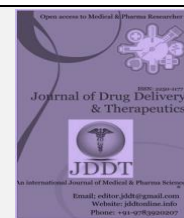
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Review Article

## Solid Dispersion: Solubility Enhancement Technique of Poorly Water Soluble Drug

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### ABSTRACT

Solid dispersion is a technique which is widely and successfully applied to improve the solubility, dissolution rates and consequently the bioavailability of poorly soluble drugs. Dispersion of one or more active ingredients (hydrophobic) is done with an inert carrier (hydrophilic) at solid-state prepared by fusion method, solvent, and melting solvent method. In this review article, we have focused on the methods of preparation, advantages, disadvantages and characterization of the solid dispersions.

**Keywords:** Solid dispersion; dissolution; solubility.

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### INTRODUCTION:

Solid dispersion is defined as a group of solid products which should contain at least two different components, like a hydrophilic matrix and a hydrophobic drug. Hydrophilic matrix can be crystalline or amorphous. The first drug whose rate and extent of absorption was significantly enhanced using solid dispersion was sulfathiazole in which eutectic mixture of sulfathiazole with urea as the inert carrier was formed. Lyophilization is a molecular mixing technique where the drug and carrier were co-dissolved in cyclohexanol, frozen and then sublimed under vacuum to obtain a lyophilized molecular dispersion [1].

Solubility is not to be confused with the ability to dissolve or liquefy a substance, since these processes may occur not only because of a chemical reaction. Solubility does not depend on particle size or other kinetic factors; given enough time, even large particles will eventually dissolve [2, 3].

Several factors such as complicated preparation method, low reproducibility of physicochemical properties, difficulty of formulation development and scale-up and physical instability for solid dispersion make it difficult to apply the systems to solid dispersion dosage forms. Especially in order to maintain a supersaturation level of drug for an extended time, re-crystallization of drug must be prevented during its release from dosage form<sup>4</sup>.

After administration of a drug orally, it firstly dissolves in gastric media and then permeates the membranes of GI tract to reach into the blood. Therefore, a drug with poor aqueous solubility will exhibit dissolution rate limited absorption. 35-40% of newer drugs suffer from poor aqueous solubility<sup>5,6</sup>.

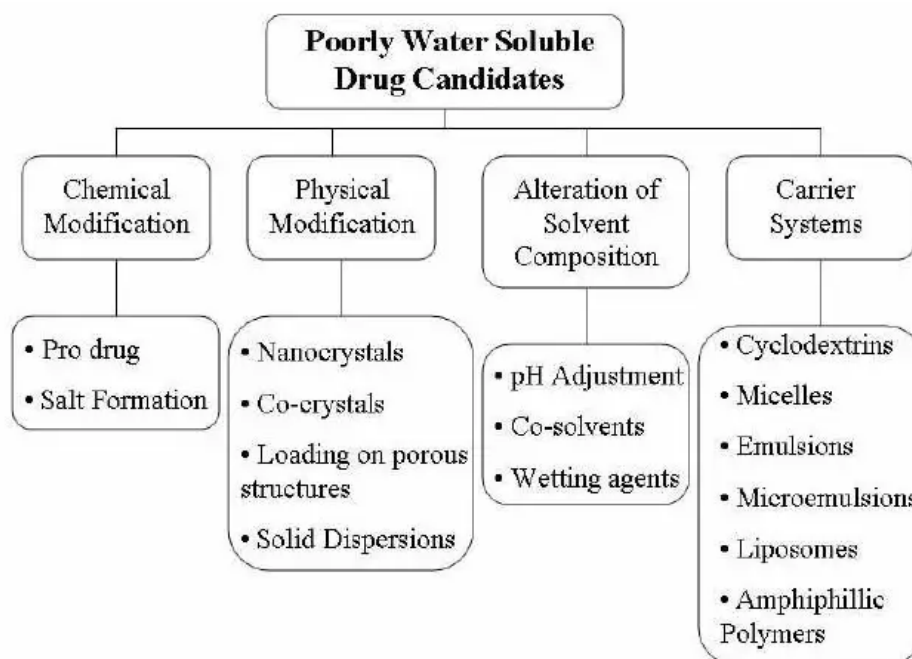


Figure 1. Approaches to Increase solubility/ Dissolution

#### ADVANTAGES OF SOLID DISPERSION

1. Improving drug bioavailability by changing water solubility which is possible only by solid dispersion<sup>7</sup>.
2. Increase in dissolution rate & extent of absorption and reduction in Pre systemic metabolism.
3. Transformation of liquid form to solid form.
4. It is more efficient than particle size reduction technique<sup>[8]</sup>.

#### DISADVANTAGES OF SOLID DISPERSION

1. Major disadvantage is their instability. They show changes in crystallinity and a decrease in dissolution rate with ageing.
2. Temperature and moisture have more deteriorating effect on solid dispersions than on physical mixtures.
3. Difficulty in handling because of tackiness<sup>[9,10]</sup>.

#### METHODS OF PREPARATION OF SOLID DISPERSIONS:

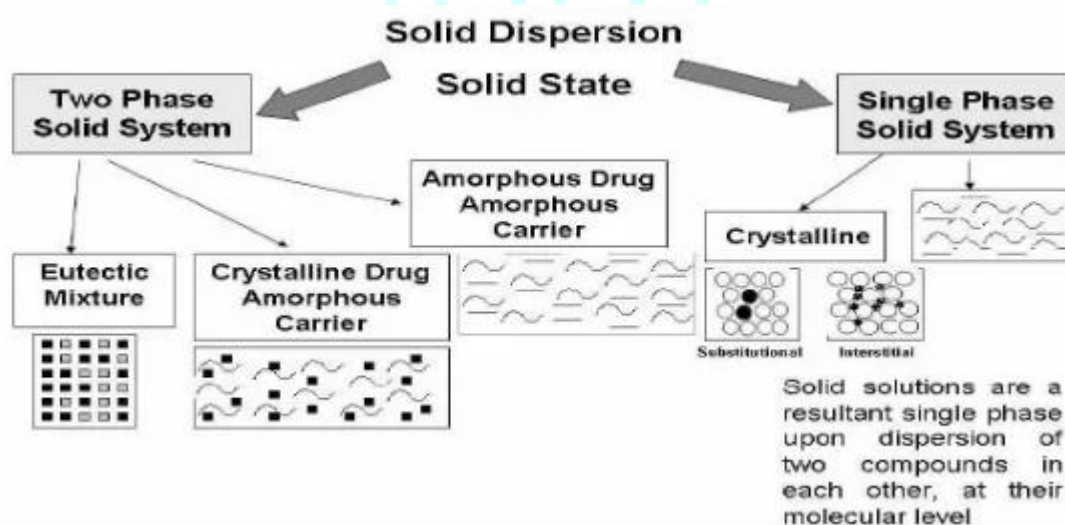


Figure 2. Solid State Solid Dispersions

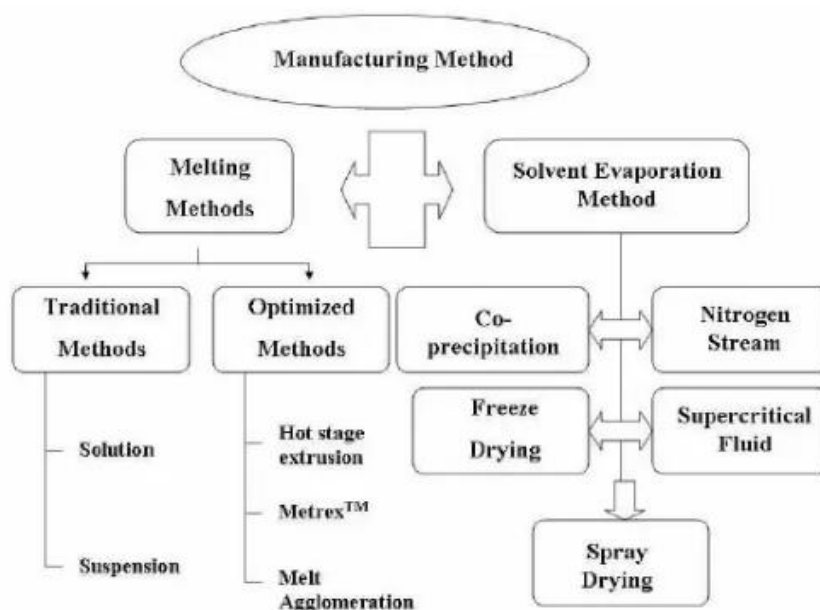


Figure 3. Methods of preparation of Solid Dispersion

Various methods used for preparation of solid dispersion system. These methods are given below.

**1. Melting solvent method:** This method is prepared by physical mixture of a drug and a water soluble carrier and heating it directly until it is melted. Final solid mass is crushed and sieved and then it passed with other modification procedures [11,12].

**2. Solvent evaporation method:** In this type of method dissolve the drug and polymeric carrier in a common solvent, such as ethanol, chloroform, mixture of ethanol and dichloromethane, resulting films are pulverized and milled [13-17].

**3. Hot melt extrusion method:** In this method extruder is utilized for intense mixing of components. Physical mixture of both the drug and carrier is introduced into the hopper then passed through screw and finally it is extruded from the die [18].

**4. Melt agglomeration Process:** This technique has been used to prepare solid dispersion wherein the binder acts as a carrier. Solid dispersion are prepared by heating binder, drug & excipient to a temperature above the melting point of the binder or by spraying a dispersion of drug in molten binder on the heated excipient by using shear mixer [19-21].

**5. Lyophilization:** it is a phenomenon of transfer of heat and mass from and to the product. It's an alternative method to solvent evaporation in which molecular mixture technique is used [22].

#### EVALUATION PARAMETERS OF SOLID DISPERSION:

Various methods to evaluate the solid dispersion are as follows:

Drug -carrier miscibility

- Hot stage microscopy

- Differential scanning calorimetry – Helps to determine that the treated drug melting is similar to the original form of the drug.

- Powder X-ray diffraction – The intensity peaks shows the crystal lattice of the treated drug. Low and high intensity peaks are evaluated for the crystallization index.

- Spectroscopic methods like Raman spectroscopy, FT-IR spectroscopy – the functional groups of the treated drug produces similar peaks as that of the original drug form which helps to determine that the no changes in the functional structure of the drug moiety<sup>22</sup>.

#### Physical Structure

- **Scanning electron microscopy** – SEM shows the surface morphology of the drug particles and to evaluate them with the treated drug<sup>23</sup>.

- **Surface area analysis** – The surface area is directly proportional to the solubility of the drug.

- Dynamic vapour sorption

- Inverse gas chromatograph

- Atomic force microscopy

- Raman microscopy

#### Amorphous content

- Polarised light optical microscopy

- Hot stage microscopy

- Humidity stage microscopy

- DSC (MTDSC)

- Powder X-ray diffraction<sup>24</sup>

#### Stability

- Humidity studies

- Isothermal Calorimetry

- DSC (TG, Temperature recrystallization)

- Saturated solubility studies

#### Dissolution enhancement

- Dissolution

- Intrinsic dissolution
- Dynamic solubility
- Dissolution in bio-relevant media<sup>25</sup>

### Applications of solid Dispersion:

The solid dispersion technique may have numerous pharmaceutical applications, which are:

1. To stabilize unstable drugs and protect against decomposition by processes such as hydrolysis, oxidation, racemization, photo oxidation etc<sup>26</sup>.
2. To reduce side effects of certain drugs:- A third factor that **affects** the **rate of dissolving** is the **size** of solute **particles**. For a given amount of solute, smaller **particles** have greater surface area. With greater surface area, there can be more contact between **particles** of solute and solvent<sup>27</sup>.
3. Masking of unpleasant taste and smell of drugs:- Taste masking has always been the integral part of formulation especially for pediatric formulations. During almost last three decades advanced novel formulation techniques have been utilized to improve the aesthetics of the final products.
4. To avoid undesirable incompatibility.
5. To obtain a homogeneous distribution of a small amount of drug in solid state :- Solubility is the property of a solid, liquid, or gaseous chemical substance called *solute* to dissolve in a solid, liquid, or gaseous solvent to form a homogeneous solution of the solute in the solvent. The solubility of a substance fundamentally depends on the solvent used as well as on temperature and pressure.
6. To dispense liquid or gaseous compounds<sup>28</sup>.
7. To formulate a fast release priming dose in a sustained release dosage form.
8. To formulate sustained release preparation of soluble drugs by dispersing the drug in poorly soluble or insolub to formulate sustained release preparation of soluble drugs by dispersing the drug in poorly soluble or insoluble carrier<sup>29</sup>.
9. To enhance the absorption of drug.
10. To reduce side effects:-
  - (A). The binding ability of drugs for example to the erythrocyte membrane is decreased by making its inclusion complex.
  - (B). The damage to the stomach mucous membranes by certain non-steroidal anti-inflammatory drugs can be reduced by administration as an inclusion compound<sup>30</sup>.

### Challenging future for Solid Dispersion Technique:

- A. Inability to scale bench top formulations to manufacturing sized batches,
- B. Difficulty to control physiochemical properties ,
- C. Difficulty in delivering solid dispersion formulations as tablet or capsule dosage forms and
- D. Physical and chemical instability of the drug and/or the formulation [31].

### Commercial Solid Dispersion Products:

List of products available in the market [6]

Brand name	Manufacturer	Drug	Carrier
Gris-PEG	Pedinol Pharmacal Inc.	Griseofulvin	PEG6000
Cesamet	Valeant Pharmaceuticals	Nabilone	PVP
Kaletra	Abbott	Lopinavir, ritonavir	PVPVA
Sporanox	Janssen Pharmaceutica	Itraconazole	HPMC
Intelence	Tibotec	Etravirin	HPMC
Certican	Novartis	Everolimus	HPMC
Isoptin SR-E	Abbott	Verapamil	HPC/HPMC
Nivadil	Fujisawa Pharmaceutical Co., Ltd	Nivaldipine	HPMC
Prograf	Fujisawa Pharmaceutical Co., Ltd	Tacrolimus	HPMC
Rezulin	Developed by Sankyo, manufactured by Parke-Davis division of Warner-Lambert	Troglitazone	PVP

## CONCLUSION

Increasing the Bioavailability of a poorly soluble drug is a challenging aspect of drug development. On the basis of back literature we have concluding solid dispersion is the promisable technique increment of solubility and bioavailability of water insoluble (BCS Class II). Because of the poor aqueous solubility the drug possesses dissolution problems due to which the in vivo absorption of the drug is reduced and thus the bioavailability is reduced, making the drug inappropriate for oral consumption and therefore solubility enhancement become necessary for such drug candidate. Solid dispersion is a most simple and efficient technique for increasing the aqueous solubility of a drug. Solid dispersion systems have been realized as extremely useful tool in improving the dissolution properties of poorly water-soluble drugs based on the observed entrapment

rates and pesticide loadings, the processes for preparing the solid dispersions were optimized.

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