# Dissolution Media For In Vitro Testing Of Waterinsoluble

Explore the cutting-edge of dissolution testing in an authoritative, one-stop resource In Pharmaceutical Dissolution Testing, Bioavailability, and Bioequivalence: Science, Applications, and Beyond, distinguished pharmaceutical advisor and consultant Dr. Umesh Banakar delivers a comprehensive and up-to-date reference covering the established and emerging roles of dissolution testing in pharmaceutical drug development. After discussing the fundamentals of the subject, the included resources go on to explore common testing practices and

methods, along with their associated challenges and issues, in the drug development life cycle. Over 19 chapters and 1100 references allow practicing scientists to fully understand the role of dissolution, apart from mere quality control. Readers will discover a wide range of topics, including automation, generic and biosimilar drug development, patents, and clinical safety. This volume offers a one-stop resource for information otherwise scattered amongst several different regulatory regimes. It also includes: A thorough introduction to the fundamentals and essential applications of pharmaceutical dissolution testing Comprehensive explorations of the foundations and drug development applications of bioavailability and bioequivalence Practical discussions

about solubility, dissolution, permeability, and classification systems in drug development In-depth examinations of the mechanics of dissolution, including mathematical models and simulations An elaborate assessment of biophysiologically relevant dissolution testing and IVIVCs, and their unique applications A complete understanding of the methods, requirements, and global regulatory expectations pertaining to dissolution testing of generic drug products Ideal for drug product development and formulation scientists, quality control and assurance professionals, and regulators, Pharmaceutical Dissolution Testing, Bioavailability, and Bioequivalence is also the perfect resource for intellectual property assessors.

In this era of increased pharmaceutical industry competition, success for generic drug companies is dependent on their ability to manufacture therapeutic-equivalent drug products in an economical and timely manner, while also being cognizant of patent infringement and other legal and regulatory concerns.Generic Drug Product Development: Solid Oral

This book describes the theories, applications, and challenges for different oral controlled release formulations. This book differs from most in its focus on oral controlled release formulation design and process development. It also covers the related areas like preformulation, biopharmaceutics, in vitro-in vivo correlations (IVIVC), quality by design (QbD), and regulatory issues.

Scientists have attributed more than 40 percent of the failures in new drug development to poor biopharmaceutical properties, particularly water insolubility. Issues surrounding water insolubility can postpone, or completely derail, important new drug development. Even much-needed reformulation of currently marketed products can be significantly affected by these challenges. Water Insolubility is the Primary Culprit in over 40% of New Drug Development Failures The most comprehensive resource on the topic, this second edition of Water Insoluble Drug Formulation brings together a distinguished team of experts to provide the scientific background and step-by-step guidance needed to deal with solubility issues in drug development. Twenty-three chapters

systematically describe solubility properties and their impact on formulation, from theory to industrial practice. With detailed discussion on how these properties contribute to solubilization and dissolution, the text also features six brand new chapters on water-insoluble drugs, exploring regulatory aspects, pharmacokinetic behavior, early phase formulation strategies, lipid based systems for oral delivery, modified release of insoluble drugs, and scalable manufacturing aspects. The book includes more than 15 water-insoluble drug delivery systems or technologies, illustrated with case studies featuring oral and parenteral applications. Highlighting the most current information and data available, this seminal volume reflects the significant progress that

has been made in nearly all aspects of this field.

Oral Controlled Release Formulation Design and Drug Delivery

Pharmaceutical Dissolution Testing, Bioavailability, and Bioequivalence

Generic Drug Product Development

Media for in Vitro Dissolution Testing of Polysaccharide Based CDDS

Handbook of Lung Targeted Drug Delivery Systems

Investigation of Dissolution and Dispersion Behavior of Ritonavir from Amorphous Solid Dispersion

Guides readers on the proper use of in vitro drug release methodologies in order to evaluate the performance of special dosage forms In the last decade, the application of

drug release testing has widened to a variety of novel/special dosage forms. In order to predict the in vivo behavior of such dosage forms, the design and development of the in vitro test methods need to take into account various aspects, including the dosage form design and the conditions at the site of application and the site of drug release. This unique book is the first to cover the field of in vitro release testing of special dosage forms in one volume. Featuring contributions

from an international team of experts, it presents the state of the art of the use of in vitro drug release methodologies for assessing special dosage forms' performances and describes the different techniques required for each one. In Vitro Drug Release Testing of Special Dosage Forms covers the in vitro release testing of: lipid based oral formulations; chewable oral drug products; injectables; drug eluting stents; inhalation products; transdermal formulations; topical formulations; vaginal

and rectal delivery systems and ophthalmics. The book concludes with a look at regulatory aspects. Covers both oral and non-oral dosage forms Describes current regulatory conditions for in vitro drug release testing Features contributions from well respected global experts in dissolution testing In Vitro Drug Release Testing of Special Dosage Forms will find a place on the bookshelves of anyone working with special dosage forms, dissolution testing, drug formulation and

delivery, pharmaceutics, and regulatory affairs.
This volume offers a comprehensive guide on the theory and practice of amorphous solid dispersions (ASD) for handling challenges associated with poorly soluble drugs. In twenty-three inclusive chapters, the book examines thermodynamics and kinetics of the amorphous state and amorphous solid dispersions, ASD technologies, excipients for stabilizing amorphous solid dispersions such as polymers, and ASD

manufacturing technologies, including spray drying, hot melt extrusion, fluid bed layering and solvent-controlled micro-precipitation technology (MBP). Each technology is illustrated by specific case studies. In addition, dedicated sections cover analytical tools and technologies for characterization of amorphous solid dispersions, the prediction of long-term stability, and the development of suitable dissolution methods and regulatory aspects. The book

also highlights future technologies on the horizon, such as supercritical fluid processing, mesoporous silica, KinetiSol®, and the use of non-salt-forming organic acids and amino acids for the stabilization of amorphous systems. Amorphous Solid Dispersions: Theory and Practice is a valuable reference to pharmaceutical scientists interested in developing bioavailable and therapeutically effective formulations of poorly soluble molecules in order to advance these technologies

and develop better medicines for the future. This book serves as a reference text for regulatory, industry and academic statisticians and also a handy manual for entry level Statisticians. Additionally it aims to stimulate academic interest in the field of Nonclinical Statistics and promote this as an important discipline in its own right. This text brings together for the first time in a single volume a comprehensive survey of methods important to the nonclinical science areas

within the pharmaceutical and biotechnology industries. Specifically the Discovery and Translational sciences, the Safety/Toxiology sciences, and the Chemistry, Manufacturing and Controls sciences. Drug discovery and development is a long and costly process. Most decisions in the drug development process are made with incomplete information. The data is rife with uncertainties and hence risky by nature. This is therefore the purview of Statistics. As such, this book

aims to introduce readers to important statistical thinking and its application in these nonclinical areas. The chapters provide as appropriate, a scientific background to the topic, relevant regulatory guidance, current statistical practice, and further research directions.
Dissolution in different steps of pharmaceutical drug development was considered in this work. Dissolution is used as informative tool throughout the entire development process: After identification of a possible

drug candidate, intrinsic dissolution in different buffer media is tested for physicochemical characterization. In galenics dissolution is used to develop and optimize formulations by comparative release studies. During scale-up dissolution testing is used to observe influence of process or parameter changes. For regulatory affairs all of these dissolution studies are of interest and many have to be presented to the authorities. Most of the dissolution testing designs

in pharmaceutical development are following pharmacopoeial monographs or general chapters and official guidelines. In addition these “official” dissolution testing setups, a progression of more innovative dissolution methods closer to physiological conditions are used. Devices simulating movement and flow of the GIT combined with media simulating the gastrointestinal fluids are often used. Disadvantages of these methods are that they are time-consuming and

expensive, both of which limit throughput. The aims of this thesis were to (a) reduce time consumption regarding preparation of biorelevant dissolution, (b) increase biorelevance of the media FaSSIF and FeSSIF by substituting the non-physiological buffer systems for bicarbonate and (c) to increase throughput by miniaturization of dissolution devices. To meet the first goal a novel preparation method for the biorelevant media FaSSIF and FeSSIF was established. The conventional method

uses chlorinated organic solvent, is time-consuming in preparation (approx. 2 hours) and needs to be done daily. The investigated method uses freeze-drying for the preparation of instant biorelevant media. The instant media only consist of bile salt and lecithin in mixed micelles. In situ preparation is done by simply adding blank buffer to the rapidly dissolving lyophilisate. Freeze-dried product gave comparable results to freshly prepared media and improved reproducibility. Comparison

to commercial available instant media indicated superiority of the freeze-drying method. Next, a buffer system based on the more physiological bicarbonate buffer was investigated. A method to maintain a stable buffer system throughout the dissolution testing. The buffer therefore was created by sparging carbon dioxide into alkali saline solution to forming carbonate and bicarbonate as buffer system. At equilibrium the media was transferred to the vessels and supply of carbon

dioxide continued by sparging the gas above the solution. Therewith bubble formation could be minimized, although not excluded. Only a small range of buffer strength and pH combinations was possible. The lowest pH still providing effective buffer capacity (5 mmol/l/ΔpH) was 5.5. Physiologically relevant buffer capacities of 10 and 30 mmol/l/ΔpH were tested at pH 6.5. The buffer turned out to be very sensitive against pH modifying agents by loosening its buffer capacity and strength.

Standard deviations were generally higher. No superiority over conventional buffer systems like phosphate or acetate buffer regarding IVIVC was given. Therefore it is concluded that bicarbonate buffer is not a suitable medium for in vitro dissolution testing. Subsequently methods for small scale dissolution testing were established. Improvement of throughput in dissolution testing was achieved. The investigated BI miniDiss method can be used to test release profiles

of small particulate formulations or intermediates. High throughput excipient screening for early formulation is possible by using the well-plate method. In the first series of tests, downscaling by factor 10 was conducted by miniaturizing and automating standard dissolution apparatus. Small vessels of 20 ml volume and paddles of about 8 mm diameter were used. Automating was done by sampling through paddle hollow shafts and online

UV/VIS measurement. Since no filtration was possible due to the small sample volume, the true % dissolved was calculated using mathematical scatter correction of spectra from turbid solutions. In this way, release profiles comparable to standard dissolution testing were obtained. Cleaning and restart is accelerated and therewith throughput increased. The 10fold reduced consumption of drug formulation reduces API consumption, so that a larger variety of formulations can be

prepared and tested with the same amount of API. The BI miniDiss is limited to multiparticulates like pellets, extrudates, minitablets, granules or intermediates. Downscaling of matrix or IR tablets will likely result in different results due to changed surface to volume ratio. The well-plate method offers a miniaturization of factor 100. Dissolution of multiparticulates showed significant differences compared to standard methods. However, ranking of formulations was possible

in several cases. The well-plate method is not suitable for conducting comparative release profiles. However, it can be used for selection of excipients by supersaturation testing. It is an informative tool in early formulation screening helping to optimize formulation of poorly soluble compounds. As last part of the work, the BI miniDiss was used to screen various buffers to finding the best media for IVIVC, retrospectively. The BI miniDiss proved to be useful as a fast and cost and

effective screening method. In summary, several improvements in dissolution for pharmaceutical development purposes have been developed regarding consumption of API, costs and efficiency. An easy and rapid preparation of biorelevant media was established making their use in pharmaceutical development and routine quality control more feasible. The miniaturized dissolution methods and the improved high-throughput fulfil demands from pharmaceutical industries to

facilitate API-saving methods in development.
In-vitro In-vivo Correlation
Developed Using a Biorelevant In-vitro Dissolution Test in the Prediction of In-vivo Pharmacokinetic Parameters for the Treatment of Multiple Sclerosis
Amorphous Solid Dispersions
Correlation of In Vitro Dissolution Rate with Apparent Solubility
Water-Insoluble Drug Formulation
Poorly Soluble Drugs
Generics and Bioequivalence

**This detailed volume addresses key issues and subtle nuances involved in developing hydrophilic matrix tablets as an approach to oral controlled release. It brings together information from more than five decades of research and development on hydrophilic matrix tablets and provides perspective on contemporary issues. Twelve comprehensive chapters explore a variety of topics including polymers (hypromellose, natural polysaccharides and polyethylene oxide) and their utilization in hydrophilic matrices, critical interactions impacting tablet performance, in vitro physical and imaging techniques, and microenvironmental pH control**

**and mixed polymer approaches, among others. In one collective volume, Hydrophilic Matrix Tablets for Oral Controlled Release provides a single source of current knowledge, including sections of previously unpublished data. It is an important resource for industrial and academic scientists investigating and developing these oral controlled release formulations.**

**Learn about the analytical tools used to characterize particulate drug delivery systems with this comprehensive overview Edited by a leading expert in the field, Characterization of Pharmaceutical Nano- and Microsystems provides a complete description of the**

**analytical techniques used to characterize particulate drug systems on the micro- and nanoscale. The book offers readers a full understanding of the basic physicochemical characteristics, material properties and differences between micro- and nanosystems. It explains how and why greater experience and more reliable measurement techniques are required as particle size shrinks, and the measured phenomena grow weaker. Characterization of Pharmaceutical Nano- and Microsystems deals with a wide variety of topics relevant to chemical and solid-state analysis of drug delivery systems, including drug release, permeation, cell interaction, and**

**safety. It is a complete resource for those interested in the development and manufacture of new medicines, the drug development process, and the translation of those drugs into life-enriching and lifesaving medicines. Characterization of Pharmaceutical Nano- and Microsystems covers all of the following topics: An introduction to the analytical tools applied to determine particle size, morphology, and shape Common chemical approaches to drug system characterization A description of solid-state characterization of drug systems Drug release and permeation studies Toxicity and safety issues The interaction of drug particles with cells Perfect for**

**pharmaceutical chemists and engineers, as well as all other industry professionals and researchers who deal with drug delivery systems on a regular basis, Characterization of Pharmaceutical Nano- and Microsystems also belongs on bookshelves of interested students and faculty who interact with this topic.**

**Published in 1994: This text focuses on the determination of bioequivalence between formulations that are pharmaceutically equivalent and manufactured using acceptable chemistry, manufacturing and controls and in accordance with Good Manufacturing Practices. Developing Solid Oral Dosage Forms is intended for**

**pharmaceutical professionals engaged in research and development of oral dosage forms. It covers essential principles of physical pharmacy, biopharmaceutics and industrial pharmacy as well as various aspects of state-of-the-art techniques and approaches in pharmaceutical sciences and technologies along with examples and/or case studies in product development. The objective of this book is to offer updated (or current) knowledge and skills required for rational oral product design and development. The specific goals are to provide readers with: Basics of modern theories of physical pharmacy, biopharmaceutics and industrial pharmacy and their applications**

**throughout the entire process of research and development of oral dosage forms Tools and approaches of preformulation investigation, formulation/process design, characterization and scale-up in pharmaceutical sciences and technologies New developments, challenges, trends, opportunities, intellectual property issues and regulations in solid product development The first book (ever) that provides comprehensive and in-depth coverage of what's required for developing high quality pharmaceutical products to meet international standards It covers a broad scope of topics that encompass the entire spectrum of solid dosage form development for the global**

**market, including the most updated science and technologies, practice, applications, regulation, intellectual property protection and new development trends with case studies in every chapter A strong team of more than 50 well-established authors/co-authors of diverse background, knowledge, skills and experience from industry, academia and regulatory agencies**
**Science, Applications, and Beyond**
**Recent Trends and Clinical Evidences**
**Hydrophilic Matrix Tablets for Oral Controlled Release**
**Nonclinical Statistics for Pharmaceutical and Biotechnology Industries**

**Bioequivalence Requirements in Various Global Jurisdictions**
**Characterization of Pharmaceutical Nano- and Microsystems**

This book presents some of the state-of-the-art methods for the study of the gastrointestinal variables affecting oral drug absorption. Practical applications of new in vitro release/dissolution methods are presented, as well as in vitro permeability studies to explore segmental differences. The application of MRI methods for the study of colon physiology is presented to illustrate its potential applications in controlled release dosage form design. Some examples

of successful in vitro–in vivo correlations show how implementing the gastrointestinal physiological variables in the new in vitro methods can improve the predictions of in vivo drug product performance. The book contains an updated review of the experimental, computational, and in vivo approaches for measuring intestinal permeability.

A clear, straightforward resource to guide you through preclinical drug development Following this book's step-by-step guidance, you can successfully initiate and complete critical phases of preclinical drug development. The book serves as a basic, comprehensive reference to

prioritizing and optimizing leads, dose formulation, ADME, pharmacokinetics, modeling, and regulations. This authoritative, easy-to-use resource covers all the issues that need to be considered and provides detailed instructions for current methods and techniques. Each chapter is written by one or more leading experts in the field. These authors, representing the many disciplines involved in preclinical toxicology screening and testing, give you the tools needed to apply an effective multidisciplinary approach. The editor has carefully reviewed all the chapters to ensure that each one is thorough, accurate, and clear. Among the key topics

covered are: * Modeling and informatics in drug design * Bioanalytical chemistry * Absorption of drugs after oral administration * Transporter interactions in the ADME pathway of drugs * Metabolism kinetics * Mechanisms and consequences of drug-drug interactions Each chapter offers a full exploration of problems that may be encountered and their solutions. The authors also set forth the limitations of various methods and techniques used in determining the safety and efficacy of a drug during the preclinical stage. This publication should be readily accessible to all pharmaceutical scientists involved in preclinical

testing, enabling them to perform and document preclinical safety tests to meet all FDA requirements before clinical trials may begin.

This book represents the invited presentations and some of the posters presented at the conference entitled "In Vitro-In Vivo Relationship (IVIVR) Workshop" held in Sep tember, 1996. The workshop was organized by the IVIVR Cooperative Working Group which has drawn together scientists from a number of organizations and institutions, both academic and industrial. In addition to Elan Corporation, which is a drug delivery com pany specializing in the development of ER (Extended

Release) dosage forms, the IVIVR Cooperative Working Group consists of collaborators from the University of Maryland at Baltimore, University College Dublin, Trinity College Dublin, and the University of Not tingham in the UK. The principal collaborators are: Dr. Jackie Butler, Elan Corporation Prof. Owen Corrigan, Trinity College Dublin Dr. lain Cumming, Elan Corporation Dr. John Devane, Elan Corporation Dr. Adrian Dunne, University College Dublin Dr. Stuart Madden, Elan Corporation Dr. Colin Melia, University of Nottingham Mr. Tom O'Hara, Elan Corporation Dr. Deborah Piscitelli, University of Maryland at Baltimore

Dr. Araz Raoof, Elan Corporation
Mr. Paul Stark, Elan Corporation
Dr. David Young, University of Maryland at Baltimore The purpose of the workshop was to discuss new concepts and methods in the devel opment of in vitro-in vivo relationships for ER products. The original idea went back ap proximately 15 months prior to the workshop itself. For some time, the principal collaborators had been working together on various aspects of dosage form development.
The ultimate goal of drug product development is to design a system that maximizes the therapeutic potential of the drug substance and facilitates its access to patients.

Pharmaceutical Dosage Forms: Tablets, Third Edition is a comprehensive resource of the design, formulation, manufacture, and evaluation of the tablet dosage form, an

med 16 Sider farvetrykte Kort m.m., 64 Sider almennyttige Oplysninger, 64 Sider til Noteringer, Schemaer m.m

A Practical Guide from Candidate Drug Selection to Commercial Dosage Form

The Effects of Temperature and Dissolution Media on Crystallization of Amorphous Drugs and Potential Effects on Predicting Bioavailability

A Comprehensive Guide on

Biopharmacy and Pharmacokinetics
Basic Pharmacokinetics and Pharmacodynamics
Pharmaceutical Preformulation and Formulation
***This thesis describes evaluation of a gastric retention device (GRD) developed at Oregon State University. The device was originally fabricated from Xanthan gum and Locust bean gum. A modified gastric retention device containing other additives was developed and investigated in this work. The modified device was evaluated in vitro for swelling and dissolution properties using riboflavin as a model drug.***

*Different shapes and sizes of GRDs were tested in dogs to study the gastric retention potential of these devices. The effect of the device on food emptying from the stomach in dogs was also investigated. Endoscopic studies in dogs also showed that the device swells rapidly and considerably in gastric fluid. The bioavailability of riboflavin from three different size GRDs was determined in six fasted human volunteers and compared to an immediate release formulation. The biostudy indicated that the bioavailability of riboflavin from a large size*

*GRD was more than triple that measured after administration of the immediate release formulation. Deconvolution was used to determine gastric residence time of the different size GRDs. A new colonic delivery system made of acetaminophen loaded beads produced by extrusion and spheronization and coated with different ratios of pectin and ethylcellulose coating solutions in a spray coating apparatus was also developed in this work. Such beads release their drug content in the colon due to susceptibility of pectin in the outer coat to enzymatic action of colonic bacteria.*

*The new delivery system was evaluated in vitro by conducting release studies in different dissolution media to mimic transit times, pH and enzyme conditions in the gastrointestinal tract. The gastrointestinal transit behavior of drug beads was also assessed by conducting gamma-scintigraphic studies in dogs. The bioavailability and pharmacokinetic parameters of acetaminophen from several colonic delivery system formulations were determined in human volunteers and compared to the immediate release commercial product Tylenol®. A selected pectin-*

*ethylcellulose coat formulation in the ratio 1:3 was further evaluated in six volunteers under both fed and fasting conditions and was found to be effective and to provide sustained drug release in the colon over a period of 12 hours. Till date, pursuit for cost effective and animal sparing colon specific bio-relevant dissolution media has been a foremost challenge facing pharmaceutical scientists over many decades.It is problematic to mimic the dynamic and ecologically diverse features of the colon in dissolution vessel.With the knowledge of enormous colonic microflora,*

*the predominant species Bacteroides, Bifidobacterium, Eubacterium, Streptococcus and Lactobacillus species were cultured in 12% w/v skimmed milk powder and 5%w/v grade "A" honey. Probiotic culture was added to the dissolution media in order to test the drug release of polysaccharide based formulations. USP dissolution apparatus I/II with gradient pH dissolution method were used to evaluate the drug release from formulations meant for colonic drug delivery. Drug release from 5-fluorouracil granules and metronidazole tablets were assed under*

*gastric, small intestine conditions and also within a simulated colonic environment involving existing rat caecal, human fecal media and compared with novel probiotic media. The present method can be successfully applied for the drug release testing of any oral formulations meant for colonic delivery.*

*This book presents a collection of articles that represent individual and expert perspectives in both preclinical and clinical development, including case studies on real-life examples of successful drugs that add value to the pharmacokinetic principles*

*learned and applied. Unlike existing books that focus on pharmacokinetic theory, the current book emphasizes application of pharmacokinetic principles in new drug development. Pharmaceutical Preformulation and Formulation: A Practical Guide from Candidate Drug Selection to Commercial Dosage Form reflects the mounting pressure on pharmaceutical companies to accelerate the new drug development and launch process, as well as the shift from developing small molecules to the growth of biopharmaceuticals. The book meets the need for advanced*

*information for drug preformulation and formulation and addresses the current trends in the continually evolving pharmaceutical industry. Topics include: Candidate drug selection Drug discovery and development Preformulation predictions and drug selections Product design to commercial dosage form Biopharmaceutical support in formulation Development The book is ideal for practitioners working in the pharmaceutical arena—including R&D scientists, technicians, and managers—as well as for undergraduate and*

***postgraduate courses in industrial pharmacy and pharmaceutical technology.***

***Analytics of dissolution testing of products containing nanosized drugs with a view to predicting plasma profiles***

***Theory to Practice***

***The Impact of Biorelevant Media on the In-Vitro Dissolution of Azole Anti-Fungal Drugs***

***In Vitro-In Vivo Correlations***

***Pharmaceutical Dosage Forms - Tablets***

***Applications of Pharmacokinetic Principles in Drug Development***

*Poorly soluble crystalline drug*

*candidates are often made amorphous to increase their solubility with the intent to enhance oral bioavailability, thus improving the likelihood of becoming a commercial drug product. Currently, considerable time, material and effort are expended to determine whether an amorphous approach will provide the required bioavailability improvement. However, often the solubility enhancement of the amorphous form is not fully realized in vivo due to solution-mediated phase transformation (SMPT). This study investigated the effects of key factors, through experimentation and modeling, that affect SMPT and*

*model the potential effects of SMPT on bioavailability. Sparsely parameterized biopharmaceutical models were developed to quickly obtain estimates of the bioavailability from in vitro dissolution data for compounds that precipitate in the gastrointestinal tract. The models highlight the complex effects of drug absorption rate on expected in vivo drug peak concentration and duration in the small intestinal lumen from where orally administered drug is absorbed, depending on whether the peak concentration or the peak duration is assumed to better translate from in vitro to in vivo. Furthermore, a model with limited*

*number of input variables allowed us to quantify variation in bioavailability based on known variations of one or more model input parameters. The differences in SMPT of a supersaturating system were compared in biorelevant media and a medium without surfactants. Amorphous spironolactone underwent SMPT to a channel hydrate in all three media which was confirmed by the decrease in dissolution rates assessed in a flow-through dissolution apparatus, as well as by the appearance of crystals on the amorphous solid surface detected by polarized light microscopy. Longer duration of supersaturation was found in both*

*biorelevant media, compared to the medium without surfactants. The contribution(s) of the molecular mobility of the hydrated amorphous drug and degree of supersaturation to the rate of SMPT of amorphous spironolactone. The degree of supersaturation was not the sole determinant of SMPT. Rather, mobility of the solid at/near the dissolution surface of amorphous material, relative to 37°C (id est, physiological relevant temperature) is more likely to be govern the extent and time course of dissolution enhancement by amorphous drugs. This book covers the essentials of drug delivery research and provides a unique forum for scientific*

*experimental methods that are exclusively focused by the in-vitro, ex-vivo, and in-vivo methodologies of drug delivery research and felicitates translational research. The book includes recent and novel approaches in evaluation methods of transdermal, nasal, ocular, oral and intraoral, gastro-retentive, colon-targeted, and brain-targeted drug delivery systems. Providing up to date and comprehensive information, this text is invaluable to students, teachers, scientists, and others employed in the field of drug delivery.*

*Although the Bioequivalence (BE) requirements in many global jurisdictions have much in common,*

*differences in certain approaches and requirements such as definitions and terms, choice of comparator (reference) product, acceptance criteria, fasted and fed studies, single and multi-dose studies, biowaivers and products not intended for absorption into the systemic circulation (locally acting medicines and dosage forms), amongst others, provide food for thought that standardisation should be a high priority objective in order to result in a harmonized international process for the market approval of products using BE. An important objective of Bioequivalence Requirements in Various Global Jurisdictions is to*

*attempt to gather the various BE requirements used in different global jurisdictions to provide a single source of relevant information. This information from, Brazil, Canada, China, European Union, India, Japan, MENA, Russia South Africa, the USA and WHO will be of value to drug manufacturers, regulatory agencies, pharmaceutical scientists and related health organizations and governments around the world in the quest to harmonize regulatory requirements for the market approval of generic products.*
*Oral Drug Absorption, Second Edition thoroughly examines the special equipment and methods used*

*to test whether drugs are released adequately when administered orally. The contributors discuss methods for accurately establishing and validating in vitro/in vivo correlations for both MR and IR formulations, as well as alternative approaches for MR an*
*Aarhuus Stiftstidendes Lommebog for Avislæsere*
*In-Vitro and In-Vivo Tools in Drug Delivery Research for Optimum Clinical Outcomes*
*An Integrated Textbook and Computer Simulations*
*Pharmaceutical Theory and Practice*
*Principles in Drug Development*
*Computer-aided applications in*

*pharmaceutical technology*

*Handbook of Lung Targeted Drug Delivery Systems: Recent Trends and Clinical Evidences covers every aspect of the drug delivery to lungs, the physiology and pharmacology of the lung, modelling for lung delivery, drug devices focused on lung treatment, regulatory requirements, and recent trends in clinical applications. With the advent of nano sciences and significant development in the nano particulate drug delivery systems there has been a*

*renewed interest in the lung as an absorption surface for various drugs. The emergence of the COVID-19 virus has brought lung and lung delivery systems into focus, this book covers new developments and research used to address the prevention and treatment of respiratory diseases. Written by well-known scientists with years of experience in the field this timely handbook is an excellent reference book for the scientists and industry professionals. Key Features: Focuses*

*particularly on the chemistry, clinical pharmacology, and biological developments in this field of research. Presents comprehensive information on emerging nanotechnology applications in diagnosing and treating pulmonary diseases Explores drug devices focused on lung treatment, regulatory requirements, and recent trends in clinical applications Examines specific formulations targeted to pulmonary systems*

*A human, regional*

*absorption study was undertaken, in-vivo data for the systemic exposure of Firategrast, a multiple sclerosis treatment was obtained. Immediate release, Modified release over 3, 6 and 9 hour solid oral tablet formulations in the fasted state, alongside the modified release 6 hour formulation administered with food were administered. As part of pharmaceutical development, understanding the release profile of the formulation is critical to understanding the bioavailability the*

*product. A theory in understanding Firategrast bioavailability was tasked; could in-vitro dissolution be used to understand the bioavailability at the time of 'gastric emptying' and be used to predict in-vivo absorption of Firategrast. In order to investigate bioavailability, a range of biorelevant in-vitro dissolution tests were developed, with the aim of developing an IVIVC. The biorelevant dissolution test focussed on mimicking two key areas of in-vivo*

*gastro-intestinal transit that are critical to bioavailability; gastric media and gastric agitation. The dissolution tests developed were validated for use with an analytical HPLC method. No trends were observed in using fasted and fed media or using the peristaltic pump to mimic the gastric hydrodynamics. The data was then applied to the 'gastric emptying window' theory for bioavailability. The percentage in-vitro dissolution at 1 hour (fasted gastric emptying*

*time), 3 and 4 hours (fed gastric emptying times) were correlated with the in-vivo pharmacokinetic data parameters such as AUC and plasma concentration (ng/mL). A multiple level C correlation was observed according to FDA guidelines. Correlations show weaknesses in the form of variable dissolution data and potentially skewed in-vivo data. Further work is recommended to increase the statistical power of the correlations.*
*The oral bioavailability*

*of a drug substance is strongly related to its aqueous solubility. Only complete dissolution during the GI-passage can maintain an optimal bioavailability. Poor aqueous drug solubility results, according to the Nernst-Brunner equation into a slow dissolution rate, sometimes too slow for complete dissolution in the GI tract. The dissolution rate increases with decreasing particle size and therefore increasing surface area of the drug particles. In consequence,,*

*micronization of the drug is applied to increase oral bioavailability, but often meets with modest success. Recently developed techniques were applied to decrease the particle size into the nanometer range. For some substances, pharmacokinetic parameters could be influenced decisively, e.g. the obviation of a food effect for the drugs aprepitant and fenofibrate. The assessment of a dosage form is investigated by dissolution testing. For a reasonable assessment of*

*such tests, a separation of solid and liquids has to be ensured within an appropriate time frame. For particle sizes of about 150 nm it appears questionable whether such separation can be succeeded by classical techniques, e.g. the use of syringe filters with a pore size of 0.45 µm. The aims of this thesis were to investigate the suitability of various analytical techniques in analysis of dissolution tests containing nanosized drug substance. Furthermore, a suitable*

*analytical tool is applied to establish an in vitro – in vivo correlation of the nanosized drug fenofibrate. At first, several techniques were investigated in theory to assess their ability to ensure a rapid and complete separation of solids and liquids. The classical dialysis, turbidity measurement and UV-measurement via fiber optics were excluded from further investigation due to various reasons, e.g. the speed of separation for dyialisis. The asymmetrical flow field-*

*flow fractionation appeared to be a promising tool, but lack of equipment precluded further investigation. The ultrasonic resonance technology (ResoScan), the microdialysis and the use of centrifugal filter devices have shown to be inappropriate for the analytics of nanosized drugs in dissolution test. The use of syringe filters with various pore sizes and the ionselective electrode (ISE) was promising, so these techniques were examined more intensively. The*

*syringe filters with various filter pore sizes were investigated for their ability to hold back colloidal drug. Fenofibrate was chosen as model drug, since this is commercially available both as micronized and nanosized formulation (Lipidil TerR and Lipidil 145 ONER), enabling direct comparison. The experiments with micronized fenofibrate which contains little or no colloidal fenofibrate yielded similar dissolution profiles, irrespective of filter*

*pore size; f2 was always greater than 65, indicating less than 5% difference between the dissolution profiles in any medium. Using a pore size of 0.1 µm or less, the maximum concentration of drug achieved in solution from the nanosized formulation was commensurate with the saturation solubility of fenofibrate in all tested media. Filtration with a pore size of 0.2 µm or 0.45 µm generated concentrations exceeding the saturation solubility. These results, in*

*combination with higher standard deviations of the analytical results, indicate that the apparent "supersaturation" is caused by colloidal fenofibrate, which is too fine to be held back by these filters. The f2-value of less than 50 when comparing the profiles obtained from 0.1 µm and 0.2 µm filter pore size indicates that the choice of filter pore size is crucial to the interpretation of the dissolution profiles. To separate nanosized drug from molecularly dissolved*

*fenofibrate in Lipidil 145 ONER, a filter pore size of 0.1 µm or less appears to be appropriate. It was observed that the experimental increase of dissolution rate is not congruent with common hypothesis regarding the boundary layer h for decreasing particle sizes and subsequent application of the Nernst-Brunner equation. The initial dissolution rates of both formulations were investigated by using a filter pore size of 0.1 µm. The results were utilized in an in silico*

*model (STELLAc) to correlate the in vitro results with in vivo data (Model A). In the preprandial state a good in correlation was established for the micronized fenofibrate, while for the nanosized fenofibrate the plasma levels were overpredicted. The model was expanded to investigate the impact of an absorption step at the intestinal membrane on the in vitro – in vivo correlation. It was found that even a minor deceleration of absorption results in varied plasma*

*profiles caused by a lagged appearance of drug in the blood. For both formulations the rate determining step was identified: When changing from the micronized to the nanosized formulation, the rate-determining step for absorption may change from completely dissolution-controlled to at least partly permeationcontrolled in the fasted state. In the fed state, gastric emptying appears to be rate-determining for absorption of fenofibrate from both the micronized*

*and the nanosized formulation. Another technique appears to be suitable for analysis of nanosized drugs in dissolution testing. The Ion-selective electrode (ISE) is a recently developed analytical system measuring the changes of the electrochemical potential in solutions. A transformation via the Nikolski – Eisenmann equation results into the concentration of the respective drug in solution. Since only dissolved drug is*

*detected, obviating the need for separation of dissolved from undissolved drug, this system appears to be very promising in the analytics of nanocrystalline drugs. Diphenhydramine_HCl was chosen as model substance for the ISE studies. It was the goal of investigation to test compatibility of the ISE with complex media, e.g. all biorelevant dissolution media. This is done in advance of application of the ISE in these media for nanocrystalline drug*

*substance. The results were compared to manual sampling, filtration and subsequent HPLC-UV analysis. The results demonstrate that the ion-selective electrode is suitable for measurements of diphenhydramine HCl in fasted state biorelevant media (FaSSGF, FaSSIF, FaSSIF-V2) as both a stand-alone system (Method A) and in conjunction with a single point conventional assay (Method B). The results acquired are similar to those obtained by manual sampling and subsequent HPLC-UV*

*analysis. The ISE also delivers satisfactory results in a milk-based medium (FeSSGF), in which it has distinct advantages over manual sampling with HPLC-UV analysis by obviating the need for sample preparation. The application of the ISE in FeSSIF type media will need further study. Finally, as an on-line technology, ISE offers more efficient generation of dissolution profiles than conventional sample-based methods.*
*This book is the first text to provide a*

*comprehensive assessment of the application of fundamental principles of dissolution and drug release testing to poorly soluble compounds and formulations. Such drug products are, vis-à-vis their physical and chemical properties, inherently incompatible with aqueous dissolution. However, dissolution methods are required for product development and selection, as well as for the fulfillment of regulatory obligations with respect to biopharmaceutical*

*assessment and product quality understanding. The percentage of poorly soluble drugs, defined in classes 2 and 4 of the Biopharmaceutics Classification System (BCS), has significantly increased in the modern pharmaceutical development pipeline. This book provides a thorough exposition of general method development strategies for such drugs, including instrumentation and media selection, the use of compendial and non-compendial techniques in product development, and*

*phase-appropriate approaches to dissolution development. Emerging topics in the field of dissolution are also discussed, including biorelevant and biphasic dissolution, the use on enzymes in dissolution testing, dissolution of suspensions, and drug release of non-oral products. Of particular interest to the industrial pharmaceutical professional, a brief overview of the formulation and solubilization techniques employed in the*

*development of BCS class 2 and 4 drugs to overcome solubility challenges is provided and is complemented by a collection of chapters that survey the approaches and considerations in developing dissolution methodologies for enabling drug delivery technologies, including nanosuspensions, lipid-based formulations, and stabilized amorphous drug formulations.*

*Theory and Practice*

*Oral Drug Absorption*

*6. Computer-aided biopharmaceutical*

*characterization: gastrointestinal absorption simulation*
*ADME and Biopharmaceutical Properties*
*Preclinical Development Handbook*
*Development and Evaluation of a New Colonic Delivery System*

**Updated with new chapters and topics, this book provides a comprehensive description of all essential topics in contemporary pharmacokinetics and pharmacodynamics. It also features interactive computer simulations for students to**

**experiment and observe PK/PD models in action. • Presents the essentials of pharmacokinetics and pharmacodynamics in a clear and progressive manner • Helps students better appreciate important concepts and gain a greater understanding of the mechanism of action of drugs by reinforcing practical applications in both the book and the computer modules • Features interactive computer simulations, available online through a companion website at: https://web.uri.edu/pharmacy/research/rosenbaum/sims/ •**

**Adds new chapters on physiologically based pharmacokinetic models, predicting drug-drug interactions, and pharmacogenetics while also strengthening original chapters to better prepare students for more advanced applications • Reviews of the 1st edition: “This is an ideal textbook for those starting out ... and also for use as a reference book ...." (International Society for the Study of Xenobiotics) and “I could recommend Rosenbaum’s book for pharmacology students**

**because it is written from a perspective of drug action . . . Overall, this is a well-written introduction to PK/PD .... " (British Toxicology Society Newsletter)**

**This chapter introduces the concept of gastrointestinal absorption simulation using in silico methodology. Parameters used for model construction and the sensitivity predicted pharmacokinetic responses to various input parameters are described. Virtual trials for in silico modeling of drug absorption are presented. The influence of food on drug**

**absorption, as well as correlation between the in vitro and in vivo results, are also addressed, followed by biowaiver considerations. Numerous examples are provided throughout the chapter.**

**ORAL DRUG DELIVERY FOR MODIFIED RELEASE FORMULATIONS Provides pharmaceutical development scientists with a detailed reference guide for the development of MR formulations Oral Drug Delivery for Modified Release Formulations is an up-to-date review of the key aspects of**

**oral absorption from modified-release (MR) dosage forms. This edited volume provides in-depth coverage of the physiological factors that influence drug release and of the design and evaluation of MR formulations. Divided into three sections, the book begins by describing the gastrointestinal tract (GIT) and detailing the conditions and absorption processes occurring in the GIT that determine a formulation's oral bioavailability. The second section explores the design of modified release formulations, covering early drug substance**

**testing, the biopharmaceutics classification system, an array of formulation technologies that can be used for MR dosage forms, and more. The final section focuses on in vitro, in silico, and in vivo evaluation and regulatory considerations for MR formulations. Topics include biorelevant dissolution testing, preclinical evaluation, and physiologically-based pharmacokinetic modelling (PBPK) of in vivo behaviour. Featuring contributions from leading researchers with expertise in the different aspects of MR formulations,**

**this volume: Provides authoritative coverage of physiology, physicochemical determinants, and in-vitro in-vivo correlation (IVIVC) Explains the different types of MR formulations and defines the key terms used in the field Discusses the present status of MR technologies and identifies current gaps in research Includes a summary of regulatory guidelines from both the US and the EU Shares industrial experiences and perspectives on the evaluation of MR dosage formulations Oral Drug Delivery for Modified Release**

**Formulations is an invaluable reference and guide for researchers, industrial scientists, and graduate students in general areas of drug delivery including pharmaceutics, pharmaceutical sciences, biomedical engineering, polymer and materials science, and chemical and biochemical engineering. The aim of this study was to develop ritonavir amorphous solid dispersion (ASD) formulation, investigate its aqueous dissolution and dispersion behavior, and predict potential**

**pharmacokinetic parameters by in-silico modeling. The binary/ternary ASDs of ritonavir with PVPVA or HPMCAS-MG in the absence or presence of surfactants were prepared by using the hot-melt extrusion method. The amount of ritonavir was fixed at 20 %w/w, while amount of polymer and surfactant in the formulation was varied. The film-casting technique was used to confirm the miscibility of drug and polymer in the absence and presence of surfactant in different formulations. PXRD and DSC analyze were carried**

**out to determine solid state properties of the neat ritonavir and solid dispersion formulations prior to conducting dissolution and dispersion testing. All in-vitro dissolution and dispersion studies were performed under non-sink condition at pH 2 (0.01N HCl), pH 4.5 (acetate buffer), and pH 6.8 (phosphate buffer), as well as in a biorelevant medium (FeSSIF-V2). Particle size analysis of the dispersed phase after dispersion of the extrudates in aqueous media was carried out in-line using a particle size analyzer. Raman spectroscopy**

**coupling with chemometrics method was used to identify the polymorphic form of the precipitates from the extrudates after exposing to dissolution medium. The software simulation was then carried out to predict the oral absorption based on in-vitro studies. Stability studies of the ASDs were carried out at 25°C/60%RH for 1 year and 40°C/75%RH for 1 month. Ritonavir, 20%w/w, was found to be miscible with various ratios of polymers and surfactants used. Supersaturated solutions were formed and the**

**supersaturation was maintained throughout 2 h of dissolution testing. However, above certain concentration in dissolution media, ritonavir phase separated and formed milky dispersions. Particle size analysis of the dispersed phase revealed that nano/micro particles were generated by all ASD formulations. The biorelevant media provided much higher drug dissolution as compared to that in standard phosphate buffer medium. The slurries from the extrudates containing ritonavir:PVPVA:sorbitan**

**monolaurate at 20:70:10 % w/w revealed that mixtures of amorphous and crystalline of ritonavir were present. The predicted fraction absorbed ranged from 65 to 90%. In the solid state, all ASDs did not show any ritonavir crystallization under both the stability testing conditions. In the present study, various factors influencing formulations, physical stability and drug release of ASDs of ritonavir were studied. It was observed that there was a good correlation between in-vitro dissolution, in-line particle size monitoring and in-**

**silico modeling which can served as a predictive tool in pharmaceutical development of the ASD for ritonavir as well as other poorly water-soluble drugs. The dissolution and dispersion testing using biorelevant media provided more accurate results on the behavior of the drug formulation than only the result from dissolution testing in standard buffers.**

**Improvements to biorelevant dissolution testing: lyophilized media, buffer alternatives and miniaturized apparatus**

**Developing Solid Oral Dosage Forms**

**In Vitro and in Vivo Testing of a Gastric Retention Device**
**Solid Oral Dosage Forms, Second Edition**
**Federal Register**
**Experimental, Computational and In Vitro Predictive Approaches**