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SOLID DISPERSION: TYPES OF SOLID DISPERSION AND MECHANISM OF SOLID DISPERSION IMPROVED SOLUBILITY

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ABSTRACT

Solid dispersions have garnered a great deal of attention as an effective way to increase the rate of dissolution and, consequently, the bioavailability of a variety of hydrophobic drugs. This article summarizes some recent technology transfers and reviews various solid dispersion preparation methods. On the basis of molecular arrangement, the various kinds of solid dispersions have been highlighted. A look at the molecular arrangement of drugs in solid dispersions is also covered, along with some of the practical considerations for the preparation of solid dispersions, such as carrier selection and physicochemical characterization techniques. The limited commercialization of solid dispersions and its recent revival have been thoroughly justified.

Keywords: Solid dispersions, carrier, solubility, dissolution, bioavailability.

Introduction

Because it is convenient and simple to consume, the oral route of drug administration is the most popular and preferred method of delivery. From the perspective of the patient, swallowing a dosage form is a convenient and common way to take medication. As a consequence, compared to other routes of administration, such as parenteral, oral medication administration generally results in greater patient compliance and, consequently, more successful drug therapy.

Although the oral route of administration is preferred, it can be a challenging and ineffective mode of delivery for many medications for a variety of reasons. Confined drug among the possible issues that can arise when delivering an active agent orally, poor absorption leading to low bioavailability is the most serious. Poor aqueous solubility and/or poor membrane permeability of the drug molecule are the most important contributors to limited drug absorption from the gastrointestinal (GI) system. In the pharmaceutical literature, a variety of solid dispersion systems have been shown to enhance the dissolution characteristics of drugs with low water solubility. Other techniques have been used to enhance the dissolution properties of poorly water-soluble drugs, such as salt formation, complexation with cyclodextrins, solubilization of drugs in solvent(s), and

particle size reduction, but each of these approaches has significant drawbacks. On the other hand, when creating oral delivery systems for medications that are poorly water soluble, the formulation of drugs as solid dispersions provides a wide range of processing and excipient choices.

Solubility:

The quantity of a substance that has entered solution when equilibrium is reached between the excess, or undissolved substance, and the solution at a specific temperature and pressure is the substance's solubility. Together, the terms "solute" and "solvent" designate the material to be dissolved and the dissolving medium in which it is accomplished.

Definition of Solid Dispersions:

A collection of solid products with at least two distinct components, typically a hydrophilic matrix and a hydrophobic drug, are referred to as solid dispersion. Either the material is crystalline or amorphous. The medication can be distributed molecularly, in crystalline or amorphous particles (clusters).

Advantages of solid dispersion

Particles with reduced particle size

After carrier dissolution, the drug is molecularly distributed in the solid state of particle size reduction known as molecular dispersions medium for disintegration. Solid dispersions combine a drug that is poorly water soluble with carriers that are highly soluble to apply this concept to drug release. A high surface area is created, increasing the dissolution rate and, as a consequence, the bioavailability.

Particles with improved wettability

The drug wettability increase observed in solid dispersions has a significant impact on the improvement of drug solubility. Even carriers with no surface activity, like urea, were found to enhance drug wettability. carriers that have surface action, such as bile salts and cholic acid. When used, can greatly improve the drug's wettability characteristic. In addition, carriers may have direct dissolution or co-solvent impacts that alter the drug's dissolution profile.

Particles with higher porosity

It has been discovered that dense dispersions of particles exhibit more porosity. Additionally, the carrier characteristics affect the increase in porosity. For example, solid dispersions containing linear polymers create larger and more porous particles than those containing reticular polymers, leading to a higher dissolution rate. The increased porosity of solid dispersion particles also hastens the drug release profile.

Drugs in amorphous state

When in the amorphous state, drugs that are not very soluble in water typically have a greater solubility. Since no energy is needed to disrupt the crystal lattice during the dissolution process, the drug can typically be used in its amorphous form to enhance drug release. After system dissolution, drugs in solid dispersions appear as supersaturated solutions. If drugs precipitate, it is thought to be in a metastable polymorphic form with a greater solubility than the most stable crystal form.

The amorphous composition of drugs with low crystal energy (low melting temperature or heat of fusion) is mainly determined by the difference in melting temperatures between the drug and carrier. Higher amorphous compositions for drugs with high crystal energy can be achieved by selecting carriers that have particular interactions with them.

Disadvantage of Solid Dispersion:

- Poor scale-up for production results from this.
- The polymers used in solid dispersion have the ability to absorb moisture and bring about phase separation, crystal development, and crystalline transformation. As a consequence, solubility and dissolution rate are reduced.
- It is a time-consuming technique of preparation.
- It results in reproducibility of physicochemical properties.

Based on their molecular arrangement, six different types of solid dispersions can be distinguished as shown in table 1.

Solid dispersion type		Matrix *	Drug **	Remarks	No. phases	Ref. to lit.
I	Eutectics	C	C	The first type of solid dispersion prepared	2	(Chiou and Riegelman, 1971)
II	Amorphous precipitations in crystalline matrix	C	A	Rarely encountered	2	(Breitenbach AH, 2002); (Mullins and Macek, 1960)
III	Solid solutions					
	Continuous solid	C	M	Miscible at all composition, never prepared	1	(Goldberg *et al.*, 1965]

	solutions					
	Discontinuous solidsolutions	C	M	Partially miscible, 2 phases eventhough drug is molecularly dispersed.	2	Sekiguchi K and Obi N(1961)
	Substitutional solidsolutions	C	M	Molecular diameter of drug (solute) differs less than 15% from the matrix(solvent) diameter. In that case the drug and matrix are substitutional. Can be continuous or discontinuous.When discontinuous: 2 phases even though drug is molecularly dispersed.	1 or 2	(Rastogi and Verma, 1956);(Wilcox *et al*., 1964)
	Interstitial solid solutions	C	M	Drug (solute) molecular diameterless than 59% of matrix (solvent)diameter. Usually limited miscibility, discontinuous. Example: Drug in helical interstitial spaces of PEG.	2	(Chiou and Riegelman, 1971);(Chiou and Riegelman, 1969)
IV	Glass suspension	A	C	Particle size of dispersed phase dependent on cooling/evaporation rate. Obtained after crystallization of drug in amorphous matrix	2	(Chiou and Riegelman, 1971);(Sarkari M et al., 2002)
V	Glass suspension	A	A	Particle size of dispersed phase dependent on cooling/evaporationrate many solid dispersions are of this type	2	(Chiou and Riegelman, 1971);(Sarkari M *et al*., 2002)
VI	Glass solution	A	M	Requires miscibility OR solid solubility, complex formation or upon fast cooling OR evaporation	1	Simonelli AP *et al*., 1969

				during preparation, many (recent) examples especially with PVP		

*A: matrix in the amorphous state, C: matrix in the crystalline state, **: A: drug dispersed as amorphous clusters in the matrix, C: drug dispersed as crystalline particles in the matrix, M: drug molecularly dispersed throughout the matrix

Preparation of solid dispersions:

Various methods of preparation solid dispersions are summarized as:

a) Kneading technique,
b) Hot-melt extrusion,
c) Solvent evaporation,
d) Solvent melt fusion,
e) Complexes of inclusion Surface active carriers,
f) Direct capsule filling,
g) Particle size reduction Solid deposition on super disintegrants,
h) Adsorption on insoluble carriers/fluidized bed system,
i) Melt agglomeration technique,
j) Dropping technique.

- **Applications of the solid dispersion:**
- It was demonstrated that solid dispersion systems could deliver bioavailable oral dosage forms for anti-cancer medications, which could be used in place of conventional injections to increase patient compliance and comfort.
- Additionally, solid dispersion serves as the functional carrier that has the additional advantage of directing the release of the highly soluble forms of the drugs that are poorly water soluble for absorption at the best location.
- Additionally, it was discovered that the solid dispersion systems reduced the impact of food on drug absorption, making drug treatment more convenient by doing away with the requirement that some medications be taken with food.
- For medications like NSAIDS [non-steroidal anti-inflammatory drugs], where immediate action is important in reducing acute pain and inflammation, it has been shown that solid dispersion formulations can hasten the onset of action.
- The cost of these drug therapies is reduced due to the solid dispersion systems' better absorption efficiency, which enables a reduction in the amount of active agent required per dose.
- The solid dispersion is made as a dry powder formulation for inhalation to enhance immunosuppressive therapy in lung transplant patients. Numerous issues, such as the use of irritant solvents and local anesthesia, can be prevented.

Limitations of Solid Dispersions:

- costly and time-consuming preparation techniques.
- Physical and chemical traits that are easy to reproduce.
- difficulty incorporating into dosage form formulation.
- The manufacturing procedure being scaled up.
- Stability of the drug and vehicle.

Conclusion:

Solid dispersion systems have been identified as a very practical tool for enhancing the dissolution characteristics of drugs with low water solubility. Solid dispersion technology has seen a lot of research in recent years, but their practical use has been relatively sparse. To get around the restriction and make the preparation practicable, various strategies have recently been attempted. With the development of alternative strategies, the issues associated with incorporating into the formulation of dosage forms have been progressively resolved. These include direct capsule filling and techniques like spraying on sugar crystals. Although there are some challenges, such as scale-up and manufacturing costs, solid dispersion technology holds out a lot of potential for accelerating the drug release profile of poorly water soluble drugs.

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