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Review Article

A review: permeability, porosity, tortuosity and physicochemical properties of controlled release oral dosage formulations

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ABSTRACT

Drug dissolution is a part of drug flux governed by biopharmaceutical properties in correlation with fluid dynamic principles. It is essentially significant to determine the importance of fluid dynamics by observing the fate of essential fluids, namely, the air intake, foods eaten, water consumed, and body fluids. This study aimed to observe the correlation between different factors that influence fluid mechanics, specifically, permeability, porosity, and tortuosity with various physicochemical characteristics of drug substa nces, namely, drug solubility and dissolution rate, particle size and punch surface, polymorphism and amorphism, pseudo polymorphism (hydrates/solvates), and drug stability. Thus, this literature review aimed to compare the permeability of ambient conditio ns to different dosage forms of varying properties and determine its effects and liberation of active components to its ambient context of diffusion. Ergun equation is a tool for mathematical modelling of the fluid dynamics that can be used to calculate the fluid flow transition resulting to drug dissolution. Several imaging techniques, namely, x -ray microcomputed microtomography, magnetic resonance imaging (MRI) and nuclear magnetic resonance (NMR) can be used in determining the permeability of Newtonian fluid and analysis of ratio of porosity and tortuosity needed for regulation of the release of active therapeutic components. Flow rate control is necessary in controlled release oral dosage formulations in order to reduce adverse effects brought about by c onventional release. Permeability of Newtonian fluid is influenced by the inverse relationship of porosity and tortuosity. The size of the void space in porous medium is affected by the degree of compression of drug materials. Hence, punch surface and other physicochemical properties of drugs, namely, solubility, particle size, polymorphism, solvates, hydrates and drug stability are coerced by the permeability of Newtonian fluid into the drug. Therefore, porosity and tortuosity are modified by change in physicochemical properties of drugs.

Keywords: Ergun; darcy's law; dissolution; drug delivery; fluid dynamics; flow rate; flux .

INTRODUCTION

Fluid is a substance that will constantly undergo deformation upon subjection to a tangential or shear force. Its rate depends not only on the magnitude of the applied force but also on viscosity (Wilkes, 2006). Mechanics deals with application, analysis, interpretation and evaluation of forces and motions. Hence, fluid dynamics involves the study of mechanisms and principles of fluid forces and its motions. There are four (4) basic concepts for generalization of its applied fluid flows, namely, the principle of the conservation of mass, the first and second law of thermodynamics, and Newton's law of motion. Each idea is a reasoning summary of experimental data due on their ability to predict accurately the data results (de Nevers, 1991).

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A packed bed following Darcy's law at low Reynolds numbers for the flow evaluation of Newtonian fluid is usually assessed as a porous medium. The total decline in pressure across bed particles is the outcome of interaction by friction between the fluid and the particles in connection with gravitational potential energy change brought about by the fluid rise and is explained by Eq.:

$$\Delta P = \Delta P_{fr} + \rho_f g L$$

The pressure decline by friction across a packed bed is expressed by two terms, namely, a viscous energy loss term, directly associated to fluid velocity, and an inertial energy loss term, directly associated to fluid velocity squared, throughout the one-dimensional flow:

$$\frac{\Delta P_{fr}}{L} = AU + BU^2$$

where A and B are heuristic constants (Koekemoer & Luckos, 2015).

It is very important to know the significance of fluid mechanics by understanding the behavior of essential fluids, specifically, the air breathed, foods consumed,

water taken, and body fluids. This paper aims to determine the correlation between various parameters that affect fluid dynamics, namely, permeability, porosity, and tortuosity with several physicochemical properties of drug substances, specifically, drug solubility and dissolution rate, particle size and punch surface, polymorphism and amorphism, pseudo polymorphism (hydrates/solvates), and drug stability. Hence, this literature review aims to compare the permeability of surrounding medium to various dosage forms of varying properties and understand its effects and release of active components to its immediate medium of diffusion. Therefore, evaluate the importance of drug formulation innovation for the health of the people.

Porous Media

A porous material is a solid matrix penetrated by an inter-connected mesh of pores suffused with a fluid. A number of natural substances, namely, rocks, soils, biological tissues (e.g. bones) and man-made substances, namely, cements, foams and ceramics are all classified as porous media. Certain determinants have been created for categorization of these porous materials like porosity, permeability and solid phase dimensions. The porous substance porosity is the void space fraction that is filled up by air or some other fluid to complete the volume of the material (Crawford et al., 2011).

Porosity

Hydraulic Permeability

Fluid mechanics study by random porous media has a major impact in various related fields of science and technology. This issue has been widely involved in diverse domains of scientific literature. Fluid dynamics has an extensive range of applications in chemical, ceramic, environmental, and mechanical engineering, food technology, petroleum firms, separation processes, paper production, geophysics and many other technological processes. Some technological methodologies connected with the study of fluid flow by porous substances comprise filtration, drying process, fuel cells, insulators, binary mixture solidification and heat liquefaction, elevated heat transfer by surfa ce alteration, flow of oil and gas in reservoirs, natural gas yield, improved oil production, oil extraction from porous rocks, chromatography, flow of ground water, contamination travel in groundwater, liquid filtration in snow, soil remediation by steam injection, hazardous waste spread in soils, and the building material degradation such as concrete (Zaman & Jalali, 2010).

The hydraulic permeability estimation for porous media still has debating issues from both theoretical and empirical perceptions. An enormous attempt has been done to accurately correlate and predict the permeability based on geometric properties. There are several proposed associations to easily connect permeability to porosity and a pore size factor like the particle diameter in the packed bed of spherical particles. The famous correlation introduced was done by Kozeny and Carman in which the hydraulic radius concept was utilized in a semi-experimental model and is commonly called the Carman-Kozeny theory. Rumpf and Gupte illustrated another correlation for spherical particle packed beds with a restricted distribution range in size which has a greater consistency with the empirical results in the porosity range of 0.35 to 0.70. Brinkman proposed an estimation of consistency for the porous matrix permeability. Subsequent to that, Childress, Howells, and Hinch gathered total convergent cluster type expansions for the randomly dispersed single size sphere beds (Zaman & Jalali, 2010).

Darcy Equation

The porous media fluid permeability has been a topic in several literatures, from the middle of the XIX century. Darcy (1856) in his novel paper proposed the lead equation that associates fluid velocity and the pressure gradient in a porous substance. This equation is called Darcy's law which involves two (2) substance constants, namely, fluid viscosity and fluid permeability (Berndt & Sevostianov, 2012).

Darcy's law is the most commonly used heuristic correlation for the computation in terms of pressure decline throughout an isotropic, homogeneous, unbounded and non-deformable porous substance. Its validity is narrow in terms of incompressible and isothermal Stokes flow (Re = 0) of Newtonian fluids. Although its application commonly accepted in engineering applications for Re < 1, defined by

$$Re = -\frac{\rho U l}{\mu}$$

where 1 and ρ are the typical structure pore size and fluid density, respectively. Darcy's law has no flow inhomogeneity/variability, therefore, Re = 1 is invalid at the porous medium-solid or porous medium-free flow junction. Brinkman included a flux-type term to the Darcy's law, resulting to

$$-\bar{V}p = \frac{\mu}{K} U - \mu\bar{V}^2 U$$

Brinkman's equation is similar to Darcy's law. Inertia - free is acceptable only for creeping flows. Recently, Auriault explained the acceptability and delimitations of Brinkman's equation for ''traditional'' porous media, low concentration particles swarm and fibrous media at elevated porosities (Yazdchi & Luding, 2012).

Pressure Drop

Fluid flow by solid particle packed beds occurs in diverse essential applications in various engineering areas. A portion of main interest is the pressure decline, also known as the head loss, yielded as an outcome of fluid dynamics by the porous medium. The equation proposed by Ergun about six (6) decades ago stays the

most famous and most commonly-quoted correlation of pressure drop-flow rate by packed beds (Erdim, Akgiray & Demir, 2015).

Friction Factor

The presence of porous material and oscillatory flow has assured the heat elevation. Therefore, Nusselt number for flow of oscillation in a porous substance can be up to a number of times larger than in void medium. Losses by friction increase a number of times by flow of oscillation in porous material as well as thermodynamics. Zhao and Cheng investigated empirically declines of pressure by oscillation through a woven-screen dense column. They exhibited associations for maximum pressure decline determinant and cycle mean pressure decline determinant in the kinetic Reynolds number ranging from 0.001-0.13 and in dimensionless fluid range of displacement from 614.73 - 2827.56, under the sinusoidal condition of air motion. They observed that the values of cycle mean pressure decline of flow of oscillation were a number of times greater than that of steady flow (Pamuk & Ozdemir, 2012).

Jin and Leong, and Leong and Jin have done an empirical study regarding steady and oscillating flows by open cell aluminum foams. By numerous porosity and permeability considerations, they generalize that flow resistance augments with form coefficient and diminishes with the escalating permeability for a given porosity. Form drag is the main reason for pressure drop by augmenting flow velocity. They illustrated linear regression analysis of friction factors as cited by Zhao and Cheng. They also exhibited that the pressure drop is elevated both increasing the area (Ao) and kinetic Reynolds number (Rex) (Pamuk & Ozdemir, 2012).

Hsu et al. conducted heuristic studies to encompass an extensive range of too low and too high Reynolds numbers in order to compare the linear regression analysis of pressure loss for both steady and oscillating flows. In terms of oscillating flows, the velocity resulted in quite significant correlation to the pressure drop. This illustrates that Darcy's law is acceptable for small amplitude flow of oscillation (Pamuk & Ozdemir, 2012).

Cha et al. have observed empirically and mathematically eight (8) various microporous material on flow of oscillation. They answered the problem mathematically by the use of the computational fluid dynamics (CFD) code called Fluent in order to do permeability and inertial coefficient prediction of the porous material under the flow of steady-periodic conditions. Their results have shown that pressure loss in flow of oscillation is not definitely lower than that of steady flow (Pamuk & Ozdemir, 2012).

Fluid Flow

Fluid dynamics in porous material has been one of the primary research interests of scientists for several decades. A number of applications have already been established for porous material flow in biological, civil and mechanical systems, such as the flow by endothelial glycocalyx in the red cell motion by capillaries, the past muscle cell flow in the artery wall, the flow by brush border microvilli in the proximal tubule, the flow by fenestral pores in the capillary wall and the internal elastic arterial lamina, the fluid shear stress transmission to the intracellular actin endothelial cell cytoskeleton, molding methods, and soil dynamics, etc. In spite of the vast researches of porous material flow in diverse fields, recent study for the possible lift creation in soft porous material has been observed. This phenomenon is deeply connected to the permeability change of the soft porous material in reaction to compression (Crawford et al., 2011).

The fundamental physics behind the lift creation phenomenon in a soft porous material is in alignment with the porous material compression leading to sharp decline in relation to Darcy permeability and hence, significant elevation in fluid resistance it meets as it flows by. Thus, it is important to know the mechanism of Darcy permeability changes as a compression function (Crawford et al., 2011).

Permeability

The permeable particle motion in a fluid has long gained acceptable notice in several areas like colloid science, biomedical, chemical, and environmental engineering. Due to the fact that fluid can permeate into a porous particle, flow associated with porous material firm skeleton has been observed. The hydrodynamic areas outside and inside the particles required to be handled simultaneously, which disagrees much from those of solid impenetrable particles. Various studies have been committed to the comprehension of transfer phenomena by movement of porous material for applications, such as sedimentation, flotation, agglomeration, and filtration (Wang et al., 2015).

Conservation equations which exactly control the fluid dynamics are needed for the porous domain leading to acquisition of fluid velocity within a penetrable particle. In relation to creeping flow conditions and acknowledging the force of resistance from the surface of the solid of moving porous material, two (2) models for the motion of fluid inside the porous material are commonly utilized in the literature, namely, Darcy's law and Brinkman equation. Through the application of the Stokes equation and Darcy's law, Payatakes and Dassios studied the porous sphere motion moving in the direction of solid planar wall. Afterwards, Burganos et al. supplied their work revision in regard to the drag force employed on the porous particle. Due to the viscous dissipation term negligence, the momentum equation responsible for the porous material internal fluid consists only of law of Darcy's first order spatial derivatives, whereas the momentum equation for the external fluid involves spatial derivatives leading to the second order. This would generate a common fact that

Darcy's law is sequestered to the condition that the penetrability of the porous material is accurately low. In the meantime, the fluid velocity and the stress continuity at the junction between the porous medium and the external fluids do not have assurance. Corresponding boundary treatment is thus, required to complete the continuity at the junction of a moving porous material. In contradiction to the Brinkman equation, the velocity gradient term dealing to viscous fluid dissipation inside the porous material is integrated in the momentum equation, and the fluid velocity continuity is satisfied at the permeable body surface. From this equation, the Brinkman equation is more appropriate than Darcy's law in the permeable particulate systems (Pamuk & Ozdemir, 2012).

In reference with Brinkman equation, various postulatory and numerical researches have been done regarding moving porous particles. Citing one study, Jones computed the forces and torques on moving permeable particles with a reflection method, and some articles were also conducted to study the porous particle suspension flow using the Brinkman equation with other supporting procedures. Nowadays, the Brinkman model was also applied to investigate the hydrodynamic motion and composite particle interactions (Wang et al., 2015).

In summation of all the cited investigations, the flow internal to the moving porous particle is explained using either Darcy's law or the Brinkman model. By the use of these two mathematical models, the transient term and the non-linear inertial term are not involved in the momentum equation. It accompanies that there is a mechanism absence to treat the flow field unsteady evolution, and the Reynolds number for fluid flows must be hoarded adequately small. Although as noted by Wood, the inertial effect on the flow and transfer in porous material must be regarded in many empirical methods. Applying the best method based on knowledge, no postulatory and computational methods have been generated to solve this delimitation. A novel model is hence, predicted for moving permeable particulate systems at finite flow Reynolds numbers (Wang et al., 2015).

Tortuosity

Categorization in the flow and transfer phenomena in porous material is beneficia l for an extensive array of approaches in science and engineering starting from oil recovery and carbon sequestration to fuel cells. Tortuosity, τ, is a determinant mostly used in continuum models throughout effective flow estimates and transfer phenomena inside the porous material. The tortuosity concept was first proposed by Carman in 1937 as a factor that explains the mean elongation of microscopic fluid flow pathways in porous material in regard to free flow. In relation to the commonly applied Kozeny-Carman relationship, tortuosity is utilized to investigate the permeability, *K*, of porous material, as follows:

$$K = \frac{1}{C_{KC}} \frac{\varphi^3}{S^2\tau^2}$$

where C_{KC}, φ, and *S* are the Kozeny–Carman constant (shape factor), porosity, and specific surface area, in that order.

In most investigated tortuosity literatures, it involves porous material involving of mono-sized (same-sized) particles, like the analytical experiments by Yun et al, Yu & Li and Jian-Long et al or the computational studies by Koponen et al and Matykaetal. Moreover, granular porous material, occasionally fibrous porous media have wide fiber diameter distributions (Khabbazi, Hinebaugh & Bazylak, 2015).

Ergun Equation

The famous and most extensively used Ergun (1952) equation was first formulated semi-heuristically for prediction of pressure loss for Newtonian flow by a packed bed of chiefly spherical particles. It has been utilized well and still applied extensively, especially in chemical engineering. The classic Ergun equation was claimed by direct addition of the Blake-Kozeny and the Burke–Plummer equations (du Plessis & Woudberg, 2008).

$$\frac{\Delta p}{L} = 180\,\frac{(1-\varphi)^2}{\varphi^3}\,\frac{\mu q}{D_h^2} + 1.75\,\frac{(1-\varphi)}{\varphi^3}\,\frac{\rho q^2}{D_h}$$

Kozeny-Carman Equation

The CK equation was first introduced by Kozeny (1927) and was later altered by Carman (1937). Kozeny (1927) formulated a derivation relationship between permeability and porosity in regard with the porous material as a channel group of numerous cross sections with the same length. The viscous governed by Navier-Stokes equations was calculated for all channels moving a cross section normal with the flow, which resulted to the Kozeny's equation

$$Kp = c\,\frac{\varphi^3}{s^2}$$

where φ is the porosity; c is the Kozeny constant whose value depends on the capillary shape; s is the specific channel surface (surface area per unit volume of the channel). Carman confirmed Kozeny's equation, proposed the hydraulic radius concept, expressed the specific surface, regarded fluid does not pass in straight channels but throughout irregularly shaped solid particles, and enhanced Kozeny's equation to acquire

$$Kp = \varphi\,\frac{r_H^2}{k}$$

where r_H is the hydraulic radius explained as the pore volume to surface area ratio, k is the heuristically investigated Carman-Kozeny constant. With rH=φD/6(1-φ) where D is the average particle diameter, k=5, the moer familiar form of the CK equation is shown as (Crawford et al., 2011)

$$Kp = [\frac{\varphi^3 D^2}{36(1-\varphi)^2 k} = \frac{\varphi D^2}{180} (\frac{\varphi}{(1-\varphi)})^2$$

The CK equation has been observed and was utilized in numerous settings and in varied modifications. This analytical permeability is nearly associated to the porous material microstructures, involving fractal dimensions, porosity and maximal pore size (Crawford et al., 2011).

Burke Plummer Equation

The conditions of inertial flow in the Forchheimer rule were mathematically designed as turbulent flow where it is presented that the friction factor, f, defined as

$$f = \frac{-\Delta p}{\rho q^2} \frac{D_h}{L} \frac{\varphi^3}{(1-\varphi)}$$

is independent on the Reynolds number, defined as

$$Re = \frac{\rho q D_h}{\mu(1-\varphi)}$$

but a constant for a relative roughness so that

f = constant = B.

For the Darcy rule, the relation friction factor-Reynolds number can be expressed as

$$f = \frac{A}{Re}$$

A value of 1. 75 was formulated for the coefficient B, generating

$$\frac{\Delta p}{L} = 1.75 \frac{(1-\varphi)}{\varphi^3} \frac{\rho q^2}{D_h}$$

which is recognized as the Burke–Plummer equation (du Plessis & Woudberg, 2008).

Oral dosage formulations

In a number of years, investigation into the drug formulation domain has centered on the look for systems that slow the drug release subsequent to administration. There have been substantial developments in the field, and can be found naturally in the scientific database. Among other explanations that have resulted to the sustained release drug delivery systems stem formulation from the hope to obtain the delayed release of highly water-soluble compounds, lead those compounds to the target organ or cell, obtain release rates that complement a given desire, diminish the daily number of administrations, and enhance compliance and reduce side effects (Maderuelo, Zarzuelo & Lanao, 2011).

Solid oral drug delivery systems may be classified into two main categories in accordance to the drug release rate (Mantle, 2013).

Conventional Release

Immediate release (IR) systems, like aspirin and paracetamol, are the most usual drug delivery type device amidst commercial drugs. Here a rapid release rate results to a fast uptake and high drug concentration in the blood plasma, allowing the dosage form to transport the rapid action to its intended receptor. However, the fast increase in blood plasma drug concentration can result to elevated occurrence risk of side effects or overdosing (Mantle, 2013).

Controlled Release

The second general type of solid oral drug delivery matrix, which is modelled to resolve the problems of IR delivery systems, is termed as sustained or controlled release (CR) drug delivery system which controls a safe drug label concentration in the blood plasma for a prolonged time period. In the ideal setting, a sustained release device would regulate a sustained drug therapeutic level (zero order release kinetics) within the blood over a longer time period but in reality this is seldomly found to be the case. Alternatively, a slow first order drug release profile is analyzed. Controlled release drug delivery devices may be considered as a sustained release delivery device subset but where a number of spatio- and/or temporal therapeutic management form is shaped into the delivery device thereby regulating the concentration of drug in a drug tissue. Controlled drug delivery also involves site specific or targeted drug delivery whose main objectives are localization of drugs and may not definitely require zero order drug release kinetics (Mantle, 2013).

Physicochemical properties of drug substances

Active pharmaceutical ingredient (API) dissolution fixed into a finished dosage form (FDF) is a requirement for absorption of drugs and thus, bioavailability. This explains the dissolution testing omnipresence in FDF development and quality assurance. During which disintegration and drug dissolution are vital modes, essential gaps in FDF dissolution characterization stay for more than 115 years subsequent to the pioneering work by Noyes and Whitney (1897) (Horkovics-Kovats, 2015).

Drug solubility and dissolution rate

API dissolution involves the dissolution medium interaction with the FDF. In regard with immediate release FDF, disintegration and API dissolution happen all the same time; during which the disintegration process starts, the already released API particles dissolve in the dissolution medium. This resulted to the heterogenous mass particle elevation, although the FDF held homog-

enous particles. The system complexity is further elevated by the drug concentration modification in the dissolution medium that influences the dissolution particle kinetics released from the FDF (Horkovics - Kovats, 2015).

Punch Surface and Particle Size

The pharmaceutical compression surface is of critical value for their properties. Compact disintegration and drug dissolution are strongly affected by the surface layer structure. Although it is also a precise compact part which may have properties that vary from those of the bulk. The surface structure and roughness are affected by the powder properties like the mechanical behavior or the grain size. Although the surface particularity is also responsible for the compression process itself. During the procedure, the surface is the compact part which is in contact with the punches. Hence, the stress employed to the surface particle layer varies from that employed to the bulk particles. In connection with that, surface particles are in touch with the punch on one side and with the other particles on the other side while the bulk particles are only in touch with other particles (Mazel et al., 2013).

Polymorphism and amorphism

Existing theories and models are unable to explain some dissolution profile types that are analyzed when API exists in the FDF in different polymorphic forms with varying solubility. If several polymorphic forms exist, the API can dissolve from the form with the greatest free energy and all at the same time, crystallize into more stable solid form(s) [i.e. form(s) with lower solubility] (Horkovics-Kovats, 2015).

Pseudo polymorphism (hydrates/solvates)

Pseudopolymorphism is the contact outcome between the solid form and liquids. Interaction products are hydrates and solvates. The principle is discussed as the water molecule permeability into the bulk solid structure and with further crystalline structure modification. The responsibility of this polymorphism type in pharmaceutical science is important since hydrates and solvates are famous to control enormous variations in pharmacokinetic profiles in comparison to non-hydrous crystals (Pobudkowska, Domanska & Kryska, 2014).

Drug stability

Dissolved API chemical instability illustrates an added problem that may affect the dissolution profiles and bioavailability. Optimization of FDF disintegration properties are precisely essential for drugs that are chemically unstable in the stomach or that are fully absorbed throughout a strict absorption 'window' in the gastrointestinal (GI) tract. Knowing the FDF disintegration impact on bioavailability may improve the concepts supplied by the Biopharmaceutical Classification System (Horkovics-Kovats, 2015).

Drug delivery mathematical modeling

Models of drug release can be categorized as heuristic models or mechanistic models. A heuristic approach can be referred on the empirical system behavior analyzed. No physical principles are regarded in the problem description. These model kinds can often mimic the actual system behavior very well, most likely if a corresponding number of determinants are involved in the model. Meanwhile, such a mathematical design does not supply any instruction on the principles that regulate the procedure. Subsequently, a heuristic model cannot be utilized for prediction of what result an alteration in the cited conditions like modification in film thickness of a reservoir system and its gained result on the release rate. Hence, these designs assist the same role as any mathematical polynomial with adequate properties to suit the experimental data. The heuristic model utilization for drug release profile simulation is, thus, narrowed to simple curve-fitting procedures (Kaunisto, 2011).

Models of mechanistic drug release are referred on the physical principles that affect the release process. Hence, the model determinants have physical importance, and it is hence, practical to utilize a mechanistic model to generate predictive simulations. Although it is still important to verify the model validity against experimental data. In this procedure it is necessary to confirm not only the model output but also all the determinant values involved in the model. This confirmation is practical because the factors have physical importance, in contradiction to the heuristic factors. Another significant topic is to narrow the model to a suitable complexity level. A general rule is to determine rate-limiting system processes. This is mainly significant if the determinant values of the methods are unknown and are to be identified from determinant fitting procedures. The more precise the model explanation, the more accurate the empirical validation procedure must be. The varying model presentations should be observed in the reason of this leading modelling concept (Kaunisto, 2011).

Various instrumental techniques

Throughout recent decade, there has been a remarkable elevation in the imaging technique approaches in the pharmaceutical sciences. The chief explanation for such extended attention is the various spectroscopic technique developments, which allow researchers to gather one-, two or three-dimensional distribution maps of physical or chemical quantities inside the computed sample. Imaging expands knowledge regarding structural or physico-chemical properties of a sample, and the temporal modifications that occur in such samples throughout hydration and dosage form dissolution; these are the primary methods that affect the in vitro and in vivo controlled-release (CR) performance of dosage forms (Dorozynski et al., 2012).

X-ray Microcomputed Microtomography

The relationship between the excipient structures and coated granules in tablets and properties of tablet is not completely answered, possibly due to the gap of non-destructive structural information and in-situ quantitative analyses. X-ray computed tomography (CT) has been effectively utilized to investigate non-destructively the various pharmaceutical material internal structures with the inclusion of tablets. Although microstructure details within the tablet are still not clear due to their structural information spatial resolution was micro to millimeters because of the performance delimitation of the CT instruments and X-ray generator. Nowadays, it is now workable to do visualization of the fine particle three-dimensional internal structures through the utilization of X-ray computed microtomography (μCT). The synchrotron X-ray radiation benefit is high brilliance and monochromatic characteristic, which makes it feasible to acquire highly precise CT images out of tiny samples in fast measurement time. The utilization purpose of μCT is to study the microgranular formulation internal structures with a diameter of sub-millimeter, and to evaluate its high potency for visualization with sub-micrometer spatial resolution (Kajihara et al., 2015).

Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) supplies an option to work on nondestructive and noninvasive recording of certain particle spatial distribution and mobility, like protons, in the sample. MRI is commonly utilized in medical, material and food sciences. It is also gaining increasing attention in the pharmaceutical technology area. Although MRI is chiefly employed for in vivo studies, there has been a remarkable elevation in the number of researches searching at the in vitro preformulation of solid oral dosage forms (Dorozynski et al., 2012).

Nuclear Magnetic Resonance (NMR)

Magnetic resonance imaging and its closely related analogue nuclear magnetic resonance (NMR) spectroscopy are perfectly appropriate to investigate drug dissolution phenomena at a local level within a dosage form for several purposes. Both MRI and NMR spectroscopic techniques are quantitative, non-invasive, chemical and nuclear specific techniques that can also be utilized to measure molecular mass transport phenomena in the molecular diffusion form and flow (Mantle, 2013).

Comparison of permeability, porosity, tortuosity with physicochemical properties of controlled release oral dosage formulations

Controlled release oral dosage formulations are mathematically designed to regulate the release of active ingredients to the body by following the biological aspects of pharmacokinetic process, namely, absorption, distribution, metabolism and excretion. This type of drug delivery has an advantage of reducing the adverse effects observed during its immediate release. Hence, the regulation of the therapeutic components is governed by several parameters following the principle of fluid dynamics in correlation with the physicochemical properties of drugs. Fluid dynamics can be logically understood by inter-relating the concepts of permeability, porosity and tortuosity. Thus, an ideal fluid flow rate for permeability through a porous medium for dissolution involves high porosity and low tortuosity wherein physicochemical properties of drugs, like the drug compaction, greatly affects the void space needed for water transport. Hence, particle size, drug solubility, polymorphism, pseudopolymorphism and drug stability are physicochemical properties that also affects the permeability of drugs for dissolution. Therefore, a heavily compacted drug will a ffect the size of the void space and tortuosity in which permeability will be low in which other physicochemical properties will also be affected. These drug phenomena can be observed and analyzed by imaging techniques, namely, x-ray micro-computed microtomography, magnetic resonance imaging (MRI) and nuclear magnetic resonance (NMR). Hence, fluid dynamics for drug dissolution can be studied for correlations and mathematical modelling.

Evaluation using ergun equation

Ergun equation is used to evaluate the friction loss for fluid flow through a packed bed in terms of pressure drop. The transition from laminar to turbulent flow as observed in drug dissolution can be evaluated using Ergun formula derived from Kozeny-Carman Equation and Burke Plummer Equation. Thus, fluid dynamics in drug dissolution can be modelled mathematically using this equation in order to determine the flow rate, hence, it can give a better understanding on the permeability, porosity and tortuosity.

CONCLUSION

Fluid dynamics is a mathematical tool to understand the behavior of several porous media. Drug dissolution is a pharmacokinetic process involved in the release of pharmaceutical therapeutic components in a medium. Regulating the void space or its porosity can lessen deleterious effects of drugs, thus, providing optimum therapeutic care to patients. Porosity is inversely proportional to tortuosity in terms of permeability and is affected by the degree of drug compaction as well as other physicochemical properties of drugs. Hence, drug dissolution is governed by the relationship of fluid dynamics together with its physicochemical properties.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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