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SOLID DISPERSION METHODS AND POLYMERS TO ENHANCE SOLUBILITY OF LOW SOLUBLE DRUGS

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ABSTRACT

The solubility behaviour of the drug is still one of the most important aspects of formulation development. Nowadays, the number of new drugs is increasing, but they have problems of poor solubility and poor permeability. For drugs with poor water solubility, solid dispersions have become a better option than dosage forms. Solid dispersion within water-soluble carriers have attracted considerable attention as a way to improve the dissolution rate and bioavailability of hydrophobic drugs. Solid dispersion has the ability to increase the solubility of the drug. There are many ways to increase the solubility of new drugs in which solid dispersion are promising. Solid dispersions usually have two components - drug and polymer matrix. Number of methods are present to prepare the solid dispersions such as solvent evaporation method, melting method, spray

drying method, fusion method, kneading method, co-grinding method, hot melt extrusion, melt agglomeration, lyophilization technique, supercritical fluid (SCF) technology etc. Various hydrophilic carriers have been investigated to enhance the solubility and bioavailability properties of poorly water-soluble drugs.

Keywords: Solubility, Dissolution, Hydrophobic Drugs, Polymer, Carriers, Solid Dispersion

INTRODUCTION

Solubility is an important physical and chemical factor that affects the absorption and therapeutic effect of the drug. If the drug has poor water solubility, the formulation will fail. In aqueous G.I.T. fluid, the low dissolution rate and low solubility of drugs often result in inadequate bioavailability. Increasing the solubility and solubility of hydrophobic drugs is still one of the most difficult tasks in drug development. Different methods have been proposed to solve this problem **[1]**. The oral drug delivery is the most commonly used method of administration because it is easy to administer, easy to handle and cost-effective, thus ensuring good patient compliance **[2-3]**. Drug dissolution in intestinal fluid is a limiting step in determining bioavailability for Biologics Classification System (BCS) Class II drugs as they pass through the intestinal mucosa **[4]**. There are many commercial methods to improve the solubility and dissolution of poorly soluble substances, such as liqui-solid, where drug is in solution phase or over insoluble carriers dissolved drug is adsorbed **[5-7]**. Surfactants can also be used in preparing formulation to improve the wettability and solubility of various lipophilic substances **[8]**. Micronization of the drug is not ideal because the micronized product has a tendency to agglomerate, resulting in reduced surface area for good dissolution. However, solid dispersion is the best trustful method due to their ease of preparation, ease of processing, and repeatability **[9-10]**. The term "dispersion" is often used to describe many types of drugs in which the drug is dispersed within a bioinert matrix to improve oral bioavailability **[11]**.

Mechanisms that increase the solubility and dissolution rate of the drug include reducing the particle size of the drug to submicron size. Reducing particle size often increases dissolution power; transition from crystalline state to amorphous state, higher energy state easy to dissolve; and finally improve the wettability content of the drug molecule **[1]**. Despite these benefits, there are still some limitations in the use of solid dispersion in the pharmaceutical industry.

With the recent beginning of screening for potential treatments, the number of low soluble drugs has increased significantly, and for orally deliver the formulation of low soluble compounds currently, one of the most common and biggest challenge for scientist in the pharmaceutical industry. Only small quantities of solid dispersions are commercially available. This is due to poor physical properties for formulation manufacturing. Solid dispersions prepared using water-soluble carriers are soft, sticky lumps and difficult to handle. This is especially true when developing fillable capsules and manufacturing tablets. e.g. sieving, pulverization and mixing **[11]**.

APPLIED STRATEGIES FOR DISSOLUTION RATE ENHANCEMENT:

Accepted strategies to increase the solubility and dissolution rate of drugs are generally divided into physical and chemical modifications. **Figure 1** shows the media system and media modifications **[12-15]**.

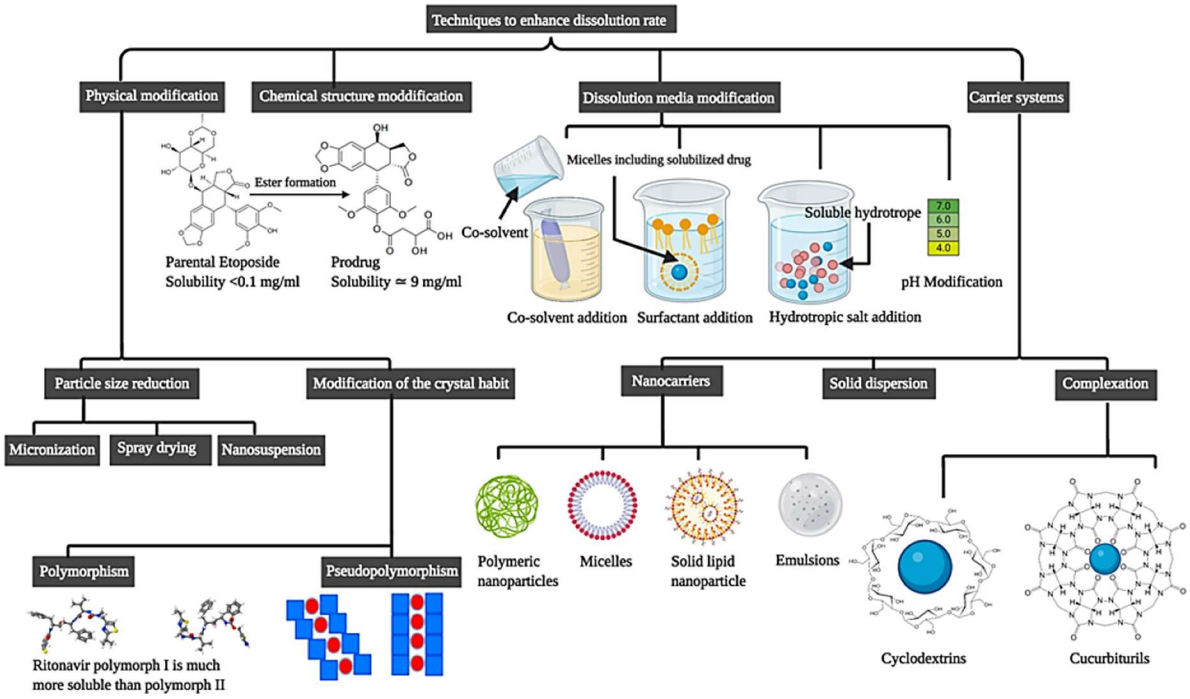

Figure 1: Enhancement strategies for drug solubility and dissolution rate [89]

Increasing dissolution using solid dispersion methods is one of the most direct and commonly used methods to improve the rate of drug absorption into systemic circulation. The term "solid dispersion" refers to the solid product (amorphous or crystalline) most commonly formed by incorporating a hydrophobic drug into a hydrophilic carrier

[16]. The drug is distributed to the selected polymer, creating six different dispersions depending on the molecular arrangement, which affects the properties of the prepared solid dispersion **[17]**.

ADVANTAGES AND DISADVANTAGES OF SOLID DISPERSIONS:

Solid dispersion has some advantages as well as some disadvantages which are mentioned in **Table 1 [13, 18-20]**.

Table 01: Advantages and Disadvantages of solid dispersion

Advantages of SD	Disadvantages of SD
• **Dissolution rate and bioavailability are improved by: Increased exposed surface area due to reduced particle size; converting the crystalline state to a more soluble amorphous state; increased wettability; Increased porosity.**	• **It is generally not used as a commercial product because the amorphous drug is converted to a less soluble crystalline form. This is because exposure to moisture during storage and the resulting increased mobility of the drug may cause phase separation and instability.**
• **The use of sugar carriers can mask the bitter taste of some drugs.**	• **Expensive preparation methods limit large-scale production.**
• **Formulated as a rapidly disintegrating tablet (FDT), it is easy to apply.**	• **Reproducibility cannot be guaranteed.**

Classification of SD based on recent developments:

- **First-generation solid dispersion**

In this type, a dispersed system is formed by incorporating the drug into a crystalline carrier such as urea and sugar to produce a slowly released thermodynamically stable crystalline SD **[21-23]**. Eutectic mixtures were the first SD formulas. Monolithic mixtures are undesirable because the melting points of the product and support do not change. In contrast, eutectic dispersions have a melting point that is lower than the melting points of the carrier and drug. This is preferred over monomixtures as the product and support crystallize immediately during the cooling phase of the eutectic mixture **[22, 24]** Reduced particle size increases specific surface area, increasing dissolution rate and bioavailability **[24]**.

- **Second generation solid dispersion**

This generation contains amorphous carriers and is thermodynamically stable compared to the first generation, such as polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) **[22, 25]**. Amorphous carriers can be synthetic or natural polymers. Depending on the physical state of the drug, amorphous solid dispersions (ASDs) can be classified as amorphous solid suspensions, solutions (free solutions), or mixtures of the two **[25, 26]**.

Amorphous solid suspensions consist of two different phases due to the limited solubility of the drug dispersed in the chosen medium **[27]**. In an amorphous solid solution, the

components are molecularly dispersed into one homogeneous phase **[28]**. During storage, the drug may recrystallize, forming fewer dissolved crystals. The use of highly viscous polymers can reduce the drug dissolution rate, but is often used to overcome recrystallization problems and provide more stable formulations suitable for production **[24]**.

- **Third generation solid dispersion**

In this generation, carriers are believed to have surface or emulsifying activity that promotes nucleation and aggregation of the drug **[13, 23]**. This function prevents recrystallization and simultaneously increases the dissolution rate and physicochemical stability of the drug **[29]**. Gelucire 44/14 and Solutol HS 15 are two examples of surfactants used to speed drug dissolution, while low glass transition temperature (Tg) polymers such as poloxamer (P188) can inhibit recrystallization **[29-31]**.

- **Fourth-generation solid dispersion**

Unlike ASD, fourth generation dispersions are controlled release solid dispersions (CRSD). Proposed carriers such as hydroxypropylcellulose (HPC) and Eudragit RS are used to support the release of drugs with short biological half-lives **[21, 32]**. Increasing solubility and controlled prolongation of drug release are the main goals of CSRD **[32]**.

CLASSIFICATION OF SOLID DISPERSION ACCORDING TO THE DRUG DISPERSION INTO THE CARRIER:

Solid dispersions are classified into six types depending on the crystalline state of the drug incorporated with the carrier, such as eutectic mixture, **[33]** solid solution, glass solution, **[34]** glass suspension, **[35]** amorphous precipitate of the drug in a crystalline carrier, complex or formation of a new compound **[36]**. Solid solution systems are generally divided into substitutional solid solutions and interstitial solid solutions, depending on the molecular size of the drug **[18]**.

MECHANISM OF DRUG INCORPORATION AND RELEASE FROM SOLID DISPERSION:

In theory, when a drug and a polymer come into close contact at the molecular level, the drug molecule inserts itself into the broken portion within the weakened polymer chain. Because heat is used to achieve this flexibility, whether through hot melt extrusion or melt methods, loosening the polymer chains is necessary to incorporate drug molecules **[24]**. Many methods, such as solvent evaporation and coprecipitation, are solvent-based. The solvent used serves two purposes. In addition to converting the drug into a molecular state, solvents also generate weak intermolecular

and intramolecular cohesive forces of polymer chain interactions, which further develops the interaction of polymers with various solvents **[16]**.

One effective strategy to improve dissolution is to convert the crystalline form of a poorly soluble drug to an amorphous state **[37, 38]**. Therefore, the drug release mechanism depends on the type of dispersive system containing different generations of ASDs and CRSDs.

- **Drug release from Amorphous Solid Dispersion**

Drug release from Amorphous Solid Dispersions is a process that can be divided into three groups according to the release rate of the drug carrier: vehicle-controlled release, drug-controlled release, and dissolution-controlled release **[34]**. In vehicle-controlled release, water penetrates the polymer, forming a viscous gel layer, and the drug is released slowly. In the case of controlled drug release, the amorphous drug is dissolved at a controlled rate after the polymer is initially dissolved in the dissolution medium.

- **Drug release from Controlled Release Solid Dispersion**

The release profile of the fourth-generation solid dispersions shows a controlled dissolution behaviour that is different from that of the first three generations. In this generation, Controlled Release Solid Dispersion releases the drug into the environment through diffusion and erosion mechanisms.

SOLID DISPERSION PREPARATION TECHNIQUES:

SD can be produced through a variety of approaches, including kneading, fusion, co-milling, solvent melting and solvent evaporation techniques. The advantages and limitations of these methods are summarized in **Table 2**.

1. **Kneading method**

   The carrier is ground together with the drug to form a dense paste using minimal amounts of organic solvents such as alcohol, acetone, or water. Then, the input amount of solvent is extracted in a vacuum oven, and the resulting lump is ground into a fine powder **[39, 40]**. The kneading method is cost-effective but suffers from heavy residue remaining **[41]**.

2. **Hot-Melt Methods (Fusion-Based Method)**

   In this process, a mixture of drug and hydrophilic carrier is directly heated until melted. The molten mixture is then rapidly cooled and solidified under vigorous stirring in an ice bath. The final solid mass is then crushed to reduce particle size for homogeneous inclusion in a suitable

dosage form **[42]**. The melting point of this binary system depends on the composition, choice of carrier, and mass fraction of drug in the system. For example, poloxamer (P188) has a low melting point and is a good candidate for melting methods **[43]**. Because the melting point of some carriers is higher than the decomposition temperature of the drug, the melting method is limited by the thermal stability and miscibility of the components **[44]**.

The fusion method can be easily applied in the laboratory using a conventional oven or microwave. Microwaves with frequencies of 0.3-300 GHz can be used to produce solid dispersions. These waves pass through the drug/carrier mixture and cause it to oscillate in response to external radiation, generating enough heat for fusion **[45]**. This method is cost-effective and generates heat quickly and evenly **[41]**.

The KinetiSol ® method was introduced into the pharmaceutical industry as an external heat-free fusion process. In this process, fusion relies on friction generated by high-speed rotating blades. The high shear forces of quenching are sufficient to melt the mixture without applying heat. Therefore, it is used for large-scale production of ASDs of thermolabile drugs **[45]**.

3. **Co-milling**

The co-milling method is the simplest process to prepare solid dispersions. The drug and carrier are mixed for several hours without solvent or heat until a homogeneous solid is obtained **[46]**. This process also reduces the drug's particle size and converts the substance into an amorphous form. It is assumed that at low temperatures an amorphous form of the drug is formed, whereas milling at temperatures above the Tg may lead to the formation of a crystalline form. However, the main drawback is the formation of heterogeneous mixtures with weak drug-polymer interactions and low physical stability **[47]**.

4. **Solvent Evaporation**

Solvent evaporation (SE) methods are available and widely used in both small laboratories and large plants. The basic procedure involves using a volatile solvent to dissolve the drug and carrier until a homogeneous mixture is obtained **[1]**. The introduced amount of solvent is then evaporated under various conditions (room temperature, heating or freezing) to obtain a solid dispersion. The choice of evaporation method depends on the

stability of each ingredient. Additionally, surfactant concentration is important because the evaporation process gradually forms a diffusion layer that can delay drug release. Additionally, the evaporation rate, type of solvent or co-solvent, and evaporation technique used can greatly affect the uniformity of yield. Hu *et al* reported that uniformity was much higher when using a rotary vacuum evaporator **[13, 48]**.

Table 2: Advantages and Limitations of Solid Dispersion Preparation Methods

Method	Carrier Drug	Limitations	Advantages
1. Kneading	**Poloxamer P188 and 407/Boswellic acid**	**• Heterogeneity. • Solvent residuals.**	**• A simple and economical method.**
2. Co-milling (comminution)	**α-Lactose / Budesonide**	**• Thermodynamic instability. • Alteration of the particle size distribution.**	**• A simple and economical method.**
3. Fusion		**• Require drug/carrier miscibility. • Thermolabile drugs.**	**• Solvent-free method.**
i. Simple fusion	**Urea/ Rofecoxib PEG 4000/Gliclazide**	**• Phase separation. • Scale-up.**	**• A simple and economical method.**
iii. Microwave induced fusion	**PEG 6000 / Atorvastatin**	**• Scale-up.**	**• A rapid, uniform heating Short heating time. • Cost-effective.**
ii. Hot-melt extrusion	**Soluplus®/ Telmisartan**	**• Processes at a high temp. • High input energy. • High shear force.**	**• Continuous process suitable for large scale. • Short heating time.**
iv. KinetiSol®	**Polyvinyl alcohol/ Ritonavir**	**N/A**	**• Processes at a lower temp. • Processing thermolabile drugs. • Semi-continuous with output 1000 kg/hr.**
4. Solvent evaporation		**• Presence of toxic solvent residuals and high risk of phase separation.**	**• No heating. • Suitable for thermolabile drugs.**
i. Simple solvent evaporation	**Phospholipid complex or TPGS 1000 or SiO_2 /Berberine**	**• High cost. • Phase separation may occur under slow evaporation condition.**	**• Simple. • Suitable for heat-labile ingredients.**
ii. Lyophilization	**Skimmed milk/ Simvastatin**	**• High cost.**	**• Homogeneity.**
iii. Spray drying	**Mannitol/Diazepam**	**• Require high solubility of the drug/carrier mixture in the organic solvents.**	**• Particle size control. • Fair powder flowability. • A rapid and economical method. • Scale-up.**
iv. Fluid-bed coating	**PEG 6000/resveratrol**	**• Tedious process**	**• Suitable for tableting and encapsulation • Higher drug loading • Scale-up**
v. Electrostatic spinning	**PVP VA64/ Itraconazole**	**• Scale-up**	**• High surface area for evaporation**

Because the SE method does not use heat or uses mild heating, it is mainly widely used to overcome the problem of instability of drugs under heat stress. SE can be exploited through scale-up methods with efficient throughput, such as spray drying **[49]**, freeze-drying, and high-speed electrospinning **[50]**. Hot plate agitation, rotary evaporation **[51]**, single needle electrospinning **[50]**, and laboratory spray drying are suitable small-scale methods. The high pressure used in spray drying causes evaporation by spraying the solution into the drying vessel through an adjustable diameter nozzle **[20, 52]**. Because the atomized particles are small and have a large area, they evaporate faster than traditional methods. The faster the drying process, the more homogeneous the product will be. This is because reproducible products can be obtained by avoiding the heterogeneity that occurs in traditional manufacturing methods. The atomization process also controls the particle size of the resulting dispersion. Particle size control helps improve powder flowability by creating particles in a size range that cannot stick together or form clumps **[53-56]**.

The electrostatic spinning process is achieved by electrostatically charging a polymer solution or melt stream under the influence of a strong electric field **[57]**. The electrical acceleration and large surface area provided by this method cause flash evaporation. Therefore, the product falls in the form of solid fibres **[58, 59]**. Several attempts have been made to combine electrospinning with other available techniques that involve introducing mechanical force **[60, 61]** or thermal energy **[62, 63]** into the traditional electrospinning process. In electrospinning, commutators come in many types, including the traditional solid commutator types as well as various types of radial commutators, which can be rotating mandrels, rotating wire drums, or rotating disks **[64, 65]**.

In this method, the applied electric field strength, temperature, and flow rate are important factors that control the size and shape of the product **[66, 67]**. The electrospinning process is dependent on polymer concentration because it increases the amount of polymer in the precursor solution. It begins to form uniform fibres. In the case of a low-concentration solution, fine powder is electro sprayed to form the product. As the concentration increases, beads are formed in the fiber structure and begin to precipitate, ultimately forming fibers containing a high-concentration precursor **[66, 68]**.

The freeze-drying method does not involve immersing the drug in a freezing environment

and heating it. Typically, applying negative pressure to a water-containing solution initiates the subsequent sublimation process **[69]**. The freeze-drying process can be used using spray freeze-drying **[70]** or ultra-fast freezing **[71, 72]**. Maintaining the temperature of the components below their Tg during freeze-drying rate and sublimation plays an important role in controlling phase separation **[13]**. Therefore, the choice of lyophilization method is important to prepare stable SD preparations.

Fluidized bed coating has recently been introduced as an effective method for loading mixtures of drugs and carriers into inert granules that are evaporated by air flow **[73, 74]**. This method can be used industrially due to its easy flow during encapsulation and tableting **[75]**.

CARRIERS

1. **Polyethylene glycol (PEG)**

   Polyethylene glycol (PEG) is an ethylene oxide polymer with a molecular weight (MW) typically in the 200-300,000 range. PEG with a molecular weight of 1,500 to 20,000 is generally used to prepare solid dispersions and solutions, and as the molecular weight increases, the viscosity of PEG also increases. At molecular weights up to 600, PEG is liquid, between 800 and 1500 it has a consistency best described as vaseline, between 2000 and 6000 it has a waxy texture, and at molecular weights above 20,000 it forms hard, brittle crystals at room temperature. do. Solubility in water is generally good but decreases with increasing molecular weight. The biggest advantage of PEG over solid dispersions is that it is highly soluble in many organic solvents. In each case, the melting point of the PEG of interest is below 65°C (e.g., PEG 1000 has a melting point of 30 -40°C, PEG 4000 has a melting point of 50–58°C, and PEG 20000 has a melting point of 60°C -63°C) **[76]**. Additional attractive features of PEG include its ability to solubilize certain compounds **[77]** and its ability to improve the wettability of compounds. Even for drugs with relatively high solubility, such as aspirin, the dissolution rate can be improved if formulated as a solid dispersion in PEG 6000 **[78]**.

Problems with PEGs

Overall, there are few toxicity issues associated with PEG and it is approved for a variety of purposes as an excipient. However, low molecular weight PEGs tend to be slightly more toxic than higher molecular weight PEGs **[76]**. Additionally, numerous medications have been linked to PEG. There

have been virtually no cases of PEG stability issues during hot melt production.

2. **Polyvinylpyrrolidone (PVP)**

Polymerization of vinylpyrrolidone produces polyvinylpyrrolidone (PVP) with a molecular weight of 2,500 to 3,000,000. This can be categorized by the K value, which is calculated using the Fickentscher equation **[79]**. The temperature of a particular PVP depends on its molecular weight as well as its moisture content. Generally, the glass transition temperature (Tg) is high. For example, PVP K25 has a Tg of 155°C **[80]**. For this reason, PVP is of limited use in the preparation of solid dispersions by the hot melt method. Because it has excellent solubility in many organic solvents, it is most suitable for preparing solid dispersions by the solvent method. fufenamic acid **[81]** has been shown to enhance the dissolution rate of solid dispersions in PVP due to improved wettability. As chain length increases, the solubility of PVP in water becomes even lower, and another disadvantage of high molecular weight PVP is that its viscosity is much higher at a given concentration **[79]**. Similarly, the slower dissolution of indomethacin observed in PVP K90 compared to PVP K12 is due to the higher viscosity generated by PVP K90 in the diffusion boundary layer adjacent to the dissolution surface of the dispersion **[82]**.

3. **Cellulose Derivatives**

1. ***Hydroxypropyl methylcellulose (HMPC):***

HPMC is a mixed cellulose ester in which 16.5–30% of the hydroxyl groups are methylated and 4–32% are derivatized with hydroxypropyl groups. For example, type 2910 has an average methoxy content of 29% and a hydroxypropyl content of 10%. HPMC has a molecular weight of approximately 10,000 to 1,500,000 and is soluble in water and ethanol-dichloromethane and methanol-dichloromethane mixtures **[82]**. Other drugs that exhibit faster release from solid dispersions of HPMC include nilvadipine **[82]** and benidipine **[83]**, which are poorly soluble weak acids.

2. ***Hydroxypropylcellulose (HPC):***

Hydroxypropylcellulose (HPC) exhibits excellent solubility in a variety of solvents, including water (up to 40°C), ethanol, methanol and chloroform. Average HPC MW ranges from 37,000 (SSL type) to 1,150,000 (H type) **[84]**. an extensive study on the effect of chain length and

HPC ratio in solid dispersion on the release behaviour of flurbiprofen conducted [85]. As the HPC ratio increased, and when low molecular weight HPC was used as the carrier, the release rate also increased.

3. ***Carboxymethylethylcellulose (CMEC)***

Carboxymethylethylcellulose is also a cellulose ether, but unlike many others, it is difficult to dissolve in gastric (acidic) conditions. Easily soluble at pH values above 5-6, it has the lowest dissolution pH depending on the grade of carboxymethyl ethyl cellulose.

Carboxymethylethylcellulose is also readily soluble in acetone, 70% isopropanol, 60% ethanol, and a 1:1 mixture of dichloromethane and ethanol. Amorphous solid dispersions of nifedipine and spironolactone showed a significant increase in drug dissolution rate at pH value 6.8 **[84]**.

4. ***Hydroxypropylmethylcellulose phthalate (HPMCP)***

HPMCP is a cellulose ester often used as an enteric coating. Depending on the grade, it first dissolves at pH 5 (HP 50) or pH 5.5 (HP 55). Solubility in organic solvents varies depending on the type. MW ranges from 20,000 to 2,000,000 **[81]**, and integration into HPMCP co-evaporator can significantly increase the dissolution rate of griseofulvin at pH 6.8 **[82]**.

4. **Polyacrylates and polymethacrylates**

Polyacrylates and polymethacrylates are glassy substances obtained by polymerizing acrylic acid and methacrylic acid, as well as derivatives of polymers such as esters, amides, and nitriles. In pharmaceuticals, they are primarily used as coatings to modify the release of drugs from dosage forms. They are commonly called by the brand name Eudragit drugs. Among Eudragit, Eudragit E is frequently used to improve release rate as it is soluble in buffers up to pH 5 and swells at higher pH values, while Eudragit L can be used when gastric release is desired to be avoided. When benipidine was evaporated with Eudragit E, the dissolution rate was much higher than that of pure drug powder **[86, 87]**. On the other hand, Eudragit L was successfully used to increase the dissolution of griseofulvin and spironolactone at pH 6.8 **[84]**.

5. **Urea**

Urea is the end product of human protein metabolism, has a mild diuretic effect and is considered non-toxic. Its solubility in water is greater than 1 and it is also soluble

in some common organic solvents. One of the first studies on the bioavailability of solid dispersions showed that sulphathiazole was better absorbed in rabbits when administered as a eutectic with urea **[84]**.

For ursodeoxycholic acid, the release rate of the hot melt urea dispersion was higher than that of other carriers tested, including PEG 6000. The use of urea also doubled the rate of phenytoin dissolution. However, in this case PEG 6000 was much more effective **[83]**.

6. **Sugar, polyols and their polymers**

Although sugars and related compounds are highly soluble in water and pose few toxicity problems, they are less suitable than other carriers for the production of solid dispersions. Most sugars have high melting points, which poses a problem in making hot melts, and their low solubility in most organic solvents makes it difficult to obtain co-evaporated products. Despite these shortcomings, several attempts to produce solid dispersions using sugars and their derivatives have been reported. Mannitol, which has a melting point of 165-168 ℃ and decomposes only at temperatures above 250 ℃, can in some cases be used to prepare dispersions using the hot melt method **[88]**.

7. **Organic acids and their derivatives**

Organic acids such as succinic acid and citric acid were also initially used as carriers in solid dispersions to increase the release rate of the griseofulvin method **[89]**.

CHARACTERIZATION OF SOLID DISPERSIONS

Methods for Characterizing Solid Dispersions

- Dissolution testing.
- X-Ray diffraction (XRD) and Differential scanning calorimetry (DSC).
- Microscopic methods including polarization microscopy and scanning electron microscopy.
- Spectroscopic methods, e.g. IR spectroscopy.
- Thermoanalytical methods: differential thermo-analysis and hot stage microscopy.

CONCLUSION:

Knowledge of solid dispersions over the past decades indicates that this is a very profitable approach to improve the release rate and oral bioavailability of hydrophobic drugs. Two trends are significantly increasing the role of solid dispersions in drug development. One is the increase in poorly soluble drug candidates and the significant improvements in solid dispersion manufacturing technology that

have occurred over the past few years. Another advantage of solid dispersions over other approaches is that many of the possible carriers are already widely used as excipients in the pharmaceutical industry and no toxicity studies are required. Solid dispersions are one of the most attractive methods to improve the water solubility of drugs. Various solubility enhancers such as water-soluble carriers, co-solvents, surfactants, and super disintegrants manufactured through solid dispersion methods (melting method, solvent evaporation method) help improve solubility. This greatly helps improve bioavailability and bioequivalence.

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