World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 7.409

REVIEW ON SOLID DISPERSION AND THEIR FORMULATION TECHNIQUES

Vankudavath Manthru Naik*[1], Chennu M M Prasada Rao[2]

[1]Research Scholar, School of Pharmacy, Raffles University, Neemrana-301705.
[2]Professor, School of Pharmacy, Raffles University, Neemrana-301705.

***Corresponding Author: Vankudavath Manthru Naik**

Research Scholar, School of Pharmacy, Raffles University, Neemrana-301705.

Article Received on 07/03/2025 **Article Revised on 27/03/2025** **Article Accepted on 17/04/2025**

ABSTRACT

Solid dispersions have garnered considerable scholarly attention as a proficient strategy for augmenting the dissolution rate and, consequently, the bioavailability of various weakly water-soluble pharmaceuticals. The formulation of solid dispersions comprising weakly water-soluble drugs in conjunction with water-soluble carriers has mitigated the prevalence of associated challenges and has enhanced dissolution rates. Solid dispersion represents a solubilization methodology that predominantly focuses on drug-polymer binary systems, wherein the dispersion of the drug and its stabilization serve as pivotal elements in the formulation development process. As such, this methodology is acknowledged as an advantageous approach for ameliorating the dissolution characteristics of poorly soluble pharmacological agents. In recent years, a substantial body of knowledge has been amassed regarding solid dispersions; nevertheless, their practical application within the commercial sector remains constrained. This review article emphasizes critical aspects such as solubility, the Biopharmaceutical Classification System (BCS) classification, and the selection of carriers. Furthermore, this article delineates various preparation methodologies for solid dispersions and compiles recent technological advancements in this arena. The distinct categories of solid dispersions are highlighted based on the utilized carrier and the molecular configurations involved. Additionally, it encapsulates the underlying mechanisms, the preparatory techniques for solid dispersions, and the commercially available pharmaceuticals that utilize solid dispersion methodologies.

KEY WORDS: Solid Dispersion, New method, BCS Classification. Solubility enhancement, evaluation.

INTRODUCTION

Solid dispersion pertains to a classification of solid formulations comprising a minimum of two distinct components, typically a hydrophilic matrix alongside a hydrophobic pharmaceutical agent. The matrix may exist in either a crystalline or amorphous state. The pharmaceutical agent can be distributed at a molecular level, in amorphous aggregates (clusters), or in a crystalline form. Consequently, one can delineate six distinct categories of solid dispersions based on their molecular configuration. Furthermore, specific combinations may be observed; for instance, within a single sample, specific molecules may be present as clusters while others are dispersed at a molecular level. Additionally, the molecular configuration, rather than the preparation method, indicates the characteristics of solid dispersions.[1]

Drugs that exhibit moderate solubility in gastrointestinal fluids demonstrate complete oral absorption and, consequently, enhanced bioavailability. Approximately 40% of pharmaceutical compounds exhibit poor solubility in aqueous environments, leading to slow absorption rates, culminating in inadequate and inconsistent bioavailability and gastrointestinal toxicity. Thus, one of the most critical phases in the drug development process, particularly concerning oral dosage forms, is the enhancement of drug solubility, thereby improving its oral bioavailability. Bioavailability is defined as the extent to which a therapeutically active drug reaches systemic circulation and, as a result, is accessible at the site of therapeutic action. Two primary hypotheses are put forth to explain the inadequate aqueous solubility of drugs.[2]

- High lipophilicity
- Strong intermolecular forces which cause the insolubilization of drugs.

Various approaches have been proposed to enhance solubilization of poorly water-soluble drugs for the improvement of their bioavailability commonly used for drug solubilisation includes micronization, chemical modification, pH adjustment, solid dispersion, complexation, co-solvency, micellar solubilisation and hydrotropy.

Biopharmaceutics Classification System (BCS)[3]

This methodology is predicated upon the pharmaceutical compound's aqueous solubility and permeation through the gastrointestinal system. The categorization framework is derived from applying Fick's first law to a selective membrane.

Jw= PwCw

In this equation, Jw represents the drug flux (mass per unit area per unit time) traversing the intestinal barrier at any given location and moment, Pw denotes the membrane's permeability, and Cw signifies the drug's concentration at the surface of the intestinal membrane.

This methodology presupposes that no other constituents within the formulation influence the membrane's permeability and/or the transport processes within the intestine. Employing this framework, an investigation into the solubility and permeability traits of diverse representative pharmaceuticals was conducted, leading to the establishment of a biopharmaceutical drug classification system to forecast the in vitro drug dissolution of immediate-release solid oral dosage forms alongside their in vivo absorption profiles.

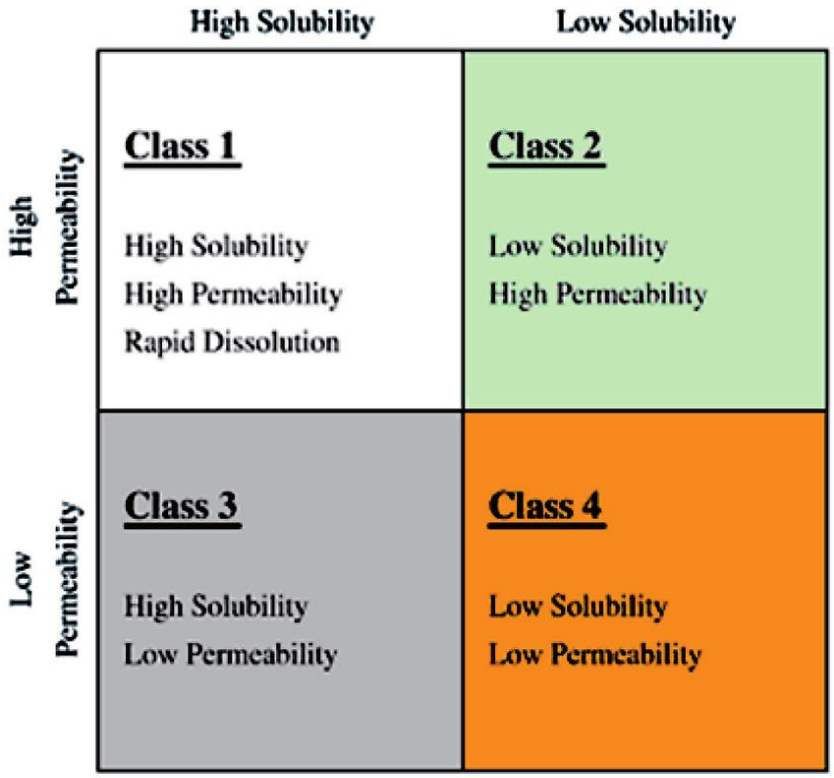

Figure 1 : BCS classification system.

Class I - High Permeability, High Solubility

Those compounds are well absorbed and their absorption rate is usually higher than excretion.

Example: Metoprolol

Class II - High Permeability, Low Solubility

The bioavailability of those products is limited by their solvation rate. A correlation between the in vivo bioavailability and the in vitro solvation can be found.

Example: Glibenclamide, Lacidipine

Class III - Low Permeability, High Solubility

The absorption is limited by the permeation rate but the drug is solvated very fast. If the formulation does not change the permeability or gastro-intestinal duration time, then class I criteria can be applied.

Example: Cimetidine.

Class IV - Low Permeability, Low Solubility

Those compounds have a poor bioavailability. Usually, they are not well absorbed over the intestinal mucosa and a high variability is expected.

Example: Hydrochlorothiazide.

Solubility[4]

Solubility is quantitatively characterized as the concentration of solute present in a saturated solution at a designated temperature. At the same time, qualitatively, it can be conceptualized as the inherent tendency of two or more substances to engage in a spontaneous interaction that results in a homogeneous molecular dispersion (Martin, 2006). The expressions of solubility are conveyed through a descriptive terminology and are specifically intended to be applicable within the temperature range of 20-30°C. The subsequent table elucidates the significance of the terminology employed in delineating statements concerning approximate solubilities.

Table 1: Descriptive terms of solubility.

Descriptive Term	Parts of solvent per one part of solute
Very Soluble	Less than 1 part
Freely Soluble	1 to 10 parts
Soluble	10 to 30 parts
Sparingly soluble	30 to 100 parts
Very insoluble	1000 to 10,000 parts
Insoluble	More than 10,000 parts.

Theories of drug dissolution[5]

Dissolution is a process wherein a solid substance is rendered soluble within a designated solvent, specifically involving the transference of mass from the solid interface to the liquid phase. Numerous theoretical frameworks have been posited to elucidate the phenomenon of drug dissolution, and several significant theories are noteworthy.

Diffusion layer model/film theory

This theoretical framework represents the most fundamental and prevalent explanation for the dissolution process. According to this theory, the dissolution of solid particles within a liquid comprises two sequential stages in the absence of reactive or chemical interactions.

The initial stage involves the solid solvating, forming a thin film or layer at the solid/liquid interface referred to as the stagnant film or diffusion layer, which becomes saturated with the drug. This particular phase is generally characterized by rapid kinetics.

The subsequent stage entails the diffusion of the soluble solute from the stagnant layer into the bulk of the solvent, which is comparatively slower and, hence, serves as the rate-determining step in the drug's dissolution. The model is illustrated in Figure 2.

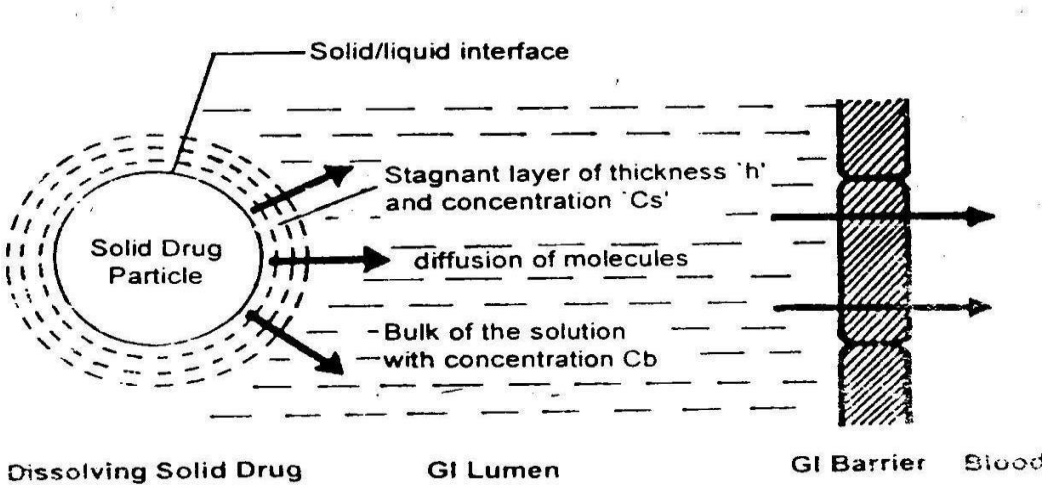

Figure 2: Diffusion layer model for drug dissolution.

Noyes and Whitney gave the earlier equation to explain the rate of dissolution when the process is diffusion controlled and involves no chemical reaction

dc/dt=k (Cs-Cb)

Where,

k=dissolution rate constant (first order).
Cs=concentration of drug in the stagnant layer.
Cb=Concentration of drug in the bulk of the solvation at time t.

The above equation was based on Fick's second law of diffusion. Brunner incorporated Fick's first law of diffusion. The modified Noyes-Whitney's equation is as follows:

dC/dt=DAK w/o (Cs-Cb)/ Vh

Where, D = Diffusion coefficient of the drug.
A=Surface area of the dissolving solid.
Kw/o=Water/Oil partition coefficient of the drug considering the fact that are aqueous. Since the rapidity with which a drug dissolves depends on the Kw/o, it is also called as the intrinsic dissolution rate constant.

Danckwert's model (Penetration or Surface renewal theory)

Danckwert contested the notion of a stagnant layer and posited that turbulence within the dissolution medium is present at the solid/liquid interface. Consequently, the disturbed fluid, characterized by a macroscopic aggregation of eddies or packets, encounters the solid/liquid interface in a stochastic manner due to the influence of eddy currents, facilitating the absorption of the solute through diffusion and subsequently transporting it to the bulk of the solvation packets containing solute, which are incessantly supplanted with novel packets of fresh solvent. This dynamic ensures that

the drug concentration at the solid/liquid interface remains inferior to Cs, establishing a lower limiting value of Ci. Given that the solvent packets interact with a fresh solid surface on each occasion, this theoretical framework is termed the surface renewal theory.

The Danckwert model is represented by the equation:
V dc/dt=dm/dt = A (Cs-Cb) (γD) ½
Wherein, m denotes the mass of solid dissolved and γ signifies the rate of surface renewal.

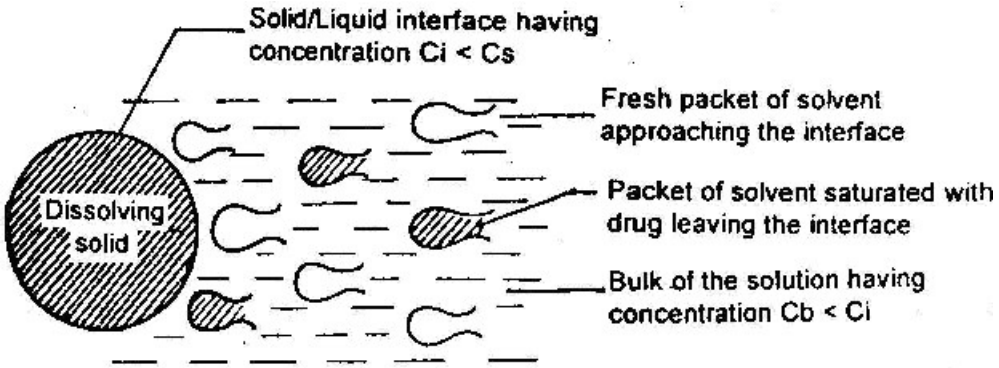

Figure 3: Danckwert's model for drug dissolution.

Interfacial barrier model (Double barrier or Limited salvation theory)
The diffusion layer model and Danckwert's model are predicated upon two fundamental assumptions:
The mass transport phenomenon represents the rate-determining step that governs the dissolution process.
The solid and solvation phases attain equilibrium at the solid/liquid interface.

In accordance with the interfacial barrier model, an intermediate concentration may be present at the interface due to the solvation mechanism, which is contingent upon solubility rather than diffusion. Each crystal face exhibits a distinct interfacial barrier in the context of a crystal's dissolution. The following equation encapsulates this concept.
G=Ki (Cs-Cb)
Where G denotes the dissolution rate per unit area and Ki signifies the effective interfacial transport constant.

The diffusibility D may not remain independent of the saturation concentration Cs within this theoretical framework.

Advantages of Solid Dispersions improving bioavailability of Poorly soluble drugs[6-7]
The utilization of solid dispersions as a pharmaceutical formulation strategy presents many benefits when compared to alternative methodologies aimed at enhancing the bioavailability of drugs that exhibit poor solubility in aqueous environments. This particular approach not only facilitates an increase in the effective surface area of the drug particles, thus promoting a more rapid dissolution rate, but it also aids in the stabilization of the drug's amorphous form, which is often associated with enhanced solubility characteristics, thereby yielding a superior therapeutic effect.

Furthermore, the implementation of solid dispersions allows for the incorporation of various hydrophilic carriers, which can significantly improve the drug's dissolution profile, thereby mitigating the challenges posed by the inherent physicochemical properties of poorly soluble compounds. This versatile technique not only encompasses the potential for enhanced drug release kinetics but also provides a platform for the tailoring of release mechanisms, offering a strategic advantage in the design of dosage forms that can meet specific pharmacokinetic and pharmacodynamic objectives.

Moreover, solid dispersions can effectively minimize the reliance on excipients that may be employed in other formulation strategies, thus reducing the overall complexity of the formulation process and potentially lowering production costs. By utilizing this innovative approach, researchers and formulators are afforded the opportunity to explore a broader range of formulation possibilities, which can lead to the development of more effective and patient-friendly drug delivery systems that ultimately improve patient compliance and treatment outcomes.

Solid dispersions disadvantages[8]
Despite considerable expertise in the realm of solid dispersions, their application in commercial products remains limited, primarily due to the inherent risk that the amorphous state may transition to a crystalline state during processing (mechanical stress) or storage (temperature and humidity stress).

The influence of moisture on the storage stability of amorphous pharmaceuticals is a notable concern, as it has the potential to augment drug mobility and facilitate drug crystallization.

Most of the polymers employed in solid dispersions possess the capacity to absorb moisture, which may lead to phase separation, crystal development, or a transformation from the amorphous state to the

crystalline state or from a metastable crystalline form to a more stable configuration during storage.

This phenomenon may culminate in diminished solubility and a reduced dissolution rate. Consequently, the comprehensive utilization of the inherent advantages of amorphous solids necessitates their stabilization in the solid state and during in-vivo performance.

Limitations

Labourious and economically demanding techniques for the synthesis process.

Consistency in the physicochemical properties.

There are challenges in integrating the pharmaceutical agent into the formulation of dosage forms, scaling up the manufacturing procedure, and ensuring the stability of both the pharmaceutical agent and the carrier.

Methods of preparation of solid dispersions[8-12]

Various methods used for preparation of solid dispersion system.

- Melting method
- Solvent method
- Melting solvent method (melt evaporation)
- Melt extrusion methods
- Lyophilization techniques
- Melt agglomeration Process
- The use of surfactant
- Electrospining
- Super Critical Fluid (Scf) technology
- Dropping method

Melting method

The melting or fusion method is the preparation of physical mixture of a drug and a water-soluble carrier and heating it directly until it melted. The melted mixture is then solidified rapidly in an ice-bath under vigorous stirring. The final solid mass is crushed, pulverized and sieved.

Solvent method

In this method, the physical mixture of the drug and carrier is dissolved in a common solvent, which is evaporated until a clear, solvent free film is left. The film is further dried to constant weight.

Melting solvent method (melt evaporation)

It involves preparation of solid dispersions by dissolving the drug in a suitable liquid solvent and then incorporating the solvation directly into the melt of polyethylene glycol, which is then evaporated until a clear, solvent free film is left. The film is further dried to constant weight.

Melt extrusion methods

The drug/carrier mix is typically processed with a twin screw extruder. The drug/carrier mix is simultaneously melted, homogenized and then extruded and shaped as tablets, granules, pellets, sheets, sticks or powder.

Lyophilization techniques

Lyophilization involves transfer of heat and mass to and from the product under preparation. This technique was proposed as an alternative technique to solventevaporation. Lyophilization has been thought of a molecular mixing technique where the drug and carrier are co dissolved in a common solvent, frozen and sublimed to obtain a lyophilized molecular dispersion.

Melt agglomeration Process

This technique has been used to prepare solid dispersion where in the binder acts as a carrier. In addition, solid dispersion is prepared either by heating binder, drug and excipient to a temperature above the melting point of the binder (melt- in procedure) or by spraying a dispersion of drug in molten binder on the heated excipient (spray-on procedure) by using a high shear mixer.

Melting method

The melting or fusion technique entails the formulation of a physical amalgamation of a pharmaceutical compound and a hydrophilic carrier through direct thermal application until liquefaction occurs. The resultant molten mixture is subsequently subjected to rapid solidification within an ice bath while undergoing vigorous agitation. The final solidified mass is then subjected to crushing, pulverization, and sieving processes.

Solvent method

In this approach, the physical amalgamation of the pharmaceutical compound and the carrier is solubilized in a common solvent, which evaporates until a coherent, solvent-free film is produced. The film is then subjected to further drying until a constant weight is achieved.

Melting solvent method (melt evaporation)

This method involves preparing solid dispersions by dissolving the pharmaceutical compound in an appropriate liquid solvent, followed by the direct incorporation of the resultant solvate into the molten polyethylene glycol matrix. Subsequently, the polyethylene glycol is evaporated until a transparent, solvent-free film is obtained. The film is further dried until it reaches a constant weight.

Melt extrusion methods

The pharmaceutical compound and carrier combination is typically processed using a twin-screw extruder. This mixture is concurrently melted, homogenized, and subsequently extruded into various forms, including tablets, granules, pellets, sheets, sticks, or powders.

Lyophilisation techniques

Lyophilization encompasses the transfer of heat and mass to and from the product under formulation. This methodology has been proposed as a viable alternative to solvent evaporation techniques. Lyophilization is a molecular mixing process wherein the pharmaceutical compound and carrier are solubilized in a common

solvent, frozen, and subsequently subjected to sublimation to yield a lyophilized molecular dispersion.

Melt agglomeration process

This technique has been employed in preparing solid dispersions, wherein the binder functions as a carrier. Furthermore, solid dispersions can be formulated either by elevating the temperature of the binder, pharmaceutical compound, and excipient above the binder's melting threshold (melt-in procedure) or by atomizing a dispersion of the pharmaceutical compound in a molten binder onto the preheated excipient (spray-on procedure) utilizing a high-shear mixer.

The use of surfactant

Surfactants have been documented to induce salivation/plasticization, thereby diminishing the melting point of active pharmaceutical ingredients, the glass transition temperature, and the overall glass transition temperature of solid dispersions. Due to these distinctive characteristics, surfactants have garnered significant attention from researchers in forming solid dispersions.

Electrospinning

Electrospinning is a sophisticated technique whereby solid fibers are generated from a polymeric fluid stream, either in a solvate state or molten form, which is extruded through a millimeter-scale nozzle. This process necessitates the application of a potent electrostatic field over a conductive capillary linked to a reservoir containing the polymer solvate or melt, along with a conductive collection screen**.**

Super Critical Fluid (Scf) technology

The supercritical fluid (Scf) methodology involves atomizing a solvate composed of the solute and an organic solvent into a continuous, concurrent supercritical phase.

Dropping method

Solid dispersion of a molten drug-carrier mixture is pipetted and subsequently released onto a designated plate, where it solidifies into spherical particles. Factors such as the molten mixture's viscosity and the pipette's dimensions may significantly influence the resultant size and morphology of the particles.

Formulation strategies for solubility and bio enhancement[13-14]

To facilitate the ongoing early-stage drug discovery initiative, it is essential to achieve a sufficient concentration of either amorphous or crystalline drug forms that are solubilized in aqueous testing environments for both appropriate in vitro and in vivo evaluations. In instances where the solubility of compounds within aqueous media is constrained, implementing formulation strategies becomes imperative at the initial stages of drug discovery. Such strategies are indispensable for the selection of lead compounds and the advancement of commercially viable pharmaceutical products. The fundamental methodologies for drug solubilization are delineated herein.

- Particle size reduction
- Solid state engineering
- Solid dispersions
- Microemulsions
- Liposomes
- Complexation (e.g. cyclodextrins)
- Lyophilization
- Co-solvent systems
- Micellar/surfactant systems
- Salt formation
- Prodrug approach
- Nanotechnology approaches
- Hydrotrophy
- Osmotic drug delivery
- Combination with other drugs

Microionization

Microionization presents several significant drawbacks, with the primary concern being the restricted capacity to regulate critical attributes of the resultant particle, including dimensions, morphology, structural characteristics, surface traits, and electrostatic properties. Furthermore, microionization represents a high-energy procedure that induces perturbations within the drug's crystalline lattice, thereby forming disordered or amorphous regions in the final formulation. These amorphous regions exhibit thermodynamic instability and are consequently prone to recrystallization during storage, particularly under elevated temperature and humidity conditions. Notably, not all poorly water-soluble pharmaceuticals are amenable to solubility enhancement via salt formation. A specific salt's dissolution kinetics typically diverge from its parent compound's. Nevertheless, sodium and potassium salts derived from weak acids generally exhibit a more rapid dissolution rate than their unprotonated counterparts. Potential drawbacks associated with salt forms encompass heightened reactivity with atmospheric carbon dioxide and moisture, culminating in the precipitation of poorly soluble pharmaceuticals. Although applying a cosolvent to augment dissolution rates is advantageous, it also presents challenges related to patient adherence and market viability.

Solubility enhancing agents

Numerous investigations documented in the scientific literature have thoroughly explored methodologies aimed at augmenting the solubility of drugs exhibiting poor aqueous solubility. A thorough examination conducted by Yalkowsky delineates the various strategies and techniques employed in the solubilization of hydrophobic pharmaceutical agents. Chiou and Riegelman have critically assessed the function of water-soluble polymers in enhancing both the solubility and dissolution kinetics of drugs characterized by low solubility profiles.

Sodium lauryl sulfate (SLS) is classified as an anionic surfactant with remarkable wetting characteristics across an extensive range of pH levels. Its utility spans multiple pharmaceutical and cosmetic applications. SLS has achieved recognition as a Generally Regarded as Safe (GRAS) substance and is cataloged in the FDA's Inactive Ingredients Guide, encompassing dental formulations, oral capsules, suspensions, tablets, as well as topical and vaginal preparations. Integrating a substantial quantity of SLS into a direct compression tablet formulation facilitates the rapid and nearly complete in vitro release of a poorly water-soluble drug from a tablet matrix that maintains acceptable mechanical integrity. Drug solubilization can be accomplished by establishing a locally elevated concentration of SLS micelles that directly interact with crystalline drug particles during the continuous erosion of the surfactant-enriched tablet core. Polyethylene glycol (PEG) enhances the dissolution rate by optimizing water wettability and capillary absorption during disintegration. Polyvinylpyrrolidone (PVP) is recognized as a water-soluble polymer and is noted for its exceptional wetting properties. It has been extensively employed to enhance the solubility and dissolution kinetics of drugs with low solubility. In physical mixtures, the influence of the PVP polymer is believed to function as a complex formation agent during solvation at intermediate polymer weight fractions and likely acts as a disintegration-promoting matrix at elevated polymer weight fractions.

Solid dispersions

The solid dispersion (SD) methodology has been extensively implemented to enhance the dissolution kinetics, solubility, and oral bioavailability of drugs with poor water solubility. The nomenclature of solid dispersions has been adopted to characterize a category of dosage forms wherein the drug is dispersed within a biologically inert matrix, typically to improve oral bioavailability.

Superdisintegrants

A drug administered in an orally ingested tablet must dissolve before absorption and subsequent transport into systemic circulation. For numerous pharmaceuticals, the dissolution process must be preceded by the disintegration of the tablet matrix. In order to facilitate tablet dissolution, it is imperative to surmount the cohesive strength conferred upon the mass by compression. Consequently, the conventional practice of incorporating disintegrants is intended to catalyze this process. Disintegration is frequently regarded as a necessary precursor to drug dissolution; however, it does not guarantee that the drug will dissolve, thus potentially impacting bioavailability. Therefore, it is crucial to evaluate the efficacy of disintegrants in terms of their influence on the dissolution rate of a drug from a tablet formulation. The advancement of rapidly dispersible tablets utilizing super disintegrants has garnered popularity for many reasons. For tablets containing sparingly water-soluble drugs, the onset of dissolution is frequently impeded by inadequate wettability of the tablet or sluggish liquid infiltration into the tablet matrix. This leads to prolonged disintegration times and consequently hinders drug release. The incorporation of a super disintegrant serves to ameliorate this issue.

A group of superdisintegrants including Crosscarmellosesodium (Ac-Di-Sol) sodium starch glycolate (Primojel and Explotab) and Crospovidone (Polyplasdone XL) alleviate most of these problems. Use of the super disintegrants in fast dispersible tablet is possible as tablet shows optimum physical properties. The total porosity and pore mean diameter decrease, when applied pressure increase and, consequently, the disintegration time increase, as has been also reported by number of authors Under certain condition, the superdisintegrant makes enough pressure in the pores of the tablets as to produce an efficient disintegration . Although the rate of capillary penetration in tablets of narrower pore size distribution are lower than those for structure of wide pore size distribution, larger parts of pore structure participate in liquid uptake. So the final saturation volume is superior at the intermediate level of disintegrants.

Wicking and swelling were found to be the primary mechanism of action for tablet disintegrants, while other mechanisms such as deformation recovery, particles repulsion theory, heat of wetting and evolution of a gas etcmay play a role in particulate cases of tablet disintegration. G.K Bolhuis demonstrated that dissolution from tablets and capsules of poorly soluble, hydrophobic drugs can be improved by solid deposition of the drug upon hydrophilic, strongly swelling carriers like the super disintegrants sodium starch glycolate, crosscarmellose, and crosspovidone. This increased in dissolution is because of micronized drug particles are fairly evenly distributed on relatively large hydrophilic carrier particles can prevent reagglomeration and increase the drug dissolution rate as an effect of the large effective surface for dissolution . A prerequisite for fast dissolution from an ordered mixture seemed to be that the carrier particles dissolve rapidly, delivering a fine particulate suspension of drug particles.

The crosspovidone is a water in-soluble type of cross-linked polyvinylpyrollidone used as tablet disintegrant at concentration of 5-10%, exhibiting high capacity with little tendency to gel formation.

The advantageous properties of solid dispersions[15]

Particles with higher porosity

Particles in solid dispersions have been found to have a higher degree of porosity. The increase in porosity also depends on the carrier properties, for instance, solid dispersions containing linear polymers produce larger and more porous particles than those containing reticular polymers and, therefore, result in a higher dissolution rate. The increased porosity of solid dispersion particles also hastens the drug release profile.

Particles with improved wettability
Carriers with surface activity, such as cholic acid and bile salts.When used, can significantly increase the wettability property of drug. Even carriers without any surface activity, such as urea, improved drug wettability. Carriers can influence the drug dissolution profile by direct dissolution or co-solvent effects.

Particles with reduced particle size
Molecular dispersions, as solid dispersions, represent the last state on particle size reduction, and after carrier dissolution the drug is molecularly dispersed in the dissolution medium. Solid dispersions apply this principle to drug release by creating a mixture of a poorly water soluble drug and highly soluble carriers. A high surface area is formed, resulting in an increased dissolution rate and, consequently, improved bioavailability.

Drugs in Amorphous State
Poorly water-soluble crystalline drugs, when in the amorphous state tend to have higher solubility. The enhancement of drug release can usually be achieved using the drug in its amorphous state, because no energy is requiredto break up the crystal lattice during the dissolution process.

Types Of Solid Dispersions
Based on their molecular arrangement, 6 different types of solid dispersions can be distinguished

- Eutectics
- Amorphous precipitations in crystalline matrix
- Solid solvations
- Continuous solid solvations
- Discontinuous solid solvations
- Substitutional solid solvations
- Interstitial solid solvations
- Glass suspension (contain 2 phases)
- Glass suspension (contain1 phase)
- Glass solvation

Applications of Solid Dispersions[16]
To increase the solubility of poorly soluble drugs thereby increase the dissolution rate, absorption and bioavailability.

- To stabilize unstable drugs against hydrolysis, oxidation, recrimination, isomerisation, photo oxidation and other decomposition procedures.
- To reduce side effect of certain drugs.
- Masking of unpleasant taste and smell of drugs.
- Improvement of drug release from ointment, creams and gels.
- To avoid undesirable incompatibilities.
- To obtain a homogeneous distribution of a small amount of drug in solid state.
- To dispense liquid (up to 10%) or gaseous compounds in a solid dosage.
- To formulate a fast release primary dose in a sustained released dosage form.
- To formulate sustained release regimen of soluble drugs by using poorly soluble or insoluble carriers.
- To reduce pre systemic inactivation of drugs like morphine and progesterone.

Factors affecting solubility and drug release from solid dispersion[16]
There are mainly three factors:

- Drug-carrier concentration ratio.
- Molecular weight of polymer used as carrier.
- Physical form of drug in dispersion.

Drug carrier concentration ratio
Solubility and dissolution rate of drug from solid dispersion is affected by drug carrier concentration ratio to some extent. For e.g. Sulfathiazole- PVP solid dispersion. Tablets were made using powders composed of different ratio of Sufathiazole to PVP and their dissolution profiles were obtained. The 1:1, 2:1, 3:1 (Sulfathiazole: PVP) ratio shows non-linear relationship whereas the 1:2, 1:3, 1:5 (Sulfathiazole: PVP) ration shows liner relationship. From this data, one can expect that increase in PVP concentration improve dissolution rate. But when experiment carried out by using 1:3, 1:5, 1:10, 1:15 (Sulfathiazole: PVP) ratio, it was found that as further the PVP concentration increases there is decrease in dissolution rate. From this one can conclude that optimum drug-carrier ratio is required to enhance dissolution rate of drug from solid dispersion.

Molecular weight of polymer used as carrier
Molecular weight of polymer used for preparation of solid dispersion, also affect the release profile of the drug. For e.g. Sulfathiazole-PVP solid dispersion. For this study again Sulfathiazole and different molecular weight PVPs are used. Solid dispersions of 1:2 & 1:3 (Sulfathiazole: PVP) ratio using PVP of 10000, 40000, 60000 molecular weight were prepared. They were compressed in to tablets and their dissolution rates were determined. It is seen that as the molecular weight of PVP increases the dissolution rate of sulfathiazole decreases.

Physical form of drug in solid dispersion
Dissolution of drug from solid dispersion also depends upon the physical form of the drug, which is incorporated in the solid dispersion. For e.g Ritonavir – PEG (8000) solid dispersion, the drug was incorporated into two different forms i.e. crystalline Ritonavir and amorphous Ritonavir. This is observed that the dispersion containing amorphous drug gives improved dissolution profile than crystalline drug.

Over the surfaces of dissolving plugs, which prevented further dissolution of drug from solid dispersions. Therefore, surface-active or self-emulsifying agents including bile salts, lecithin, lipid mixtures, Gelucire 44/14 and Vitamin E TPGS NF were used as additional additives, acting as dispersing or emulsifying carriers for the liberated drug to prevent the formation of any water-

insoluble surface layer. In addition, the release behaviors of many drugs are also improved by using water insoluble polymers such as crospovidone and enteric polymers such as hydroxypropyl methylcellulose phthalate (HPMCP), cellulose acetate phthalate (CAP), Eudragit L100 and S100 and Eudragit E.

Characterization of solid dispersion[17]

- Drug -carrier miscibility
- Hot stage microscopy
- HSM is used to characterize the interactions of many drugs with polymer.

Differential scanning calorimetry

Differential Scanning Calorimetry (DSC) technique is used to detect theamount of crystalline material10.

Powder X-ray diffraction.

Powder X-ray diffraction can be used to qualitatively detect material with long rangeorder. Sharper diffraction peaks indicate more crystalline material.

Drug carrier interactions

FT-IR spectroscopy

Infrared spectroscopy (IR) can be used to detect the variation in the energy distribution of interactions between drug and matrix. Sharp vibrational bands indicate crystallinity. Fourier Transform Infrared Spectroscopy (FTIR) was used to accurately detect crystallinities ranging from 1 to 99% in purematerial. Using IR or FTIR, the extent of interactions between drug and matrix can be measured.

Raman spectroscopy

Confocal Raman Spectroscopy was used to measure the homogeneity of the solid mixture.

Physical Structure

Scanning electron microscopy

Macroscopic techniques that measure mechanical properties that are different for amorphous and crystalline material can be indicative for the degree of crystallinity.

Dynamic vapor sorption: Water vapour sorption can be used to discriminate between amorphous and crystalline material when the hygroscopicity is different.

DSC (MTDSC): Temperature Modulated Differential Scanning Calorimetry (TMDSC) can be used to assess the degree of mixing of an incorporated drug.

ITC: Isothermal Micro calorimetry measures the crystallization energy of amorphous material that is heated above its glass transition temperature (Tg).

CONCLUSION

Solid dispersions are increasingly recognized for enhancing the dissolution rate and bioavailability of poorly water-soluble drugs. They effectively reduce dissolution issues when combined with water-soluble carriers. This technology focuses on drug-polymer systems, where drug dispersion and stabilization are critical for formulation. Consequently, it is acknowledged as a promising strategy for improving the dissolution characteristics of such drugs. Despite advancements in understanding solid dispersions, their commercial use remains limited. This review highlights solubility, BCS classification, and various carriers. It also discusses preparation techniques for solid dispersions and recent technological advancements. The article categorizes solid dispersions based on carrier type and molecular configuration. Furthermore, it outlines the mechanisms, preparation methods, and commercially available drugs utilizing solid dispersion techniques.

REFERENCES

1. GL, A. (1995). Theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res, 22: 11-23.
2. Chaudhari, P. D. (2006). Current trend in solid dispersion techniques. Pharm. Rev, 4(1): 3.
3. Dhirendra, K., Lewis, S., Udupa, N., & Atin, K. (2009). Solid dispersions: a review. Pakistan journal of pharmaceutical sciences, 22(2).
4. Brahmankar, D. M., & Jaiswal, S. B. (2019). Biopharmaceutics and pharmacokinetics. Vallabh prakashan.
5. Sugimoto, M., Okagaki, T., Narisawa, S., Koida, Y., & Nakajima, K. (1998). Improvement of dissolution characteristics and bioavailability of poorly water-soluble drugs by novel cogrinding method using water-soluble polymer. International Journal of Pharmaceutics, 160(1): 11-19.
6. Molčányiová, A., Stančáková, A., Javorský, M., & Tkáč, I. (2006). Beneficial effect of simvastatin treatment on LDL oxidation and antioxidant protection is more pronounced in combined hyperlipidemia than in hypercholesterolemia. Pharmacological research, 54(3): 203-207.
7. Shete Amol, S., Shinde Sunita, S., Patil Manisha, V., Mevekari Fatima, I., Shete Amol, S., Bhagwat Durgacharan, A., & D'Souza, J. I. Physicochemical Characterization And Solubility Enhancement of Simvastatin Using Solid Dispersion Technology. World journal of pharmaceutical Research, 1(2): 297-308.
8. Kumar, A., & Kumar, K. (2017). Solid dispersion-strategy to enhance solubility and dissolution of poorly water soluble drugs. Universal Journal of Pharmaceutical Research.
9. Jatwani, S., Rana, A. C., Singh, G., & Aggarwal, G. (2011). Solubility and dissolution enhancement of simvastatin using synergistic effect of hydrophilic carriers. *Der Pharm Lett*, *3*(6): 280-93.
10. Bley, H., Fussnegger, B., & Bodmeier, R. (2010). Characterization and stability of solid dispersions based on PEG/polymer blends. International Journal of Pharmaceutics, 390(2): 165-173.

11. Modi, A., & Tayade, P. (2006). Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS pharmscitech, 7(3): 68.
12. Nagarsenker, M. S., & Joshi, M. S. (2005). Celecoxib-cyclodextrin systems: characterization and evaluation of in vitro and in vivo advantage. Drug development and industrial pharmacy, 31(2): 169-178.
13. Raymond C Rowe, Paul J Sheskey, Sian C Owen. Handbook of pharmaceutical excepients, pharmaceutical press and American Pharmacist Association, London, Chicago, Fifth edition, 132, 385, 188, 430, 687, 767, 214, 701, 211, 449, 142, (2006).
14. Osol, A., Hoover, J. E., & Chase, G. D. (1980). Remington's pharmaceutical sciences. (No Title).
15. Allen Jr, L. V. (1990). Pharmaceutical Dosage Forms and Drug Delivery Systems.
16. Darekar, A. B., Bele, M. H., Wagh, M. P., & Derle, D. V. (2024). Preparation and characterization of microwave assisted bionanocomposites for enhancement of physicochemical properties of olmesartan. Research Journal of Pharmacy and Technology, 17(3): 1332-1335.
17. Singh, S., Baghel, R. S., & Yadav, L. (2011). A review on solid dispersion. International journal of pharmacy & life sciences, 2(9).