C. IVRT Study: Using the deconvoluted *in vivo* profile as a target profile, two accelerated IVRT methods were developed using the USP apparatus 2; method 1 utilized a suspension cup and nominal agitation (75 rpm paddle speed) to predict the initial burst and intermediate release, and method 2 employed HPMC capsule and high agitation (250 rpm for the first 10 minutes followed by 100 rpm) to reflect the terminal profile. The same release medium, 10 mM sodium phosphate buffer with 0.75% w/v cremophor, pH 7.4, 900 mL at 37℃, was applied for both release testing methods.
D. IVIVC: The *in vitro* release profiles using both these accelerated methods were time-scaled independently and then combined to predict the complete 'real-time' *in vivo* release profiles lasting over 2000 hours. IVIVCs were developed separately for the two drugs and the two IVRT methods. Finally, the IVIVCs were validated using the combination (internal validation) and single agent (external validation) formulations (***Figure 1***).

Results: All LAI formulations formed a depot in aqueous media. Suspension cup (method 1) allowed exposure of only the depot surface to the media, resulting in a gradual, biphasic drug release lasting for more than 48 hours, capturing the initial burst and intermediate release phases observed *in vivo* (deconvoluted profiles). On the other hand, high agitation employed with method 2, comminuted the depot and resulted in complete drug release within about an hour, reflecting the monophasic release observed approximately 1000 hours post-injection *in vivo*. Upon time scaling the profiles obtained using both these IVRT methods separately, the IVIVCs developed for drugs A and B were successfully validated (***Figure 1***). The predicted release profiles showed good agreement with the deconvoluted (observed) profiles both in the initial and later phases for the combination and single agent formulations (***Figure 1***). In general, a significantly higher exposure (C_{max} and AUC_{0-t}) and percent release of drugs A and B was both predicted and observed from the single agent



formulations, relative to the combination formulations. This suggests that the presence of drug A likely retards the release of drug B and vice versa (***Figure 1***).

Figure 1: Outline of the 2-method IVRT strategy to predict the *in vivo* performance of LAI formulations

Conclusions: To predict the *in vivo* performance of LAI formulations and ensure their safety and efficacy, it may be critical to capture all the phases of drug release with reliable IVRT methods. While a slow method may successfully capture the initial release, the method can be too lengthy and impractical to capture the terminal phase. A highly accelerated method, on the other hand, can result in excessive time scale compression and limit the prediction of the initial phase. A novel 2-method strategy introduced in this study combines the release profiles obtained separately using the slow and fast methods to predict the complete release from an LAI. Acceleration of drug release can be attained by varying the temperature, agitation, surfactant concentration or sample introduction. In this study, different agitation rates and sample introduction methods were utilized to vary the surface area of the suspension formulation that was exposed to the media to in turn vary the drug release kinetics. IVIVCs were developed for both the drugs with methods 1 and 2 independently and further validated. Through a successful implementation of IVIVC, accelerated *in vitro* studies can be used to accurately predict the *in vivo* performance of LAIs, thereby minimizing animal or human studies and expediting the drug development process.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Dissolution & Solubility Modulation

Redefining Solubility Enhancement: Unveiling the Potential of Acid-Base Supersolubilization to Improve Indomethacin Dissolution

Vishvesh Raje (vishveshraje7@gmail.com) [1], Abu Serajuddin (serajuda@stjohns.edu)[1], Ida Lu[1], Raya Keir[1]

[1]**College of Pharmacy and Health Sciences, St. John's University, Jamaica, New York**

Purpose: Over two-thirds of drugs under development in the pharmaceutical industry are extremely insoluble in aqueous media and fall into BCS Class II or IV. This abstract describes how the aqueous solubility of a poorly water-soluble weakly acidic drug, indomethacin, can be greatly improved and its dissolution rate from amorphous solid dispersions (ASD) can be enhanced by applying a novel physicochemical principle called acid-base supersolubilization (ABS). The application of the ABS principle was previously described for basic drugs (1,2). According to the classical pH-solubility theory (3), the solubility of a free base and its salt with an acidic counterion may be described by two independent curves, one where the free base is the equilibrium species and the other where the salt is the equilibrium species; the point where the two curves intersect is the pH of maximum solubility (pH_{max}). When an acid is used to lower the pH of the suspension of a basic drug in water, the solubility of the drug increases until pH_{max} is reached, and upon further lowering of pH to $<pH_{max}$, a phase transition of the drug occurs resulting in the crystallization of its salt form. Acids used to adjust the pH of the suspensions must be strong enough to lower pH below pH_{max}; if relatively weaker acids are used, pH_{max} may never be reached, and solubility of the drug in aqueous medium keeps increasing according to the Handerson-Hasselbach equation without any salt precipitation until a very high solubility is attained. It has been reported that, while aqueous solubilities of phosphate and HCl salts of haloperidol are 1 and 4 mg/mL, respectively, the solubility of the compound could be increased to >300 mg per gram of solution by adjusting pH with such weak acids as malic acid, succinic acid, and citric acid, which did not form haloperidol salts. The phenomenon has been named acid-base supersolubilization (ABS) since extremely high aqueous solubility was obtained via interactions between basic drugs and weak acids. ASDs were formed when such solutions were dried. Later, it was demonstrated that ASDs may also be obtained by the melt extrusion of the acid-base mixture without the need for any water to dissolve the drug (4).

Although the ABS principle has previously been used for basic drugs, no study on its application to improve the solubility and dissolution rates of acidic drugs has been reported. In this study, the ABS principle was applied to greatly increase the dissolution rates of a model acidic drug, indomethacin (IND), from ASDs under gastric pH conditions. Indomethacin has a solubility of 0.001 mg/mL, at pH 1.2, and because of such a low solubility, all reports in the literature show that it precipitates out from ASDs at relatively low pH of 1 to 2.

Methods: The aqueous solubility of IND in the presence of a weak base, tromethamine, was determined by using the shake-flask method at 25°C and analyzing samples by HPLC. ASDs were prepared by hot melt extrusion (HME) using a Thermo Scientific Process 11 extruder. Rheology as a function of temperature, hot-stage microscopy, DSC, and PXRD were performed to determine HME experimental conditions and characterize ASDs. *In vitro* dissolution testing of 25-mg IND equivalent was performed in 250mL of 0.1M HCl (pH 1.2) using USP II apparatus at 50 RPM and 37°C.

Results: Figure 1 shows the solubility of IND as a function of increasing concentration of tromethamine that reached >240 mg/ml at pH~8, demonstrating supersolubilization of the drug. When dried, the concentrated solution converted to an amorphous semisolid mass that did not crystallize to free acid or salt. The supersolubilized system was, therefore, processed into solid ASD using the solvent-free HME process. IND-tromethamine mixtures at 1:1 and 1:2 molar ratios, without or with added surfactant (poloxamer 407; P407) at 10 and 20% levels were used for ASDs. Physically and chemically stable ASDs were formed in all cases. Figure 1 shows that <5% IND dissolved when ASD was produced using 10% IND in KVA64 alone. Although the addition of P407 improved drug release, the maximum release was still ~40% which subsequently precipitated out from the solution. On the other hand, the acid-base supersolubilization using tromethamine greatly improved drug release and prolonged supersaturation of dissolution media. The ABS phenomenon also improved the processability of ASD as HME could be conducted at as low as 80°C, thus avoiding any potential of drug degradation at high HME temperatures.

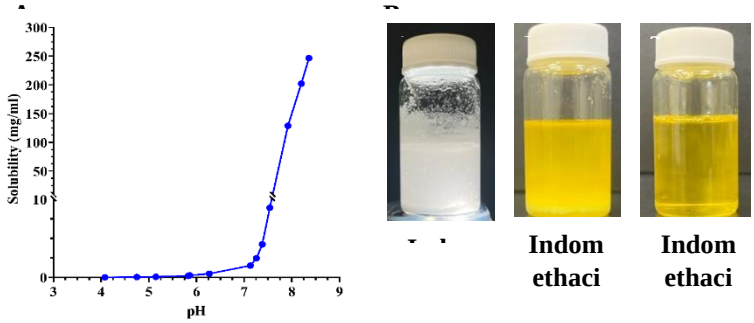
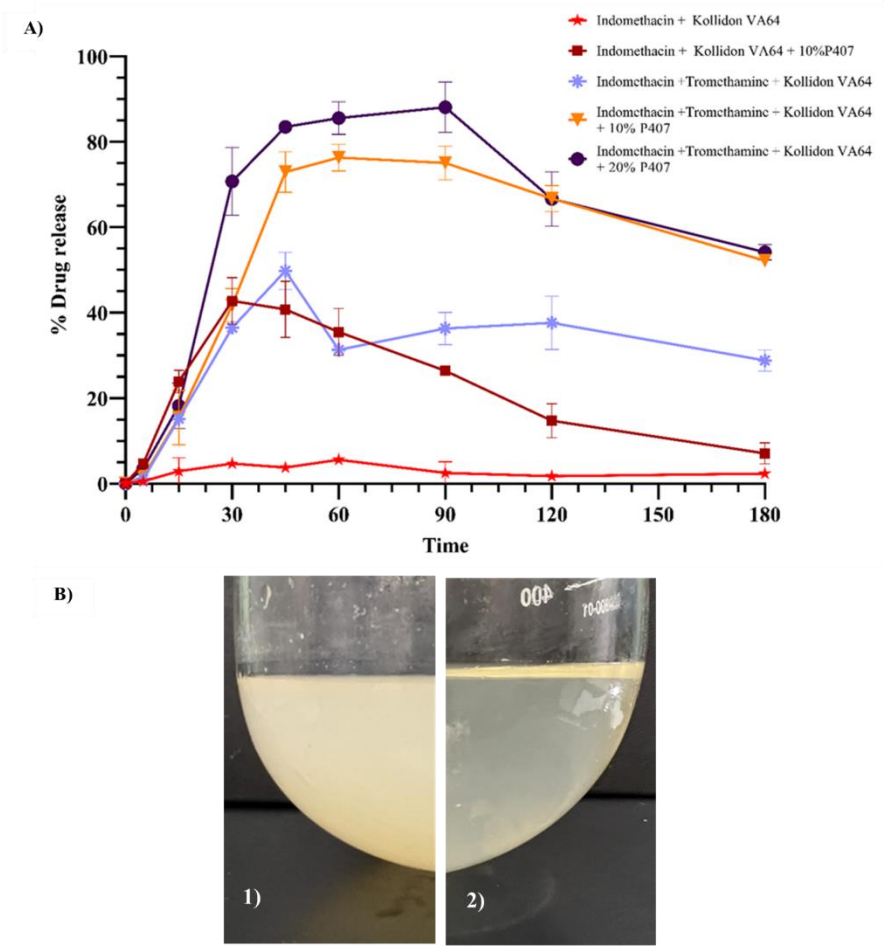


Figure 1 pH-solubility profile of indomethacin. The increasing pH values obtained by addition of tromethamine.

Conclusions: The application of acid-base supersolubilization yielded a remarkable and substantial enhancement in the solubility of indomethacin (IND). The exceptionally high drug release of >80% under gastric pH conditions was particularly surprising because literature reports that the release of IND from ASDs at low pH is very limited (usually <10-15%).

Figure 2 A: In Vitro drug release of capsules filled with powdered extrudates with dose equivalent to 25 mg of indomethacin.
B: (1) The cloudy dissolution media suggest undissolved or precipitated indomethacin for the extrudates of indomethacin-Kollidon VA64. (2) Clear media suggest completely dissolved indomethacin (particle analysis shows particle size of 46nm ± 5nm) for the batch containing Indomethacin +Tromethamine Kollidon VA64 + 20% P407.



References:

1. Singh, S., Parikh, T., Sandhu, H.K., Shah, N.H., Malick, A.W., Singhal, D. and Serajuddin, A.T., 2013. Supersolubilization and amorphization of a model basic drug, haloperidol, by interaction with weak acids. Pharmaceutical Research, 30, pp.1561-1573.
2. Shah, A. and Serajuddin, A.T., 2014. Supersolubilization by using nonsalt-forming Acid-Base interaction. Amorphous Solid Dispersions: Theory and Practice, pp.595-611.
3. Kramer, S.F. and Flynn, G.L., 1972. Solubility of organic hydrochlorides. Journal of Pharmaceutical Sciences, 61(12), pp.1896-1904.
4. Parikh, T. and Serajuddin, A.T., 2018. Development of fast-dissolving amorphous solid dispersion of itraconazole by melt extrusion of its mixture with weak organic carboxylic acid and polymer. Pharmaceutical Research, 35, pp.1-10.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD

Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Development and Validation of Microdialysis-Based Discriminatory and Biorelevant In vitro Release Testing Instrument for Complex Ophthalmic Products

Sushesh Srivatsa Palakurthi (susheshsrivatsa98@gmail.com)[1], Nitin B Charbe (nitinunimi@gmail.com)[1], Srinath Palakurthi[1]

[1]**Department of Pharmaceutical Sciences, Irma Lerma Rangel School of Pharmacy, Texas A&M University, Kingsville, TX 78363, USA**

Purpose: Ophthalmic emulsions are considered complex products due to the involved manufacturing process. Unlike other dosage formulation like solid oral, reliable instruments which could be used for the discrimination of complex ophthalmic with high degree of reproducibility is not available. Following topical administration of eye drops, dilution with the tears and rapid clearance from the eye necessitate appropriate methods that allow monitoring the drug release from the formulations in the first few minutes. Microdialysis is the only biorelevant technique that can be optimized and automated to simulate in vivo conditions for testing drug release from topical ophthalmic formulations. Unlike other classical IVRT techniques, microdialysis is sensitive enough to study the release of drug from the formulation as early as 1 min.

As a part of our current investigation, the microdialysis based instrument was developed and validated by studying the drug release from difluprednate (DFBA/ Butyrate ester of 6(alpha),9(alpha) difluoro prednisolone acetate) formulations of different strengths (F1, F2, F3 & F4), formulations of same strength prepared by changing the process parameters (F1 & F4) compared to that of RLD (DUREZOL®) and micellar formulations prepared without oil (F5). In the current investigation the in-house developed instrument which is based on microdialysis was found to be a reliable IVRT tool for ophthalmic emulsions in terms of reproducibility and discriminatory ability.

Methods: In the present study, drug release profiles of DFBA 0.05% (RLD, F1=In house, and F4=In house- Higher globule size), DFBA 0.025% (F2), and DFBA 0.1% (F3) were studied. DFBA ophthalmic emulsion formulations were prepared in two steps using high-pressure homogenization followed by microfluidzation. Micellar formulation was prepared by solubilizing DFBA 0.05% in surfactant but not oil, having all the other excipients constant. F1 & F4 were prepared by changing the process parameters. These formulations were then studied using the inhouse developed instrument. The microdialysis-based equipment utilized in this study comprises of a syringe pump, a magnetic heating block with a stirrer, and an autosampler. Our laboratory personnel assembled this equipment to ensure its compatibility with the experimental procedures and specific requirements of the study. Microdialysis of the formulations has been performed using 0.1X PBS with 1% albumin as the perfusion fluid at a flow rate of 4 µl/min. 5X diluted formulations were stirred at 800 rpm and the temperature was maintained at 35°C. Samples were collected at 2-minute intervals for 30 minutes and analyzed using HPLC-UV. Polyether sulfone (PES) probes of 10 mm length and 35kD MWCO were used. Globule size distribution of the emulsions were measured using ZetaPals. Nonparametric Wilcoxon Rank Sum/Mann- Whitney rank test was conducted at 90% CI to compare the sameness of RLD and In-house prepared DFBA 0.05% (F1) ophthalmic emulsions (n=6). The developed method and the customized equipment setup were validated by comparing release profiles of different formulations of DFBA nano emulsion.

Results: The release profiles of F1 (DFBA 0.05%) and F2 (DFBA 0.05%, larger globular size) were compared to that of RLD. F1 exhibited a similar release as RLD whereas the drug release profile of F4 formulation was significantly different from that of RLD and F1. The observed difference in the drug release profile of F4 and RLD could be attributed to the globular size variation as globule size distribution is considered as a critical quality attribute of an ophthalmic emulsion. Drug release from different strengths of formulation was easily differentiated using Microdialysis (Fig 1). The cumulative amount of DFBA release over a period of 30 min with RLD, F1, F2, F3, F4 and F5 were 0.124609±0.033, 0.085877±0.016, 0.044134±0.005, 0.106101±0.033, 0.068169± 0.019, and 0.145185 ± 0.02258 µg, respectively. The sameness of RLD and In-house prepared DFBA 0.05% (F1) ophthalmic emulsions was confirmed when the formulations passed the Wilcoxon Rank Sum/Mann- Whitney rank test. On the other hand, all the other formulations (F2, F3, F4, and F5) fail the test. Effective globular size distribution measures (Table 1) of the emulsion formulations can be correlated to the drug release. Formulations with smaller size (RLD, F1) show better release than the formulation with higher particle size (F4). SPAN value explains the globular size distribution in a formulation. The greater the SPAN value, wider is the globule size distribution. SPAN value is calculated using the formula: $(D_{90}-D_{10})/D_{50}$.

Conclusions: The bioequivalence of the in-house developed (Q1/Q2) formulation was demonstrated by comparing its drug release profile to that of the reference listed drug (RLD). The experiments were conducted using a microdialysis-based instrument developed in-house. The results revealed that all formulations could be distinguished based on their formulation strength and physicochemical

properties. These findings highlight the capability of the in-house developed tool to effectively differentiate between formulations of varying strengths and characteristics. The application of this technique could highly be advantageous for both the industry and academia in the development of generic ophthalmic products.

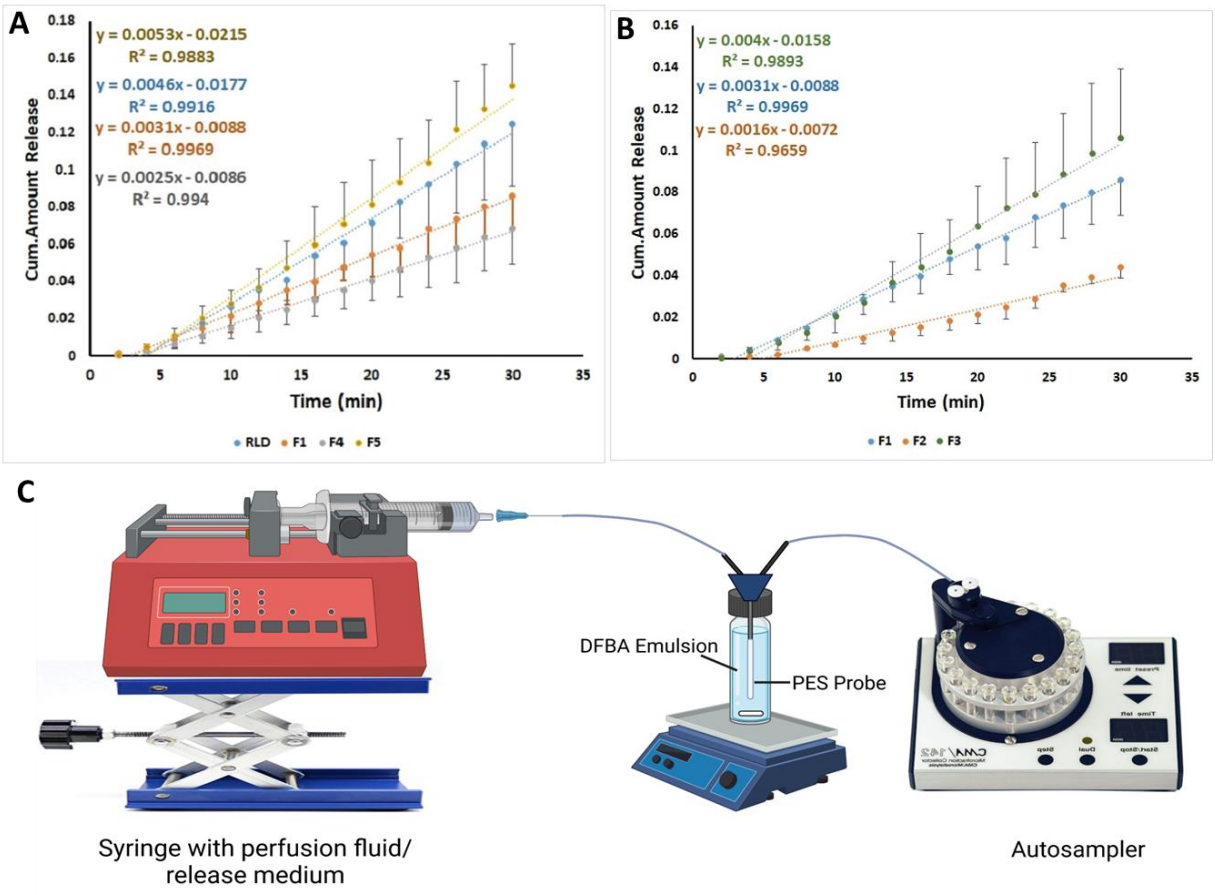


Figure 1: **A.** Cumulative amount drug release (µg) from 0.05% DFBA nano emulsions, RLD, F1 (In-house), F4 (In-house Higher globule size), and F5 (Micellar formulation). **B.** Cumulative amount drug release (µg) from 0.05% (F1), 0.025% (F2), and 0.1% (F3) in house prepared DFBA nano emulsions (n=6). **C.** Schematic representation of the customized microdialysis equipment setup.

Table 1: Globule size distribution and SPAN values of emulsion and micellar formulations of DFBA (n=12).

Formulations	Effective diameter (nm)	D10	D50	D90	SPAN
RLD	102.013	50.763	93.013	170.43	1.286
F1	105.856	63.693	105.856	175.973	1.060
F2	118.6	70.68	118.6	198.99	1.081872
F3	119.91	63.11	119.91	227.82	1.373614
F4	171.75	86.26	171.75	341.95	1.488734
F5	12.031	6.693	12.128	22.283	1.280

References:

1. Bellantone, R.A.; Shah, K.B.; Patel, P.G.; Kaplan, M.; Xu, X.; Li, V.; Newman, B.; Abul Kaisar, M. Cyclosporine Release and Distribution in Ophthalmic Emulsions Determined by Pulsatile Microdialysis. *Int. J. Pharm.* **2022**, *615*, 121521, doi:10.1016/J.IJPHARM.2022.121521.

DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: Computational Tools, PBPK Modelling

Semi-Mechanistic Reduced Order Model of Pharmaceutical Tablet Dissolution for Design, Optimization, and Control Of Manufacturing Processes

Shumaiya Ferdoush (shumaiyaferdoush30@gmail.com)[1], Marcial Gonzalez (marcial-gonzalez@purdue.edu)[1]

[1]**School of Mechanical Engineering, Purdue University, West Lafayette, Indiana**

Background: Dissolution profile is one of the most important critical quality attributes for pharmaceutical solid oral dosage forms as failure to meet the dissolution specification can impact bioavailability [1, 2]. Dissolution tests are time-consuming destructive tests performed offline to ensure batch-to-batch manufacturing consistency, guide the development of new formulations, and provide continuing product quality and performance after specific changes [3]. Therefore, predictive dissolution models are crucial for the successful implementation of any real-time release testing (RTRT) strategy [4, 5, 6] and, eventually, for ensuring consistent product quality based on process data. The development of mechanistic and semi-mechanistic reduced order models (ROMs), resulting from a trade-off between complexity and performance but still based on product and process understanding, forms an essential cornerstone for process design, optimization, and control in pharmaceutical manufacturing. First-principles models, such as the population balance model (PBM), have been used for a long time to understand the effect of crystal size distribution (CSD) on dissolution [7, 8, 9]. However, using the PBM approach to predict the dissolution of complex formulations in a tablet form is rarely found in the open literature. In the current study, a modified version of the PBM is proposed to understand the effect of active pharmaceutical ingredient's (API) CSD and the wetting phenomena controlled by the porous microstructure formed by the compacted excipients on tablet dissolution. The performance of the proposed model is demonstrated using experimental dissolution data of lomustine tablets (an oral antineoplastic agent for the treatment of primary and metastatic brain tumors).

Methods: A. Experimental procedures: Sieve analysis was first performed on the lomustine crystal manufactured by our team to obtain the following two sieved fractions of particles, (i) CSD: 0-180 μm (ii) CSD: 125-250 μm. Next, morphology analysis was performed using a Malvern G3SE-ID particle size analyzer to obtain the initial particle size distribution of the sieved fractions. Using the above two sieve size ranges, two blends were prepared of formulation 4.41% lomustine, 70.59% lactose monohydrate, 24% mannitol, and 1% MgSt, all % w/w. Flat-faced, 114 mg, 6 mm tablets of seven different porosities and two different CSDs were fabricated in a Gamlen D Series bench-top compaction simulator. Four different sets of tablets were manufactured by changing MgSt lubricant concentration (0-2)% and mixing time. Finally, the dissolution tests were performed on all the tablets in 900 mL of 0.05 M phosphate buffer media at temperature 37.0 ± 0.5 ◦C. The tests were done on a USP II apparatus at 75 rpm. The API absorbance was measured at 231 nm.

2.2 Mathematical modeling and parameter identification

Figure 1: Model input-output

A discrete implementation of a high-resolution finite volume method (HR-FVM) was used to solve the PBM. A parameter identification method was developed based on a nonlinear multivariate minimization problem. This method is based on the similarity factor $f2$ described in the FDA dissolution guidance [3], i.e., two dissolution profiles are similar if $f2 = 100$, and are equivalent if $f2 > 50$. Specifically, the method minimizes $(100 - f2)$ between dissolution experimental data and model predictions by choosing optimal model parameters. The nonlinear multivariate minimization problem was solved in MATLAB [10] using the constrained optimization function fmincon with the default interior-point algorithm.

Results: Lomustine tablets exhibit negligible sensitivity to MgSt lubrication conditions. However, lomustine tablets showed sensitivity to the CSD of the API and tablet porosity, as shown in figure 2. Notably, the tablets with smaller CSD (0-180 μm) showed faster dissolution compared to the larger CSD, and tablets of higher porosity exhibited faster dissolution. The modified version of the PBM, which is a function of tablet porosity and API CSD, was calibrated to the experimental data points of tablets having two different CSD and seven different porosities and the model parameters were estimated. The calibrated model had a similarity factor, $f2$, which exemplifies the goodness of fit for each set of predicted and measured dissolution profiles, i.e., $f2 > 50$. Due to its high accuracy, the model can further be used to create a design space to obtain the desired release characteristics.

Conclusion: In the current study, we showed that the modified version of the PBM models can be used to accurately predict tablet dissolution which is controlled by the API CSD and the porous microstructure formed by the compacted excipients of the tablet. The estimations of the proposed pharmaceutical tablet dissolution model are in good agreement with experimental data. The integration of these models with in-line and at-line process analytical technology (PAT) tools can enable RTRT and quality-bycontrol (QbC) strategies in continuous pharmaceutical manufacturing.

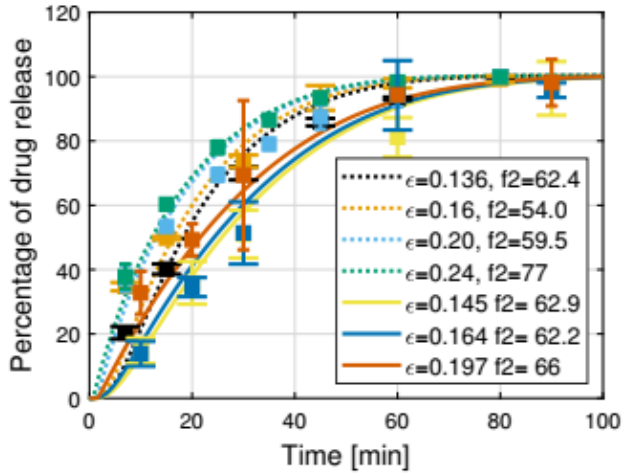


Figure 2: Effect of CSD and tablet porosity on dissolution. Squares represent experimental data, solid lines represent model prediction for CSD of 125-250, dotted lines represent model prediction for CSD of 0-180 μm , and *f*2 represents similarity factor.

References

[1] Jennifer Maguire and Daniel Peng. How to identify critical quality attributes and critical process parameters. In *presented FDA/PQRI 2nd Conference North Bethesda, Maryland*, 2015.

2] X Yu Lawrence, Gregory Amidon, Mansoor A Khan, Stephen W Hoag, James Polli, GK Raju, and Janet Woodcock. Understanding pharmaceutical quality by design. *The AAPS journal*, 16 (4):771–783, 2014.

[3] FDA Guidance. Guidance for industry: Dissolution testing of immediate release solid oral dosage forms. us department of health and human services. *Food and Drug Administration, Center for Drug Evaluation and Research (CDER)*, 1997.

[4] FDA. Guidance for industry: PAT-A framework for innovative pharmaceutical development, manufacturing and quality ssurance. http://www.fda.gov/cder/guidance/published.hml, 2004.

[5] FDA. Guidance for industry: Q11 development and manufacture of drug substances. US department of health and human services. 2012.

[6] Huiquan Wu, Robbe C Lyon, Mansoor A Khan, Randall J Voytilla, and James K Drennen III. Integration of near-infrared spectroscopy and mechanistic modeling for predicting film-coating and dissolution of modified release tablets. *Industrial & Engineering Chemistry Research*, 54 (22):6012–6023, 2015.

[7] Nikolay Zaborenko, Zhenqi Shi, Claudia C Corredor, Brandye M Smith-Goettler, Limin Zhang, Andre Hermans, Colleen M Neu, Md Anik Alam, Michael J Cohen, Xujin Lu, et al. First principles and empirical approaches to predicting in vitro dissolution for pharmaceutical formulation and process development and for product release testing. *The AAPS journal*, 21(3):1–20, 2019.

[8] David Wilson, Stephen Wren, and Gavin Reynolds. Linking dissolution to disintegration in immediate release tablets using image analysis and a population balance modelling approach. *Pharmaceutical research*, 29(1):198–208, 2012.

[9] Brigitta Nagy, Botond Szilagyi, Andr ´ as Domokos, Blanka V ´ eszi, Korn ´ elia Tacsi, Zsolt Rapi, ´ Hajnalka Pataki, Gyorgy Marosi, Zolt ¨ an K Nagy, and Zsombor Krist ´ of Nagy. Dynamic flow- ´ sheet model development and digital design of continuous pharmaceutical manufacturing with dissolution modeling of the final product. *Chemical Engineering Journal*, 419:129947, 2021.

[10] *MATLAB version 9.8.0.1380330 (R2020a)*. The Mathworks, Inc., Natick, Massachusetts, 2020.

Acknowledgements: This research is supported by the U.S. Food and Drug Administration through Grant No. 1U01FD006738-01, 5U01FD006738-02, and 5U01FD006738-03 entitled “Risk-based process synthesis and Industry 4.0 framework for pharmaceutical manufacturing processes”. The authors gratefully acknowledge Gamlen Instruments (London, UK) for the availability of the Gamlen D Series bench-top compaction simulator, and Professor Tonglei Li at Purdue University for providing access to the Distek 2100C dissolution system. The authors would also like to express gratitude to Dr. Jaron Mackey and Professor Zoltan Nagy at Purdue University for manufacturing the lomustine crystals used in the experiments reported in this abstract.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Comparative Evaluation of Dissolution Performance in USP 2 Setup and Alternative Stirrers and Vessel Designs: A Systematic Computational Investigation

Niloufar Salehi (nilousa@umich.edu)[1], Gregory Amidon (geamidon@umich.edu)[2], Jozef Al-Gousous[3] | Bart Hens[4] | Gordon Amidon[2] | Robert Ziff[5]

[1]Eli Lilly & Company, Indianapolis, Indiana | [2]Department of Pharmaceutical Sciences, University of Michigan | [3]Institute of Pharmaceutical and Biomedical Sciences, Johannes Gutenberg University Mainz | [4]Drug Product Design, Pfizer | [5]Department of Chemical Engineering, University of Michigan |

Background & Rationale: The dissolution testing method described in the United States Pharmacopeia (USP) Chapter <711> is widely used for assessing the release of active pharmaceutical ingredients from solid dosage forms. However, extensive use over the years has revealed certain issues, including high experimental inter-variability observed in specific formulations and the settling of particles in the dead zone of the vessel. To address these concerns and gain a comprehensive understanding of the hydrodynamic conditions within the USP 2 apparatus, computational fluid dynamic (CFD) simulations have been employed in this study. This enables a more robust analysis of the USP hydrodynamics and facilitates the evaluation of alternative designs that may offer advantages over the current system.

Methods: The base design employed in this study is the 900 mL USP 2 vessel along with a paddle stirrer at 50 rpm rotational speed. Additionally, alternative stirrer designs, including the hydrofoil, pitched blade, and Rushton impellers, are investigated as shown in Fig.1. A comparison is also made between a flat bottom tank and the USP round bottom vessel of the same volume and diameter. Furthermore, this work examines the impact of various parameters, such as clearance distance (distance between the bottom of the impeller and bottom of the vessel), number of impeller blades, impeller diameter, and impeller attachment angle. The volume-average shear rate (S_{tv}), fluid velocity (U_{tv}), and energy dissipation rates (ϵ_{tv}) represent the key properties evaluated in this study.

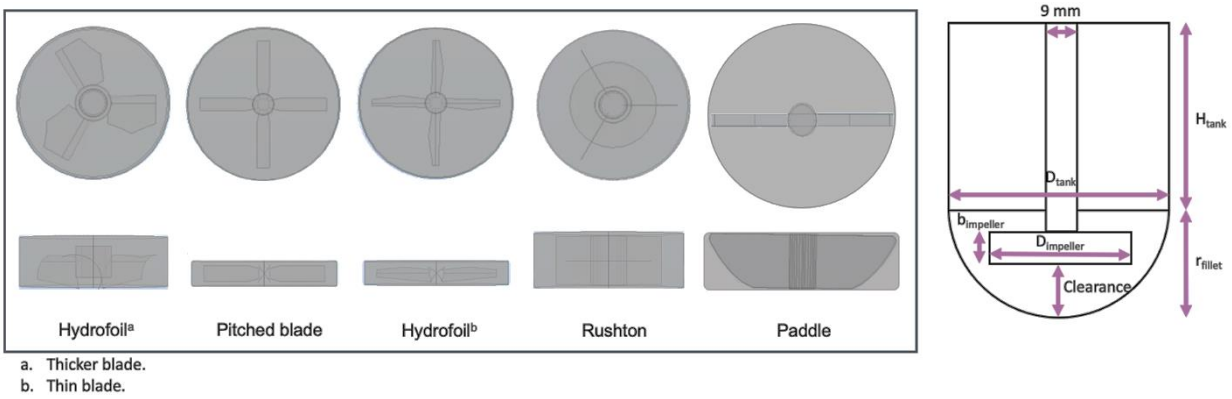


Figure 3. schematic of the stirrer and vessel designs used in this study and the corresponding parameters investigated.

Results and Discussion: Comparing the USP2 design and systems with the same stirrer but flat-bottom vessel reveals a skewed fluid velocity and shear rate distribution for the flat-bottom design, indicating more homogeneous mixing compared to the wide distribution observed in the USP2 design. This suggests that a flat bottom vessel offers better mixing homogeneity compared to a round bottom vessel. Analyzing fluid flow streamlines in different designs demonstrates that hydrofoil stirrers generate more suspension or upward movement of fluid compared to paddle stirrers as shown in Fig.2. Therefore, when impellers are of similar size, hydrofoil designs generate higher fluid velocities in the coning area. Furthermore, the angle of blade attachment to the hub influences the fluid velocity in the coning area in a way that 60° angle design generates more suspension than 45° angle design. Finally, it was observed that the volume-average shear rates and fluid velocities were higher in the USP 2 design compared to the other designs at the same rotational speed. This indicates a greater dissolution rate and hydrodynamic impact in the USP 2 design[1].

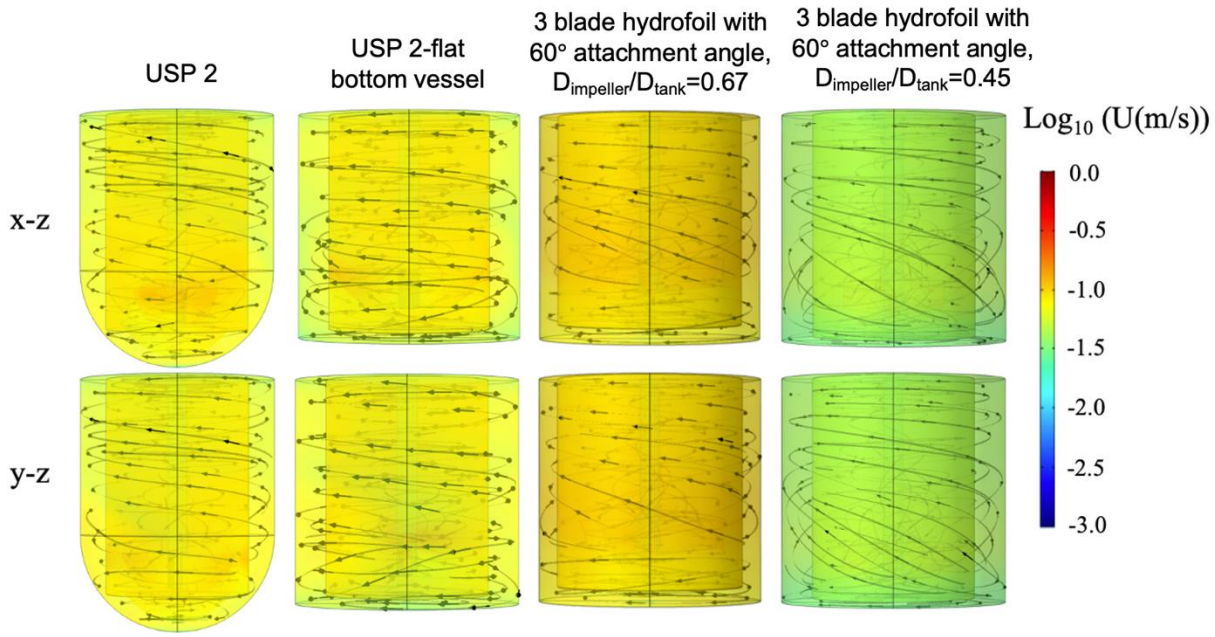


Figure 2. The fluid pattern in different design systems from different views.

Conclusions: The findings indicate that the paddle stirrer design leads to heterogeneous shear rate and velocity distributions within the vessel compared to the other designs, suggesting suboptimal performance. In contrast, the simulations demonstrate that the use of a hydrofoil stirrer promotes upward fluid movement, resulting in a more homogeneous distribution of shear rate and velocity. Additionally, the adoption of a flat bottom vessel reduces hydrodynamic heterogeneity compared to a round bottom vessel. These insights provide valuable guidance for the development of improved in vitro dissolution testing devices, emphasizing the importance of optimized design considerations to minimize hydrodynamic variability, enhance dissolution characterization, and reduce variability in dissolution test results. Ultimately, such advancements hold potential for improving in vitro-in vivo correlations in drug development.

Reference:

1- Niloufar Salehi et al., *Hierarchical Mass Transfer Analysis of Drug Particle Dissolution, Highlighting the Hydrodynamics, pH, Particle Size, and Buffer Effects for the Dissolution of Ionizable and Nonionizable Drugs in a Compendial Dissolution Vessel*, Mol. Pharmaceutics, 2020, **17** (10): p.3870–3884.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Three Complementary Autonomous In-Vitro Release Test (IVRT) Methods for Liposomal Doxorubicin Formulations

Savithra Jayaraj (savithra.jayaraj@fda.hhs.gov)[1], Thilak Mudalige (thilak.mudalige@fda.hhs.gov)[1], Prabhath Gamage[1], Wenlei Jiang[1], Isabelle Niyonshuti[1], Fatma Yurtsever[1]

[1]U.S. Food and Drug Administration, Jefferson, Arkansas

Purpose: A considerable amount of research has been conducted over the past six decades on the use of liposomes as drug delivery systems, and the in vitro drug release test (IVRT) is a critical method in both premarket development and post-approval quality control of liposomal drug products. Most IVRTs for liposomes require a separation step such as dialysis or solid phase extraction to separate and then quantitate the released active pharmaceutical ingredient (API) from the liposome-bound API. However, these separation methods are lengthy and have been known to induce an artificial drug concentration gradient or liposome rupture, resulting in inaccurate quantitation of released drug. The objective of the current work was to develop new IVRT methods to acquire accurate, real-time release of doxorubicin (DOX) from liposomal encapsulated doxorubicin hydrochloride formulations without additional separation steps.

Methods: Five liposomal doxorubicin formulations manufactured by Baxter Healthcare Corporation (Baxter), Sun Pharmaceutical Industries Ltd (Sun Pharma), Dr. Reddy's Laboratories Ltd (Dr. Reddy), Ayanna Pharma Ltd (Ayana Pharma), and Zydus Pharmaceuticals (Zydus) were obtained for the in vitro release study. We developed three automated drug release profiling methods based on capillary electrophoresis (CE), nanoparticle exclusion chromatography (NEC), and electroanalytical chemistry (EC). CE and NEC methods automated sampling and separation, and quantitated released DOX using optical absorbance and fluorescence, respectively. The separation mechanism of each method and the release media used are in Table 1. The DOX release studies were conducted at different temperatures (37.0 °C, 47.0 °C and 52.0 °C) and pH (5.5, 6.0, 6.5 and 7.4) conditions in ammonium formate-based release media, and the released sample were automatically collected and analyzed up to 24 hours.

Results and Discussion: The automated IVRT methods can separate liposomal DOX from released DOX and provide quantitative measurements over time without additional sample preparation. The methods were validated according to the ICH M10 guidelines for bioanalytical method validation. For all three-methods, the regression analysis correlation coefficient (R^2) was greater than 0.995. The limits of quantifications (LOQ) for DOX were calculated to be 9.68 µM, 3.00 µM and 3.00 µM, respectively, for CE, NEC, and EC methods, and the limits of detection (LOD) were 3.19 µM, 1.00 µM and 1.00 µM, respectively.

The effect of ammonium formate concentration, media pH and temperature on DOX release were studied with all three analytical methods and shows similar trends. For example, Figure 1 shows data collected using NEC method. With the increase of ammonium formate concentration, there is slight increase on DOX release (Figure 1A) and DOX release rates significantly increases with temperature (Figure 1B) and media pH (Figure 1C/D). Complete doxorubicin release (100%) was obtained in 6 hours at pH 6.5 at 47.0 °C with 200 mM ammonium formate release buffer using NEC method and these conditions were used for further formulation comparison with different IVRT methods.

Figure 2 shows the drug release profiles obtained for different liposomal doxorubicin formulations at pH 6.5 and 47 ºC using NEC, CE or EC methods. About 100% Dox release was observed with NEC and CE methods at 6-8 hours while less than 90% release with EC methods at 16 hours. In addition, some dox degradation was observed at later hours with NEC method. All tested formulations showed similar dissolution profiles with each IVRT method.

Conclusions: We have developed three new fully automated IVRT methods for liposomal formulations that use small sample volumes, accommodates continuous sampling, separates and quantitates the released DOX simultaneously, resulting in less labor-intensive and more accurate analysis capabilities without the introduction of error from separation methodologies. These IVRT methods were successfully demonstrated for the release profiling of liposomal doxorubicin formulations. The advantages and limitations of each method were also compared, facilitating the application of optimal method for release profiling of other liposomal drug products, e.g., Vyxeos.

Table 1. Comparison of Three Autonomous In Vitro Release Methods for Doxorubicin HCl Liposomes

Method	Separation and/or Quantitation Mechanism	Release Media	Formulation volume	Injection volume	Advantage	Limitation
Capillary Electrophoresis (CE)	Released and liposomal DOX separated based on different electrophoretic mobility.	500 µL; 20 mM L-histidine, 200 mM ammonium formate, 5% sucrose	10-25 µL	Few nL	Small sample volume; all aqueous solvents. Minimal drug degradation	Applicable to charged APIs
Nanoparticle Exclusion Chromatography (NEC)	Released and liposomal DOX separated based on different partition/separation into through-pores (1 µm) or mesopores (10 nm).	2 mL; same as above	25-50 µL	Few µL	Separate released intact DOX from degraded DOX	Liposomal must be stable
Electroanalytical Chemistry (EC)	Square wave voltammetry mode used to quantitate the released DOX (the only redox-active analyte) by measuring the current at the pulsed potential ranges.	5 mL; 20 mM L-histidine, 200 mM ammonium formate, 150 mM NaCl, 5% sucrose	50-100 µL	No sampling	Direct measurement of released Dox in the presence of liposomal DOX	Limited to redox-active analytes; sensitive to air in the container

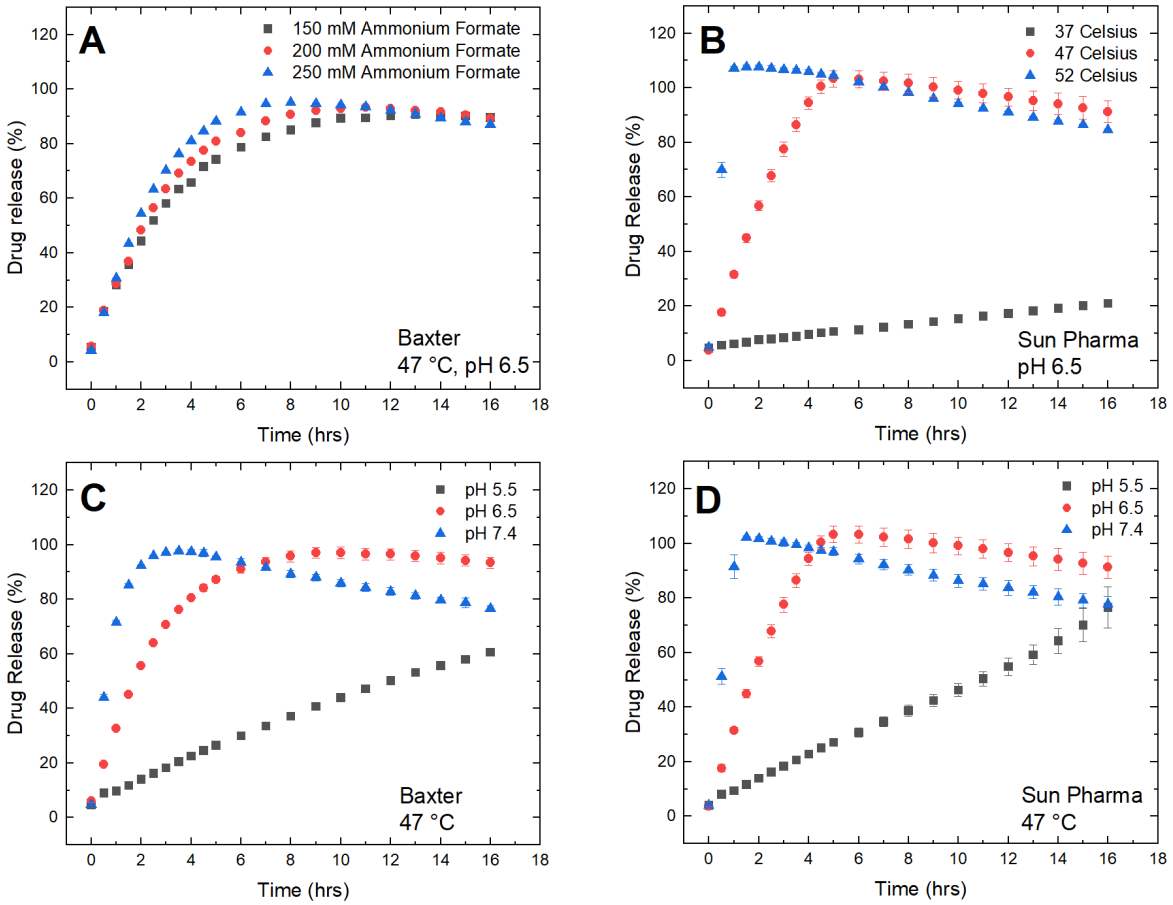


Figure 1. Effect of ammonium formate concentration (A), temperature (B) and pH (C and D) on DOX release profiles of liposomal doxorubicin HCl formulations in different release media using the Nanoparticle Exclusion Chromatography (NEC) method (mean ± SD, N=3). Histidine buffer pH was adjusted with HCl or NaOH.

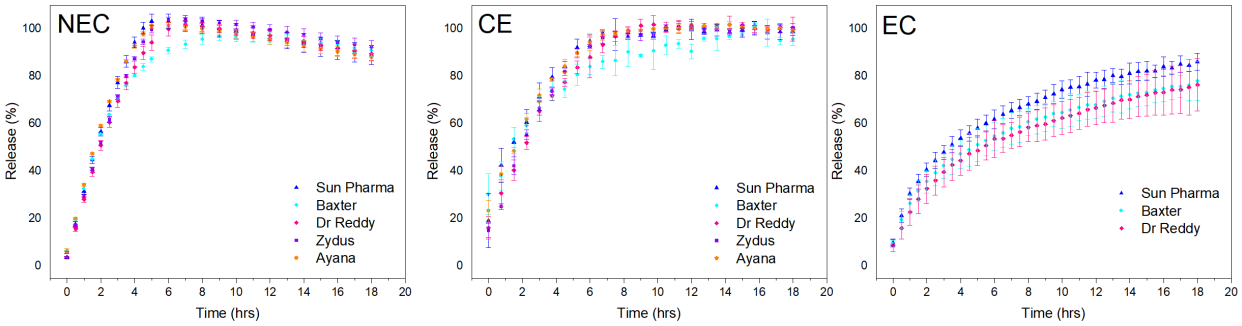


Figure 2. Drug release profiles of different formulations of the liposomal doxorubicin HCl at pH 6.5 and 47 ºC using NEC, CE and EC methods (mean ± SD, N=3).

Acknowledgements: This project was supported in part by an appointment to the Research Participation Program at the U.S. Food and Drug Administration administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and the U.S. Food and Drug Administration. The authors would like to acknowledge Drs. Paul Howard, Marilyn Khanna, Sean Linder, Jennifer Brzezinski and Selen Stromgren of FDA/ORA and Drs. Lei Zhang and Robert Lionberger of FDA/CDER for their support.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Assessment of 250-mL Volume Vessels for Use in Biorelevant Dissolution

Angela Hu (angela.hu2@bms.com)[1], Wei Chen (wei.chen1@bms.com)[1], Xujin Lu[1]

Bristol Myers Squibb, New Brunswick, New Jersey

Purpose: To compare Chinese Small Volume (CSV) vessel with USP standard vessel for dissolution using 250 mL volume of media targeted for biorelevant dissolution. To establish testing parameters for using the CSV that can generate comparable dissolution results as using the USP standard vessels.

In-vitro biorelevant dissolution is an important tool for drug development that allows for prediction of in-vivo performance of drug products. Biorelevant dissolution is typically performed in 250 milliliters (mL) of media to simulate the average volume of gastrointestinal fluids in the body. But current biorelevant methods mostly use either a 500-mL or 1-Liter (L) sized vessels on a USP apparatus 2. Several challenges have been encountered with using in-situ UV-fiber optics (UVFO) for such dissolution. Due to the low volume of medium in the vessel, 250 mL, conventional dip-in probes cannot be placed in the vessel above the paddle at the USP recommended sampling point. J-shaped probes have been utilized and placed under the paddle. However, placement of these j-shaped probes is inconvenient and increases measurement variability. 250 mL Chinese Small Volume (CSV) vessels have been considered as an alternative to overcome the challenges. The CSV vessel is commercially available and in compliance with the Chinese Pharmacopeia. It also allows for easier placement of the UVFO dip-in rod-shaped probes above the paddle and better experimental repeatability was observed. As the CSV vessels with paddles have different size, shape, and hydrodynamics from the USP standard vessels, in this work, these differences of the two types of vessels were studied, and efforts were made to define the agitation parameter for using the CSV vessels so that the dissolution results are comparable to that from using the USP standard vessels.

Methods:(1) Dissolution testing: An Agilent 708-DS bath was fitted with TruAlign 1000 mL and 250 mL CSV vessels. All vessels were filled with 250 mL of media. USP Prednisone calibrator tablets were used as a model drug. UV fiber optic j-shaped probes were used in the USP apparatus 2 vessels and the dip-in rod-shaped probes were used in the CSV vessels. A Rainbow® Dynamic Dissolution system (Pion Inc.) was used to measure absorbance and determine concentration of the released drug.

(2) Computational Fluid Dynamics (CFD) simulation with Noyes-Whitney equation model [1]: This model was developed to mimic the hydrodynamics in the dissolution vessels and the testing parameters. A Sherwood number was calculated using the model for the testing condition of the USP standard vessels with a paddle speed of 50 rpm. The Sherwood number was then used to predict the paddle speed for the CSV vessels to generate a comparable dissolution result as using the USP standard vessels for the model drug. Dissolution tests in FaSSIF for two drug products (D1 and D2) were performed to confirm the prediction.

Results: Initial dissolution studies were performed with 10 mg Prednisone tablets in 250 mL of water in a CSV vessel at 50 rpm, 100 rpm, and 140 rpm, and in a USP vessel at 50 rpm. Data from the initial studies were supplemented to CFD modeling. A scaling factor Sherwood number of 15.8 was calculated by utilizing the model as described in Cao et al [2] through a dimensionless correlation with energy dissipation rate (power draw by CFD divided by liquid weight) simulated by CFD and inputs of conditions in a USP standard vessel with a stirring speed of 50 rpm and 250 ml fill volume (see Figure 1). The developed dissolution model combined CFD simulation and the Noyes-Whitney equation model was used to predict a stirring speed of 84 rpm in CSV with 250 ml fill volume for dissolution profiles of the 10 mg Prednisone tablets. Experimentation was performed in FaSSIF for two drug products (D1 and D2) that confirmed the predicted paddle speed generated a similar dissolution profile to that of the one from the USP standard vessel with a paddle speed of 50 rpm (see Figure 2).

Conclusion: In this work, we developed a model to predict dissolution of the USP calibrator prednisone tablets in water in both the USP apparatus 2 and CSV vessels using data collected from initial experiments run with different agitation speeds and utilizing a combination of CFD modeling and the modified Noyes-Whitney equation. A scaling factor was calculated and used in prediction of an agitation speed in the CSV vessels that generated a comparable dissolution profile to that in the USP standard vessels. The predicted agitation speed resulted in comparable dissolution profiles observed in experiments run with the two vessels.

References:

1. Noyes, A. A.; Whitney, W. R. The rate of solution of solid substances in their own solutions. Journal of the American Chemical Society 1897, 19, 930–934.
2. Cao, H.; Amador, C.; Jia, X.; Li, Y.; Ding, Y. A modelling framework for bulk particles dissolving in turbulent regime. Chemical Engineering Research and Design 2016, 114, 108–118.

Figure 1:

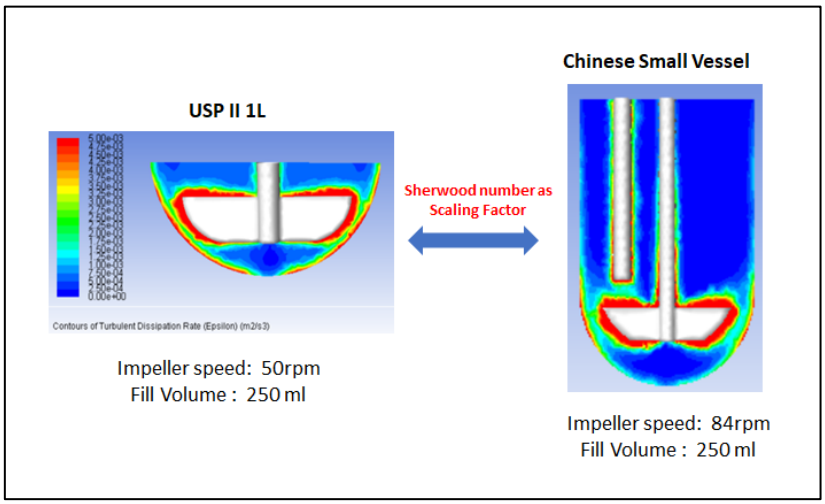
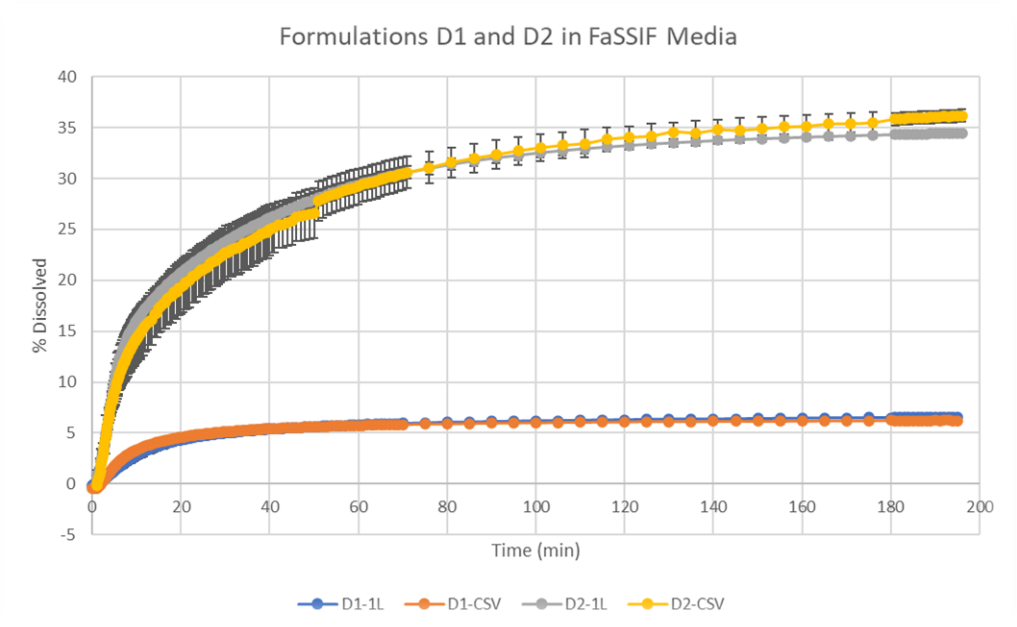


Figure 2:



DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Revolutionizing Drug Delivery: Twin-Screw Melt Coating Granulation for Enhanced Oral Bioavailability, Immediate and Controlled Release

Zankrut Vyas (zankrut.vyas@rutgers.edu)[1], Fernando Muzzio (muzzio@soe.rutgers.edu)[1], Riya Shinde[1], James Scicolone[1]

[1]**Rutgers University, Piscataway, New Jersey**

Purpose: As human understanding of diseases expands, novel drug molecules are being discovered each year. However, formulating these drugs for oral dosages poses a significant challenge due to limited drug bioavailability which is preliminary attributed to poor solubility. It is estimated that nearly 40% of newly discovered drugs are poorly soluble [1]. To address this problem, several techniques are deployed including melt granulation [2,3]. Melt granulation is a process that does not require solvents but uses a solid powder binder to transform powder into granules at elevated temperatures. When heated to a specific temperature, the low melting point solid binder melts and coat the active pharmaceutical ingredient (API) to produce well flowing granules through either distribution or coalescence. Melt granulation also allows us to produce granules with high drug loading (> 80 weight percent API). In addition to that, melt granulation facilitates continuous manufacturing process, i.e., enabling the production of solid dosage forms in a continuous flow system, thereby reduction in number of process steps and time, energy consumption, costs to produce a final product. This study explores the utilization of melt granulation technique, using a twin-screw granulator (TSG), to improve the solubility and manufacturability of fenofibrate, an API that exhibits poor flow and low solubility. The study also focuses on creating direct compaction (DC) formulation for making tablets with modified release profiles.

Methods: A granule formulation comprising a primarily API (>80 wt.%), disintegrant (3 to 5 wt.%) and low melting point surfactant (10 to 15 wt.%), was used to determine the range of operational process parameters for TSG, such as screw configuration, screw rotational speed, granulation temperature, and feeder throughput. After identifying the acceptable values of the process parameters, a 2-level 2-factor 2k full factorial design of experiments (DOE), with center points, focusing on screw speed and mass throughput, was conducted to find optimal conditions for granulation. The granules size distribution, true and bulk density, and dissolution rate were evaluated for all DOE conditions. The granules can be filled into capsules or compact into tablets with direct compaction formulation. Granules with immediate release dissolution profile were obtained and developed into several DC formulations to generate tablets with immediate, sustained, and controlled release profiles.

Results: The analysis of melt-coated granules shows a good flowability, consistently uniform product and exhibits significantly enhanced dissolution profile when compared to the pure API under all experimental conditions specified by the DOE. The addition of 10% surfactant in granule formulation results in a 60% increase in the dissolution rate, while the addition of 15% surfactant yields immediate release (IR) granules with a remarkable 110% improvement in dissolution rate compared to the pure API. Figure 1 provides a visual representation of this data. Figure 2 depicts distinct release profiles of a direct compaction tablet formulation developed using immediate release granules. This tablet formulation primarily comprises melt-coated granules, binder, and lubricant.

Conclusion: An effective method for converting a poorly flowing and poorly soluble API into granules with excellent flow properties and immediate release characteristics has been successfully demonstrated. Once the immediate release granules are obtained, additional granular material can be incorporated to create a direct compaction tablet formulation. The utilization of immediate release granules to the development of a tablet formulation that exhibits a controlled and sustained release profile is also successfully shown.

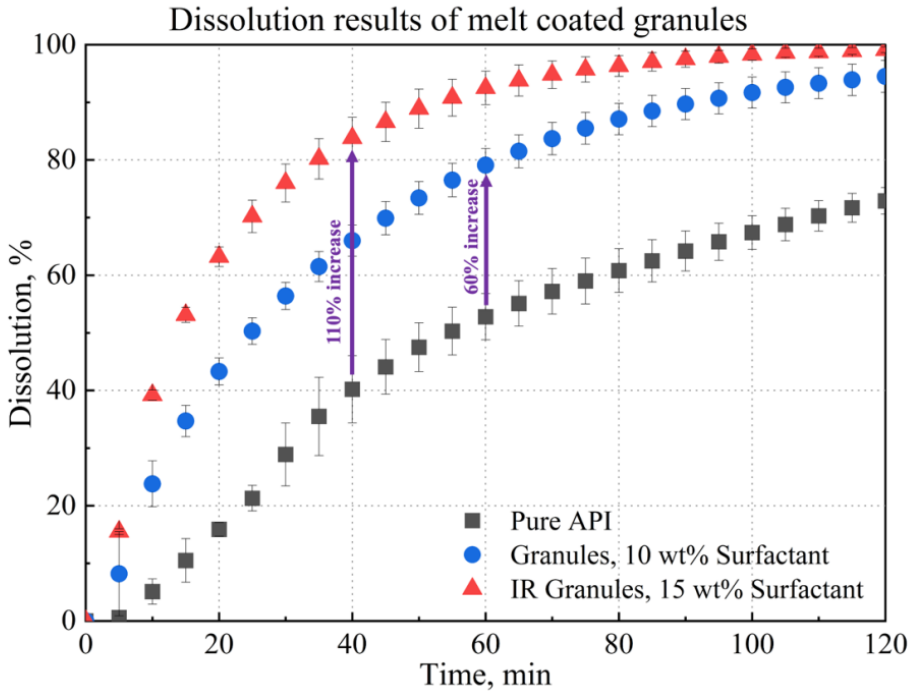


Figure 1: Dissolution enhancement of melt coated granules

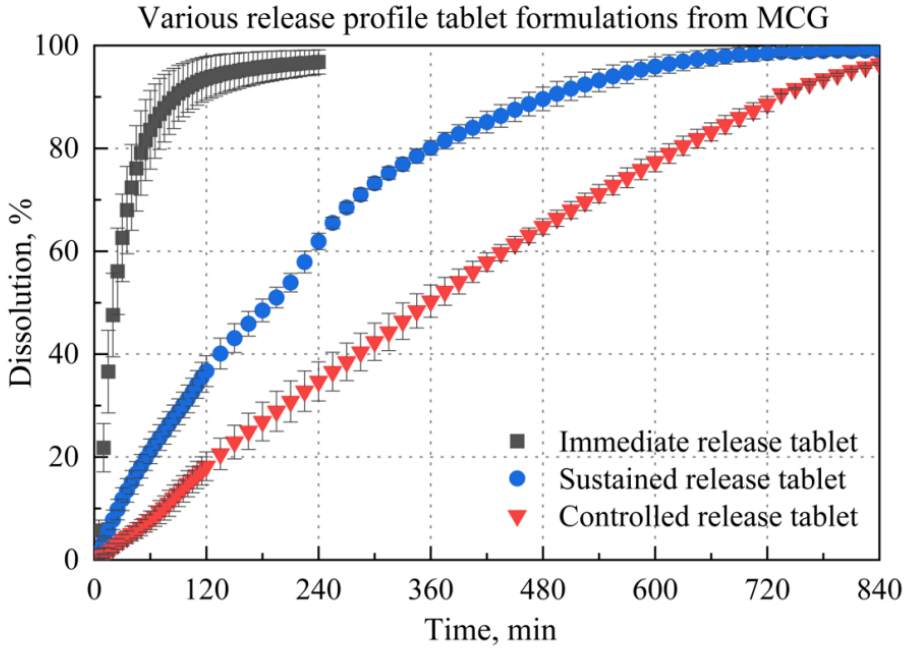


Figure 2: Immediate and modified release tablets from immidiate release melt-coated granules

References:

1. Savjani, K. T., Gajjar, A. K., & Savjani, J. K. (2012). Drug Solubility: Importance and Enhancement Techniques. *ISRN Pharmaceutics*, *2012*, 195727. L

2. Lakshman, J. P., Kowalski, J., Vasanthavada, M., Tong, W.-Q., Joshi, Y. M., & Serajuddin, A. T. M. (2011). Application of melt granulation technology to enhance tabletting properties of poorly compactible high-dose drugs. *Journal of Pharmaceutical Sciences*, *100*(4), 1553-1565.

3. Yang, D., Kulkarni, R., Behme, R. J., & Kotiyan, P. N. (2007). Effect of the melt granulation technique on the dissolution characteristics of griseofulvin. *International Journal of Pharmaceutics*, *329*(1), 72-80.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: Computational Tools, PBPK Modelling

Effect of Surface pH on Acidulant's Dissolution under Buffered Condition

Venkata Krishna Kowthavarapu (kowthavarapu.v@ufl.edu)[1], Rodrigo Cristofoletti (rcristofoletti@ufl.edu)[1], Tatiana Lakovleva[1], Stephan Schmidt[1], Cordula Stillhart[2], Neil John Parrott[3]

[1]Center for Pharmacometrics and Systems Pharmacology, Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL 32827, USA, Orlando, Florida | [2]Pharmaceutical Research & Development, Formulation | [3]Pharmaceutical Research & Early Development, Roche Innovation Center Basel, F. Hoffmann—La Roche Ltd., 4070 Basel, Switzerland

Background & Rationale: Orally delivered drug products must first pass through the gastrointestinal (GI) tract, where they will dissolve, before being absorbed through the intestinal epithelium. In vivo dissolution is the rate limiting factor for the oral administration of BCS class II drugs with low solubility and high permeability. The *in vivo* dissolution rate of drug products is determined by physicochemical drug properties, formulation parameters, as well as physiological parameters like gastric emptying rate, hydrodynamic conditions caused by intestinal motility, ionic strength, buffer concentrations, bile salt concentrations, and pH. The solubility of weakly basic BCS II drugs is pH-dependent, with higher solubility at low pH and significantly lower solubility at higher pH. Since the GI tract has a pH range from acidic to basic, this will greatly alter the solubility of ionizable weak base drugs. These drugs are more prone to ionization and solubilization at the stomach's acidic pH and to precipitation at the small intestine's basic pH. Moreover, food, drug treatment and pathological conditions have the potential to alter pH of fluids in the GI tract, which has an impact on drug dissolution. To overcome the challenges associated with these alterations in gut pH for weak base drugs, different techniques, such as addition of acidulant, solubilizers, or complexing agents, are being used. There are different factors to be considered while formulating a weak base drug with acidulant as an excipient such as physicochemical properties of drug and acidulant, amount of acidulant, dosage form and other considerations. The purpose of this study was to establish a stepwise biopharmaceutical modeling framework for BCS class II, weakly basic drugs, in which the relevant biopharmaceutical parameters are estimated from in vitro data and are subsequently integrated into PBPK models to predict the in vivo exposure of drug products. Based on drug, acidulant, and reactant diffusion coefficients, model equations for calculating surface pH for monoprotic and diprotic bases with monoprotic or diprotic acidulants in buffered species are proposed in this study (Figure 1a).

Methods: This work applies a model-based framework to describe the effect of monoprotic (betaine hydrochloride-BET) and diprotic (tartaric acid-TAR) acidulants in the buffered environment using mass transport models. The mass transport analysis relies on the film theory, which suggests the presence of a diffusion boundary layer adjacent to the drug dissolving surface. In view of ionization capabilities and the concentration gradient across the diffusion boundary layer, acidulant can undergo simultaneous diffusion and chemical interactions with reactive species in the bulk solution, altering the pH at the dissolving solid surface and in the surrounding boundary layer. Expanding on Mooney et al.'s classical approaches, Fick's law of diffusion was applied with simultaneous chemical reactions, followed by the application of boundary conditions and a numerical solution for surface pH, yielding a third-degree and fourth-degree polynomial equation for monoprotic and diprotic acidulants, respectively [1,2]. These polynomial equations are solved using MATLAB R2022b software.

Results and Discussion: The model was evaluated over a wide range of buffer concentrations using acetate buffer at bulk pH 4.5. The critical physicochemical properties that are required for accurate surface pH predictions such as molecular weight, ionization constants, density and intrinsic solubility were adapted from the literature, and the diffusion coefficient was calculated using the Stokes Einstein equation for monoprotic (BET) and diprotic (TAR) acidulants listed in Table 1. The surface pH of monoprotic (BET) and diprotic (TAR) acidulants is predicted using algebraically solved polynomial equations, based on their physicochemical properties.

When the total buffer concentration in the bulk solution is increased at constant bulk pH, the steady-state pH that exists at the solid-liquid interface, namely surface pH or pH_0, is increased more in the monoprotic acidulant than in the diprotic acidulant (Figure 1b). As the buffer concentration increases, the buffer species swamps the diffusion layer and will control the surface pH. As a result, the total bulk concentration of the dissolving acidulant tends to be critical, in determining the initial dissolution rate of that acidulant.

Conclusion: This study provides a mechanistic insight into the dissolution behavior of monoprotic and diprotic acidulants. The acidulants lower the surface pH, which improves the dissolution rate of a weakly basic drug. Mass transfer analysis of the surface pH allows for the evaluation of the acidulant's ability to dissolve the weakly basic drug at the dissolving surface. The findings indicate that diprotic acidulant (TAR) is more efficient in reducing surface pH than monoprotic acidulant (BET). This gives useful information about the thermodynamic behavior of the acidulants, which can help to select the most suitable acidulant for orally administered weakly basic drug product development.

References:

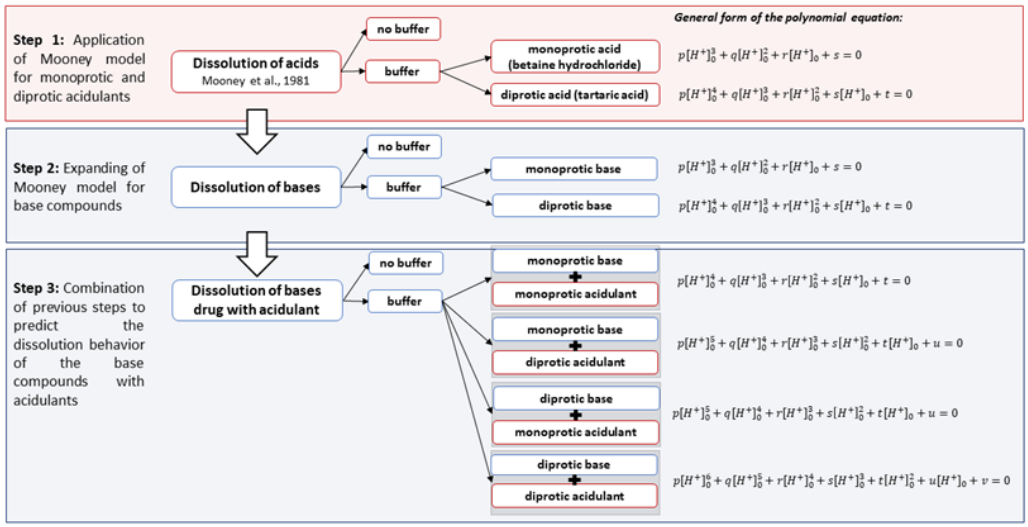
1. Mooney, K.G.; Mintun, M.A.; Himmelstein, K.J.; Stella, V.J. Dissolution Kinetics of Carboxylic Acids II: Effect of Buffers. *J. Pharm. Sci.* **1981**, *70*, 22–32.

2. Mooney, K.G.; Mintun, M.A.; Himmelstein, K.J.; Stella, V.J. Dissolution Kinetics of Carboxylic Acids I: Effect of PH under Unbuffered Conditions. *J. Pharm. Sci.* **1981**, *70*, 13–22.

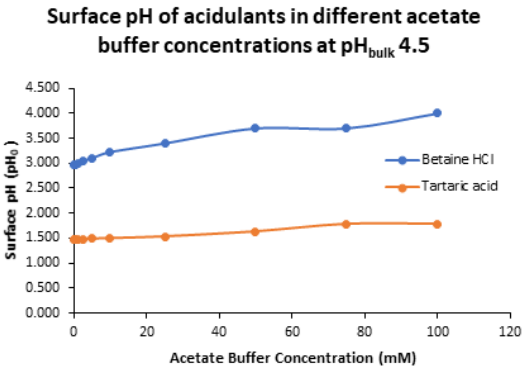
Table 1: Physicochemical properties of acidulants

Acidulant	pKa[a]	Intrinsic solubility[b] (mg/mL)	Diffusion coefficient[c] (cm^2/sec)	Molecular weight[d] (g/mol)	Density[e] (g/cm^3)
Betaine Hydrochloride (BET)	1.94	647	5.79×10^{-7}	153.61	1.65
Tartaric acid (TAR)	2.90, 4.03	21	7.03×10^{-7}	150.10	1.75

[a, b, d, e]pKa, intrinsic solubility, molecular weight and density were adopted from the literature. [c]Diffusion coefficient is calculated using the Stokes Einstein equation



(a)



(b)

Figure 1: (a) Schematic representation of the model equations for calculating surface pH using (i) Mooney model for monoprotic and diprotic acids in buffered species, (ii) Expanding Mooney model for monoprotic and diprotic bases in buffered species and (iii) Expanding Mooney model for the combination of monoprotic or diprotic bases with monoprotic or diprotic acidulants in buffered species, (b) Surface pH of acidulants in different acetate buffer concentrations at bulk pH 4.5

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Dissolution & Solubility Modulation

Assessing the In Vitro Performance of Solid Dosage Forms Over-encapsulated with the ID-Cap System for Improved Compliance

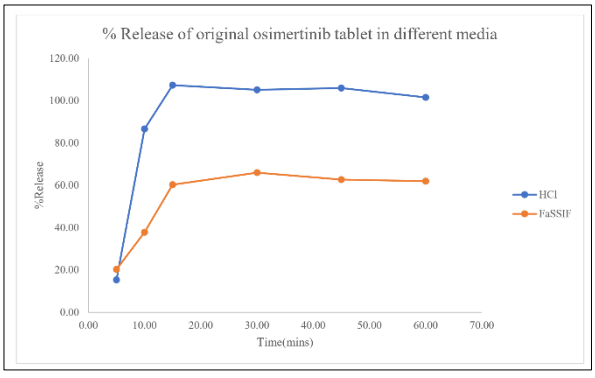
Kajal Gupta (guptak@ufl.edu)[1], Rodrigo Cristofoletti (rcristofoletti@cop.ufl.edu)[1], Nitin Charbe[1]

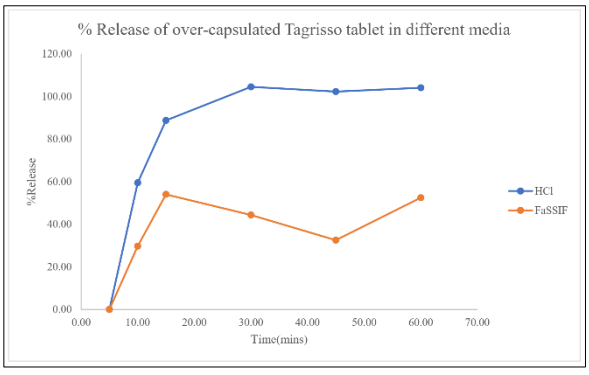
[1]**University of Florida, Orlando, Florida**

Purpose: The ID-Cap™ System is a novel approach for monitoring and tracking oral medication adherence in clinical studies. We have investigated the *in vitro* performance of solid dosage forms over-encapsulated with the ID-Cap™ System, with a focus on Tagrisso® (osimertinib mesylate). The research aims to investigate whether the over-encapsulation process affects the dissolution profile and overall performance of the original drug product. We tested the hypothesis that the IDCap™ System does not compromise the dissolution behavior of the over-encapsulated dosage form, ensuring its effectiveness and therapeutic outcomes while improving patient compliance in clinical settings.

Methodology: *In vitro* dissolution experiments were conducted in simulated gastric (0.1 N Hydrochloric acid) and Fasted State Simulated Intestinal Fluid (FaSSIF) condition. The experiment used original tablet and over encapsulated tablets with ID-Cap™ System. A liquid chromatography method was developed using osimertinib and nilotinib as internal standard, and the samples were quantified using LC-diode array detector. The two-dissolution profile results were compared using f2 statistics, as per current regulatory FDA and ICH guidelines.

Results: The dissolution profile of the drug indicates a comparable release profile, with a 5-minute time lag observed when using the tablet in ID-Cap System encapsulated form. The f2 statistic used to assess the similarity of two dissolution profiles, with a value of 56.14 in gastric pH media (0.1 N Hydrochloric acid) and 51.51 in simulated intestinal media (FaSSIF). The results obtained show that the f2 values are greater than 50 indicating similarity between the two dissolution profiles of original and over encapsulated tablet. The ID-Cap™ System consisted of an ingestible microsensor that is embedded in an oral dosage form and, once activated by stomach or intestinal fluid it communicates through digital messages to an external wearable device to confirm ingestion, which was also recorded during the study.





Conclusion: Osimertinib is a BCS class III drug, and it showed a very rapid *in vitro* dissolution profile under defined conditions. The investigation on the use of ID-Cap system also gave similar dissolution profile when compared via f2 statistics. Hence, the over-encapsulation with novel ID-Cap System does not affect the performance of the original drug product, beyond a slight delay in dissolution start and the time to achieve 85% of the dose dissolved in the media.

References:

1. MedSurgPI LLC, 3700 Lark Farm Road, Franklinton, NC 27525, USA & Klein, G. L. The Case for digital Pill Use in Clinical Trials. *Clin. Trials Pract. – Open J.* **4**, 16–21 (2021).
2. Flores, G. P. *et al.* Performance, Reliability, Usability, and Safety of the ID-Cap System for Ingestion Event Monitoring in Healthy Volunteers: A Pilot Study. *Innov. Clin. Neurosci.* **13**, 12– 19 (2016)

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps® American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Multi-functionalization of 3D Printed Scaffolds with Quercetin and Vitamin D3 Encapsulated Solid Lipid Nanoparticles for Orthopedic Applications

Vishal Chaudhari (vishal.chaudhari@wsu.edu)[1], Susmita Bose (sbose@wsu.edu)[1]

[1]**W. M. Keck Biomedical Materials Research Laboratory, School of Mechanical and Materials Engineering, Washington State University, Pullman, WA 99164, USA, Pullman, Washington**

Purpose: With an aging population possessing longer life expectancies, bone diseases, and anomalies have served as a constant impediment to bone regeneration. Host body rejection of transplants may be caused by the intricate biology of bone tissues, the biocompatibility of scaffold materials, the potential for metastasis initiation, and bacterial infections [1]. The 3D printed calcium phosphate scaffolds provide an ideal option with their biocompatibility and biodegradability but still need upgradation to multifaceted devices. Therefore, the integration of natural medicinal compounds (NMCs) having potent osteogenic and antimicrobial properties could address the issue. Quercetin and Vitamin D3, obtained from edible sources have been reported to induce bone regeneration and reduce inflammation, bacterial growth, and cancer metastasis [2, 3]. But poor physicochemical properties halt their clinical applications and need to be formulated in the delivery system. Solid lipid nanoparticles (SLNs) have been shown to be a promising carrier system for lipophilic drugs [4]. Finally, the functionalization of a 3D printed CaP scaffold with quercetin and vitamin D3 encapsulated SLNs can address issues associated with host body rejection of transplants and improve patient compliance.

Methods: The 3DP scaffolds were fabricated using a binder jet printer (Innovent+, ExOne LLC, Irwin, PA, USA). Solid lipid nanoparticles were prepared with the melt emulsification method followed by probe sonication. Quercetin and vitamin D3 were encapsulated within a matrix of the solid lipid Compritol 888 ATO and characterized thoroughly. Approximately 200µg drug solution and SLNs were drop-cast over 3DP CaP scaffolds individually and used further in the study.A drug release study for functionalized scaffolds was carried out at 37°C and 150 rpm. The release media of phosphate buffer (pH 7.4) and an acetate buffer (pH 5.0) were used. Aliquots were taken at specific times and replenished with fresh media. Samples were analyzed for quercetin and vitamin D3 at respective wavelengths of 370nm and 260nm using a UV-Vis multimode spectrophotometer (BioTek, Winooski, VT, USA). Cumulative drug release (%) vs time (days) comprised the release profile. Additionally, data was submitted to various curve-fitting equations using MATLAB®. Microscopic analysis was performed for surface morphology. Further, *in-vitro* cell material interactions were studied for developed functionalized scaffolds against human fetal osteoblast (hfOB) cells, MG-63 osteosarcoma cells, and the bacteria *Staphylococcus aureus* strain [5, 6].

Results:

• Multi-functional scaffolds direct toward a newer dimension of drug delivery. Integration of nanocarriers with 3D printed CaP scaffolds is a novel approach that aims to obtain localized delivery of NMCs and can aid in faster bone recovery and prevent revision surgery.
• Quercetin and vitamin D3 were successfully encapsulated within a solid lipid matrix as SLNs. Particle size for developed SLNs showed ~ 90 nm, polydispersity index <0.25, with negative zeta potential.
• The lipidic matrix encapsulated ~97% of NMCs with amorphous conversion during processing as confirmed with DSC and XRD.
• The drug release showed a biphasic release pattern with initial burst release followed by a long-term release up to 60 days. Quercetin and vitamin D3 from SLN-loaded scaffolds showed ~82% and ~98% release at pH 5 and ~49% and ~73% at pH 7.4, respectively.
• Quercetin and vitamin D3 from drug solution-loaded scaffolds showed ~72% and ~55% release at pH 5 and ~31% and ~50% at pH 7.4, respectively.
• Higher and controlled drug release was observed with lipid formulation due to enhanced solubility of the drug as compared to pure drug solution.
• Release profiles followed the Power law showing non-linear diffusion-mediated release kinetics with R2 >0.99.
• The surface morphology for scaffolds analyzed before and after the release study showed higher degradation in acidic pH as compared to phosphate buffer.

• SLNs loaded scaffold showed ~89% reduction in bacterial cell growth as compared to control TCP due to DNA damage and ruptured bilayer lipid membranes induced by the phenolic group from drugs.
• Also, the developed scaffold showed 4.2-fold higher cytotoxicity on day 11 towards osteosarcoma cells as compared to the control. Quercetin induces a reduction in mitochondrial membrane potential and prevents cell growth through the arrest of the G2/M phase and inhibition of metalloproteinases.
• The osteoblastic differentiation and mineralization through alkaline phosphatase activity was observed through hfOB culture. Treated scaffolds showed ~1.27-fold enhancement in hfOB cell viability and supporting bone-forming cell growth.

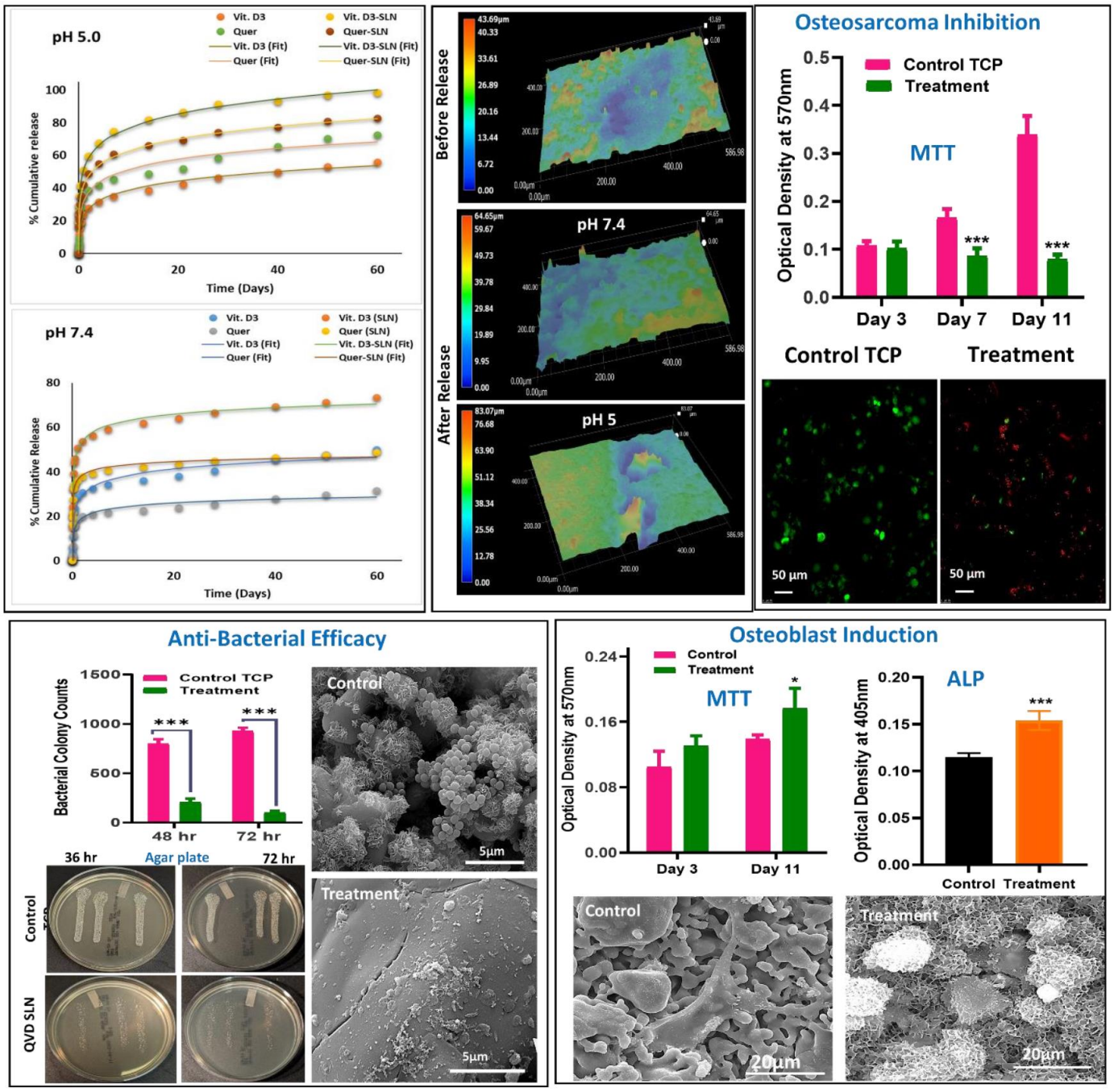


Figure: Characterizations of functionalized 3D printed CaP scaffold in terms of *in vitro* release and surface morphology evaluations followed by cellular evaluation.

Conclusion: Overall, we developed a 3DP scaffold-based localized drug delivery system with the integration of quercetin and vitamin D3 encapsulated SLNs. NMCs were delivered in tandem and showed controlled release of quercetin and vitamin D3 for a longer period. The biocompatibility of scaffolds was assessed through potentiated fibroblast growth. Also, it showed promise in reducing bacterial and cancer cell growth on the scaffold. Our results

promisingly suggest that orthopedic and bone tissue engineering applications can take advantage of tailored CaP scaffolds.

References:

1. S. Bose, M. Roy, A. Bandyopadhyay, Recent advances in bone tissue engineering scaffolds, Trends in biotechnology, 30 (2012) 546-554.
2. Z. Yuan, J. Min, Y. Zhao, Q. Cheng, K. Wang, S. Lin, J. Luo, H. Liu, Quercetin rescued TNFalpha-induced impairments in bone marrow-derived mesenchymal stem cell osteogenesis and improved osteoporosis in rats, American journal of translational research, 10 (2018) 4313.
3. M. Sattary, M. Rafienia, M. Kazemi, H. Salehi, M. Mahmoudzadeh, Promoting effect of nanohydroxyapatite and vitamin D3 on the osteogenic differentiation of human adipose derived stem cells in poly-caprolactone/ gelatin scaffold for bone tissue engineering, Materials Science and Engineering: C, 97 (2019) 141-155.
4. V.S. Chaudhari, P.K. Hazam, S. Banerjee, Lipid nanoarchitectonics for natural products delivery in cancer therapy, in: Sustainable Agriculture Reviews 44, Springer, 2020, pp. 169-203.
5. N. Sarkar, S. Bose, Liposome-encapsulated curcumin-loaded 3D printed scaffold for bone tissue engineering, ACS applied materials & interfaces, 11 (2019) 17184-17192.
6. Bhattacharjee, S. Bose, Zinc curcumin complex on fluoride doped hydroxyapatite with enhanced biological properties for dental and orthopedic applications, Journal of materials research, 37 (2022) 2009-2020.

Acknowledgements: The authors acknowledge the financial support from the National Institute of Dental and Craniofacial Research (NIDCR) of the NIH Grant Number R01 DE029204-01 (PI: Bose) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institute of Health, USA under Award Number R56 AR066361-06 (PI: Bose).

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Modified Dissolution Equipment & Methodologies, including Biorelevant Media & Automation

Hydroxypropyl-β-cyclodextrin (HPBCD) in Insoluble Drug-Loaded Nanoparticles Dissolution Studying: A New Approach to Overcoming Sink Limitations

Yihan Wang (yihanwang@rx.umaryland.edu)[1], Stephen Hoag (shoag@umaryland.edu)[1], Dongyue Yu[1], Xun Li[1], Haixi Cui[1], Iram Maqsood[1], Ryan Pearson[1]

[1]University of Maryland, Baltimore, Maryland

Purpose: Modern drug discovery is revealing a rising number of BCS Class II compounds, representing a substantial portion (50%-60%) of the pharmaceutical pipeline.[1] Maintaining sink condition is vital for accurate dissolution characterization, particularly for BCS Class II compounds with low solubility and high permeability. Achieving adequate dissolution in aqueous solutions, which may mimic physiological conditions, can be challenging for low solubility drugs. Alternative strategies such as increasing the volume of the dissolution medium, using flow-through apparatus, addition of cosolvents, surfactants, or using biphasic media can be employed; however, most of these methods impose greater demands on the analysis instruments and processes. Hydroxypropyl-beta-cyclodextrin (HPBCD) is a modified form of beta-cyclodextrin (β-CD) that improves the solubility and stability of the cyclodextrin. Like the β-CD, HPBCD is a cyclic oligosaccharide with a hydrophobic truncated cone-shaped core that can encapsulate or complex with a wide range of guest molecules. [2] (Figure 1A) Typically, β-CD is used as solubilizer, stabilizer, or taste masking agent. In our study, HPBCD was used as a component of dissolution buffer to help maintain sink condition for BCS Class II compounds. Three BCS Class II drugs with different solubility, Cholecalciferol (VD3, MW 384.6, LogP7.5), lovastatin (LVT, MW 404.5, LogP4.5), and Indomethacin (IND, MW 357.8, LogP3.4) were used as model drugs. The saturation concentrations of model drugs are detected in four different dissolution mediums. For the dissolution studies, the model drugs were incorporated into nanoparticles (NPs) and their release behaviors were evaluated in dissolution medium with or without HPBCD.

Methods: The solubility of model drugs was measured in PBS, 20% methanol in PBS, 200 mM HPBCD in PBS, and 0.1% SDS. Excess amounts of drugs were added to each solution. The saturation concentrations of the 3 drugs were measured via UPLC after 3 days' shaking at room temperature. The recovery and stability of model drugs at 37℃ were measured. For the recovery study, different concentration of drug solutions mixed with blank NPs. After shaking, supernatant was collected by centrifuge and measured by UPLC. For the stability studies, different drug solution concentrations were kept under 37 ℃ for 48 hours. The oil in water (O/W) emulsion method was used to prepare VD3, LVT, and IND loaded nanoparticles. The nanoparticles were dispersed in 10 mL PBS, 200 mM HPBCD in PBS and placed in 50mL centrifuge tubes. The tubes were shaken at 110 rpm and 37 °C. At predetermined intervals, 1 mL of the suspension was withdrawn and replenished with fresh media. The supernatant was collected after centrifugation and analyzed by UPLC for drug release. The cumulative release rate (Q) was determined according to the equation: $Q = \frac{\sum_{n=1}^{i} C_i V_i + C_n V}{W * P}$ (Ci and Cn are sample concentration at given times; Vi is solution volume taken out at each time; V is the total solution volume; W and P are the weight and the drug loading capacity of NPs, respectively). SPSS Statistics (v26) were used to fit the release model.

Results: Compared with the other three commonly used dissolution buffers, HPBCD can help the drug to obtain the best solubility. (Figure 2A) HPBCD also has the best effect in increasing solubility ratios (Sbuffer/SPBS). (Figure 2B) Both the absolute solubility of the drug in HPBCD buffer and the increase ratio relative to PBS are proportional to the LogP of the drug itself. (Figure 2B) The results indicated that the drugs with stronger hydrophobicity (e.g., VD3) were preferring to remain in the hydrophobic cavity of HPBCD and form solubilization complexes. (Figure 1B-F) In the recovery study at 37℃, 48 hours stability study that prior to the nanoparticle release experiment, three drugs are stable in HPBCD buffer. The presence of blank nanoparticles did not interfere with the measurement of the drugs. (Figure 2C)

In the nanoparticle release study, the release behavior of the three drug nanoparticles in PBS and HPBCD was compared. Except for IND, which has the maximum solubility and minimum LogP, there was not an observed difference in release behavior between PBS and HPBCD. (Figure 2D) The release rate of LVT and VD3 increased in HPBCD compared with PBS. (Figure 2E, 2F) IND NPs' release curve in either PBS or HPBCD fit the First order model (R2=0.799 and

0.679 respectively); LVT NPs' fit the Higuchi equation (R2=0.982 and 0.830 respectively); VD3 NPs' release curve of HPBCD buffer (VD3 release was not detected in PBS) also fit the Higuchi equation (R2=0.995).

HPBCD can encapsulate the drug into its hydrophobic cavity that creates sink conditions for subsequent release processes. HPBCD doesn't influence the drug release mechanism from the view that the release model has not been changed.

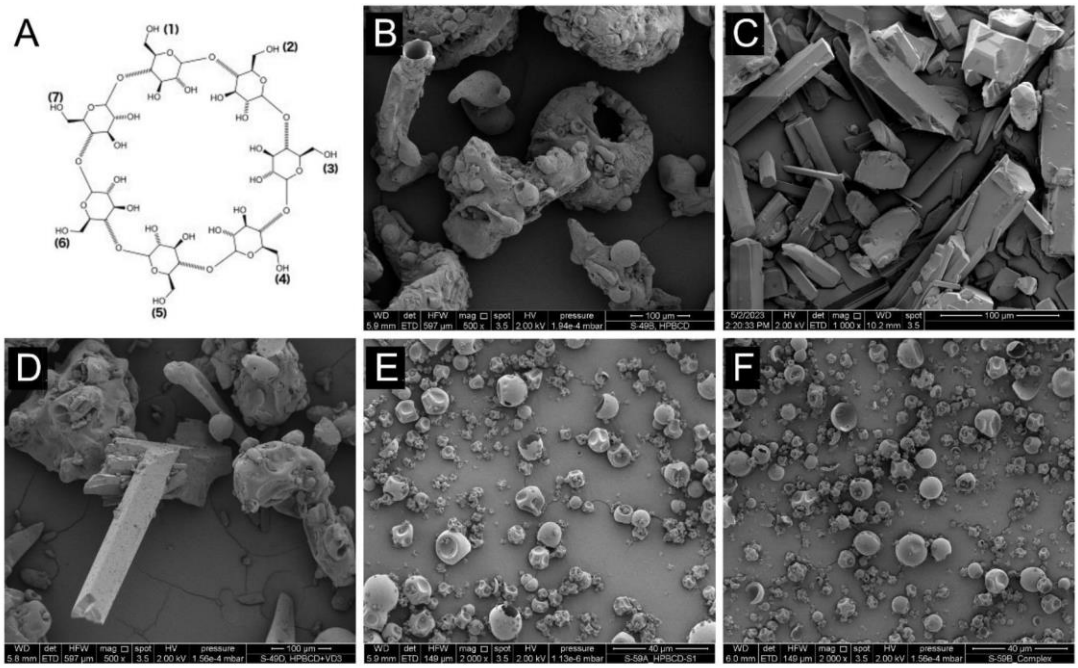


Figure. 1: (A) 2D structure of HPBCD; (B) HPBCD; (C) cholecalciferol (VD3), (D) physical mixture of VD3 and HPBCD; (E) spray dried HPBCD; (F) spray dried cholecalciferol–HPBCD complex particles.

Conclusions: HPBCD could significantly enhance the solubility of hydrophobic drugs. This phenomenon is proportional to the drugs' LogP value. In dissolution medium HPBCD play a solubilizing role. The drug release mechanism from the nano particles was not affected while sink conditions were maintained.

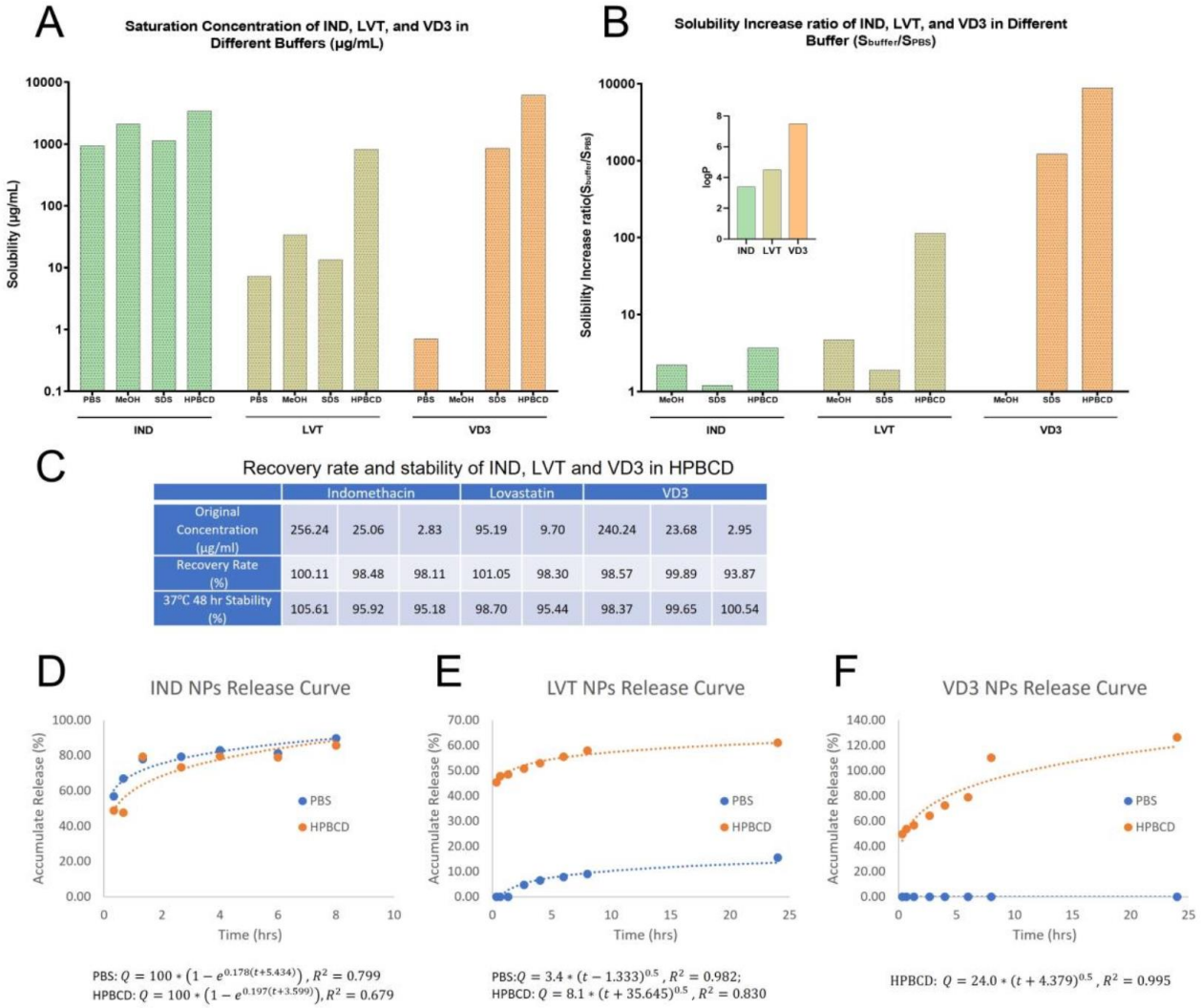


Figure 2. Solubility changes of hydrophobic drugs in different dissolution medium, and IND, LVT, VD3 nanoparticles release curves in PBS and HPBCD. (A) Saturated concentration of IND, LVT and VD3 in different dissolution medium (μg/ml); (B) Solubility increase ratio of IND, LVT and VD3 in different dissolution medium to PBS; (C) IND, LVT and VD3 recovery and stability in HPBCD solution; (D) IND NPs release curves fit the First order model both in PBS and HPBCD; (E) LVT NPs release curves fit the Higuchi model both in PBS and HPBCD; (F) VD3 nanoparticles in HPBCD release curves fit the Higuchi model

References

1. Ku, M.S., *Use of the Biopharmaceutical Classification System in early drug development.* Aaps j, 2008. **10**(1): p. 208-12.
2. Wang, F., et al., *Cholecalciferol complexation with hydroxypropyl-β-cyclodextrin (HPBCD) and its molecular dynamics simulation.* Pharmaceutical Development and Technology, 2022. **27**(4): p. 389-398.

Acknowledgements: Nostopharm Inc. and Maryland Industrial Partnerships (MIPS) for technical assistance and financial support.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: Dissolution & Solubility Modulation

Programmable Pulsatile Dissolution of Drug Nanocrystals from Core-Shell Hydrogel Particles

Lucas Attia (lattia@mit.edu)[1], Patrick Doyle[1], Liang-Hsun Chen[1]

[1]**Massachusetts Institute of Technology, Cambridge, Massachusetts**

Purpose: Core-shell structures have emerged as a drug product geometry that can structure drugs in distinct excipient layers, control release of multiple payloads, and engineer stimuli-responsive functionality.[1–6] Core-shell functionality is vital for delayed release applications, which are important delivery routes to target enteric and colorectal diseases.[7–9] Yet, manufacturing core-shell polymeric structures typically relies on 3-D printing, emulsification with an oil or lipid phase, or multi-step gelations, which have various limitations for the formulation of therapeutics for oral drug delivery.[10,11]

Here, we address these limitations by developing a novel 'dual gelation' process that uses two simultaneous biopolymer gelations to synthesize core-shell particles with non-interpenetrating layers in a single processing step. Through encapsulating API-loaded nanoemulsions in the core hydrogel matrix followed by evaporation of the organic and aqueous phase solvents,[12] we apply a 'bottom-up' method to generate drug nanocrystals inside these core-shell particles. We use this approach to demonstrate tunable pulsatile dissolution of a model hydrophobic API.

Methods: Core-shell hydrogel particles were synthesized using a dripping process (**Figure 1a**). First, we designed thermogelling methylcellulose (MC) nanoemulsions, with a dispersed phase of drug-loaded anisole and a continuous phase of $CaCl_2$ and MC. We use a model hydrophobic API, fenofibrate (FEN), since it is practically water insoluble (0.3 µg mL^{-1} at 37 °C),[13] and can benefit from nanoformulation.[14] These nanoemulsions were synthesized using ultrasonication, then dripped from a syringe into a heated sodium alginate bath. Contacting the bath simultaneously triggers two orthogonal gelations, resulting in a core-shell hydrogel particle (**Figure 1b-d**). The MC first thermally gels and immobilizes FEN-loaded anisole nanodroplets in the MC network, producing an MC hydrogel core. As Ca^{2+} ions diffuse from the core, they crosslink alginate polymers in the bath and produce the alginate hydrogel shell. Next, we extract and dry the particles at 70 °C to evaporate the anisole and water, generating FEN nanocrystals embedded in dried core-shell particles (**Figure 1e**). These dried particles are harvested for solid state characterization and drug dissolution testing. We perform compendial *in vitro* drug dissolution tests in biorelevant release media at 37° C, following FDA guidance for BCS class II APIs.

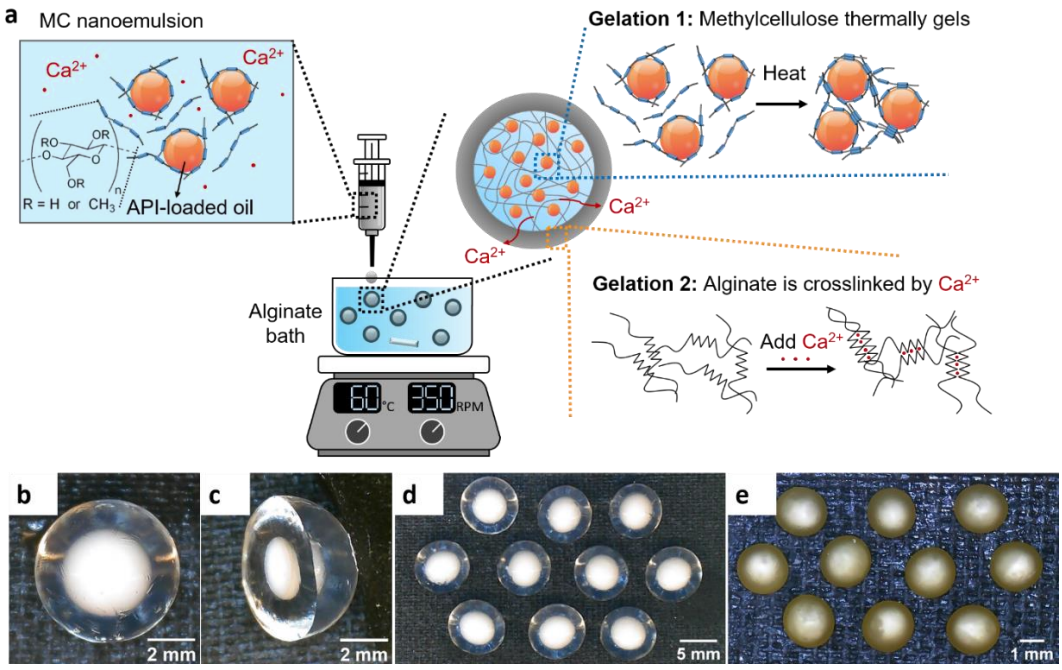


Figure 1. *'Dual gelations' synthesize core-shell hydrogel particles.* (a) Schematic describing the dual gelation dripping method. (b) Digital microscopy image of a hydrated particle, (c) which is halved to visualize the sharp interface between gel layers. Scale bar is 2 mm. Digital microscopy images of (d) hydrated and (e) dried particles highlight monodispersity. Scale bar is 5 mm for (d) and 1 mm for (e).

Results: We demonstrate programmable pulsatile dissolution of the FEN nanocrystals from the core-shell particles over varied formulation conditions. First, we observe that the nanocrystalline formulation of FEN exhibits a substantial improvement in the release rate of FEN compared to the bulk FEN crystals (gray curve in **Figure 2**). We establish control over the release profile by modulating the amount of $CaCl_2$ in the formulation, where the programmed release point increases with increasing $CaCl_2$ concentration (blue curves in **Figure 2**). For all formulations, release 'suppression' is effective, with minimal drug release from the particles until the release pulse.

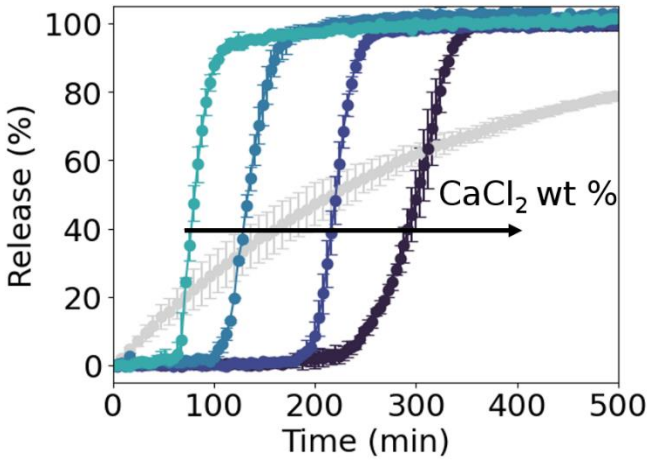


Figure 2. *$CaCl_2$ concentration controls delayed release timescale.* Dissolution profiles for increasing *$CaCl_2$ concentration* from left to right. Gray curve corresponds to bulk, as-received FEN crystals. Y-axis error bars indicate standard deviation of experimentally calculated dissolution proportion, n = 3.

The strong release suppression and programmable timed release we report suggests that this formulation approach could be applicable in oral delayed and sustained release applications. The programmability of the release based on process parameters highlights how this platform can access a diverse range of drug product profiles. We demonstrate release suppression between 1-4 h, which correlates well to *in vivo* residence time of drug products in the stomach (5 min-1 h)[15,16] and the small intestine (3-4 h).[7,17] The tunability of this release suppression timescale suggests that this approach could target pulsatile enteric or colonic release, ensuring a therapeutic is protected from the gastric environment. Oral drug delivery systems with this pulsatile release behavior could also be useful in treating disease processes that exhibit circadian rhythms in their pathology, so-called 'chronotherapy.'[18–20] Simple mixtures of particles with different suppression timescales could enable sustained-release functionality to reduce pill burden, an important clinical challenge in chronic disease.[21]

Conclusion: Our approach exploits the advantages of hydrogels and nanoemulsions to design small molecule nanoformulations. We synthesize core-shell particles with tunable geometry that enables programmable drug release. This method requires few unit operations compared to the current state-of-the-art core-shell particle manufacturing methods, while also structuring distinct hydrogel layers. The modular nature of this platform suggests that minimal adaptation can generalize this approach for the formulation of small molecule therapeutics for diverse applications in oral delivery.

References

1. Shams, T., Parhizkar, M., Illangakoon, U. E., Orlu, M. & Edirisinghe, M. Core/shell microencapsulation of indomethacin/ paracetamol by co-axial electrohydrodynamic atomization. *Mater. Des.* **136**, 204–213 (2017).
2. Alzahrani, A. *et al.* Fabrication of a shell-core fixed-dose combination tablet using fused deposition modeling 3D printing. *Eur. J. Pharm. Biopharm.* **177**, 211–223 (2022).
3. Ding, Y. *et al.* Precision combination therapy for triple negative breast cancer via biomimetic polydopamine polymer core-shell nanostructures. *Biomaterials* **113**, 243–252 (2017).
4. Zu, S. *et al.* 4D printing of core–shell hydrogel capsules for smart controlled drug release. *Bio-Design and Manufacturing* **5**, 294–304 (2022).
5. Yin, W.-H. *et al.* Dual-functional polyetheretherketone surface with programmed sequential drug release coating. *Colloids Surf. B Biointerfaces* **219**, 112806 (2022).
6. Zarket, B. C. & Raghavan, S. R. Onion-like multilayered polymer capsules synthesized by a bioinspired inside-out technique. *Nat. Commun.* **8**, 193 (2017).
7. Wilding, I. R., Davis, S. S., Pozzi, F., Furlani, P. & Gazzaniga, A. Enteric coated timed release systems for colonic targeting. *Int. J. Pharm.* **111**, 99–102 (1994).

8. Cole, E. T. *et al.* Enteric coated HPMC capsules designed to achieve intestinal targeting. *Int. J. Pharm.* **231**, 83–95 (2002).
9. Gazzaniga, A., Iamartino, P., Maffione, G. & Sangalli, M. E. Oral delayed-release system for colonic specific delivery. *Int. J. Pharm.* **108**, 77–83 (1994).
10. Alhnan, M. A. *et al.* Emergence of 3D Printed Dosage Forms: Opportunities and Challenges. *Pharm. Res.* **33**, 1817–1832 (2016).
11. Zhang, L., Huang, J., Si, T. & Xu, R. X. Coaxial electrospray of microparticles and nanoparticles for biomedical applications. *Expert Rev. Med. Devices* **9**, 595–612 (2012).
12. Chen, L.-H. & Doyle, P. S. Design and Use of a Thermogelling Methylcellulose Nanoemulsion to Formulate Nanocrystalline Oral Dosage Forms. *Adv. Mater.* **33**, e2008618 (2021).
13. Vogt, M., Kunath, K. & Dressman, J. B. Dissolution enhancement of fenofibrate by micronization, cogrinding and spray-drying: comparison with commercial preparations. *Eur. J. Pharm. Biopharm.* **68**, 283–288 (2008).
14. Kawabata, Y., Wada, K., Nakatani, M., Yamada, S. & Onoue, S. Formulation design for poorly water-soluble drugs based on biopharmaceutics classification system: basic approaches and practical applications. *Int. J. Pharm.* **420**, 1–10 (2011).
15. Baumgartner, S., Kristl, J., Vrecer, F., Vodopivec, P. & Zorko, B. Optimisation of floating matrix tablets and evaluation of their gastric residence time. *Int. J. Pharm.* **195**, 125–135 (2000).
16. Singh, B. N. & Kim, K. H. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. *J. Control. Release* **63**, 235–259 (2000).
17. Davis, S. S., Hardy, J. G. & Fara, J. W. Transit of pharmaceutical dosage forms through the small intestine. *Gut* **27**, 886–892 (1986).
18. Jain, D., Raturi, R., Jain, V., Bansal, P. & Singh, R. Recent technologies in pulsatile drug delivery systems. *Biomatter* **1**, 57–65 (2011).
19. Maroni, A. *et al.* Erodible drug delivery systems for time-controlled release into the gastrointestinal tract. *J. Drug Deliv. Sci. Technol.* **32**, 229–235 (2016).
20. Youan, B.-B. C. Chronopharmaceutical drug delivery systems: Hurdles, hype or hope? *Adv. Drug Deliv. Rev.* **62**, 898–903 (2010).
21. Baryakova, T. H., Pogostin, B. H., Langer, R. & McHugh, K. J. Overcoming barriers to patient adherence: the case for developing innovative drug delivery systems. *Nat. Rev. Drug Discov.* **22**, 387–409 (2023).

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: Dissolution & Solubility Modulation

Exploring the Mechanisms Behind Increased Absorption in Rapidly Dissolving Amorphous Solid Dispersions

Akshay Narula (akshaynarula15@gmail.com)[1], Na Li (lina@uconn.edu)[1]

[1]**University of Connecticut, Storrs, Connecticut**

Purpose: The pharmaceutical industry faces a significant hurdle in formulating new active pharmaceutical ingredients due to their poor water solubility, which often results in limited bioavailability. Amorphous Solid Dispersion (ASD) has emerged as a promising approach to enhance systemic exposure by surpassing the drug's aqueous solubility. When a fast-releasing ASD dissolves, it can generate amorphous drug nanoparticles spontaneously if the dissolved drug concentration exceeds its amorphous solubility. These nanoparticles are thought to be key in enhancing absorption due to the particle drifting effect which in turn raises the concentration of the drug in the mucosal tissue[1, 2]. However, this absorption advantage is not always observed with other drug nanoparticle systems, such as nanocrystals. Therefore, this study aims to investigate the dissolution behavior and membrane permeability of different types of drug nanoparticles. By elucidating the underlying mechanisms, this research seeks to provide valuable insights into the design and development of ASDs with optimized release performance, ultimately improving the bioavailability of poorly soluble drugs.

Method: Clotrimazole was chosen as a model compound, and redispersible amorphous nanoparticles were prepared using the solvent-shift method. Eudragit® L100, a polymeric stabilizer, was used to prevent recrystallization. Dried amorphous nanoparticles were also prepared from the *in situ* particles. Nanocrystals were prepared through wet media milling. Membrane flux measurements were conducted using diffusion cells with lipophilic membranes. Dissolution studies were performed by diluting the nanoparticles to the drug's amorphous solubility in pH 6.5 phosphate buffer. Particle size and lack of crystallinity were determined using dynamic light scattering (DLS) and polarized light microscopy (PLM), respectively.

Results: The membrane flux measurements were conducted to evaluate the permeability of various drug nanoparticles. Figure 1 illustrates the results obtained for *in situ* amorphous nanoparticles, dried amorphous nanoparticles, and nanocrystals. The *in situ* amorphous nanoparticles showed an increase in membrane flux at drug concentrations exceeding the amorphous solubility threshold. As the concentration of dissolved drug particles increased, a flux plateau was observed at higher particle concentrations. This suggests that the enhanced membrane flux is primarily attributed to the dissolved drug rather than the particles themselves. On the other hand, both dried amorphous nanoparticles and nanocrystals showed minimal flux increase even at similar donor concentrations and sizes.

To elucidate the discrepancies in membrane flux measurements among the different types of particles, dissolution studies were conducted (Figure 2). The in situ amorphous particles exhibited rapid dissolution, reaching the amorphous solubility of the drug within just 5 minutes. In contrast, the dried amorphous particles displayed an extremely slow dissolution rate, failing to achieve amorphous solubility even after 5 hours. Similarly, the nanocrystals exhibited an even lower dissolution rate due to their crystalline nature. The disparity in dissolution behavior between the nanoparticles is important in explaining the observed variations in membrane permeability. Particle concentration, sink condition and drug solubility were found to play important roles in particle dissolution rate.

Conclusion: In conclusion, the study demonstrated that in situ amorphous nanoparticles exhibited superior membrane permeability compared to dried amorphous nanoparticles and nanocrystals The rapid dissolution of *in situ* particles played a crucial role in their enhanced membrane flux, thereby facilitating the particle drifting effect and increasing drug concentration in mucosal tissue. These results provide valuable mechanistic insights into the enhanced absorption observed with fast-releasing amorphous solid dispersions, paving the way for the development of optimized strategies for designing such formulations and predicting their bioavailability.

References:

(1) Narula, A.; Sabra, R.; Li, N. Mechanisms and Extent of Enhanced Passive Permeation by Colloidal Drug Particles. *Molecular Pharmaceutics* **2022**, *19* (9), 3085-3099.
(2) Sabra, R.; Narula, A.; Taylor, L. S.; Li, N. Comparisons of in Vitro Models to Evaluate the Membrane Permeability of Amorphous Drug Nanoparticles. *Molecular Pharmaceutics* **2022**, *19* (9), 3412-3428

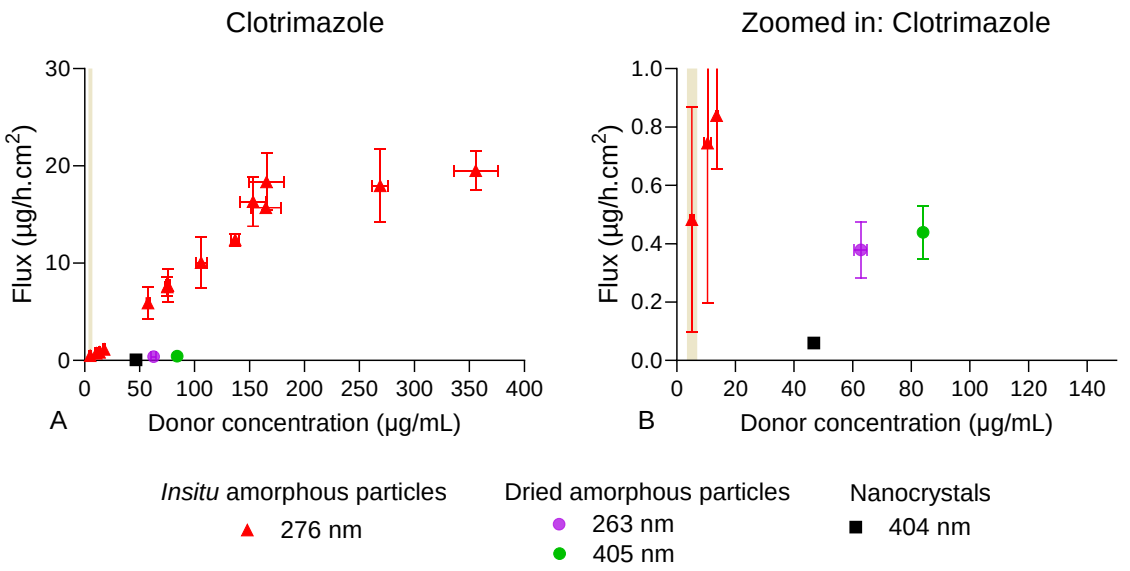


Figure 1. Flux measurements of different particle type showing minimal flux enhancement was for both dried amorphous particles and nanocrystals in comparison to *in situ* amorphous particles

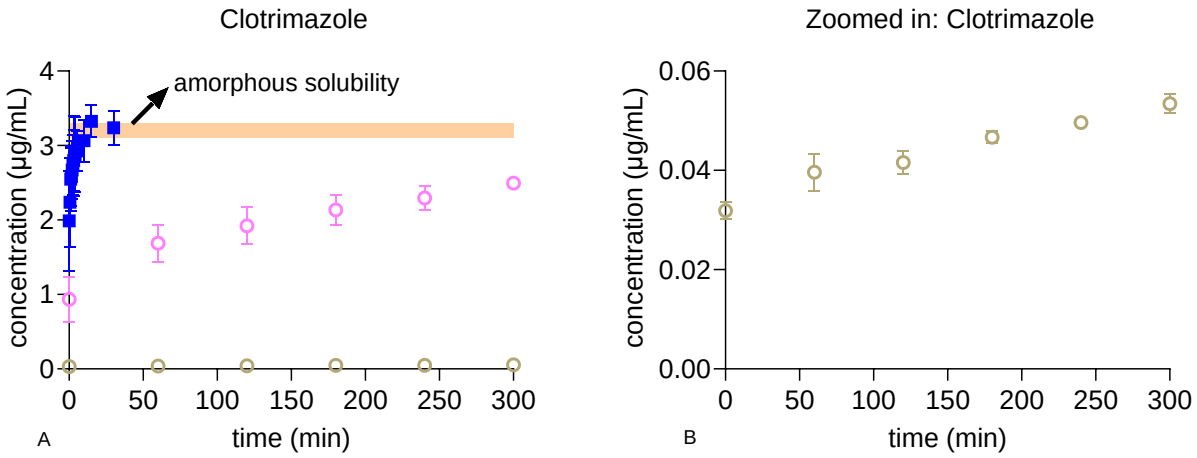


Figure 2. Impact of dissolution rate of different particle type suggesting rapid dissolution of *in situ* amorphous particles as key to enhanced membrane flux

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Side-by-side Dissolution Cells as a Novel Test to Determine Shell Properties of Delayed-Release Capsules

Miguel O. Jara (miguel.jara@utexas.edu)[1], Robert Williams (bill.williams@austin.utexas.edu)[1]

[1]**The University of Texas at Austin, Austin, Texas**

Purpose: Delayed-release capsules are commonly used for the oral delivery of probiotics, supplements, and nutraceuticals. These capsules are mainly used (1) to protect the stomach from irritating APIs or (2) to protect the API from the harsh conditions of the stomach, such as low pH and enzymatic degradation.[1] However, several research articles have shown that commercial capsules leak acid during pH-shift dissolution studies and acid-uptake tests.[2–4] These tests do not determine if acid ingresses through the capsule shell or between the locking rings. We aimed to study the properties of delayed-release capsules to guide their use during formulation. For this purpose, capsule shells were cut and used as membranes for side-by-side diffusion cells to determine the permeation of small molecules and microparticles.

Methods: Delayed-release capsules size 00 (ACGcaps™ HX) (ACG North America, Piscataway, NJ) were utilized. The 15 mm side-by-side diffusion cells (PermeGear, Hellertown, PA, USA) with a diffusion area of 1.767 cm^2 were employed to evaluate the capsules (Figure 1A). The capsules were cut as shown in Figure 2, and used as a membrane to evaluate the diffusion/permeation of caffeine (used as model small molecule) and 1.0 µm fluorescent microparticles (Thermo Fisher Scientific Inc., Waltham, MA) (Figure 1B).

During the caffeine testing, FD&C Red 40 was employed for visualization purposes to confirm that the capsule shell/membrane was correctly placed between the donor and receptor cell. The following solutions were prepared for the diffusion assays: (A) 0.1 N HCl, (B) caffeine solution at 5 mg/mL, and (C) FD&C Red 40 at 1 mg/mL in 0.1 N HCl. The donor cell was filled with 4 mL of solution A, 1 mL of solution B, and 100 µL of solution C. In contrast, the receptor cell was filled with 5 mL of solution A. The system was kept at room temperature, and both cells were fitted with cross-stir bars and stirred at 600 rpm to avoid any boundary layer effects. Samples (100 µL) were withdrawn from the receiver cell from 0 min to 60 min with a sampling interval of 5 min, and 100 µL of 0.1N HCl was replaced at each sampling point. Samples were measured using a Dionex Ultimate 3000 HPLC system (Thermo Fisher Scientific Inc., Sunnyvale, CA, USA).

In the case of the fluorescent microparticles, these were suspended in 0.1 N HCl, and because they are colored, the dye FD&C Red 40 was not needed. The rest of the conditions were maintained from the previous experiments. The fluorescence intensities were measured at excitation/emission of 542 nm/612nm using a Tecan Infinite 200 plate reader (Tecan Group Ltd., Männedorf, Switzerland).

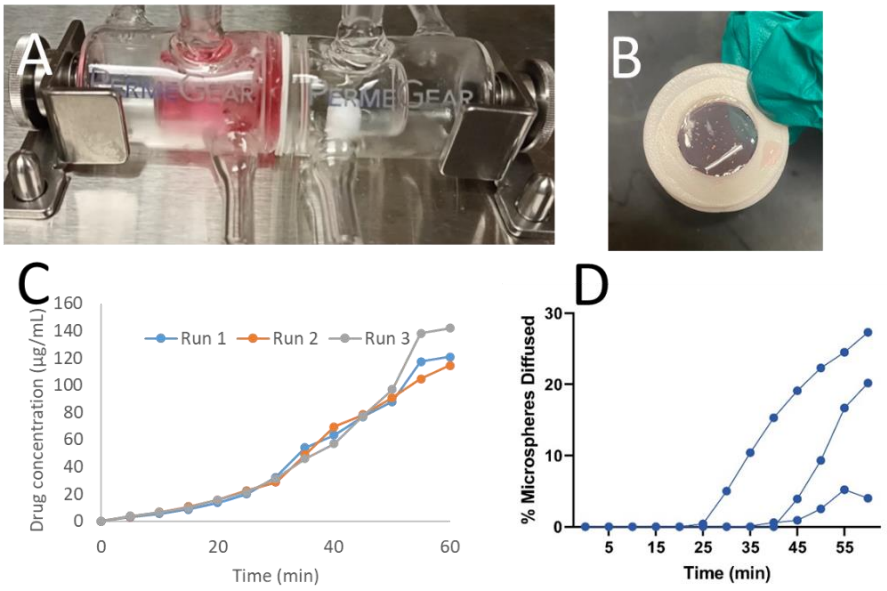


Figure 1. (A) Picture of the side-by-side diffusion cells. FD&C Red 40 was employed for visualization purposes. (B) Capsules were cut and used as membranes. (C) Caffeine concentration in the receptor cell over time. (D) microspheres permeation over time.

Results: The capsule shells were used as a semipermeable membrane surrounded by 0.1 N HCl on both sides to study the delayed-release property of the capsules. During the setting up of the cells, it is important to properly wet and place the capsule shell between the donor and receptor cells. Because of the usage of a red dye, the coloration of the receptor cell during the first 5 min of the experiment indicates that the membrane (capsule shell) was ruptured when assembling the cells.

Side-by-side diffusion cells helped to determine how capsule shells can behave as a semipermeable membrane in a simulated gastric fluid. For instance, caffeine, a small molecule, showed a two-phase diffusion profile, slow in the first 30 min but faster after 30 min (Figure 1C). It is worth noticing that caffeine concentrations detected in the receptor cell are reduced compared to the initial concentration in the donor cell (mg/mL vs µg/mL range). In the case of the 1.0 µm fluorescent microparticles, they were detected in the receptor cell after 33 ± 8 min (Figure 1D). Compared to the results employing caffeine, these results using microparticles were more variable, and further optimization is needed to determine if the variability comes from the experimental, capsules, or analytics.

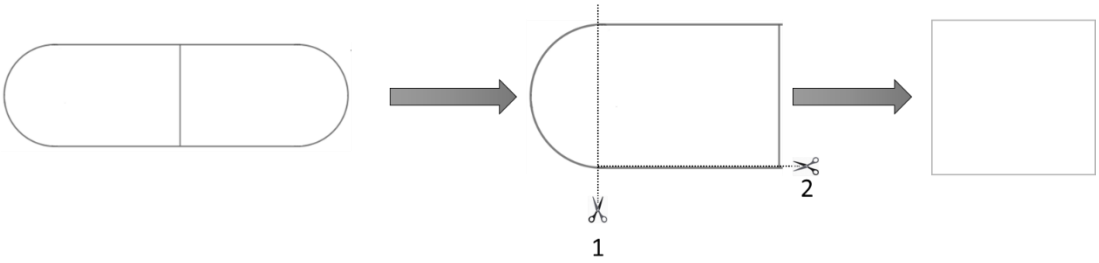


Figure 2. The diagram shows how the capsules were cut before being placed between the donor and receptor cells.

Conclusions: This study demonstrates the potential of using side-by-side diffusion cells to evaluate the properties of capsule shells. Moreover, it is possible to test different dissolution media and analytes of interest, such as small molecules, biologics, or even probiotics. Paving the way for testing modifications such as adding extra excipients, coatings, or extra layers of capsules (i.e., capsule-in-capsule dosage form). Overall, it is feasible to improve the oral delivery of pharmaceutical/nutraceutical capsule formulations by using side-by-side diffusion cells during formulation.

DRPI
DRPI.SPDS.WORLD
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

A Mechanistic Understanding of Drug Release Mechanisms from Long-Acting Ethylene Vinyl Acetate Implants

Angela Ren (a2ren@austin.utexas.edu)[1], Feng Zhang (feng.zhang@austin.utexas.edu)[1], Ziyue Zhong[1]

[1]The University of Texas at Austin, Austin, Texas

Purpose: Long-acting ethylene vinyl acetate (EVA)-based implants are designed to release drug for up to 5 years [1]. Dispersed-drug reservoir implants contain dissolved and dispersed drug in a polymer core with a rate-limiting polymer skin. Release profiles can be tailored by varying vinyl acetate (VA) content of the core and skin polymers which effectively controls drug permeability, polymer microstructure and implant mechanical properties [2]. Release through skin and ends differ due to presence of a skin layer along the implant length but not on the implant ends. This study aims to elucidate the complex drug release mechanisms of dispersed-drug EVA-based implants to facilitate rational development of long-acting implants based on fundamental understanding of drug and polymer transport properties.

Methods: The implant manufacturing setup consisted of perpendicular single-screw and a twin-screw extruder connected to a coaxial die, water bath, laser micrometer, and belt puller. The implant core contained 30% etonogestrel in EVA 28 (28% VA) while skin consisted of EVA 15 (15% VA). Implant length, diameter, and skin thickness was 4 cm, 2 mm, and 70 μm, respectively. Drug release was evaluated using an incubator shaker with 0.00075% Tween 80 in water at 37℃ and 150 rpm. Implants were tested as-is for release from the whole implant. 2 cm segments were sealed on the ends or skin using etonogestrel-impermeable glue (Loctite 4011) to assess release through skin only or ends only. X-ray microcomputed tomography (microCT) was used to investigate the implant microstructure after release. Implants depleted of drug were scanned to obtain an image stack of 963 slices with 0.7 mm x 0.7 mm x 0.7 mm field of view and 0.7 μm resolution. Scans were centered on the implant core. Image segmentation and 3D reconstruction were performed using Dragonfly.

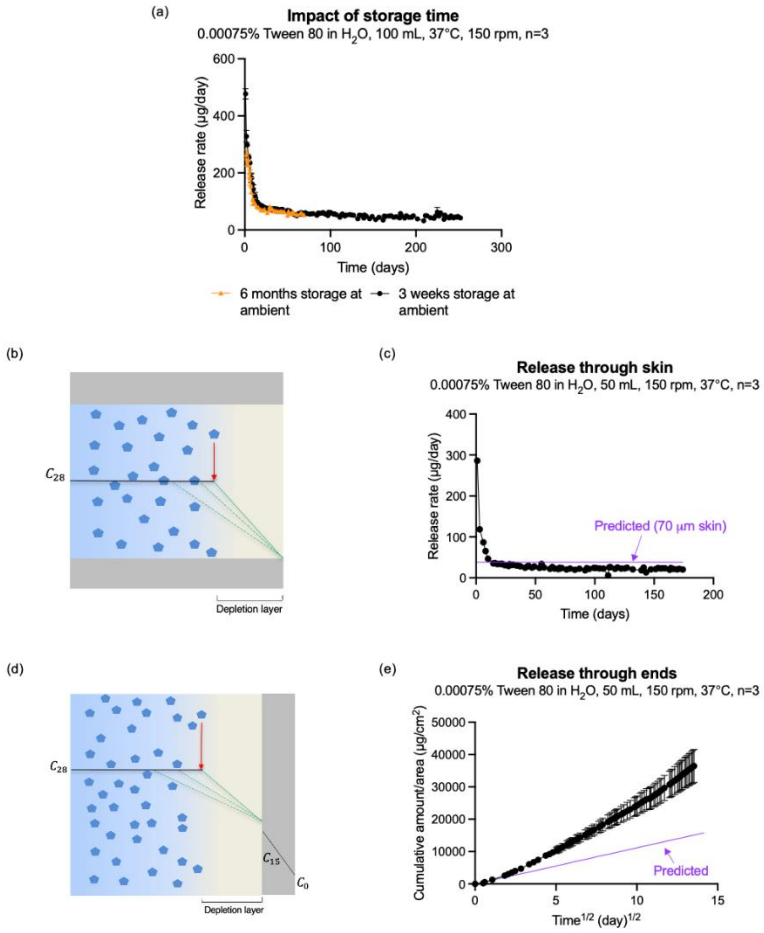
Results: Etonogestrel has negligible solubility in EVA 28 at room temperature but can be dissolved at elevated temperature during extrusion. Local heat generation from high-shear mixing enables a fraction of drug to dissolve in EVA 28. Upon cooling, a portion of drug recrystallizes but remains supersaturated [3].

During storage, supersaturated drug in the core partitions to the skin. Initial release consists of a burst portion where ½ of drug in the supersaturated skin is released. Drug recrystallization increases with storage time, causing a reduced burst (Figure 1(a)). After burst, release rate theoretically reaches steady-state as governed by skin thickness, drug permeability in EVA 15, and the concentration gradient across the skin (Figure 1(b)). Actual release depends on the ratio of drug dissolution rate/diffusion rate. Finite dissolution rate causes release rate to decrease due to slower diffusion. Additionally, release rate deviates from predicted as a depletion zone forms in the core (Figure 1 (c)). Release through ends is governed by drug transport properties in EVA 28 and the surface area of the ends (Figure 1(d)). Since there is no rate-limiting EVA 15 layer on the ends, release decreases faster over time due to an increasing depletion zone. If drug dissolution rate is infinite, release follows the Higuchi model where release is proportional to $t^{1/2}$. If drug dissolution rate is finite, release is linear with t, as observed in the early portion of release through ends (Figure 1(e)) [4]. The drug dissolution rate/diffusion rate ratio increases over time as the influence of diffusion path length dominates and release becomes linear with $t^{1/2}$.

MicroCT was employed to understand the impact of drug distribution on deviation in release through ends. Pores were assumed to originate from dispersed drug as inherent porosity was low. Analysis of the reconstructed volumes indicate presence of a few very large pores due to percolating smaller pores. The pores are nonuniformly distributed which is likely due to collapse of smaller pores due to partial melting of EVA 28 during release testing at 37℃ [5]. Percolating networks explain the higher actual release compared to predicted, as the predicted release is calculated based on drug permeability in EVA 28, not the release media [6]. A second extrusion step could be employed to improve drug dispersion and reduce drug percolation [7]. This finding highlights the importance of optimizing the manufacturing process to ensure uniform dispersion of individual drug particles in EVA 28.

Conclusion: Dispersed-drug EVA implants possess dynamic release mechanisms from skin and ends governed by the drug dissolution rate/diffusion rate ratio. The initial burst due to supersaturation during extrusion can be reduced by promoting recrystallization during storage. During release, the formation of a depletion zone reduces release rate by increasing diffusion path length. Ends are impacted more than skin as EVA 15 serves as a rate-limiting layer on release through skin. Release through ends deviates from predicted due to 1) finite drug dissolution rate and 2) percolating drug networks. Findings from this study highlight the importance of understanding fundamental transport properties of drug and polymer and implant microstructure for development of long-acting implants.

IMAGES



Predicted release rate through skin only:

$$\frac{dM}{dt} = \frac{2\pi r_i L D_{15} C_{15}}{r_o - r_i}$$

$\frac{dM}{dt}$ =release rate ($\mu g/day$), r_i =inner radius (μm), r_o =outer radius (μm), L =length (μm), D_{15} =diffusivity in EVA 15 (cm^2/s), C_{15} =solubility in EVA 15 ($\mu g/cm^3$)

Predicted cumulative release through ends only (Higuchi equation):

$$Q = \sqrt{2AD_{28}C_{28}t}$$

Q =amount released/area ($\mu g/cm^2$), A =drug load ($\mu g/cm^3$), D_{28} =diffusivity in EVA 28 (cm^2/s), C_{28} =solubility in EVA 28 ($\mu g/cm^3$)

Figure 4. (a) Impact of storage time on burst release from whole implant (skin and ends) release rate (4 cm) (b) illustration of drug release through skin (c) skin only release rate (2 cm) (d) illustration of drug release through ends (e) ends only cumulative release (2 cm). The predicted release rate through skin only was calculated using the cylindrical form of Fick's law. The predicted cumulative release through ends only was calculated using the Higuchi equation. Red and green arrows indicate dissolution and diffusion, respectively.

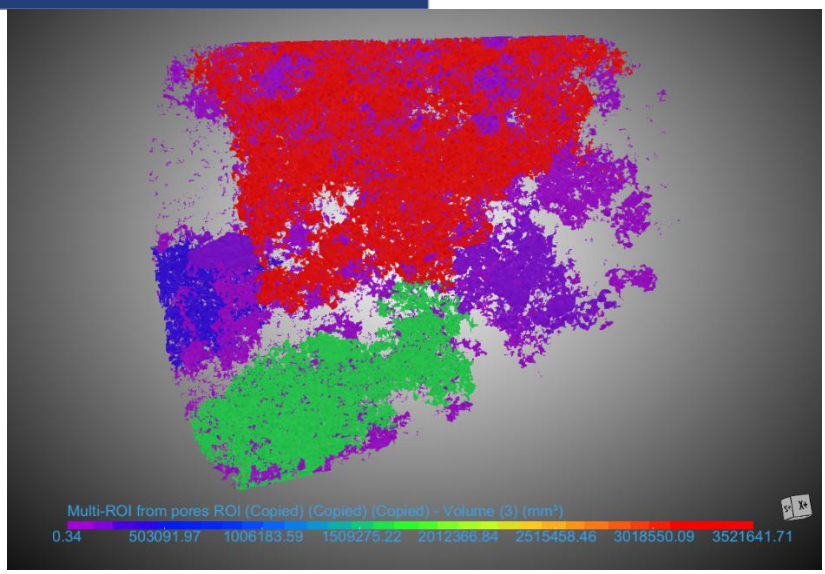


Figure 5. 3D reconstruction of an implant scanned by microCT after complete depletion of drug (axial view). Colored regions represent air-filled pores dispersed throughout the implant. Pores are colored by volume.

References:

1. Steiner, M.J., et al., *Sino-implant (II) — a levonorgestrel-releasing two-rod implant: systematic review of the randomized controlled trials.* Contraception, 2010. **81**(3): p. 197-201.
2. Van Laarhoven, J.A.H., *Physical-chemical aspects of a coaxial sustained release device based on poly-eva*. 2005.
3. Van Laarhoven, J.A.H., *Effect of supersaturation and crystallization phenomena on the release properties of a controlled release device based on EVA copolymer.* Journal of Controlled Release, 2002. **82**: p. 309-317.
4. Lindstrom, F.T. and J.W. Ayres, *Diffusion model for drug release from suspensions II: release to a perfect sink.* J Pharm Sci, 1977. **66**(5): p. 662-8.
5. Almeida, A., et al., *Ethylene vinyl acetate as matrix for oral sustained release dosage forms produced via hot-melt extrusion.* Eur J Pharm Biopharm, 2011. **77**(2): p. 297-305.
6. Veenstra, H. and W. De Graaff, *X-ray visibile drug delivery device*. 2014, Meck Sharp & Dohme B.V.: US.
7. Higuchi, T., *Rate of Release of Medicaments from Ointment Bases Containing Drugs in Suspension.* Journal of Pharmaceutical Sciences, 1961. **50**(10): p. 874-875.

Acknowledgements: This work was supported by the Broad Agency Announcement (BAA) Contract # 75F40122C00019 from the U.S. Food and Drug Administration (FDA). The content reflects the views of the authors and should not be construed to present FDA's views or policies. The authors would like to thank Jessie Maisano of the University of Texas X-ray CT Facility (NSF EAR-1762458 and 80NSSC23K0199) for her assistance in scanning and processing microCT images.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: Dissolution & Solubility Modulation

Does Dissolution Media Choice Matter when Evaluating the Performance of Hydroxypropyl Methylcellulose Acetate Succinate (HPMCAS)-Based Amorphous Solid Dispersions?

Pradnya Bapat (pradnyap2012@gmail.com)[1], Lynne Taylor (ltaylor@purdue.edu)[1], Shubhajit Paul[2], Naveen Thakral[3], Yin-Chao Tseng[2]

[1]Purdue University, West Lafayette, Indiana | [2]Boehringer Ingelheim Pharmaceuticals, Inc. | [3]Schrodinger, Inc.

Purpose: Amorphous solid dispersions (ASDs) are increasingly being used to address the poor aqueous solubility of many emerging drug candidates. Hydroxypropyl methylcellulose acetate succinate (HPMCAS), an enteric polymer, is commonly used as an ASD polymer in commercial formulations because of its ability to delay crystallization from supersaturated solutions of many drugs. Enteric polymers have been shown to have decreased pH near the polymer-water interface (unstirred water layer) compared to the bulk solution pH as a result of protons liberated during ionization of carboxylic acid groups. The impact of buffer capacity on minimizing the unstirred water layer pH gradient is well established in context of enteric-coated tablet dissolution. However, a comprehensive understanding of the combined impact of pH and buffer capacity variations on ASD dissolution is lacking. In an ASD, drug is molecularly dispersed within the polymer matrix, in contrast to an enteric coating. It is expected that the drug loading in an enteric polymer-based ASD will impact release as a function of pH and buffer capacity. The objective of this study was to gain insight into the rate limiting processes with respect to medium composition and drug loading. The ultimate goal is to optimize the maximum drug loading without sacrificing release performance, as well as to inform *in vitro* tests that better translate into the *in vivo* environment for HPMCAS-based ASDs.

Methods:

1. **ASD Preparation:** ASDs of HPMCAS and model drug, indomethacin (IND) were prepared using a rotary evaporator. ASDs were prepared by dissolving drug and polymer in 1:2 v/v methanol and dichloromethane followed by rotatory evaporation with the water bath maintained at 60 °C. ASD powders were kept under vacuum overnight to remove any residual solvents. The amorphous nature of ASDs was confirmed using powder X-ray diffraction (PXRD) and polarized light microscopy (PLM).
2. **Surface Normalized Dissolution:** Surface normalized dissolution experiments were performed using a rotating disk intrinsic dissolution rate (IDR) apparatus. Briefly, 100 mL of buffer solution was added into a jacketed beaker maintained at 37 °C. 100 mg of the ASD powder was compacted in an 8 mm die using a Carver press at 1500 psi for one minute. The die was then attached to the rotating spindle and only one surface of the compact was exposed to the dissolution medium, thus maintaining a constant surface area of the dissolving compact. The solution was sampled at regular time intervals. Drug and polymer concentration was quantified using HPLC.
3. **HPMCAS Gel Layer Properties:** Gel layer thickness was determined by directly imaging the surface of an HPMCAS compact using confocal fluorescence microscope. Prodan was added to the polymer as a fluorescence probe to aid in visualization of the gel layer. A polymer compact was partially dissolved using the IDR apparatus. The compact cross section was viewed under the confocal microscope to measure the thickness of the HPMCAS gel layer as a function of medium buffer capacity.
   Chlorophenol red was used as a pH indicator (pH range 4.5-7.0) for determining the apparent pH of the gel layer of HPMCAS formed after exposure to pH 6.8 phosphate buffer. The gel layer was physically removed and smeared on a glass slide. The slide was mounted in a UV-visible spectrophotometer and the spectrum of the gel was collected and compared against a calibration curve prepared using chlorophenol red in solutions of known pH.

Results: In dissolution experiments across all buffer capacities, drug and polymer released at similar normalized release rates, and faster than neat amorphous drug, indicating the release process was controlled by the polymer. At low buffer capacities, buffer capacity-controlled release was observed. At higher buffer capacities (plateau region), sufficient buffer capacity was achieved, and the presence of the drug had greater impact on polymer release. Importantly, fasted state simulated intestinal fluid (FaSSIF), or *in vivo* buffer capacities (4-10 mM/ΔpH) showed less impact of drug loading, whereas drug loading effects were more apparent at higher buffer capacity. ASDs showed comparable normalized release rates in FaSSIF (pH 6.5 and buffer capacity 12mM/ΔpH) and in FeSSIF (pH 5.8, buffer capacity 25mM/ΔpH) indicating that although the buffer capacity was high in case of FeSSIF, the pH was too low for complete polymer ionization. The ASDs showed comparable dissolution rates in FaSSIF and buffer for FaSSIF indicating a negligible impact of bile salts and digestive components on the release. The release pattern at different buffer capacities appeared to be controlled by the gel layer pH which was lower than the bulk buffer pH. Neat HPMCAS and ASDs showed lower

dissolution rates in pH 6.5 bicarbonate buffer compared to phosphate buffer possibly because of the inherently lower buffer capacity of bicarbonate buffer.

Conclusion: Based on pH and buffer capacity of the medium, different mechanisms controlled the release at various drug loadings and these variations should be reflected when designing *in vitro* tests for enteric-polymer based ASDs.

References:

1. Harianawala et al., Int. J. Pharm., 2002, 247(1), 139-147.
2. Mooney kg, *J pharm sci*. 1981:22-32.
3. Ozturk at al., Pharm Res. 1988;5(9):550-565.

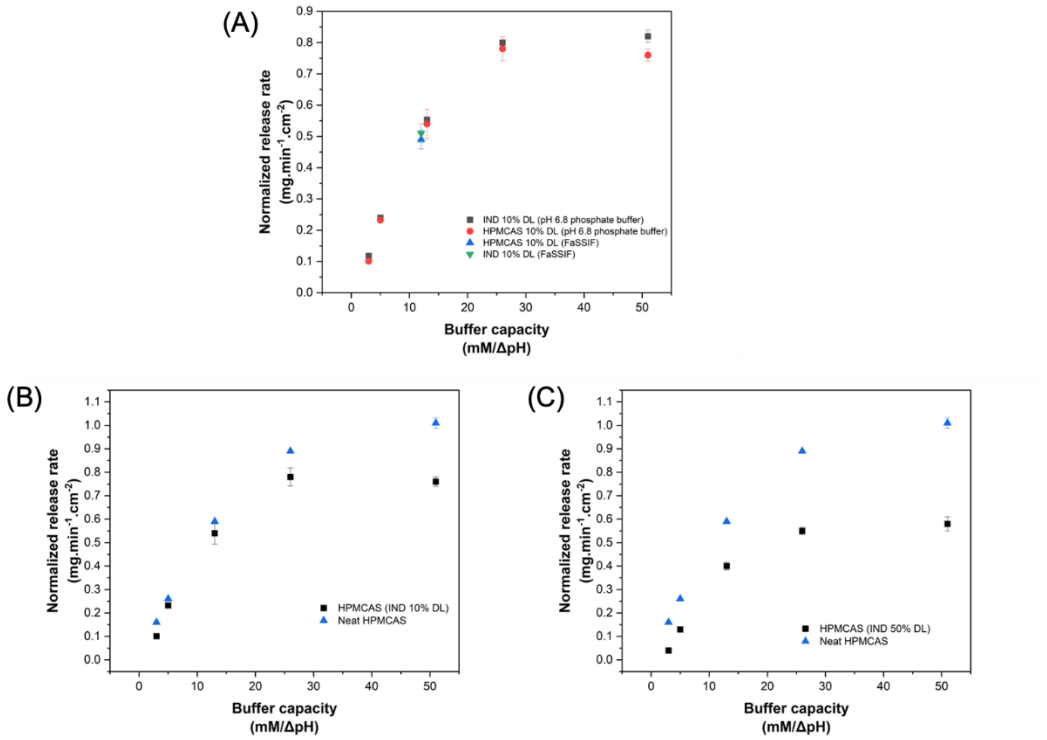


Figure 6. Normalized release rates vs buffer capacity for (A) IND and HPMCAS from IND: HPMCAS 10% DL ASD (B) neat HPMCAS and HPMCAS from 10% DL of IND: HPMCAS ASD (C) neat HPMCAS and HPMCAS from 50% DL of IND: HPMCAS ASD

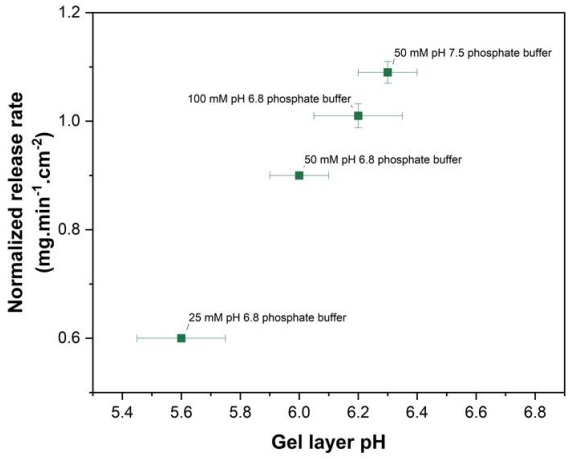


Figure 7. Relationship between normalized release rate and gel layer pH of HPMCAS in various buffers

Acknowledgements: We are thankful to Kerstin Schaefer, Olaf Behrend and Eduard Trenkenschuh for their helpful comments in the design of this research project. Boehringer Ingelheim Pharmaceuticals Inc. is thanked for providing funding for this study.

DRPI
Dissolution Research Presentations International
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists
Region: US | **Category:** PhD
Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

Understanding Microsphere In Vitro Drug Release through Imaging-based Analytics

Ruifeng Wang (ruifeng.2.wang@uconn.edu)[1], Diane Burgess (d.burgess@uconn.edu)[1], Andrew Clark[2], Quanying Bao[3], Shawn Zhang[2]

[1]**University of Connecticut, School of Pharmacy, STORSS, Connecticut** | [2]**DigiM Solution LLC** | [3]**Boehringer Ingelheim**

Purpose: Poly (lactic-co-glycolic acid) (PLGA)-based microsphere formulations continue to play a predominant role in controlled-release parenteral drug products. The release mechanism of PLGA microspheres involves diffusion, polymer erosion (degradation), or a combination thereof resulting in different release characteristics. However, there remains a need to understand the exact mechanism driving release from specific microsphere products. In the development of complex generic products such as PLGA microspheres, qualitative (Q1) and quantitative (Q2) sameness are insufficient to ensure equivalence of the two products. It is also crucial to consider similarity in microstructure (Q3), as this can affect drug release behavior and consequently, their efficacy and safety. The aim of this work is to employ imaging-based analytics to explore the relationship between microstructure and release characteristics of PLGA microspheres, thus promoting a mechanistic understanding of drug release from these products.

Methods: Minocycline hydrochloride was selected as the model drug. Four microsphere formulations were prepared *via* a coacervation method using a well-designed glass vessel assembly as previously described [1]. The physicochemical properties including drug loading, particle size, and morphology of the prepared microspheres were characterized. *In vitro* release testing of the microspheres was conducted using a sample-and-separate method (Figure 1A). Briefly, approximately 4 mg of microspheres were dispersed in 10 mL PBS (10 mM, pH 7.4, containing 0.02% (v/v) Tween 20) in screw-capped tubes mounted on a rotator set at 10 rpm, which was then incubated at 37 °C. At predetermined time intervals, the tubes were centrifuged at 3000 rpm for 3 min and the supernatants were withdrawn for further analysis. The appearance of the microspheres during release testing was captured by camera following centrifugation at the different sampling time points. The image gray values were analyzed using Image J. The internal microstructures of the different microsphere formulations were investigated through iterative focused ion beam scanning electron microscopy (FIB-SEM) (Figure 1F). The 3D microstructure properties including volume fraction, size distribution, and spatial distribution of all visible phases (PLGA, drug, and pores) were determined from the FIB-SEM images using quantitative artificial intelligence (AI)-based image analytics [2] (Figure 1G and H).

Results: Four compositionally equivalent formulations (FA, FB, FC, and FD) of minocycline hydrochloride microspheres were successfully prepared using different processing conditions. The drug loading of all four formulations was around 26% (Table 1). The four in-house formulations showed different *in vitro* drug release characteristics (Figure 1B). The release profiles of all four formulations showed a good fit with the first-order model (Figure 1C). Compared to formulations FB and FD, formulations FA and FC had lower release rates. Accordingly, more drug particles were observed inside the microspheres sampled from formulations FA and FC on Day 6 of release (Figure 1J).

Figure 1D shows the state of the prepared microspheres during *in vitro* release testing. The microspheres turned dark at the end stage of the release profiles. The dark color is due to the degradation product of minocycline hydrochloride, indicating that drug degradation may occur inside the microspheres. This microsphere discoloration at the end stage of release, showed a linear correlation with the release constant from the first-order model fitting of all four in-house formulations (Figure 1E).

All internal material phases, including the drug particles, pores, and PLGA, were identified and quantified successfully through FIB-SEM and AI image analytics (Figure 1F, G, and H). The microspheres developed a hollow appearance on Day 6 of the release study, with a PLGA shell thickness of about 35% of the radius of the microspheres (Figure 1J). Furthermore, the PLGA content in the 35% outer layer showed a linear correlation with the release constant from the first-order model fitting of all four in-house formulations (Figure 1I).

Conclusions: A hollow appearance developed during *in vitro* release for minocycline hydrochloride microspheres, which may be due to an autocatalytic effect resulting in accelerated heterogeneous degradation of PLGA (Figure 1K). The residual PLGA shell may act as a diffusion control layer, which indicates that drug release from the minocycline hydrochloride microspheres may be controlled by diffusion mechanisms. Correlation between internal phase spatial distributions and *in vitro* release characteristics can potentially provide a more comprehensive understanding of the impact of microstructural properties on the underlying release mechanisms of the microspheres, and aid in the establishment of Q3 equivalence.

References:

1. Ruifeng, W., Quanying, B., Andrew G., et al. *Int. J. of Pharm.* 628, 122292.
2. Andrew G., C., Ruifeng, W., Yuri, Q., et al. J. Control. Release. 349, 580-591.

Table 1. Drug loading and particle size of the prepared microsphere formulations. All data are presented as mean ± SD (n=3).

	Stirring rate (rpm)	Silicone oil viscosity (cSt)	Drug Loading (%, w/w)	Particle Size (D_{50}, Volume, μm)	Particle Size (D_{50}, Number, μm)
FA	350	350	26.18 ± 0.31	74.01 ± 1.81	56.10 ± 0.43
FB	350	1000	26.17 ± 0.14	62.34 ± 0.39	48.03 ± 0.18
FC	600	350	26.37 ± 0.27	72.47 ± 0.81	54.12 ± 0.16
FD	600	1000	26.41 ± 0.47	57.56 ± 0.40	41.43 ± 0.36

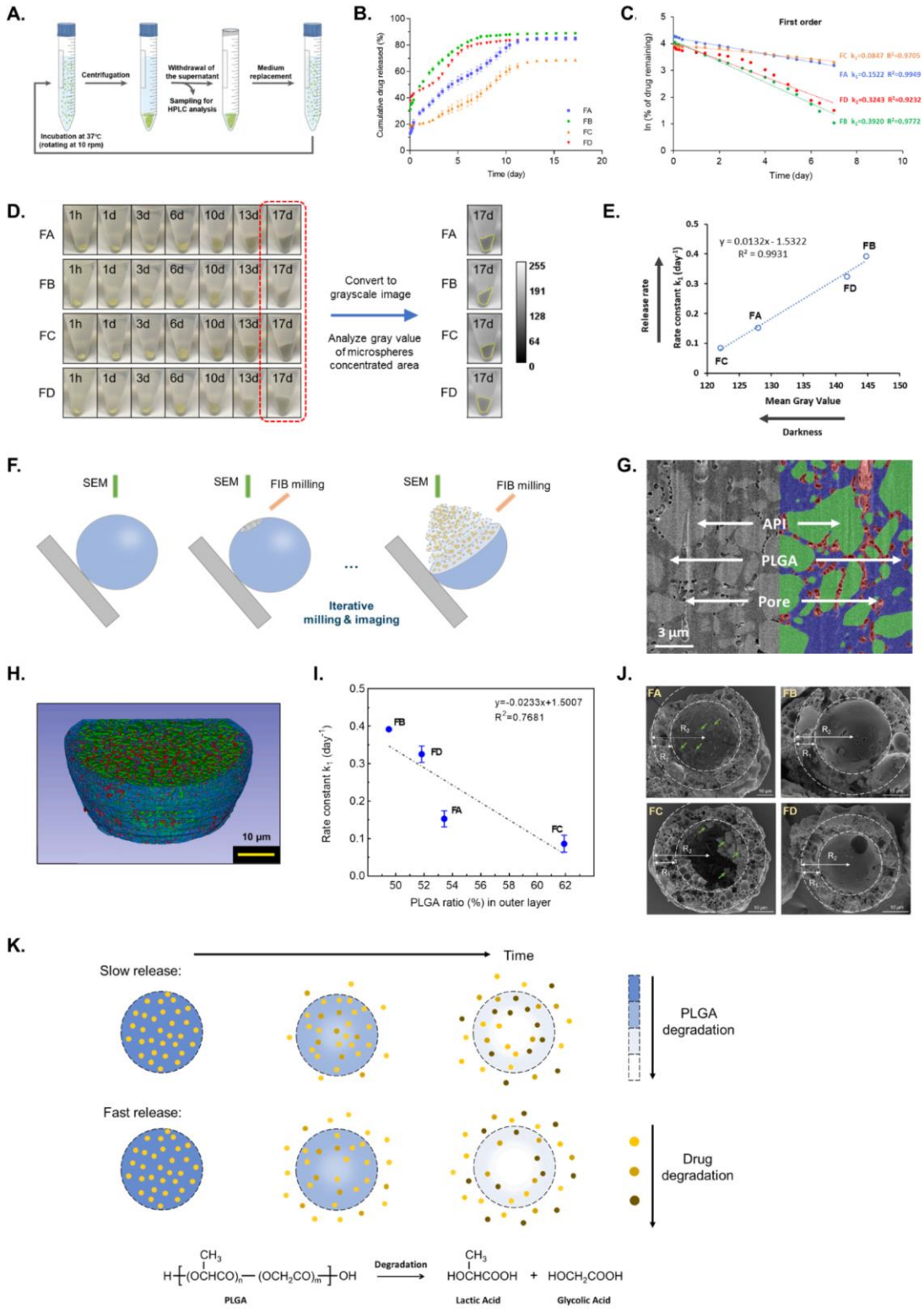


Figure 1. (A) Schematic diagram of the process of the *in vitro* release testing *via* sample-and-separation; (B) *in vitro* release profiles of the prepared microspheres using the sample-and-separate method at 37 ˚C in 10 mM PBS (pH 7.4) containing 0.02% (v/v) Tween 20 (mean ± SD,

Acknowledgements: Funding for this project was made possible, by the U.S. Food and Drug Administration through Contract # 75F40119C10157. The views expressed in this abstract do not reflect the official policies of the U.S. Food and Drug Administration or the U.S. Department of Health and Human Services.

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: US | **Category:** PhD

Theme: In vitro Release / Permeation Studies of Conventional & Novel Dosage Forms, including Herbals, Nutraceuticals & Cosmeceuticals

In Vitro Evaluation of Two Morphine Sulfate Extended-Release Products Sprinkled on Soft Foods

Md Sohel Rana (mdsohelrana.nbd@gmail.com)[1], Li Tian (li.tian@fda.hhs.gov)[1], Heather Boyce[1]

[1]US FDA, St. Louis, Missouri

Purpose: Some drug products can be sprinkled on soft foods prior to administration to improve compliance in patients affected by dysphagia. However, generic drug product formulations for the same drug substance could perform differently when mixed with soft foods. Currently FDA recommends *in vivo* pharmacokinetics studies to evaluate generic formulation differences when sprinkled on soft foods. Developing *in vitro* methodology to discriminate the effect of soft foods on the *in vitro* performance of different drug product formulations may be a useful predictor of *in vivo* performance. Two FDA approved enterically coated drugs formulations of morphine sulfate (MS) extended-release (ER) capsules, ER1 and ER2, were studied to test the impact of formulation differences on dissolution performance after exposure to soft food. The core of ER1 pellet, a reference listed drug (RLD), is a layered structure containing a sugar core coated by a layer of MS and the core of the ER2 pellet, a generic drug of the RLD, is a matrix formed with microcrystalline cellulose, where MS is mixed in. Both pellet formulations contain ethylcellulose, polyethylene glycol, and methacrylic acid copolymer. Both drug products were sprinkled on soft foods with different properties expected to influence dissolution performance and the products were subsequently characterized for the resulting changes in dissolution, water content, and mechanical strengths.

Methods: Four soft foods, applesauce, vanilla yogurt, carrot puree, and chocolate pudding, with different characteristics were selected to study the effectiveness of the *in vitro* methods in detecting product performance changes. Applesauce is the only soft food described on the product labeling approved for sprinkle administration of MS ER products while the others studied are not. The pH of the soft foods was measured with a pH meter. MS ER pellets from either ER1–10 mg, ER2–100 mg, ER2–10 mg, or ER2–100 mg was sprinkled into the soft foods for 2 h to test effectiveness of the *in vitro* method. Dissolution was performed with a 2-stage United States Pharmacopeia (USP) dissolution Test 1 for MS ER capsules (n=6). Water content was analyzed on a thermogravimeter (n=3). Pellet diameter, cracking force and cracking distance were analyzed on a texture analyzer (n=40 pellets). Cracking distance was normalized to 1 mm to account for the diameter difference in ER1 and ER2. Non-sprinkled pellets were used as controls for all tests. An f2 similarity test compared to the individual non-sprinkled control pellets was employed for dissolution profile comparison.

Results: The pH values of applesauce, vanilla yogurt, carrot puree, and chocolate pudding, were 3.69±0.01, 4.28±0.01, 5.05±0.01, and 6.19±0.01, respectively. For all four products, percent drug dissolved at 1 h (Table 1) increased in high pH compared to low pH soft food. For ER1-10 mg and ER-100 mg, the average percent MS dissolved was within individual specified ranges recommended by the USP (percent morphine-release ≤ 10% at 1 h, 25 – 50% at 4 h, 50 – 90% at 6 h, and ≥ 85% at 9 h) irrespective of the soft food. For ER2-10 mg and ER2-100 mg, this was within the USP specified range when sprinkled on applesauce and vanilla yogurt but outside the range at 1 h and 4 h when sprinkled on carrot puree and chocolate pudding. Compared to control pellets, ER1-100 mg resulted in an increase in mean percent dissolved at 1 h with chocolate pudding (8.3±1.0%), followed by carrot puree (6.8±0.3%); but f2 test for both groups passed with values of 68.9 and 68.6, respectively. In ER2-10 mg, the largest increase in drug dissolution occurred in chocolate pudding (26.7±4.2%), followed by carrot puree (21.0±2.3%); the f2 test for both groups failed with values of 28.7 and 31.9, respectively.

The mean diameters of ER1-10 mg and ER1-100 mg control pellets are 1.20±0.1 mm, and 1.26±0.1 mm, respectively; while mean diameter of ER2-10 mg and ER2-100 mg pellets are 0.86±0.2 mm, and 0.90±0.1 mm, respectively. Sprinkle administration did not show any definitive impact on the pellet diameters. Water content of sprinkled pellets were higher compared to the individual control groups for ER1 and ER2 with the highest water content occurring after being

sprinkled over high pH soft foods. Non-sprinkled pellets for each strength had lower cracking distance and higher cracking force compared to sprinkled pellets. Pellets from ER1-10 mg and ER1-100 mg formulation showed longer median normalized cracking distance compared to ER2-10 mg and ER2-100 mg when sprinkled over soft foods. These results can be useful to develop *in vitro-in vivo* relationship models for MS ER drug products sprinkled in soft food.

Conclusion: Higher percent MS release was observed for ER2 pellets sprinkled outside the labeling conditions compared to ER1 pellets which could be attributed to their difference in structure and excipients. The *in vitro* methods developed for MS ER drug products sprinkled in different types of soft food were able to detect changes in product performance after exposure to soft foods in various conditions.

Table 1. The mean percent MS release (n=6, +/- SD) at 1 h acid stage dissolution to represent influence from sprinkle administration

Sprinkle Condition	ER1 10 mg	ER1 100 mg	ER2 10 mg	ER2 100 mg
Non-Sprinkle	0.0±0.0%	1.4±0.2%	0.0±0.0%	0.3±0.1%
Applesauce	2.2±0.4%	3.9±0.7%	7.4±2.3%	7.5±1.1%
Vanilla yogurt	2.4±0.4%	3.5±0.5%	8.7±1.7%	6.6±1.3%
Carrot puree	6.0±0.6%	8.3±0.2%	21.0±2.3%	18.9±1.4%
Chocolate Pudding	7.4±0.9%	9.8±1.0%	26.7±4.2%	18.3±2.7%

Australia & New Zealand

DRPI
Dissolution Research Presentations International
DRPI.SPDS.WORLD
IN ASSOCIATION WITH
aaps American Association of Pharmaceutical Scientists

Region: AU&NZ | **Category:** PhD

Theme: Computational Tools, PBPK Modelling

Controlled Release of Vancomycin from Pegylated Fibrinogen Polyethylene Glycol Diacrylate Hydrogel

Yunong Yuan (yyua8927@uni.sydney.edu.au)[1], Duc-Viet Nguyen[2], Lingxin Wang[1], Seng Han Lim[3], Ammar Mansoor Hassanbhai[4], Mark Chong[5], Theodoros Kofidis[6], Edwin CK Tan[1], Dror Seliktar[7], Lifeng Kang[1], Abdul Jalil Rufaihah[6,8]

[1]School of Pharmacy, Faculty of Medicine and Health, University of Sydney, Australia | [2]Nusmetics Pte. Ltd. | [3]Department of Pharmacy, National University of Singapore, Singapore | [4]Osteopore International Pte Ltd, Singapore | [5] College of Design and Engineering, National University of Singapore | [6] Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore | [7] Department of Biomedical Engineering, Technion-Israel Institute of Technology, Israel | [8] School of Applied Science, Temasek Polytechnic, Singapore

Background & Rationale: Surgical site infection (SSI) is a prevalent concern in the aftermath of surgeries and contributing to approximately 3% of surgical mortality rates in the United States. These infections not only prolong hospital stays but also pose severe complications, such as sternal wound infection after cardiac surgery involving median sternotomy[1-4]. Localized delivery of high concentration antibiotics through hydrogel is still of great interest in the surgical field, as it offers targeted drug delivery, controlled drug release, minimising the risk of systemic adverse effect, in comparison with intravenous injection[5]. To optimize this approach further, changing and designing the formulation or structure of hydrogel can effectively control the drug releasing profile[6]. The aim of this study is to develop a localized, controlled-release vancomycin laden PEGylated fibrinogen–polyethylene glycol diacrylate (PF-PEDGA) hydrogel to prevent SSI effectively.

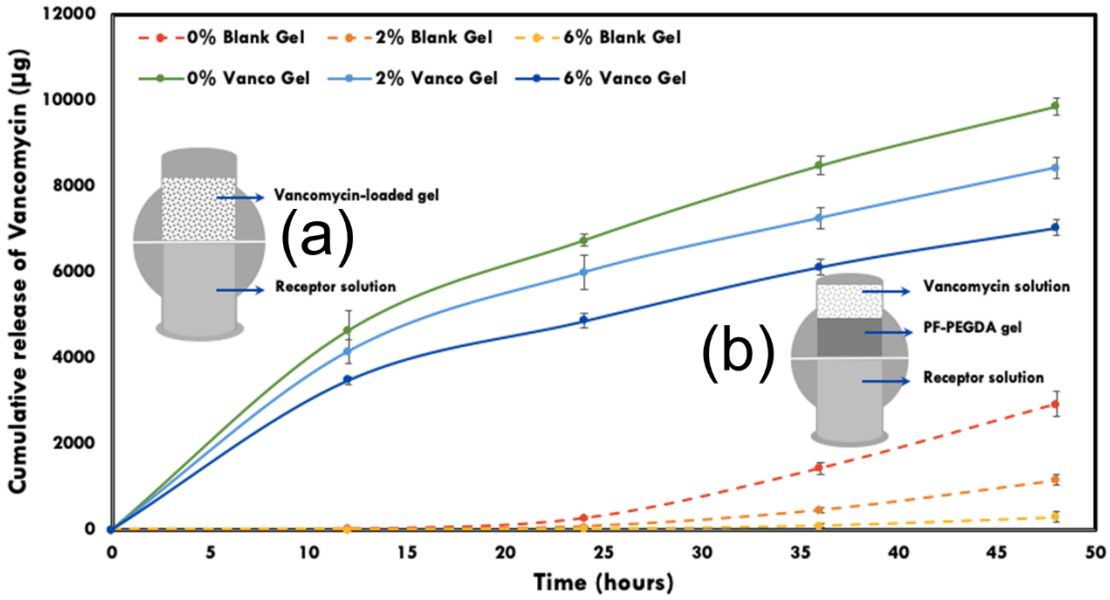
Methods: A) To prepare the hydrogels. 20% PEGDA stock solution (w/w) was prepared by dissolving PEGDA powder in PBS solution. PEGDA stock solution was mixed with PF solution to create PF hydrogel with varied PEGDA concentrations 0, 2, 6, 10% (v/v). One gram of Igacure 2959 photoinitiator powder was mixed with 1 mL of 70% ethanol to make the stock solution. The PF-PEGDA precursor solutions were mixed with 1% (v/v) of photoinitiator stock solution before UV curing. The hydrogel precursor solutions were cured under UV using either Omnicure 2000 or a portable UV lamp depending on the experiment.

B) To simulate the drug release from hydrogel. For the vancomycin laden hydrogel and the vancomycin on top of blank hydrogel, the diffusion mechanisms were calculated by Fick's second law:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}$$

The equation was further adjusted and modified according to the experimental conditions.

Results and Discussion: Two distinct configurations (vancomycin laden hydrogel and vancomycin solutions on top of blank hydrogel) were developed to achieve the burst and lag release, respectively. A controllable lag time could be designed by the structure and drug releasing rate could be accelerated via decreasing formulation concentration, which have been approved through the rheological testing of bioinks and in vitro antibacterial assessments. Modified Fick's second law was used to simulate both burst and lag drug releasing profile, where a validated mathematical model can efficiently guide the precise administration of medicine in the clinical trial. Besides, combining burst release and lag release along with the utilization of two functional of drugs could effectively tackle the dual objectives of anti-infection and accelerating wound he*aling during the appropriate phases of treatment.



Conclusions: PF-PEGDA hydrogel is a promising localized, controlled release system to deliver vancomycin in situ. As an injectable hydrogel, it offers quick gelation in minutes via photopolymerization for use in the clinical setting. Additionally, its tuneable mechanical property and structure permits the manipulation of drug release, rendering it adaptable to various therapeutic requirements. The drug release kinetics can be mathematically described by Fick's Law or modified mathematical model. These mathematical models hold significant potential in guiding the design and formulation of controlled release hydrogels for future clinical applications. With continued research and validation, this hydrogel technology holds the potential to improve patient outcomes, particularly in preventing surgical site infections and facilitating enhanced wound healing after cardiac surgery and other surgical procedures.

References:

1. Liao CH, Chen CS, Chen YC, et al. Vancomycin-loaded oxidized hyaluronic acid and adipic acid dihydrazide hydrogel: Bio-compatibility, drug release, antimicrobial activity, and biofilm model. *J Microbiol Immunol Infect.* 2020;53(4):525-531.

2. Shi YD, Qi FZ, Zhang Y. Treatment of sternal wound infections after open-heart surgery. *Asian J Surg.* 2014;37(1):24-29.

3. Gustafson CT, Boakye-Agyeman F, Brinkman CL, et al. Controlled delivery of vancomycin via charged hydrogels. *PLoS One.* 2016;11(1):e0146401.

4. Pradeep A, Rangasamy J, Varma PK. Recent developments in controlling sternal wound infection after cardiac surgery and measures to enhance sternal healing. *Med Res Rev.* 2021;41(2):709-724.

5. Narayanaswamy R, Torchilin VP. Hydrogels and their applications in targeted drug delivery. *Molecules.* 2019;24(3):603.

6. Yuan Y, Han Y, Yap CW, et al. Prediction of drug permeation through microneedled skin by machine learning. *Bioeng Transl Med.* 2023:e10512.

DRPI

DRPI.SPDS.WORLD

Dissolution Research Presentations International

IN ASSOCIATION WITH

aaps® American Association of Pharmaceutical Scientists

Partners for DRPI - 2023

SOTAX CE 7 smart

USP Apparatus 4

SOTAX CE7 Smart (USP4 Flow Through Cell) Allows you to see differences in your formulations that apparatus 1 and 2 simply do not show. Also widely recommended for poorly soluble, modified / extended release, and low dose products; Also been used for IVIVC studies and a growing range of dosage types

SOTAX India Pvt. Ltd.

Office No. 2-4, 3rd Floor,
Anupam Annapolis, Aarey Road,
Goregaon (East), Mumbai - 400063

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

PLATINUM PARTNER

www.sotax.com

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

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

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

For more details, please visit www.sotax.com

Contact Details:

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

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

It may have something to do with home schooling three children, but Lakshmi is suffering more frequently from headaches at the moment, and relies on paracetamol to help her through.

Now, as an integrated pharma supply company, ACG may not actually make the medication Lakshmi uses. But we do provide the capsules her medication is packed into, the blister packs used to protect them, and equipment used to pack and track them – ensuring they always arrive safely in her hands.

The benefits of using an integrated supplier go beyond things simply working better together. It also means having a single source of supply. So, while you help Lakshmi cope with her headaches, you should experience far fewer too.

Contact us to learn more.
www.acg-world.com

CAPSULES / ENGINEERING / FILMS & FOILS / INSPECTION

ACG

Make it better.

PLATINUM PARTNER

ACG

www.acg-world.com

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

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

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

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

Our Businesses Include:

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

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

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

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

Our Approach:

A healthier world through partnership.

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

A healthier world through integration.

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

BASF

We create chemistry

Solubilization

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

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

Product Highlights:

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

More Information

Contact us: pharma-solutions@basf.com

GOLD PARTNER

https://www.basf.com

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

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

Treasured memories from the past SPDS events

Delegate Registering for
Disso India - Hyderabad 2018
at Hotel Avassa

Lighting of the lamp
during the Inauguration
Disso India - Hyderabad 2018

Delegates interacting
with the partners

Attentive delegates
during
Disso India - Hyderabad 2018

The Organising Committee
of Disso India - Hyderabad 2018

Dr. Sandip Tiwari
during his talk
at Disso India - Hyderabad 2018

Vijay Kshirsagar, Dr. B. M. Rao,
Dr. Uday Bhaskar, Dr. Raghuram Rao,
Prof. Padma Devarajan,
Dr. Ramaswamy releasing
the Scientific Abstract Book
of Disso India - Hyderabad 2018

Dr. Ramaswamy, Dr. Alka Mukne,
Vijay Kshirsagar, Dr. Vinod Shah,
Prof. Padma Devarajan,
releasingthe Pharma Times
Dissolution Special issue
joint project of IPA & SPDS

Panel discussion during
Disso India - Hyderabad 2018

Dr. Vinod Shah answering the questions at the Panel discussion during Disso India - Hyderabad 2018

Dr. Roger William
during his talk
Disso India - Hyderabad 2018

Chairperson Dr. Rajeev Raghuvanshi presenting a momento to Dr. Jennifer Dressman

Dr. Arvind Bansal
presenting a momento
to Speaker Dr. Grove Geoffrey

Dr. Dange Veerpaneni
during his talk

Dr. Raghuram Rao
addressing the delegates
during the inauguration
at Disso India - Hyderabad 2018

Dr. Umesh Banakar
during his talk
at Disso India - Hyderabad 2018

The poster session
at Disso India - Hyderabad 2018

Delegates interacting
with the Poster presenters

Delegates interacting
with the Partners

Delegates interacting
with the Partners

Mr. Amit Lokhande from ICT, Mumbai
receiving 1st Prize
for his poster presented
at Disso India - Hyderabad 2018

Mr. Pankaj Sontakke
from BCP, Mumbai
receiving 2nd Prize
for his poster presented
at Disso India - Hyderabad 2018

Mr. Rijo John from ICT, Mumbai
receiving 3rd Prize
for his poster presented
at Disso India - Hyderabad 2018

The ACG Team
at the stall

The SOTAX India Team
at their Booth

The Lab India Team
at their stall

The Shimadzu & Electrolab
Teams
at their stall

The Inveniolife
Team
at their stall

DRPI 2024

First Announcement

We are happy to inform you that **DRPI 2024** is already being planned.

DRPI 2024 activities will begin in the month of April 2024 with a '**CALL FOR ABSTRACTS**.'

Exact dates and schedule for **DRPI 2024** would be announced online on the website: https://drpi.spds.world

Visit https://drpi.spds.world for the details of the competition and contact details.

Thank You

It may have something to do with home schooling three children, but Lakshmi is suffering more frequently from headaches at the moment, and relies on paracetamol to help her through.

Now, as an integrated pharma supply company, ACG may not actually make the medication Lakshmi uses. But we do provide the capsules her medication is packed into, the blister packs used to protect them, and equipment used to pack and track them – ensuring they always arrive safely in her hands.

The benefits of using an integrated supplier go beyond things simply working better together. It also means having a single source of supply. So, while you help Lakshmi cope with her headaches, you should experience far fewer too.

Contact us to learn more.
www.acg-world.com

CAPSULES / ENGINEERING / FILMS & FOILS / INSPECTION

ACG

Make it better.