

REVIEW ON “SOLID DISPERSION - NOVEL APPROACH FOR ENHANCEMENT OF SOLUBILITY OF POORLY SOLUBLE DRUGS”

Himani Jaisinghani*

College of Pharmacy, IPS Academy, Rajendra Nagar, A.B. Road, Indore, Madhya Pradesh- 452012.

*Corresponding Author: Himani Jaisinghani

College of Pharmacy, IPS Academy, Rajendra Nagar, A.B. Road, Indore, Madhya Pradesh- 452012.

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ABSTRACT

Improving oral bioavailability of medicine those given as solid dosage forms remains a challenge for the formulation of scientists because of solubility problems. The dissolution rate can be the rate-limiting process within the absorption of a drug from a solid dosage sort of relatively insoluble drug. Therefore, a rise in the dissolution of poorly soluble drugs by a solid dispersion technique presents a challenge to formulation scientists. Solid dispersion methods have pulled in significant enthusiasm for improving the dissolution rate of exceptionally lipophilic drugs, along these lines improving their ease of use by decreasing drug molecule size improving wettability, and forming amorphous particles. The term solid dispersion is handling a gaggle of solid products which is consisting of a minimum of two different components, generally a hydrophilic inert carrier or matrix and a hydrophobic drug. The historical background of solid dispersion technology, has limitations, classification, and various preparation techniques with its advantages and drawbacks. This review also discusses the recent advances within the field of solid dispersion technology. Supported the prevailing results and authors' reflection, this review gives rise to reasoning and suggested choices of carrier or matrix and solid dispersion procedure.

KEYWORDS: Solubility, BCS Classification, Solid dispersion, Carrier, Solvent, Methods of Preparation, Characterization, Applications.

1. INTRODUCTION

Solubility is defined in quantitative terms because of the concentration of the solute during a saturated solution at a particular temperature and in qualitative terms, it should be defined because of the spontaneous interaction of two or more substances to make a homogeneous molecular dispersion. A saturated solution is one during which the solute is in equilibrium with the solvent. The solubility of a drug could also be expressed as parts, percentage, molarity, molality, volume fraction, and mole fraction. Drug solubility is that the maximum concentration of the drug solute dissolved within the solvent under the specific condition of temperature, pH, and pressure. The drug solubility in saturated solution could be a static property where because the drug dissolution rate could be a dynamic property that relates more closely to the bioavailability rate.^[1]

Potential Causes For Poor Oral Absorption

Any drug is supposed to be inadequately dissolvable when.

1. Aqueous solubility <100µg/ml.
2. Poor dissolution: Intrinsic dissolution rate <0.1 mg/cm²/min.
3. High molecular weight: (>500), Self-association and

aggregation.

4. High crystal energy.^[2]

Process of Solubilization

Step 1 The process of solubilization involves the breaking of inter- ionic or intermolecular bonds in the solute, the separation of the molecules of the solvent to provide space in the solvent for the solute, the interaction between the solvent and the solute molecule or ion.

Step 2 Molecule of the solid breaks away from the bulk.

Step 3 The feed of the solid molecule is integrated into the hole in the Solvent.^[3]

Biopharmaceutical Classification System (BCS)

The BCS is that the scientific framework for classifying drugs substances supported their aqueous solubility and intestinal permeability. it's a drug development tool that enables estimation of the contributions of three major factors, dissolution, solubility, and intestinal permeability that affect the oral absorption of the medication. BCS Class II and IV drugs, which have low solubility, provide several challenges for formulation scientists performing on the oral delivery of medication.^[4]

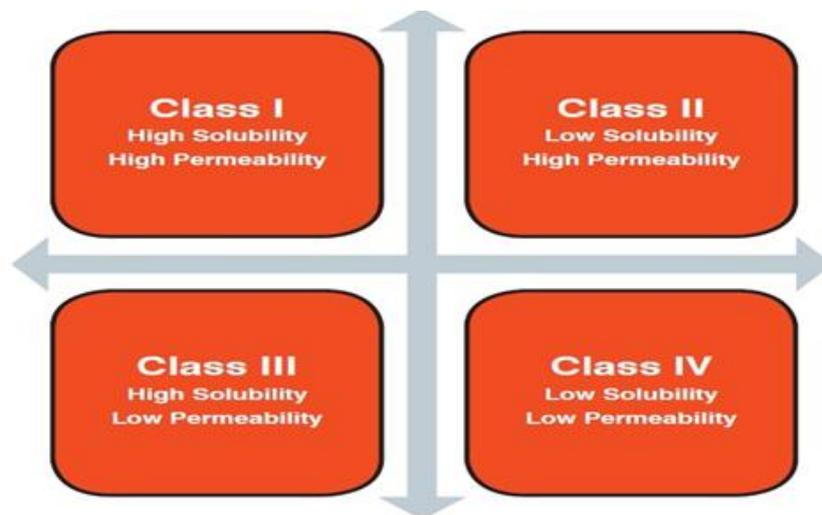


Fig. No.01 Biopharmaceutical Classification System^[4]

2. SOLID DISPERSION

Solid dispersions are one of the foremost successful strategies to enhance the drug release of poorly soluble drugs. Sekiguchi and Obi were the primary ones to explain solid dispersions in 1961. Solid dispersion is one of the important strategies to tackle dissolution- rate-limited oral absorption of poorly soluble compounds. Formulation of poorly soluble compounds as solid dispersions might cause particle size reduction, improved wetting, reduced agglomeration, changeability within

the physical state of the drug molecules, and possibly a disperse at the molecular level, in step with the physical state of the solid dispersion. The term solid dispersion refers to a bunch of solid products consisting of a minimum of two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix will be either crystalline or amorphous. The drugs will be dispersed molecularly either in amorphous particles (clusters) or in crystalline particles.^[7]

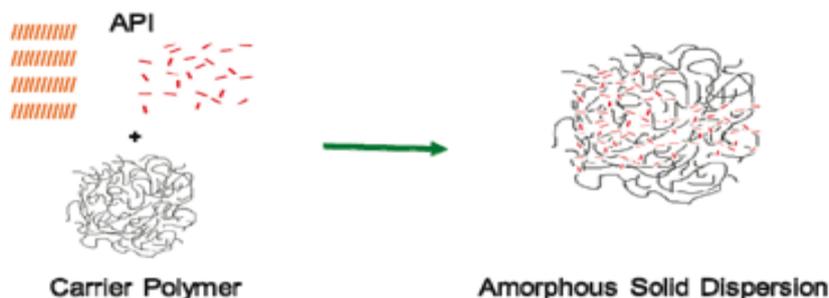


Fig. No. 2: Solid Dispersion.^[7]

Classification of Solid Dispersions

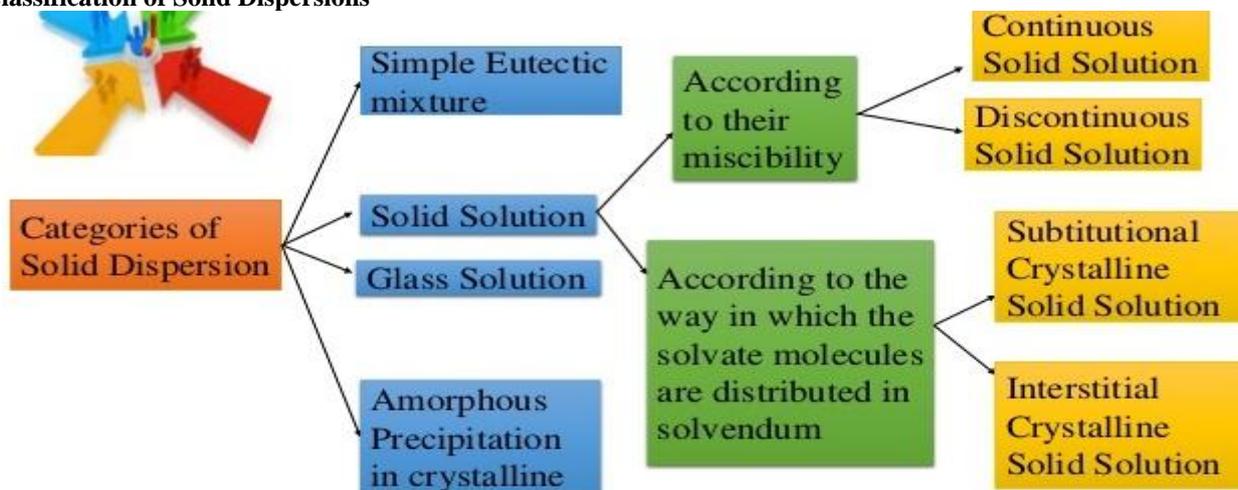


Fig. No. 3: Classification of Solid Dispersion.^[8]

Advantage of Solid Dispersion

- To improve wettability.
- To improve the porosity of drugs.
- To decrease the crystalline structure of drugs into an amorphous form.
- To mask the taste of the drug substance.
- To prepare rapid disintegration oral tablets.

Disadvantages of Solid Dispersion

- Moisture & temperature have a most deteriorating effect on solid dispersion than a physical mixture.
- Sometimes difficult to handle due to tackiness.
- Reproducibility of its physicochemical properties.
- Its formulation into dosage forms.^[9]

Selection of Carrier

- A carrier should possess the subsequent characteristics to be suitable for increasing the speed of dissolution of a drug.
- The carrier should be freely soluble in water with a high rate of dissolution.
- It should be non-toxic.
- It should be pharmacologically inert.
- Should possess heat stability with a low temperature.
- It should be able to enhance the aqueous solubility of the drug.
- It should possess chemical compatibility with the drug, and may not form strongly bonded complexes with the drug, it should be economic.^[10]

1. First Generation Carriers

Example: Crystalline carriers: Urea, Sugars, Organic acids.

2. Second Generation Carriers

Example: Fully synthetic polymers include povidone (PVP), polyethyleneglycols (PEG), and polymethacrylates. Natural product-based polymers are mainly composed of cellulose derivatives, like hydroxypropylmethylcellulose (HPMC), ethylcellulose or hydroxypropyl cellulose, or starch derivatives, like cyclodextrins.

3. Third Generation Carriers

Example: Surface active self-emulsifying carriers: Poloxamer 408, Tween 80, and Gelucire 44/141.^[11]

Selection of Solvents

Solvent to be included in the formulation of solid dispersion should have the following criteria:

- Both drug and carrier must be dissolved.
- Toxic solvents to be avoided due to the risk of residual levels after preparation e.g. chloroform and dichloromethane
- Ethanol can be used as an alternative as it is less toxic.
- Water-based systems are preferred.
- Surfactants are used to create carrier drug solutions,

but as they can reduce glass transition temperature, so care must be taken into consideration.^[12]

METHOD OF PREPARATION OF SOLID DISPERSION^[13]**1. Melting Or Fusion Method**

A physical mixture of a vigorous agent and a water-soluble carrier is heated until it's melted. The melt is solidified rapidly in an ice bath under vigorous stirring, pulverizing then sieving.

The melting method is straightforward and economical because the solvent isn't utilized in this method. But this method might not be suitable if the drug or the carrier is unstable at the fusion temperature or evaporate at extreme temperature.^[14]

2. Melting Solvent Method

During this method, the drug is first dissolved in a very suitable liquid solvent, then the drug is incorporated into the melt of the carrier without removing the liquid solvent.^[15]

3. Solvent Evaporation method

The solvent evaporation method consists of the solubilization of the drug and carrier in a very volatile solvent that's later evaporated. In this method, the thermal decomposition of medication or carriers is often prevented, since organic solvent evaporation occurs at low temperatures. A basic process of preparing solid dispersions of this kind consists of dissolving the drug and their polymeric carriers in a very common solvent, like ethanol, chloroform mixture of ethanol, and dichloromethane. Normally, the resulting films are pulverized and milled.

4. Lyophilization Techniques

Lyophilization has been thought of as a molecular mixing technique. The drug and carrier are co dissolved during a common solvent, Frozen, and sublimed to get a lyophilized molecular dispersion.^[16]

5. Kneading Method

A mixture of the drug and polymer was wetted with water and kneaded thoroughly for a half-hour during a glass mortar. The paste formed is then dried under a vacuum for twenty-four h. The dried powder is saw sieve no. 60 and stored during desiccators until further evaluation.^[17]

6. Co-Grinding Method

A physical mixture of drug and carrier is mixed a few times employing a blender at a selected speed. The powder mixture is pulverized. The blend is then charged into the office of a vibration ball factory steel balls are included. The powder blend is pummeled. Then the sample is collected and kept at temperature during a screw-capped glass vial until use. Ex. chlordiazepoxide solid dispersion was prepared by this method.^[18]

7. Spray Drying Method

The drug is dissolved during a suitable solvent and also the required amount of carrier is dissolved in water. Solutions are then mixed by sonication or another suitable method to provide a transparent solution, which is evaporated under a vacuum. Solid dispersions are reduced in size by mortar and sieved.^[19]

Characterization Of Solid Dispersions.^[20]

- Thermo-Gravimetric Analysis
- Hot Stage Polarized Light Microscopy
- Differential Scanning Calorimetry
- Dissolution Studies
- Wide Angle X-Ray Diffractometry
- Fourier Transformation-Infrared Spectroscopy
- Scanning Electron Microscopy
- High-Performance Liquid Chromatography.

Applications of Solid Dispersion in Pharmaceutical Field

Aside from absorption improvement, the solid dispersion method may have various pharmaceutical applications, which ought to be additionally investigated. Such a procedure might be utilized.

- To obtain a homogeneous distribution of a small amount of drug in a solid-state.
- To stabilize the unstable drug
- To dispense liquid (up to 10%) or vaporous mixes in a solid dosage.
- To plan a quick-release primary dose in a sustained release dosage form.
- To plan continued a sustained release regimen of soluble drugs by utilizing ineffectively dissolvable or insoluble carriers.
- To reduce pre systemic inactivation of drugs like morphine and progesterone.^[21,22]

CONCLUSION

The enhancement of oral bioavailability of poorly water-soluble drugs remains one of the foremost challenging aspects of drug development. The dissolution of a drug is that the speed determining step for oral absorption of medication, which could subsequently affect the in vivo absorption of the drug. Due to the solubility problem of the various drugs, the bioavailability of these gets affected and hence solubility enhancement becomes necessary. Solid dispersions are one of the foremost attractive processes to boost a drug's poor water solubility. Different solubility enhancers like water-solvent transporters, co-solvents, surfactants, and super disintegrants through solid dispersion approach (fusion technique and solvent evaporation method) help insolubility upgrade. These significantly help to boost bioavailability and bioequivalence.

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