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# Solid Dispersion tool to increases the Solubility of Scancy Water Soluble Drug

**Tikesh Agrawal*, Upadesh Lade, Santosh N. Gotefode**

Chhatrapati Shivaji College of Pharmacy, Deori, Gondia, Maharashtra - 441901, India.

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**ABSTRACT:** Oral administration of drug prerequisites need good water solubility. Whereas for better membrane permeation the drug should be lipid soluble. A drug to elicit effective therapeutic activity, its bioavailability must be good, which depends on the aqueous solubility of the drug. For improving the oral solubility as well as bioavailability, the solid dispersion is a great method for the hydrophobic drug. Dissolution rate can be the rate-limiting process in the absorption of a drug from a solid dosage form of relatively unsolvable drugs by increasing the wettability and forming amorphous particles. The term solid dispersion is a concept of kneading method in that the drug is kneaded with a group of solid products which consists of at least two different components, generally a hydrophilic inert carrier and a hydrophobic drug. The water soluble carriers that are used in solid dispersion technology are β-cyclodextrin, methyl cellulose, urea, lactose, citric acid, polyvinyl pyrrolidone and polyethylene glycols. The Purpose review focused on the historical background, techniques of solid dispersion, classifications, with its advantages, disadvantages, applications and marketed preparation.

**Corresponding author***
Mr. Tikesh Agrawal
Associate professor,
Chhatrapati Shivaji College of Pharmacy,
Deori, Maharashtra - 441901, India.
Tel: +91-7972554829
Mail ID: tikeshagrawal150@gmail.com

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## INTRODUCTION:

The solubility of drug is the most common and selected method for drug delivery due to in-convenience and ease of ingestion. Around 90 % drugs are administered orally. The sufficient absorption of drug and reproducible bioavailability, pharmacokinetic profile of orally administered drug substances is highly dependent on solubility of that compound in aqueous medium [1]. Poorly water-soluble drugs involve many difficulties in the development of pharmaceutical dosage forms for oral delivery systems due to their low bio-availability [2]. Drug absorption from the gastrointestinal tract can be limited by a variety of factors, out of which, the most

significant contributors being poor aqueous solubility and poor membrane permeability of the drug molecule. When delivering an active agent orally it must first dissolve in gastric and/or intestinal fluids before it can permeate the membranes of the GI tract to reach systemic circulation. Hence, two areas of pharmaceutical research that focus on improving the oral bioavailability of active agents include; enhancing solubility and dissolution rate of poorly water-soluble drugs and enhancing permeability of poorly water soluble drugs [3]. The solid dispersion term is being utilized where the drug is dispersed in a biologically inert matrix, usually with a view to enhancing oral bioavailability [4]. Chiou and Riegelman defined these systems as the dispersion of one or more active ingredients in an inert carrier matrix at solid-state prepared by the melting (fusion), solvent or melting- solvent method [5], while Corrigan suggested that the product formed by converting a fluid drug-carrier combination to the solid state [6].

**BCS classification of Drugs:**

The BCS (Biopharmaceutical Classification system) classification of the drug in view of aqueous solubility and membrane permeability is given in Table 1.

**Table 1. BCS classification system and solubility expression [7].**

| Solubility | Permeability | Examples | Class |
|---|---|---|---|
| High solubility | High permeability | Benzapril, Loxoprofen | I |
| High solubility | Low permeability | Valsartan, Nimesulide | II |
| Low solubility | High permeability | Gabapectin, Topiramate | III |
| Low solubility | Low permeability | Furosemide | IV |

**SOLID DISPERSION:**

Solid dispersion can be referred as a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug [8]. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles (clusters) or in crystalline particles [9].

**Advantages of solid dispersions:**

***Particles with reduced particle size*:**

Preparation of solid dispersions results in particles with reduced particle size for this reason the surface area is enhanced which results in increase in the dissolution rate, thus bioavailability of the drug gets increased [10].

**Particles with improved wettability:**

Wettability is improved during solid dispersion production. It has been suggested that the presentation of particles to the dissolution medium as physically separate entities may reduce aggregation. In addition, many of the carriers used for solid dispersions may have some wetting properties hence improved wetting may lead to reduced agglomeration and increased surface area [11,12].

**Disadvantages of solid dispersions:**

- They are not broadly used in commercial products because there is the possibility that during mechanical or temperature or humidity stress, the amorphous state may undergo crystallization [13].
- The effect of moisture on the storage stability of amorphous pharmaceuticals is also a significant concern, because it may increase drug mobility and promote drug crystallization [14].
- 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 [15].
- Reproducibility of physicochemical characteristics is poor.

**PREPARATION OF SOLID DISPERSIONS [18-25]:**

The general steps that are involved in preparation of solid dispersion are presented in Fig 1. There are basically nine methods for the preparation of the solid dispersion that are Fusion/ Melting, Solvent, Melting solvent (melt evaporation), Melt extrusion, Lyophilization techniques, Melt agglomeration process, the use of surfactant, Electrospinning and Super Critical Fluid (SCF) Technology.

**Fusion / Melting method:**

In this method, a physical mixture of a drug and a water-soluble carrier is formed. The mixture is heated directly until it melts. Followed by 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:**

The first step is the preparation of a solution containing both matrix material and drug[l].The second step involves the removal of solvent (s) resulting in formation of a solid dispersion. Mixing at the molecular level is

preferred, because this leads to optimal dissolution properties [21]. The main advantage of the solvent method is thermal decomposition of drugs or carriers can be prevented because of the relatively low temperatures required for the evaporation of organic solvents.

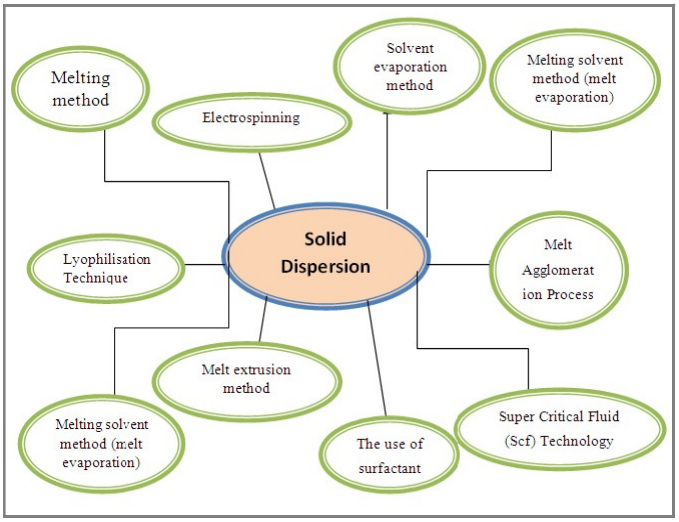


**Fig1. Steps involve in solid dispersion.**

**Melting solvent method (melt evaporation):**

About 5 to 10 % (w/w) of liquid compounds can be incorporated into polyethylene glycol 6000 without significant loss of its solid property. Also the liquid solvent used may affect the polymorphic form of the drug, which precipitates as the solid dispersion. This technique possesses unique advantages of both the fusion and solvent evaporation methods.

**Melt extrusion method:**

Hot-stage extrusion (HME) consists of the extrusion, at high rotational speed, of the drug and carrier, previously mixed, at melting temperature for a small period of time. Solid dispersion by this method is composed of active ingredient and carrier, and prepared by hot-stage extrusion using a co-rotating twin-screw extruder.

**Lyophilization Technique (Freeze-drying):**

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. This technique was proposed as an alternative technique to solvent evaporation.

**Melt Agglomeration Process:**

This technique has been used to prepare solid dispersion wherein the binder acts as a carrier. In addition, solid dispersions are 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.

**The use of surfactant:**

The utility of the surfactant systems in solubilisation is very important. Adsorption of surfactant on solid surface can modify their hydrophobicity, surface charge, and other key properties that govern interfacial processes such as flocculation/dispersion, floating, wetting, solubilisation, detergency, and enhanced oil recovery and corrosion inhibition. Surfactants have also been reported to cause solvation/plasticization, manifesting in reduction of melting the active pharmaceutical ingredients, glass transition temperature and the combined glass transition temperature of solid dispersions.

**Electrospinning:**

Electrospinning is a process in which solid fibers are produced from a polymeric fluid stream solution or melt delivered through a millimeter-scale nozzle. This process involves the application of a strong electrostatic field over a conductive capillary attaching to a reservoir containing a polymer solution or melt and a conductive collection screen.

**Super Critical Fluid (SCF) Technology:**

In this method carbon dioxide is used as anti-solvent for the solute but as a solvent with respect to the organic solvent. Different acronyms were used by various authors to denote micronization processes like solvent extraction system, precipitation, anti-solvent, gas anti-solvent, solution enhanced dispersion by supercritical fluids and supercritical anti-solvent.

**TYPES OF SOLID DISPERSIONS:**

Various type of solid dispersion are presented in Fig 2 [26-28].

**Eutectic mixtures:**

It consists of two compounds which are completely miscible in the liquid state but only to a very limited extent in the solid state. It is prepared by rapid solidification of fused melt of two components that show complete liquid miscibility but negligible solid-solid solution.

**Solid solution:**

Solid solutions are analogous to liquid solutions, consisting of just one phase irrespective of the number

of components, if the drug's particle size is reduced to its unconditional minimum. The molecular dimensions and the dissolution rate are determined by the dissolution rate of the carrier.

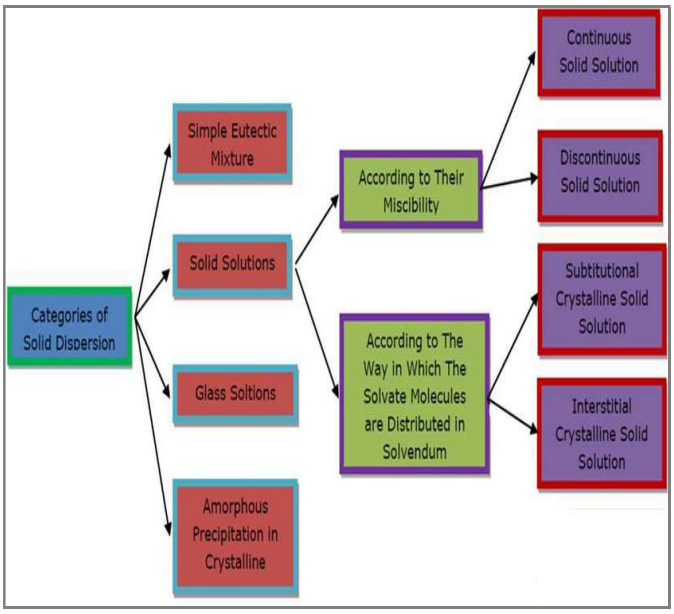


**Fig 2. Various types of solid dispersion.**

**Continuous solid solutions:**

In a continuous solid solution, the components are miscible in all proportions hypothetically, this means that the bonding strength between the two components is stronger than the bonding strength between the molecules of each of the individual components.

**Discontinuous solid solutions:**

In the case of discontinuous solid solutions, the solubility of each of the components in the other component is limited term `solid solution' should only be applied when the mutual solubility of the two components exceeds 5 %.

**Substitutional solid dispersions:**

Substitution is only possible when the size of the solute molecules differs by less than 15 % or so from that of the solvent molecules.

**Interstitial solid solutions:**

In interstitial solid solutions, the dissolved molecules occupy the interstitial spaces between the solvent molecules in the crystal lattice.

**Glass solution and suspensions:**

Glass solutions are homogeneous glassy systems in which solute dissolves in a glass carrier. Glass suspensions are mixtures in which precipitated particles are suspended in glass solvent. Lattice energy is much lower in glass solution and suspension.

**SELECTION OF SOLVENTS:**

Both drug and carrier must be dissolved in the selected solvent. Surfactants are used to create carrier drug solutions but as they can reduce glass transition temperature, so care must be taken into consideration [29].

**FUTURE PROSPECTS OF SOLID DISPERSIONS:**

Solid dispersions, preparation, parodic, formulation, scale-up and stability limited use in poorly water soluble drugs [31]. However, successful expansion has been practicable in recent years due to availability of surface-active and self-emulsifying carriers with relatively low melting points. The drugs along with carriers are filled into hard gelatine capsules because of the easy manufacturing process and improved bioavailability and enhanced dissolution rate [30].

**APPLICATIONS OF SOLID DISPERSION [31,32]:**

- To increase the solubility, dissolution rate, absorption, bioavailability and stability of drug (s).
- To formulate a fast released dosage form.
- To reduce side effects of certain drugs.
- Masking of unpleasant taste and smell of drugs
- Improvement of drug release from ointment and creams.

**CONCLUSION:**

The solid dispersion method is one of the effective approaches to achieve the goal of solubility enhancement of poorly water-soluble drugs. In developing a new solid dispersion system for a given drug, it is important to understand the physicochemical properties of the drug and carrier that best match the properties and find a solid dispersion method. The preparation method and the amount of the carrier also play a vital role in the enhancement of drug dissolution rate. With future development of this technology, solid dispersions will continue to enable novel applications in drug delivery and solve problems associated with the delivery of poorly soluble drugs.

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