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Development of in Vitro Dissolution Test for Dihydroartemisinin Capsules Oct 30 2020
DISSOLUTION TEST AND ITS CORRELATION WITH BIOAVAILABILITY OF DRUGS Mar 15 2022 1. Dissolution and its correlation with the bioavailability of drugs: For oral solid dosage forms dissolution test is the only in vitro quality control test available to date which can provide insight to predict in vivo behavior, bioavailability, the rate at which and the extent to which a drug reaches systemic circulation or the site of action from an administered dosage form, of the drug product. The dissolution test serves as a tool to distinguish between 'acceptable and unacceptable, bioequivalent, or bio inequivalent, drug products.
Generic Drug Product Development Apr 04 2021 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
Pharmaceutical Dissolution Testing Feb 26 2023 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.
Handbook of Dissolution Testing Feb 02 2021
Handbook of Dissolution Testing Nov 23 2022
Dissolution Testing of Prednisone and Salicylic Acid Calibrator Tablets at Different Tablet Locations Jun 18 2022 Dissolution testing is routinely carried out in the pharmaceutical industry to determine the rate of dissolution of solid dosage forms. This test is one of the several tests that pharmaceutical companies typically conduct on oral dosage formulations (e.g., tablets) to determine compliance. The USP Dissolution Testing Apparatus 2 is the most common of the apparatuses listed in the USP. However, it has been shown previously that the dissolution profile of a tablet undergoing dissolution in the USP Dissolution Apparatus 2 can be affected by the tablet location in the apparatus. In this work, the dissolution rates of both non-disintegrating tablets (salicylic acid) and disintegrating tablets (Prednisone) were experimentally determined for many different tablet locations, both centered on the vessel bottom and off-center. The location of the tablet was experimentally varied in very small increments in order to determine the exact location where a transition in the dissolution profile occurred. It was found that in a small region (2-4 mm in radius) centered around the vessel centerline just below the impeller the dissolution profiles were similar to those observed with a centered tablet. However, outside this region the dissolution profiles were found to be significantly different, as indicated by the values of the Similarity Factor f1 and the Difference Factor f2. These finding are consistent with previous hydrodynamic investigations that showed the existence of a poorly mixed zone below the USP Apparatus 2 impeller. The results of this work can guide the practitioner on when to accept dissolution testing results based on tablet location.
Biopharmaceutics Applications in Drug Development Nov 30 2020 The highly experienced authors here present readers with step-wise, detail-conscious information to develop quality pharmaceuticals. The book is made up of carefully crafted sections introducing key concepts and advances in the areas of dissolution, BA/BE, BCS, IVIC, and product quality. It provides a specific focus on the integration of regulatory considerations and includes case histories highlighting the biopharmaceutics strategies adopted in development of successful drugs.
Experimental Determination of the Agitation Requirements for Solids Suspension in Dissolution Systems Using a Mini Paddle Apparatus Feb 20 2020 Dissolution testing is a critical step in quality control of manufactured final products in the pharmaceutical industry. The United State Pharmacopeia (USP) Dissolution Testing Apparatus 2 (paddle) is the most widely used dissolution test devices in the pharmaceutical industry to formulate solid drug dosage forms and to develop quality control specifications for its manufacturing process. Mini vessels and mini paddle dissolution testing systems are smaller versions of the USP 2 Apparatus. The concept of the mini paddle apparatus is similar to that of the USP 2 setup but it is scaled down about to 1/5 of the volume and 40% with respect to vessel and impeller sizes. Mini vessel systems, requiring a small volume (200 mL) and a mini paddle impeller, are becoming increasing common in the pharmaceutical industry to overcome the limitations associated with the USP 2 dissolution testing method, especially for dissolution testing involving very small tablets. Mini apparatuses can be useful tools in characterizing drug release profiles since smaller sample sizes and smaller volumes of media are needed, thus offering several advantages in terms of substance, analytical, and material cost savings when evaluating release properties of drug candidates.Despite their increasing importance in dissolution testing, little information is currently available on mini vessels, and especially on the agitation speed needed to prevent "coning" effects. Typically during dissolution testing, a disintegrating tablet becomes rapidly fragmented, and the resulting solid particles may or may not become suspended depending on the agitation speed of the paddle and other geometric and operating parameters "Coning" (the accumulation of particle fragments from a disintegrating tablet) often appears in dissolution testing but can be eliminated by increasing the agitation speed N. Therefore, it is important to be able to predict the minimum rotation speed at which coning phenomena disappears in a dissolution testing system and especially in mini vessels systems.The focus of this work was the determination of the minimum agitation speed, Njs, at which the just suspended state by dispersed particles is achieved in a mini paddle system (thus removing "coning" effects). In the past, Njs, has been experimentally obtained in mixing systems by determining the agitation speed at which no particles are visually observed to be at rest on the vessel bottom for more than one to two seconds. Therefore, the first objective of this work was to develop an observer-independent method to measure experimentally Njs. This was achieved by extending to mini vessel a method that was recently developed in our laboratory and that is based on the determination of the fraction of unsuspended solids in the vessel at different agitation speed (Njs-Ds method). The results of this method agree well the visually observable values of Njs(Njs-visual).Once new method was validated in mini vessels, Njs was experimentally measured using well characterized solid particles under a number of operating conditions, such as liquid level-to-vessel diameter ratio (H/T), particle size (dp), and paddle clearance-to-vessel diameter ratio Cb/T). The results could be interpreted using the Zwietering Equation originally developed for solids suspension in baffled stirred tanks. The Zwietering "S" parameter was obtained for the mini vessel system thus enabling the use of this equation to predict when "coning" effects can be eliminated in mini vessel systems during tablet dissolution testing.
Biorelevant Dissolution Test Methods to Asses Bioequivalence of Drug Products Jun 06 2021
Dissolution of Different Commercial Aspirin Tablets Using a Novel Off-center Paddle Impeller (OPI) Dissolution Testing System Jun 25 2020 Dissolution testing is routinely conducted in the pharmaceutical industry to provide in vitro drug release information for quality control purposes. The most common dissolution testing system for solid dosage forms is the United States Pharmacopeia (USP) Dissolution Testing Apparatus 2. In this work, a modified Apparatus 2, termed "OPI" System for "off-center paddle impeller," in which the impeller is placed 8 mm off center in the vessel is tested to determine its sensitivity to differentiate between the dissolution profiles of differently formulated and manufactured tablets. Dissolution tests are conducted with both the OPI System and the Standard System using three different brands of aspirin at nine different tablet positions. The OPI system produces dissolution profiles that are highly dependent on the different brands of aspirin used, similarly to those generates in the Standard System. However, the dissolution profiles obtained with the OPI apparatus are found to be largely independent of the tablet location at the vessel bottom, whereas those

obtained in the Standard System generates statistically different profiles depending on tablet location. It can be concluded that the newly proposed OPI system can effectively eliminate artifacts generated by random settling of the tablet at the vessel bottom, thus making the test more robust, while at the same time being just as sensitive as the Standard System to actual differences in differently manufactured tablets having intrinsically different dissolution profiles.

Development and Characterization of a Novel Drug Dissolution Test Method Using a Quartz Crystal Microbalance May 05 2021

Dissolution Testing of Solid Dosage Forms Aug 20 2022 Dissolution testing has been a key tool during drug development stages and for commercial preparation of the dosage forms. At the drug development stage, dissolution testing is used to help in formulation development evaluation of stability, monitoring of product consistency and assessment of the effect of variables (changes in formulation and process parameters) affecting the characteristics of the final product. In case of the commercial products, dissolution testing applied for confirmation of manufacturing and product consistency and evaluation of process variables. With the accumulation of both in vivo and in vitro experience during a product's development cycle, the dissolution test method should be critically re-evaluated and potentially simplified for final quality control testing. This books covers dissolution testing of solid dosage forms, both conventional and novel dosage forms. Development and validation of dissolution testing method for different types of tablets have been described as separate chapters.

Hydrodynamic Effects of an Arch-shaped Fiber Optic Probe in a Dissolution Testing Apparatus 2 Nov 18 2019 Dissolution testing is widely used in the pharmaceutical industry to evaluate newly developed drug formulations and as a quality control method to insure that solid dosage forms have consistent dissolution property. Typically, samples are manually drawn from the dissolution vessel prior to analysis. An approach to overcome the limitations of manual sampling consists in the use of sampling probes, such as fiber optic probes, permanently inserted in the dissolution medium and continually sampling the drug concentration in it as the solid dosage form dissolves. Despite their advantages, permanently inserted fiber optic probes can alter the normal fluid flow within the vessel and produce different dissolution testing results. In this study, the hydrodynamic effects introduced by an arch-shaped fiber optic probe in a USP Dissolution Testing Apparatus 2 are studied by: (1) conducting dissolution tests, with and without the probe, using Prednisone tablets fixed at nine different locations at the bottom of the vessel and comparing the dissolution profiles obtained using statistical tools; and (2) experimentally determining the velocity profiles in the vessel, with and without the probe, using Particle Image Velocimetry (PIV) and quantifying changes in the flow velocities on selected horizontal iso-surfaces. The results show that the arch shaped fiber optic probe does have a baffling effect on the hydrodynamics in the dissolution vessel. This effect results in changes in the velocities in the fluid flow, and therefore in changes in the dissolution rate of the tablets undergoing testing. The baffle effect is observed mainly in the region where the probe is inserted. However, this perturbation is also found to reach the region below the impeller and to change the velocity profile there, resulting in differences in dissolution profiles when the tablets are fixed at positions that are downstream of the probe and within the low velocity region below the impeller. On the other hand, the hydrodynamic effect generated by the probe does not appear to be particularly strong. In most dissolution testing runs, the changes in dissolution profile are not large enough to fail the tests, according to the FDA criteria (f1 and f2 values). The PIV measurements additionally show that the baffle effect is not strong enough to break the overall flow pattern, or to affect the region around the impeller, which is dominated by the main flow generated by the impeller. It can be concluded that the hydrodynamic effects generated by the arch-shaped fiber optic probe are real and observable, resulting in slightly modification of the fluid flow in the dissolution vessel and therefore in detectable differences in the dissolution profiles. However, these effects are limited and do not typically lead to dissolution testing failures.

Pharmaceutical Dissolution Testing, Bioavailability, and Bioequivalence Dec 24 2022 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-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 Jan 21 2020 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.

In Vitro Drug Release Testing of Special Dosage Forms Jul 19 2022 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.

Pharmaceutical Dissolution Testing Jan 25 2023 An expertly written source on the devices, systems, and technologies used in the dissolution testing of oral pharmaceutical dosage forms, this reference provides reader-friendly chapters on currently utilized equipment, equipment qualification, consideration of the gastrointestinal physiology in test design, the analysis and interpretation of data and procedure automation -laying the foundation for the creation of appropriate and useful dissolution tests according to the anticipated location and duration of drug release from the dosage form within the gastrointestinal tract.

Predictive in Vitro Dissolution Tools May 25 2020 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 Test for Low-activity Waste Product Acceptance Sep 28 2020 We have measured the mean and standard deviation of the solution concentrations of B, Na, and Si attained in replicate dissolution tests conducted at temperatures of 20, 40, and 70 C, for durations of 3 and 7 days, and at glass/water mass ratios of 1:10 and 1:1. These and other tests were conducted to evaluate the adequacy of the test methods specified in privatization contracts and to develop a data base that can be used to evaluate the reliability of reported results for tests performed on the waste products. Tests were conducted with a glass that we formulated to be similar to low-activity waste products that will be produced during the remediation of Hanford tank wastes. Statistical analyses indicated that, while the mean concentrations of B, Na, and Si were affected by the values of test parameters, the standard deviation of replicate tests was not. The precision of the tests was determined primarily by uncertainties in the analysis of the test solutions. Replicate measurements of other glass properties that must be reported for Hanford low-activity waste products were measured to evaluate the possible adoption of the glass used in these tests as a standard test material for the product acceptance process.

Dissolution, Bioavailability & Bioequivalence Nov 11 2021 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 physicochemical properties of the drug on dissolution rate 53; 5. Factors affecting the rate of dissolution of solid dosage forms 73; 6. Effects of storage and packaging on the dissolution of drug formulations 107; 7. Factors relating to the dissolution apparatus 115; 8. Effect of the test parameters on dissolution rate 145; 9. Dissolution of suspensions 173; 10. Dissolution of topical dosage forms (creams, gels, and ointments) 189; 11. Dissolutions of suppositories 205; 12. Dissolution characteristics of controlled-release systems 215; 13. Methods for enhancement of the drug-dissolution characteristics 265; 14. Developing a new dissolution method 285; 15. Bioavailability, definitions and historical perspective 297; 17. In vitro modeling for drug absorption 315; 18. Pharmacokinetic considerations in bioavailability studies 335; 19. Bioavailability and variations in drug blood levels 367; 20. Bioavailability and the biologic response 385; 21. Measurements of bioavailability 399; 22. General issues to be considered in conducting bioavailability studies 415; 23. Bioavailability of controlled-release dosage forms 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.

Analysis of Pharmaceuticals by Capillary Electrophoresis Feb 14 2022 Dieser erste Titel einer ganzen Serie von anwendungsbezogenen Handbüchern zur Kapillarelektrophorese beschäftigt sich mit der Analytik von pharmazeutischen Substanzen. Dabei werden verschiedene Techniken praxisnah erläutert. Jeder, der im Labor - ob wissenschaftlich oder praxisnah - mit der Analyse von oft chiralen Pharmazeutika konfrontiert ist, wird viele Hinweise und Tips für seine Arbeit finden.USP: Einzige Monographie zur Analyse von Pharmazeutika mit CE This book describes the current state of the art for the analysis of pharmaceuticals by capillary electrophoresis and contains several hundred references to specific applications and methods. The main purpose of the book is to present the application possibilities of CE an therefore tabulated application data are provided. Chapters of the book are devoted to providing details of individual application areas such as chiral analysis, determination of drug related impurities, determination of drug counter-ions, drug residue monitoring and main component assay. An introductory chapter provides theoretical background to CE an related techniques. A chapter is dedicated to capillary electrochromatography which highlights the importance this technique currently possesses. Successful regulatory acceptance of CE methods is also described. A comprehensive chapter covers method validation aspects. Other chapters include discrete areas such as the use of non-aqueous solvents, forensic applications of CE, the application of experimental designs, determination of drugs in biofluids, and the analysis of vitamins by CE.

Analytics of dissolution testing of products containing nanosized drugs with a view to predicting plasma profiles Sep 21 2022 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.

Oral Drug Absorption Sep 09 2021 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

The Modification of an Automated Dissolution Test Apparatus for the Rotating Disk Method of Intrinsic Dissolution Rate Measurement, Its Validation and Use in Evaluating Tablet Diluents Mar 23 2020

Hydrodynamic Effects of a Cannula in a USP Dissolution Testing Apparatus 2 Mar 03 2021 Dissolution testing is routinely used in the pharmaceutical industry to provide in vitro drug release information for drug development and quality control purposes. The USP Testing Apparatus 2 is the most common dissolution testing system for solid dosage forms. Usually, sampling cannulas are used to take samples manually from the dissolution medium. However, the inserted cannula can alter the normal fluid flow within the vessel and produce different dissolution testing results. The hydrodynamic effects introduced by a permanently inserted cannula in a USP Dissolution Testing Apparatus 2 were evaluated by two approaches. Firstly, the dissolution tests were conducted with two dissolution systems, the testing system (with cannula) and the standard system (without cannula), for nine different tablet positions using non-disintegrating salicylic acid calibrator tablets. The dissolution profiles at each tablet location in the two systems were compared using statistical tools. Secondly, Particle Image Velocimetry (PIV) was used to obtain experimentally velocity vector maps and velocity profiles in the vessel for the two systems and to quantify changes in the velocities on selected horizontal so-surfaces. The results show that the system with the cannula produced higher dissolution profiles than that without the cannula and that the magnitude of the difference between dissolution profiles in the two systems depended on tablet location. However, in most dissolution tests, the changes in dissolution profile due to the cannula were small enough to satisfy the FDA criteria for similarity between dissolution profiles (f1 and f2 values). PIV measurements showed slightly changes in the velocities of the fluid flow in the vessel where the cannula was inserted. The most significant velocity changes were observed closest to the cannula. However, generally the hydrodynamic effect generated by the cannula did not appear to be particularly strong, which was consistent to dissolution test results. It can be concluded that the hydrodynamic effects generated by the inserted cannula are real and observable. Such effects result in slightly mod fications of the fluid flow in the dissolution vessel and in detectable differences in the dissolution profiles, which, although limited, can introduce variations in test results possibly leading to failure of routine dissolution tests.

Developing Solid Oral Dosage Forms Jan 01 2021 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

Media for in Vitro Dissolution Testing of Polysaccharide Based CDDS Aug 28 2020 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.

Poorly Soluble Drugs Oct 22 2022 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.

Effect of Tablet Compression on the Dissolution of Aspirin Tablets Using a Novel Off-center Paddle Impeller (opi) Dissolution Testing System Apr 23 2020 In the pharmaceutical industry, dissolution testing is routinely carried out to determine the dissolution rate of oral solid dosage forms. Among several testing devices, the USP Dissolution Apparatus 2 is the device most commonly used. However, despite its widespread use, this apparatus has been shown to produce test failures and to be very sensitive to a number of small geometry changes. The objective of this study was to determine whether a novel dissolution system termed "OPI" for "off-center paddle impeller" was sensitive enough to determine differences in tablet dissolution profiles caused by different compression pressure during the tablet manufacturing process. The OPI Dissolution System simply consists of a modified Apparatus 2 in which the impeller is placed 8mm off center in the vessel. In this work, aspirin tablets were manufactured from powder with a manual tablet press using three different compression pressures. The dissolution profiles of these tablets were then obtained in both the OPI system and the standard USP Apparatus 2 system. Tests were conducted by dropping the tablets in the vessels at the beginning of an experiment, and, in separate experiments, by initially immobilizing the tablets on the vessel bottom at nine different locations. This approach has been used in the past by our group to determine the sensitivity of the dissolution apparatus to minor changes in the geometry of the dissolution system. All dissolution profiles were found to be affected by the compression pressure. Faster dissolution profiles were obtained at lower compression pressures. When tablets were dropped in the vessel, a comparison of the dissolution profiles obtained in the standard Apparatus 2 system and in the OPI system showed that similarly manufactured tablets produced statistically similar dissolution profiles in both systems, i.e., that the OPI system was just as sensitive as the standard system to variations in the tablet manufacturing process. However, when the tablets were immobilized during the dissolution process, the standard system generated very different dissolution profiles even for tablets manufactured at the same compression pressure. By contrast, the dissolution profiles in the OPI system for tablets manufactured at different pressure but located at different positions were very similar. It can be concluded that the OPI system is sensitive enough to detect differences in intrinsic tablet dissolution rates (such as those caused, as in this case, by changes in the manufacturing process), while being unaffected by small changes in the system geometry that instead caused the standard system to fail. Therefore, the OPI system appears to be a more reliable dissolution testing apparatus than the current apparatus.

In Vitro-In Vivo Correlations Apr 16 2022 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.

Regulatory Implications of Dissolution Testing Jul 27 2020

Mathematical Models of Dissolution Jul 07 2021 Tablet dissolution testing where the drug release is observed as a function of time is an essential part of tablet formulation studies. These tests provide information about the dissolution mechanism and ensure the reproducibility of drug release, which is important for tablet quality assurance. However, the dissolution tests are time-consuming and thus optimal planning of experiment and sophisticated methods for its results evaluation would be needed. Identification of the parameters of specific dissolution models is crucial problem in dissolution studies. Aim of this thesis is to find the optimal time for observation of the empirical dissolution data if the parametric form of the dissolution profile is assumed to be known and the parameters should be estimated. Our approach is based on stochastic properties of the dissolution process and the Fisher information concept. Furthermore, basic models of dissolution and their stochastic modifications, including a new model based on the theory of stochastic differential equations, are presented. Parameters of studied models are estimated via maximum likelihood method.

Hydrodynamic Characterization of the USP Apparatus 2 Dissolution Test Aug 08 2021

Pharmaceutical Dissolution Testing Jan 13 2022 An expertly written source on the devices, systems, and technologies used in the dissolution testing of oral pharmaceutical dosage forms, this reference provides reader-friendly chapters on currently utilized equipment, equipment qualification, consideration of the gastrointestinal physiology in test design, the analysis and interpretation of data and procedure automation -laying the foundation for the creation of appropriate and useful dissolution tests according to the anticipated location and duration of drug release from the dosage form within the gastrointestinal tract.

Characterization of a Cascade Barrier Bed Dissolution Test Apparatus by the Methods of Dimensional Analysis Oct 18 2019

Mechanistic Studies of Drug Dissolution Testing Dec 20 2019

Improvements to biorelevant dissolution testing: lyophilized media, buffer alternatives and miniaturized apparatus Dec 12 2021 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.

Biorelevant Dissolution Test Methods for Modified Release Dosage Forms Oct 10 2021

Dissolution of Disintegrating Solid Dosage Forms in a Modified Dissolution Testing Apparatus 2 May 17 2022 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.