In Vitro Dissolution Testing For Solid Oral Dosage Forms

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In Vitro Dissolution Testing For Solid Oral Dosage Forms ***2024-06-21***

LESTER LYTA

Clinically Relevant in Vitro Dissolution/release Testing for Parenteral Formulations Springer Science & Business Media 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 Academic Press 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 September, 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 company 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.

Biopharmaceutics Applications in Drug Development John Wiley & Sons
Introduction, Historical Highlights, and the Need for Dissolution Testing
Theories of Dissolution
Dissolution Testing Devices
Automation in Dissolution Testing, by William A. Hanson and Albertha M. Paul
Factors That Influence Dissolution Testing
Interpretation of Dissolution Rate Data
Techniques and of In Vivo Dissolution, by Umesh V. Banakar, Chetan D. Lathia, and John H. Wood
Dissolution of Dosage Forms
Dissolution of Modified-Release Dosage Forms
Dissolution and Bioavailability
Dissolution Testing and the Assessment of Bioavailability/ Bioequivalence, by Santosh J. Vetticaden
Dissolution Rediscovered, by John H. Wood
Appendix: USP/NF Dissolution Test.

Pharmaceutical Dissolution Testing, Bioavailability, and Bioequivalence John Wiley & Sons
The need to validate an analytical or bioanalytical method is encountered by analysts in the pharmaceutical industry on an almost daily basis, because adequately validated methods are a necessity for approvable regulatory filings. What constitutes a validated method,

however, is subject to analyst interpretation because there is no universally accepted industry practice for assay validation. This book is intended to serve as a guide to the analyst in terms of the issues and parameters that must be considered in the development and validation of analytical methods. In addition to the critical issues surrounding method validation, this book also deals with other related factors such as method development, data acquisition, automation, cleaning validation and regulatory considerations . The book is divided into three parts. Part One, comprising two chapters, looks at some of the basic concepts of method validation. Chapter 1 discusses the general concept of validation and its role in the process of transferring methods from laboratory to laboratory. Chapter 2 looks at some of the critical parameters included in a validation program and the various statistical treatments given to these parameters. Part Two (Chapters 3, 4 and 5) of the book focuses on the regulatory perspective of analytical validation. Chapter 3 discusses in some detail how validation is treated by various regulatory agencies

around the world, including the United States, Canada, the European Community, Australia and Japan. This chapter also discusses the International Conference on Harmonization (ICH) treatment of assay validation. Chapters 4 and 5 cover the issues and various perspectives of the recent United States vs. Barr Laboratories Inc. case involving the retesting of samples. Part Three (Chapters 6 - 12) covers the development and validation of various analytical components of the pharmaceutical product development process. This part of the book contains specific chapters dedicated to bulk drug substances and finished products, dissolution studies, robotics and automated workstations, biotechnology products, biological samples, analytical methods for cleaning procedures and computer systems and computer-aided validation. Each chapter goes into some detail describing the critical development and related validation considerations for each topic. This book is not intended to be a practical description of the analytical validation process, but more of a guide to the critical parameters and considerations that must be

attended to in a pharmaceutical development program. Despite the existence of numerous guidelines including the recent attempts by the ICH to be implemented in 1998, the practical part of assay validation will always remain, to a certain extent, a matter of the personal preference of the analyst or company. Nevertheless, this book brings together the perspectives of several experts having extensive experience in different capacities in the pharmaceutical industry in an attempt to bring some consistency to analytical method development and validation. *Pharmacokinetic Evaluation and Modeling of Clinically Significant Drug Metabolites* CRC Press For inhalation drug products, the site of deposition in the lungs is assumed to be the most essential factor to control the clinical performance. Therefore, delivering the active pharmaceutical ingredient from the inhalation device to the targeted site is the only concern of the regulatory affairs. -- However, inhaled particles have to undergo dissolution in the lung fluid before being available for absorption. This implies that the dissolution kinetics of the inhaled

particles might have an effect on the therapeutic action. -- The lung fluid where dissolution occurs is one of critical factors that govern the dissolution process of the inhaled particles. Therefore, identifying the lung fluid composition is very essential during the in-vitro dissolution testing. -- The in-vitro dissolution testing can be used for different quality measures. However, it can also be employed to predict the in-vivo dissolution rate of various inhaled products, therefore, determine if the dissolution in the lung fluid is the rate limiting step for absorption or not. -- Hence, this thesis will be focusing on defining the various lung fluids and their importance regarding the dissolution process. Also, factors affecting dissolution in the lung fluid will be discussed and finally, developing an in-vitro dissolution system based upon what will be explained throughout the research. *Guidance for industry* Cuvillier Verlag 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. *Science, Applications, and Beyond* CRC Press 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. Dosage Form Design Considerations Springer Science & Business Media Dissolution has emerged as a key method during development of medicines and for quality control of marketed products. At the early stage of development, dissolution guides the selection of toxicology and first test in man formulations. At later stages of development, dissolution tests are performed to compare prototype formulations, the robustness of the manufacturing process, to indicate stability and to assure safe release and reproductibility of the products to the market. However despite they wide use in pharmaceutical development, several challenges still

exist. In particular, there is a lack of thorough identification and understanding of the critical quality attributes that control dissolution of Active Pharmaceutical Ingredient and Drug Product. Dissolution exhibits clearly a higher predictability if it can be extrapolated directly to in vivo behavior. Thepresent work focuses on the optimization of the existing and alternative dissolution techniques to lay a foundation for Quality by Design (QbD) principles, In Vitro/In Vivo Correlation (IVIVC) and In Vitro/In Vivo Relationship (IVIVR). The dissolution applied on API and on differente formulations types (Immediate release and extended release form) during the different development phases as well as for generic has been explored. Simple and cost effective dissolution methods were shown to be potential surrogate for in vivo performance and serve as well for strong quality control method. The future perspectives and central role of dissolution testing are presented and discussed.

Dissolution of Disintegrating Solid Dosage Forms in a Modified Dissolution Testing Apparatus 2

Frontiers Media SA

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 *Immediate Release Solid Oral Dosage Forms : Scale-up and Postapproval Changes, Chemistry, Manufacturing and Controls, in Vitro Dissolution Testing, and in Vivo Bioequivalence Documentation* Springer Pharmaceutical Dissolution TestingCRC Press *In Vitro Drug Release Testing of Special Dosage Forms* CRC Press 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. **Drug Delivery Systems** CRC Press Dosage Form Design Parameters, Volume I, examines the history and current state of the field within the pharmaceutical sciences, presenting key developments. Content includes drug development issues, the scale up of formulations, regulatory issues, intellectual property, solid state properties and polymorphism. Written by experts in the field, this volume in the Advances in Pharmaceutical Product Development and Research series deepens our understanding of dosage form design parameters. Chapters delve into a particular aspect of this fundamental field, covering principles, methodologies and the technologies employed by pharmaceutical scientists. In addition, the book contains a comprehensive examination suitable for researchers and advanced students working in pharmaceuticals, cosmetics, biotechnology and related industries. Examines the history and recent developments in drug dosage forms for pharmaceutical sciences Focuses on physicochemical aspects, prefomulation solid state properties and polymorphism Contains extensive

references for further discovery and learning that are appropriate for advanced undergraduates, graduate students and those interested in drug dosage design

Development and Validation of Analytical Methods

Wiley-Blackwell

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.

Pharmaceutical Theory and Practice

John Wiley & Sons

In this concise and systematic book, a team of experts select the most important, cutting-edge technologies used in drug delivery systems. They take into account significant drugs, new technologies such as nanoparticles, and therapeutic applications. The chapters present step-by-step laboratory protocols following the highly successful Methods in Molecular BiologyTM series format, offering readily reproducible results vital for pharmaceutical physicians and scientists.

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

Academic Press

1. Evolution of dissolution testing 5; 2. Theory of dissolution 11; 3. Theoretical concepts for the release of a drug from dosage forms 37; 4. Effect of the physicochemic

425; 24. In vivo release and bioavailability of topical preparations 437; 25. Methods for enhancement of bioavailability 455; 26. Bioequivalence: general definitions 477; 27. Bioequivalence: case histories 481; 28. Correlation of in vitro rate of dissolution with in vivo bioavailability 491; 29. Determination of bioequivalence and its regulatory aspects 517; 30. The official bioequivalence protocols and therapeutic equivalence 533.

Toward Biopredictive Dissolution Testing of BCS Class II Acids

Springer Science & Business Media

During the last two decades, the pharmaceutical industry has been under pressure to reduce development costs and the time needed to bring drugs to market in order to maximize return on investment and bring treatments to patients sooner. To meet these ends, pharmaceutical scientists working in the differing areas of pharmacy, pharmaceutics, and phar

Dissolution Media with Colonic Probiotics

LAP Lambert Academic Publishing

Dissolution tests are routinely carried out in the pharmaceutical industry to determine the dissolution rate of solid dosage forms.

Dissolution testing serves as a surrogate for drug bioavailability through in vitro–in vivo correlation (IVIVR), and it additionally helps in guiding the development of new formulations and in assessing lot-to-lot consistency, thus ensuring product quality. The United States Pharmacopoeia (USP) Dissolution Testing Apparatus 2 is the device most commonly used for this purpose. Despite its widespread use, dissolution testing using this apparatus remains susceptible to significant error and test failures. There is documented evidence that this apparatus is sensitive to several geometric variables that can affect the release profile of oral dosage forms, including tablet location during the dissolution process. In this work, the dissolution profiles of disintegrating calibrator tablets containing Prednisone were experimentally determined using two systems, i.e., a Standard USP Dissolution Testing Apparatus 2 (Standard System) and a Modified Standard USP Dissolution Testing Apparatus 2 (Modified System) in which the impeller was located 8 mm off the vessel centerline. The dissolving tablets were located at different off-

center positions on the vessel bottom to test the effect of tablet location in these two systems. Tablet dissolution in the Standard System was found to be strongly dependent on tablet location, as previously reported by this and other research groups. This apparatus appears to generate variable results that may not be associated with the tablets undergoing testing but with the hydrodynamic characteristics of the apparatus itself and the location of the tablet on the vessel bottom. However, when the same experiments were conducted in the Modified System, the dissolution profiles for the same tablets were found to be nearly completely insensitive to tablet location. The dissolution process in the Modified System was faster than that in the Standard System because of the improved mixing performance of the Modified System resulting from the non-symmetrical placement of the impeller. However, when the Modified System was operated at 35 rpm, the dissolution profiles for centrally located tablets were found to be very similar to those for the Standard System operating at

50 rpm. Unlike the Standard System however, the dissolution profiles obtained at 35 rpm in the Modified System were found to be insensitive to tablet location. It can be concluded that the newly proposed Modified System for dissolution testing is a simple and yet robust and valid alternative to the current dissolution testing practice using the Standard USP Dissolution Testing Apparatus. Guidance for Industry Immediate Relase Solid Oral Dosage Forms Elsevier 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 **Predictive in Vitro Dissolution Tools** Elsevier 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.

US-FDA Bioequivalence Guidance

Pharmaceutical Dissolution Testing

This is a revised and very expanded version of the previous second edition of the book. "Pharmacokinetic and Pharmacodynamic Data Analysis" provides an introduction into pharmacokinetic and pharmacodynamic concepts using simple illustrations and reasoning. It describes ways in which pharmacodynamic and pharmacodynamic theory may be used to give insight into modeling questions and how these questions can in turn lead to new knowledge. This book differentiates itself from other texts in this area in that it bridges the gap between relevant theory and the actual application of the theory to real life situations. The book is

divided into two parts; the first introduces fundamental principles of PK and PD concepts, and principles of mathematical modeling, while the second provides case studies obtained from drug industry and academia. Topics included in the first part include a discussion of the statistical principles of model fitting, including how to assess the adequacy of the fit of a model, as well as strategies for selection of time points to be included in the design of a study. The first part also introduces basic pharmacokinetic and pharmacodynamic concepts, including an excellent discussion of effect compartment (link) models as well as indirect response models. The second part of the text includes over 70 modeling case studies. These include a discussion of the selection of the model, derivation of initial parameter estimates and interpretation of the corresponding output. Finally, the authors discuss a number of pharmacodynamic modeling situations including receptor binding models, synergy, and tolerance models (feedback and precursor models). This book will be of interest to researchers, to graduate students and advanced

undergraduate students in the PK/PD area who wish to learn how to analyze biological data and build models and to become familiar with new areas of application. In addition, the text will be of interest to toxicologists interested in learning about determinants of exposure and performing toxicokinetic modeling. The inclusion of the numerous exercises and models makes it an excellent primary or adjutant text for traditional PK courses taught in pharmacy and medical schools. A diskette is included with the text that includes all of the exercises and solutions using WinNonlin.