



## Improving Solubility and Bioavailability of Poorly Water Soluble Drugs by Solid Dispersion Technique – A Review

P.Manikandan<sup>1\*</sup>, N.Subramanian<sup>2</sup>

<sup>1</sup>Research scholar, Karpagam University, Eachanari, Coimbatore, Tamilnadu, India.

<sup>2</sup>Research guide, Karpagam University, Eachanari, Coimbatore, Tamilnadu, India.

\*Corresponding author's E-mail: [psmanikandan12@gmail.com](mailto:psmanikandan12@gmail.com)

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### ABSTRACT

Among all newly, discovered chemical entities about 40 % drugs are lipophilic and fail to reach the market due to their poor water solubility. Solubility issues complicating the delivery of these new drugs also affect the delivery of many existing drugs. The various techniques are available for enhancement of poorly water solubility of drugs. Among these Solid dispersions are one of the most promising strategies to improve the oral bioavailability of BCS Class II drugs. In this review, it is intended to discuss the recent advances related on the area of solid dispersions, Such as method of preparation, carriers used, characterization, advantages, disadvantages and the application of the solid dispersion.

**Keywords:** Carrier selection, Methods of preparation, Solid dispersion, Solubility.

### INTRODUCTION

Oral drug delivery is the simplest and easiest way of administering drugs.<sup>1</sup> Because of the greater stability, smaller bulk, accurate dosage and easy production, solid oral dosages forms have many advantages over other types of oral dosage forms. Therefore, most of the new chemical entities (NCE) under development these days are intended to be used as solid dosage forms that originate an effective and reproducible in vivo plasma concentration after oral administration. Drug release is a crucial and limiting step for oral drug bioavailability, particularly for drugs with low gastrointestinal solubility and high permeability. By improving the drug release profile of these drugs, it is possible to enhance their bioavailability and reduce side effects.

Together with the permeability, the solubility behavior of a drug is a key determinant of its oral bioavailability. There have always been certain drugs which solubility has presented a challenge to the development of a suitable formulation for oral administration. Examples such as griseofulvin, digoxin, phenytoin, sulphathiazolen, and chloramphenicol come immediately to mind. With the recent advent of high throughput screening of potential therapeutic agents, the number of poorly soluble drug candidates has risen sharply and the formulation of poorly soluble compounds for oral delivery now presents one of the most frequent and greatest challenges to formulation scientists in the pharmaceutical industry.

Consideration of the modified Noyes-Whitney equation provides, some hints as to how the dissolution rate of even very poorly soluble compounds might be improved to minimize the limitations to oral availability:

$$dc/dt=AD(C_s-C)/h$$

Where  $dc/dt$  is the rate of dissolution,  $A$  is the surface area available for dissolution,  $D$  is the diffusion coefficient of the compound,  $C_s$  is the solubility of the compound in the dissolution medium,  $C$  is the concentration of drug in the medium at time  $t$  and  $h$  is the thickness of the diffusion boundary layer adjacent to the surface of the dissolving compound.

The main possibilities for improving dissolution according to this analysis are to increase the surface area available for dissolution by decreasing the particle size of the solid compound or by optimizing the wetting characteristics of the compound surface, to decrease the boundary layer thickness, to ensure sink conditions for dissolution and, last but definitely not least, to improve the apparent solubility of the drug under physiologically relevant conditions. However, the most attractive option for increasing the release rate is improvement of the solubility through formulation approaches.

Of the physical approaches, review articles have already been published on the use of polymorphs, the amorphous of the drug and complexation. Decreasing the particle size of the compound by milling the drug powder theoretically results in an increase in the available area for dissolution, but in some cases micronized powder tends to agglomerate, thereby at least partly negating the milling procedure. Presenting the compound as a molecular dispersion combines the benefits of a local increase in the solubility and maximizing the surface area of the compound that is exposed to the dissolution medium as the carrier dissolves.

Sekiguchi and obi (1961) developed a method to enhance the bioavailability of poorly water soluble drugs, which was later termed solid dispersion.<sup>2</sup> "Solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug". The matrix can be either



crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles (cluster) or crystalline particles.

**Table 1:** Summarizes the various formulation and chemical approaches that can be taken to improve the solubility or to increase the available surface area for dissolution.

Approaches to improve the solubility or to increase the available surface area for distribution

<b>I. Physical modifications</b>
Particle size
Micronization
Nano suspensions
Modifications of the crystal habit
Polymorphs
Pseudopolymorphs (including solvates)
Complexation/solubilization
Use of surfactants
Use of cyclodextrins
Drug dispersion in carriers
Eutectic mixtures
Solid dispersions (non-molecular)
Solid solutions
<b>II. Chemical modification</b>
Soluble prodrugs
Salt form

#### Ideal properties of a carrier for solid dispersion

High water solubility, improves wettability and enhances dissolution.

- i) High glass transition point (T<sub>g</sub>) and improve stability
- ii) Minimal water uptake (reduces T<sub>g</sub>).
- iii) Soluble in common solvent with drug (solvent evaporation technique).
- iv) Relatively low melting point (melting process).
- v) Capable of forming a solid solution with the drug.
- vi) Good compressibility index and flow index.
- vii) Ability to protect drug from moisture.

#### Selection of solvent

- i) Dissolve both drug and carrier
- ii) Toxic solvents to be avoided due to the risk of residual levels after preparation e.g. chloroform and dichloroform
- iii) Ethanol is a less toxic alternative
- iv) Water based systems preferable
- v) Use of surfactants to create carrier drug solutions but care should be taken as they can reduce the glass transition point.

## Solid Dispersions

### First generation solid dispersions

The first description of solid dispersions was from Sekiguchi and obi in 1961. They noted that the formulations of eutectic mixtures improve the rate of drug release and, consequently, the bioavailability of poorly water soluble drugs.<sup>2</sup> In the same decade, several solid dispersions were described using poorly water soluble drugs, such as sulfathiazol<sup>2</sup> and chloramphenicol<sup>1</sup> using urea as high water soluble carrier. These solid dispersions produced faster release and higher bioavailability than conventional formulations of the same drugs. The small particle size and the better wettability of the drug were the main reasons for the observed improvements in bioavailability. Later, Levy and Kaning developed solid dispersion systems, containing mannitol as carrier, by preparing solid solutions through molecular dispersions instead of using eutectic mixtures.

The observed improvements were attributed to faster carrier dissolution, releasing microcrystals or particles of drug. These solid dispersions, which could be designed as first generation solid dispersions, were prepared using crystalline carriers. Crystalline carriers include urea and sugars, which were the first carriers to be employed in solid dispersions. They have the disadvantage of forming crystalline solid dispersions, which were more thermodynamically stable and did not release the drug as quickly as amorphous ones.

### Second generation solid dispersions

In the late sixties<sup>3</sup> it was observed that solid dispersions, where the drug was maintained in the crystalline state, might not be as effective as the amorphous, because the former were more thermodynamically stable<sup>3</sup>. Therefore, a second generation of solid dispersions appeared, containing amorphous carriers instead of crystalline. Indeed, the most common solid dispersions do not use crystalline carriers but amorphous. In the latter, the drugs are molecularly dispersed in irregular form with in an amorphous carrier, which are usually polymers.

Polymeric carriers have been the most successful for solid dispersions, because they are able to originate amorphous solid dispersions. They are divided into synthetic polymers and natural product based polymers. Fully synthetic polymers include povidone (PVP)<sup>20</sup>, polyethyleneglycols (PEG), and polymethacrylates. Natural product based polymers are mainly composed by cellular derivatives, such as hydroxypropylmethylcellulose (HPMC), ethylcellulose or hydropropylcellulose or starch derivatives, like cyclodextrins.

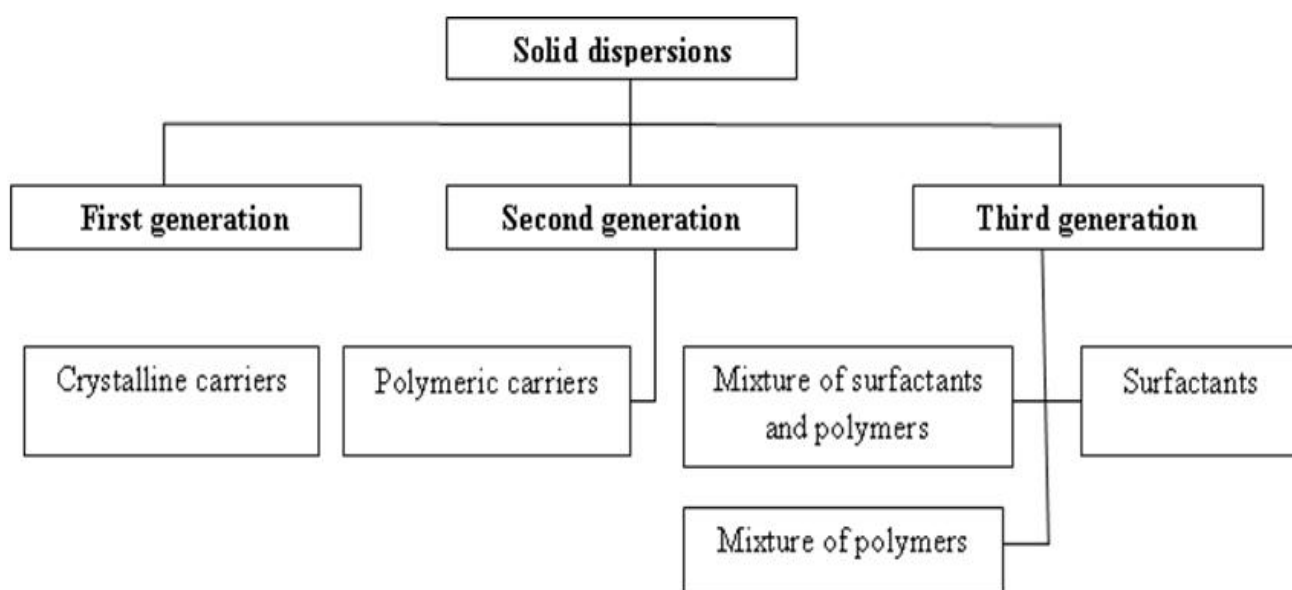
Amorphous solid dispersions can be classified according to the molecular interaction of drug and carriers in solid solutions, solid suspensions or a mixture of both<sup>28</sup>. In amorphous solid solutions, drug and carrier are totally miscible and soluble, originating a homogenous molecular interaction between them. In these systems, the drug and carrier interaction energy is extremely high, resulting in a



true solution. The use of polymers in the preparation of a true solid solution creates an amorphous product in which the crystalline drug is dissolved. This type of amorphous solid dispersion is homogenous on a molecular level. Therefore, only one phase is present.

**Table 2:** Types of solid dispersion

Solid dispersion type	Matrix	Drug**	Remarks	No.phases	Reference
I. Eutectics	C	C	The first type of solid dispersion prepared.	2	14
II. Amorphous Precipitations in crystalline matrix	C	A	Rarely encountered.	2	9.57
III. Solid solutions					
a. Continuous solid solutions	C	M	Miscible all composition, never prepared.	1	32
b. Discontinuous solid solutions	C	M	Partially miscible, 2 phases even though drug is molecularly dispersed.	2	70
c. Substitutional solid solutions	C	M	Molecular diameter of drug (solute) differs less than 15% from the matrix diameter. In that case the drug and matrix are substitutional, can be continuous and discontinuous. When discontinuous 2 phases even though drug is molecularly dispersed.	1 or 2	65,88
d. Interstitial solid solutions	C	M	Drug(solute) molecular diameter less than 59% of matrix(solvent) Diameter. Usually limited miscibility,discontinuousEg:Drug in helical interstitial spaces of PEG	2	13
IV. Glass suspension	A	C	Particle size of dispersed phase dependent on cooling/evaporation rate,obtained after cryatallization of drug in amorphous matrix.	2	68
V. Glass suspension	A	A	Particle size of dispersed phase dependent on cooling/evaporation rate much solid dispersion is of this type.	2	68
VI. Glass solution	A	M	Requires miscibility or solid solubility, complex formation or upon fast fast cooling or evaporation during preparation, manyexamplespeciallywithPVP.	1	76



**Figure 1:** The classification of solid dispersions

Amorphous solid suspensions occur when the drug has limited carrier solubility or an extremely high melting point. Drugs with a high melting point are candidates for

producing an amorphous solid suspension. Molecularly, the obtained dispersion does not have a homogenous structure, but is composed of two phases. Small drug

particles, when dispersed in polymeric carriers, are able to provide an amorphous final product.<sup>4</sup>

When a drug is both dissolved and suspended in a carrier, a heterogeneous structure is obtained with mixed properties of amorphous solid solutions and amorphous solid suspensions.

In second-generation solid dispersions, the drug is in its super-saturated state because of forced solubilization in the carrier. These systems are able to reduce the drug particle size to nearly a molecular level, to solubilize or co-dissolve the drug by the water soluble carrier, to provide better wettability of the drug by the carrier material, and to produce amorphous forms of the drug and carriers. In these solid dispersions, the carrier dissolution dictates the drug release profile.<sup>5</sup>

### Third generation solid dispersions

Recently, it has been shown that the dissolution profile can be improved if the carrier has surface activity or self-emulsifying properties, therefore third generation solid dispersion solid dispersions appeared. These contain a surfactant carrier, or a mixture of amorphous polymers and surfactants as carriers. These third generation solid dispersions are intended to achieve the highest degree of bioavailability of poorly soluble drugs and to stabilize the solid dispersion, avoiding drug recrystallization.

The use of surfactants such as inulin, inutec SPI, compritol 888 ATO, gelucire 44/14 and poloxamer 407 as carriers was shown to be effective in originating high polymorphic purity and enhanced in vivo bioavailability. The association of amorphous and surfactants has been reported. For instance, the dissolution rate and bioavailability of LAB68, a poor water soluble drug, were improved after being dispersed in a mixture of PEG and polysorbate 80. The bioavailability of this solid dispersion was 10-fold higher compared to the dry blend of micronized drug. In addition, the solid dispersion system was physically and chemically stable for at least 16 months. HPMC was also associated with poloxamer and polyethylene hydrogenated castor oil to prepare an amorphous felodipine solid dispersion. The inclusion of surfactants in the formulation containing a polymeric carrier may help to prevent precipitation and/or protect a fine crystalline precipitate from agglomeration into much larger hydrophobic particles.<sup>6</sup>

### Advantages of solid dispersions over other strategies to improve the bioavailability of poorly water-soluble drugs

Improving drug bioavailability by changing their water solubility has been possible by chemical or formulation approaches.

Chemical approaches to improving bioavailability without changing the active target can be achieved by salt formulation or by incorporating polar or ionizable groups in the main drug structure, resulting in the formulation of a pro-drug. Solid dispersions appear to be a better

approach to improve drug solubility than these techniques<sup>8</sup>, because they are easier to produce and more applicable. For instance, salt formulation can only be used for neutral. Furthermore, it is common the salt formulation does not achieve better bioavailability because of its in vivo conversion into acidic or basic forms. Moreover, these types of approaches have the major disadvantages that the sponsoring company is obliged to perform clinical trials on these forms, since the product represents a NCE.

Formulation approaches include solubilization and particle size reduction techniques, and solid dispersions, among others, Solid dispersions are most acceptable to patients than solubilization products, since they give rise to solid oral dosage forms instead of liquid as solubilization products usually do. Milling or micronization for particle size reduction are commonly performed as approaches to improve solubility, on the basis of the increase in particle size reduction techniques, since the latter have a particle size reduction limit around 2-5µm which frequently is not enough to improve considerably the drug solubility or drug release in the small intestine and, consequently, to improve the bioavailability. Moreover, solid powders with such a low particle size have poor mechanical properties, such as low flow and high adhesion, and are extremely difficult to handle.

### Solid dispersions disadvantages

Despite extensive expertise with solid dispersions, they are not broadly used in commercial products, mainly because there is the possibility that during processing or storage the amorphous state may undergo crystallization. The effect of moisture on the storage stability of amorphous pharmaceuticals is also a significant concern, because it may increase the drug mobility and promote drug crystallization. Moreover, most of the polymers used in solid dispersions can absorb moisture, which may result in phase separation, crystal growth or conversion from the amorphous to the crystalline state or from a metastable crystalline form to a more stable structure during storage. This may result in decreased solubility and dissolution rate. Therefore, exploitation of the full potential of amorphous solids requires their stabilization in the solid state, as well as during in vivo performance.

### Limitations of Solid Dispersions

Although a great research interest in solid dispersion in the past four decades, the commercial utilization is very limited. Problems of solid dispersion involve

- (i) The physical and chemical stability of drugs and vehicles,
- (ii) Method of preparation,
- (iii) Reproducibility of its physicochemical properties,
- (iv) Formulation of solid dispersion into dosage forms, and





(v) Scale-up of manufacturing processes.

### Methods of Solid Dispersion Preparation

Melting and solvent evaporation methods are the two major processes of preparing solid dispersions.

#### Melting method

Sekiguchi K<sup>1</sup>, were the first to use a melting method consisting of melting the drug within the carrier followed by cooling and pulverization of the obtained product. In the melting process, the molecular mobility of carrier is high enough to change the drug's incorporation.<sup>10</sup> The use of high temperatures, and the fact that the melting process can degrade several drugs can be a limitation of this method.

#### Hot stage extrusion

Hot stage extrusion has in recent years gained wide acceptance as a method of choice for the preparation of solid dispersions. The hot stage extrusion process is highly dependent on the physicochemical properties of the compounds and their miscibility in the molten state. Hot stage extrusion consists of the extrusion, at high rotational speed, of the drug and carrier, previously mixed, at melting temperature for a small period. Extrusion then collected after cooling at room temperature and milled.<sup>8</sup> Moreover, it was observed that solid dispersions of itraconazole/Intec SP1 prepared by hot stage extrusion presented itraconazole in a fully glassy state, whereas it was only partially glassy in solid dispersions prepared by spray drying.<sup>9</sup>

#### Melt agglomeration

Melt agglomeration allows the preparation of solid dispersions in conventional high shear mixers. It is made by adding the molten carrier containing the drug to the heated excipients.<sup>10</sup> It is prepared by heating a mixture of the drug, carrier and excipients to a temperature within or above the melting range of the carrier. It is also possible to produce stable solid dispersions by melt agglomeration in a rotary processor.<sup>5</sup>

#### Solvent evaporation method

The solvent evaporation method consists of the solubilization of the drug and carrier in a volatile solvent that is later evaporated. In this method, the thermal decomposition of drugs and carriers can be prevented, since organic solvent evaporation occurs at low temperature. A basic process of preparing solid dispersions of this type consists of dissolving the drug and the polymeric carrier in a common solvent, such as ethonal, chloroform, mixture of ethanol and dichloromethane. Normally, the resulting films are pulverized and milled.<sup>11</sup>

#### Spray drying

Spray drying is one of the most commonly used solvent evaporation procedures in the production of solid dispersion. It consists of dissolving and suspending the

carrier, then spraying it into a stream of heated airflow to remove the solvent.<sup>9</sup> Due to the large specific surface area offered by the droplets, the solvent rapidly evaporates and the solid dispersion is formed within the seconds, which may be fast enough to prevent phase separation. Van Drooge et al.<sup>12</sup> prepared an alternative solid dispersion by spraying a povidone and diazepam solution into liquid nitrogen, forming a suspension that was then lyophilized.

#### Freeze-drying (Lyophilization)

This process consists of dissolving the drug and carrier in a common solvent, which is immersed in liquid nitrogen until is fully frozen. Then, the frozen solution is further lyophilized.<sup>13</sup> Although it is concluded in literature that this is a promising and suitable technique to incorporate drug substances in stabilizing matrices, the technique is poorly exploited for the preparation of solid dispersions. An important advantage of freeze-drying is that the drug is subjected to minimal thermal stress during the formation of the solid dispersion. However, the most important advantage of freeze-drying is that the risk of phase separation is minimized as soon as the solution is verified.

#### Supercritical fluid method

Supercritical fluid methods are mostly applied either with carbon dioxide (CO<sub>2</sub>), which is used as a solvent for drug and matrix or as an anti-solvent. This technique consists of dissolving the drug and the carrier in a common solvent that is introduced into a particle formation vessel through a nozzle, simultaneously with CO<sub>2</sub>. When the solution is sprayed, the solvent is rapidly extracted by the SCF, resulting in the precipitation of solid dispersion particles on the walls and bottom of the vessel.<sup>30</sup> The use of processes using SCF reduces particle size, residual solvent content, without any degradation and often results in high yield.

#### Co-precipitation method

Co-precipitation is recognized technique for increasing the dissolution of poorly water soluble drugs, so as to consequently improve bioavailability. In this method, non-solvent is added drop wise to the drug and carrier solution, under constant stirring. In the course of the non-solvent addition, the drug and carrier co-precipitated to form micro particle suspension is filtered and dried. The required quantity of polymer and the drug were mixed and then solvent was added to obtain clear solution. The solution was first dried under vacuum at room temperature and kept inside incubator (37°C) for 12 hrs. Finally, it was passed through sieves 2.

#### Dropping method

This technique may overcome some of the difficulties inherent in the other method and developed by Ulrich et al.<sup>14</sup> To facilitate the crystallization of different chemicals is a new procedure for producing round particles from melted solid dispersions. A solid dispersion of a melted



drug carrier mixture is pipette and then dropped onto a plate, where it solidifies into round particles. The size and shape of the particles can be influenced by factors such as the viscosity of the melt and the size of the pipette. The dropping method does not use organic solvents and therefore, has none of the problems associated with solvent evaporation. This method also avoids the pulverization, sifting and compressibility difficulties.<sup>15</sup>

### Electrostatic Spinning Method

Electrostatic spinning method involves the introduction of a liquid into an electric field whereby the liquid is caused to produce fibers. After being drawn from the liquid the fibers harden, which may involve mere cooling, chemical hardening or evaporation of solvent, and then hardened fibers may be collected upon a suitably charged surface. Tubular products comprising polyurethane fiber can be prepared by this electrostatic spinning method.<sup>16</sup> One example of this type of tubular product is a vascular prosthesis, particularly a synthetic blood vessel. Other applications of this type of tubular products include the use of different kinds of ducts, e.g. urinary, air or bile as well as conduit through which for example a wire or other device or structure may pass or lie. The electrostatic spinning method has a few applications in pharmaceutical industry.

In this method, a drug-matrix solution is pumped through an orifice and then subjected to an electrical field to form fibers with a diameter of micro- or nano-scale. This method is limited to a few matrices because only a few high molecular weight materials are fiber-forming materials. In this method electrical forces are used to overcome the surface tension of drug-polymer solution at air interface, the fibers of submicron diameters are formed whose diameter depends upon feeding rate, dielectric constant, surface tension, electric field strength. Verreck et al., in 2003, assessed the application of water-soluble polymer-based nano fibers prepared by electrostatic spinning as a means of altering the dissolution rate of the poorly water-soluble drug, itraconazole. Organic solvent-based solutions of itraconazole/HPMC mixtures were electrostatically spun at 16 and 24 kV. Then they formed nanofibers were collected as a non-woven fabric. Differential scanning calorimetry (DSC) measurements found that the melting endotherm for itraconazole was not present, suggesting the formation of an amorphous solid dispersion or solution. They concluded that the application of electrostatic spinning to pharmaceutical applications resulted in dosage forms with useful and controllable dissolution properties. Verreck et al., in 2003, used electrostatic spinning method for the preparation of drug-laden non-biodegradable nanofiber for potential use in topical drug administration and wound healing. Itraconazole and ketanserin were selected as model compounds while segmented polyurethane (PU) was selected as the non-biodegradable polymer.<sup>17</sup> For both itraconazole and ketanserin, amorphous nano dispersion with PU was obtained when the drug/polymer solutions

were electrospun from dimethylformide (DMF) and dimethylacetamide (DMAc), respectively.<sup>18</sup>

### Coating on sugar beads using fluidized bed-coating system

This method involves a fluidized bed-coating system, where in a drug-carrier solution is sprayed on to the granular surface of excipients or sugar spheres to produce either granule ready for tableting or drug-coated pellets for encapsulation in one step.<sup>19</sup> The method can be applied for both controlled- and immediate-release solid dispersions. Itraconazole (Sporanox oral capsules, coated on sugar sphere, is made by layering onto sugar beads a solution of a drug and hydroxypropylmethylcellulose (HPMC)<sup>20</sup> in a mixture of suitable solvent system comprises a mixture of methylenechloride and preferably ethanol which may be denatured with butanone. As HPMC does not dissolve completely in methylenechloride, at least 10% alcohol has to be added. A solid solution of drug in HPMC is produced upon coating and controlled drying of coated beads is done in a closed Wurster apparatus.

### Characterization of solid dispersions

Thermo analytical methods include all that examine a characteristic of the system as a function of temperature. Of these, differential scanning calorimetry (DSC) is the most highly regarded method<sup>21</sup>. DSC enables the quantitative detection of all processes in which energy is required or produced (i.e. endothermic and exothermic phase transformations).

The principle behind X-ray diffraction is that when an X-ray beam is applied to the sample, interference bands can be detected. Crystallinity in the sample is reflected by a characteristic fingerprint region in the diffraction pattern. Owing to the 'specificity of the fingerprint, crystallinity in the drug can be separately identified from crystallinity in the carrier.'<sup>29</sup>

When the goal of preparing a solid dispersion is to improve the dissolution characteristics of the drug in question, the results of the rate experiments are obviously of prime importance in assessing the success of the approach. A well-designed release experiment will show whether the solubility of the drug and its dissolution rate and its dissolution rate has been enhanced, and whether the resulting supersaturated solution is stable or tends to precipitate quickly.<sup>30</sup>

### Applications of solid dispersions

- i) To increase the solubility of poorly soluble drugs thereby increase the dissolution rate, absorption and bioavailability.
- ii) To stabilize unstable drugs against hydrolysis, oxidation, racemization, isomerization, photo oxidation and other decomposition procedures.
- iii) To reduce side effect of certain drugs.



**Table 3:** Characterization of solid dispersion

Characterization	Methods	Significance
Drug-carrier interactions	FT-IR spectroscopy Raman spectroscopy Solid state NMR studies	To find out the integration between drug and carrier and formation of inclusion complex.
Drug-carrier Miscibility	Hot stage microscopy DSC (Conventional modulated) pXRD (conventional and variable temp), NMR 1H spin lattice relaxation time	To find out the complex formation between drug and carrier.
Physical structure	SEM surface area analysis	To find out the particle size and shape.
Surface properties	Dynamic vapor solution Inverse gas chromatography Atomic force microscopy Raman microscopy	To study the morphology and degree of crystallinity.
Amorphous content	Polarized light optical microscopy Hot stage microscopy Humidity stage microscopy DSC(MTDSC), ITC,pXRD	To find out the amorphous from drug.
Dissolution enhancement	Dissolution Intrinsic dissolution Dynamic solubility Dissolution in bio-relevant media	To find out the rate and extent of dissolution.
Stability	Humidity studies Isothermal calorimetry DSC (Tg.temperature recrystallization) Dynamic vapor sorption Saturated solubility studies	To find out the degree of crystallinity.

**Table 4:** Several marketed and late stage drugs are designed for improved solubility by solid dispersion

Product/Substance	Dispersion Polymer or Carrier	Technology used	Company
Gris-PEG® (Griseofulvin)	Polyethylene glycol	Melt process; exact process unknown	Novartis
Spororamax capsules (Itraconazole)	Hydroxypropylmethylcellulose (HPMC)	Spray layering	Janseen pharmaceutica
Cesamet®( Nabilone)	Povidone	process unknown	Lilly
Kaletra (lopinavir and ritonavir)	Polyvinylpyrrolidone (PVP)/polyvinyl acetate	Melt-extrusion	Abbott Laboratories
Torcetrapib	HPMC acetate succinate	Spray drying	Pfizer
Ibuprofen	Various	Melt-extrusion	Soliqs

- iv) Masking of unpleasant taste and smell of drugs.
- v) Improvement of drug release from ointment creams and gels.
- vi) To avoid undesirable incompatibilities.
- vii) To obtain a homogeneous distribution of a small amount of drug in solid state.
- viii) To dispense liquid (up to 10%) or gaseous compounds in a solid dosage.
- ix) To formulate a fast release primary dose in a sustained released dosage form.
- x) To formulate sustained release regimen of soluble drugs by using poorly soluble or insoluble carriers.
- xi) To reduce pre systemic inactivation of drugs like morphine and progesterone.

### CONCLUSION

Most of the promising NCEs are poorly water-soluble drugs, which may present a lack of therapeutic effect, due their low bioavailability. Solid dispersion systems as extremely useful tool in improving the dissolution and solubility enhancement properties of poorly water-soluble drugs. When the solid dispersion is exposed to

aqueous media, the carrier dissolves and the drug releases as fine colloidal particles. In this third generation, solid dispersions can improve their stability and performance by increasing drug-polymer solubility, amorphous fraction, particle wettability and particle porosity. Despite many advantages of solid dispersion, issues related to preparation, reproducibility, formulation, scale up, and stability limited its use in commercial dosage forms for poorly water-soluble drugs. Successful developments of solid dispersion systems for preclinical, clinical and commercial use have been feasible in recent years due to the availability of surface-active, lipid carriers and self-emulsifying carriers with relatively low melting points. Moreover, new, optimized manufacturing techniques that are easily scalable are also coming out of academic and industrial research.

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