A Review on Solid Dispersion

Kaur Sharanpreet1, Bhatti Farhan2, Amisha3 and Kumar Abhishek4

1,2,3,4Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy, Bela, Rupnagar, Punjab, INDIA.

1Corresponding Author: preetsharan240@gmail.com

ABSTRACT

The majority of patients prefer to take their medications orally. However, many drugs' limited usage in oral administration is a result of their poor solubility. One important element that influences the rate of dissolution and bioavailability is solubility. Increasing the pace at which weakly water-soluble substances dissolve through solid dispersion is useful, medicines, hence affecting its bioavailability. This study focuses on different approaches to solid dispersion preparation, their benefits and significant difficulties.

Keywords: Solid dispersion, solubility, polymers, amorphous.

I. INTRODUCTION

Due to its convenience and simplicity of ingestion, oral drug administration is the most popular and favored form of delivery. A dose form that is swallowed is a convenient and common way to take medication from the patient's standpoint. As a result, oral medication is usually more effective in terms of patient compliance and, thus, pharmacological treatment compared to other methods, such as parenteral, for delivering drugs.

Numerous solid dispersion methods have been shown in the medical literature to enhance the dissolving characteristics of medicines with low water solubility. To enhance the dissolution, other techniques have also been used, including salt production, complexation with cyclodextrins, drug solubilization in solvent(s), and particle size reduction.

However, each of these methods has significant drawbacks. characteristics of poorly water-soluble medicines. however, the formulation of medications as solid dispersions provides a range of manufacturing and excipient alternatives that allow for versatility when creating oral delivery systems for medicines that aren’t extremely water-soluble.

According to the pharmaceuticals' solubility and permeability, the Biopharmaceutical Classification System (BCS) divided them into four subclasses. The solubility of medicines in BCS classes II and IV is poor. Enhancing the solubility of these medications belonging to BCS II and IV is the most difficult task. Different strategies are employed for this aim, including solid dispersion, a decrease in particle size (Micronization and Canonization), the production of salts, a change in pH and the production of polymorphs and pseudo-polymorphs created by the complexation process with the use of a surfactant and co-solvent. Though among these Approaches for solid dispersion are simple and provide highly accurate solubility improvement results.

The carrier dissolves when the solid dispersion is in contact with water, and the medicine then releases tiny colloidal particles. This enhances the surface area of the dissolution rate and, consequently, the bioavailability of medications that are weakly water-soluble. By lowering particle size and increasing the particle surface area, the drug in soluble hydrophilic carriers increases the rate of dissolution porosity. Therefore, increasing these medications' drug release profiles will increase their bioavailability and lessen adverse consequences [1–3].

Solid Dispersion

The term "solid dispersion" refers to the dispersion of one or more active ingredients—which are hydrophobic—in an inert carrier—which are hydrophilic—in a solid form after being prepared by
melting (fusion), solvent, and melting solvent technique. Both a hydrophilic matrix and a hydrophobic drug are present in the final product.

II. CLASSIFICATION OF SOLID DISPERSION

Solid dispersions can be classified into the following categories depending on the molecular arrangement:

- **Eutectic mixtures:** The common method for creating solid eutectic mixes is to rapidly cool the co-melt of the two components to create a physical mixture of very thin crystals of the two components.

- **Solid solutions:** The two different categories of solid solutions, which depend on miscibility, are
  
a. **Continuous solid solutions:** The bonds between the components in continuous solid solutions are stronger than the bonds between the individual components because the components are miscible in all quantities.

b. **Discontinuous solid solutions:** The solubility of each component in the other component in discontinuous solid solutions is constrained.

There are two different kinds of solid solutions, depending on how the solvates are distributed in the solvent:

- **Substitutional crystalline solution:** These are the types of solid solutions that are crystalline. In nature, where the solute molecules act as the solvent molecules' replacements in the crystal lattice.

- **Interstitial crystalline solid solution:** These solid solutions contain dissolved molecules that fit in the gaps between the solvent molecules in the crystal lattice.

- **Amorphous solid solutions:** In amorphous solid solutions, the solute molecules are molecularly scattered inside the amorphous solvent but not uniformly.

- **Glass solutions and glass suspension:** When the solute dissolves in the glassy solvent, the result is a homogeneous system known as a glass solution. Below the glass transition temperature, the glassy state is defined by transparency and brittleness. Glass is a phrase used to describe a pure chemical or a combination of pure compounds in their glassy form.

Classification of solid dispersion based on of recent advancement:

- **First generation solid dispersion:** Utilizing crystalline carriers, these solid dispersions are created. To create solid dispersions, the first crystalline carriers were urea and sugars. These have the drawback of being thermodynamically unstable and do not release drugs more quickly.

- **Second generation solid dispersion:** Instead of crystalline carriers, amorphous carriers are used to create these solid dispersions. In the polymeric carrier, the medication has been molecularly distributed. There are two categories of polymeric carriers:
  
- 1. **Synthetic polymer** - polyethylene glycols, poly(methacrylates) and povidone.
- 2. **Natural polymer** - hydroxypropylmethylcellulose, ethyl cellulose, starch derivatives like cyclodextrin.

- **Third generation solid dispersion:** A surfactant carrier or a combination of amorphous polymers and surfactants serve as the carrier in these solid dispersions. Medications with weak solubility achieve the highest level of bioavailability. The third-generation solid dispersion uses surfactants like inulin, poloxamer 407, and others (4-6).

III. ADVANTAGES OF SOLID DISPERSION

Chemical or formulation methods have made it possible to increase a drug's water solubility, hence increasing its bioavailability. Chemical methods to increase bioavailability without altering the active target include salt creation and adding polar or ionizable groups to the primary drug structure, which results in the production of a salt pro-drug. Compared to these methods, solid dispersions appear to be a better strategy for enhancing drug solubility because they can be produced more quickly and are more useful.

Solid dispersions are the final stage of particle size reduction in molecular dispersions, and after carrier dissolution, the drug is molecularly distributed in the dissolving media. By combining a medication that is poorly water soluble with highly soluble carriers, solid dispersions use this principle to control drug release. There is a large surface area generated, resulting in a faster rate of dissolution and, as a result, better bioavailability. Solid dispersions additionally offer particles that have better wettability because it was discovered that even carriers with no surface activity, such as urea can bind to them enhancing medication wettability. Bile salts and cholic acid are examples of carriers with a surface activity that, when utilized, can considerably boost the drug's capacity to wettable.

Porosity has been observed to be higher in solid dispersions of particles. The increase in porosity also depends on the carrier characteristics; for example, solid dispersions including linear polymers create larger and more porous particles than those containing reticular polymers, leading to a faster rate of dissolution. That increased the porosity of solid dispersion particles also quickens the pattern of medication release. Drugs that are crystalline and have a low water solubility have a higher solubility when they are amorphous. It was improved because no energy is required to break down an amorphous drug, it is usually possible to obtain the desired level of drug release using this method. Throughout the disintegration process, the crystal lattice. Medications appear supersaturated in solid dispersions after the collapse of the system, and it is speculated.

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)
6. **Spray drying method:**

   The necessary amount of carrier is dissolved in water, and the drug is dissolved in a suitable solvent. Then, using a spray drier, the clear solution is produced by sonicating the mixture of the solutions or using another acceptable method.

7. **Melt extrusion method:**

   By employing a co-rotating twin-screw extruder, hot-stage hot-stage extrusion is used to create solid dispersion that is made up of active ingredient and carrier. Dispersions always have a 40% (w/w) drug concentration. In the pharmaceutical sector, several dosage forms, such as sustained-release, are prepared using the melt extrusion technique pellets.

8. **Melting solvent method:**

   Recently, it was demonstrated that polyethylene glycol 6000 may integrate liquid substances at a rate of 5–10% (w/w) without noticeably losing any of its solid properties. As a result, solid dispersions can be made by first dissolving a medication in a suitable liquid solvent and then adding the solution straight to the melt of polyethylene glycol, without draining the liquid solution, below 70. There is a chance that the chosen solvent or dissolved substance may be immiscible with the polyethylene glycol melt. Drug precipitated in its polymorphic form as a solid. The chosen liquid solvent may have an impact on dispersion. The benefits of this distinct approach combine both the melting and solvent-based techniques. This procedure entails dissolving the medication in an appropriate.

9. **Supercritical fluid technology:**

   SCF is a substance that has been heated or compressed past its critical point. The critical point designates the temperature and pressure combination at which a substance can coexist in equilibrium as both a liquid and a vapour. This method increases the drug's ability to dissolve by solidifying a polymer or insoluble substance into a solid dispersion. Compared to, it is SCF carbon dioxide is mostly employed in this process instead of more traditional methods (such as hot melt and spray drying), which results in incredibly quick solid mixture precipitation leaves no time for medication and polymer separation during solid preparation dispersion. It produces extremely stable, tiny particles with a high surface area for excellent flow and a minimal residue of organic solvent. In recent SCF carbon dioxide in precipitation is used to create solid dispersion of carbamazepine with PEG-4000.

10. **Solvent method:**

    This technique, also known as solvent evaporation, involves dissolving a physical mixture of the medication and the carrier in a common solvent and evaporating it until a clear solvent-free film is formed. The key benefit is that because organic solvents need to be used at low temperatures, thermal degradation of the medicine or carrier can be avoided to allow for evaporation. The difficulty in removing the solvent and

---

**By selecting carriers that interact specifically with them, higher amorphous compositions for medicines with high crystal energy can be achieved. To boost its aqueous solubility and dissolution, the drug is combined with a hydrophilic carrier as a solid dispersion. To do this, a superdisintegrant (such as croscarmellose sodium) is utilised in the formulation of tablets. Tablets made using the wet granulation process quickly disintegrate. These quickly eroding pills can be used for a substitute for parental therapy that enables patients to self-medicate without the use of water (7–11).**

**IV. METHODS OF PREPARATION OF SOLID DISPERSION**

Various methods use for preparation of solid dispersion system:-

1. **Kneading technique:**

   This technique turns the carrier into paste by allowing water to permeate it. Next, the drug is added, and the dough is worked for a specific amount of time. After drying, the kneaded dough may need to go through a sieve.

2. **Lyophilization:**

   It is a phenomenon where mass and heat are transferred from and to the product. It uses a molecular mixture process as an alternative to solvent evaporation, where the medication and carrier are mixed in a shared solvent, frozen, then sublimed.

3. **Melt Agglomeration technique:**

   Binder is used as a carrier in this method. There are two ways to prepare solid dispersions; the first is by spraying the medication onto melted excipients and binder, while the second involves melting the drug and excipients together above the binder's melting point. The rotary technique may be preferred for managing the use of high binder content temperature. Larger particle size results in densification, yet this strategy is beneficial for uniform medication mixing, fines make mass adhere.

4. **Electrosprinning method:**

   When a polymeric fluid stream solution or melt is supplied through a millimeter-scale nozzle, the process of electrosprinning creates solid fibres. As part of this procedure, an electrostatic field was created over a conducting capillary that was attached to a reservoir that contained a polymeric solution and a conductive collective screen. There is a prepared itraconazole/HPMC implementing this strategy (12–14).

5. **Melting method:**

   For heat-stable materials with low melting points, the melting process is appropriate. The primary idea behind the procedure is to combine the medication and carrier by melting them both at a temperature just above their eutectic points and combining the resulting liquid substances. Then it is chilled such that a congealed mass forms. It is broken apart and strained.
increased preparation costs are drawbacks of this technique (15-19).

V. EVALUATION OF PHYSICOCHEMICAL PROPERTIES OF SOLID DISPERSION

I. Phase Solubility Study:

Using the shaking flask method, it is done in the presence of the polymer (carrier). The Higuchi and Connors are largely followed when conducting it. The medicine is put into a 25 ml container that also contains solutions of 1%, 2%, 3%, 4%, and 5% polymer. Then, it is kept at a temperature of 37 °C 0.5 °C for 48 hours in an orbital flask shaker. Sample is then filtered and examined by Using a UV spectrophotometer to measure medication concentration.

II. Saturation Solubility Study:

Added in excess, 25 ml of distilled water is super-saturated with drug and solid dispersion batch mixtures. Then, it is heated to a temperature of 37 °C 0.5 °C and placed in an orbital flask shaker for 48 hours. It is then filtered via Whatman filtered paper and examined to determine the drug concentration using a UV spectrophotometer.

III. Drug content :

To determine the drug content, a known quantity of solid dispersion is dissolved in a solvent and examined by a UV spectrophotometer. % Drug loading = (Weight of drug in solid dispersion powder)/(Weight of solid dispersion powder) X 100 -----(1)

VI. CHARACTERIZATION OF SOLID DISPERSIONS

1. Fourier Transform Infrared Spectroscopy (FT-IR):

FT-IR mostly used for to characterize drug-polymer (carrier) compatibility study. Its main application is to study the solid state interaction between drug and polymer.

2. Differential Scanning Calorimetry (DSC):

It is an effective method for researching amorphous content. Additionally, endothermic and exothermic peaks are detected. Based on melting point, it also investigates whether the medicine was absorbed into the polymer (carrier) or not.

3. Powder X-ray Diffraction (PXRD):

It is especially helpful for determining if the solid dispersion is amorphous or crystalline. Sharper peaks denote higher crystallinity.

4. Scanning electron microscopy:

It is used for to characterize particle morphology (20-27).

VII. POLYMERS USED IN SOLID DISPERSIONS

1. Polyethylene glycol (PEG)

These substances are created when ethylene glycol and ethylene oxide combine. PEGs with a molecular weight of 300,000 or more are frequently referred to as polyethylene oxides. PEGs having molecular weights between 1500 and 20,000 are typically used to create solid dispersions and solutions. The PEG's viscosity increases along with the MW. PEGs are fluid up to MW 600; between MW 800 and 1500, they have a consistency that is best described as vaselinelike; between MW 2000 and 6000, they are waxy; and at MW 20,000 and higher, they form hard, brittle crystals at room temperature temperature. Although generally good, their solubility in water decreases with MW. PEGs' careful benefit for the The fact that they have solid dispersions.

2. Polysvinlypyrrolidone (PVP)

The PVP molecular weight ranges from 2500 to 3000000. It is soluble in solvents such as water, ethanol, chloroform, and isopropyl alcohol. PVP decomposes at high temperatures, hence it is not ideal for making solid dispersions using the melt method since melting happens at extremely high temperatures. PVP can be categorised using Fikentscher's equation to determine the K value. A certain PVP's temperature depends on not just on its MW but also on the moisture content. The glass transition temperature (Tg) is often high.Tg for PVP K25 is 1558 °C, as an illustration. For the hot melt method of making solid dispersions, PVPs have a limited range of applications. They are primarily appropriate for the manufacture of solid dispersions using the solvent method due to their good solubility in a wide array of organic solvents.

3. Cellulose derivatives :-

a. Hydroxypropylmethylcellulose (HPMC):

The hydroxyl groups in HPMCs, which are mixed cellulose ethers, are derivatized with hydroxypropyl groups in 4–32% and 16.5–30% of the total amount. The molecular weight of the HPMCs ranges from about 10,000 to 150,000, and they are soluble in water as well as mixes of ethanol and dichloromethane as well as methanol and dichloromethane.

b. Hydroxypropylcellulose (HPC):

Water (up to 400 °C), ethanol, methanol, and chloroform are just a few of the solvents in which hydroxypropylcellulose (HPC) is well soluble. HPCs range in average MW from 37 000 (Type SSL) to 1 150 000 (Type H).4

c. Carboxymethylcellulose (CMC):

CMC is a cellulose ether, but unlike many of the others, it is resistant to dissolving in an acidic environment like the stomach. The lowest dissolving pH depends on the grade of the CMC, and it dissolves easily at pH levels above 5–6. CMCs also easily dissolve in acetone, isopropanol 70%, ethanol 60%, and 1:1 combinations of these three alcohols alcohol and dichloromethane.
d. Hydroxypropylmethylcellulose phthalate (HPMCP):
Enteric coatings frequently use cellulose esters known as HPMCPs. They begin to dissolve at a pH of 5 (HP 50) or 5.5 (HP 55), depending on the grade. In organic solvents, they are soluble to a type-dependent extent. By mixing griseofulvin with a coevaporate of HPMCP, the rate at which it dissolves at pH 6.8 might be significantly increased.

e. Polyacrylates and polymethacrylates:
Glassy compounds known as polyacrylates and polymethacrylates are created through the polymerization of acrylic and methacrylic acids, as well as their derivatives such as esters, amides, and nitriles. They are mostly employed as coatings in the pharmaceutical industry to alter how quickly drugs are released from dosage forms.

f. Phospholipids:
In order to create phospholipids, the terminal hydroxyl of glycerides is modified with phosphate linked head groups. Common phospholipid head groups include choline, ethanolamine, serine, inositol and inositol phosphate, and glycerol esters. Similar to triglycerides, a variety of species are possible via different combinations of fluidity, fatty acyl substitution at the first and second locations of the glycerol backbone, and various head groups. The gel to liquid crystalline transition temperatures have an impact on the distinctions that are visible. phospholipids' solubility rather than being purely a chemical function of the molecule, is closely related to the confirmation of the aggregate material. Since they frequently form micelles, monoacyl phospholipids are typically more easily soluble in aqueous solutions.

g. Sugar, polyols and their polymers:
The production of solid dispersions is not as well suited for sugars and related molecules as it is for other carriers, despite the fact that they are extremely water soluble and have minimal to no toxicity issues. Because most sugars have a high melting point and have limited solubility in most organic solvents, it is challenging to prepare them using the hot melt method co-evaporates to get ready. There have been reported attempts to prepare solid dispersions despite these disadvantages, sugars and their derivatives are used. Mannitol, which only decomposes at 2500 degrees Celsius and has a melting point of 165-168 degrees. When preparing dispersions using the hot melt method, °C, can be used in specific circumstances.

h. Organic acids and their derivatives:
In solid dispersions, organic acids like citric acid and succinic acid have also been utilised as carriers, first to speed up the release of griseofulvin.

i. Cyclodextrins:
The main purposes of cyclodextrins are to increase solubility, chemical protection, taste masking, and enhanced handling by entrapping liquids into solids (28-32).

VIII. CONCLUSION

Even though solid dispersion systems have garnered a lot of attention over the past forty years as a way to improve the bioavailability and dissolution rate of pharmaceuticals with poor water solubility, their commercial application has been severely constrained, mostly due to manufacturing challenges and stability issues. Drugs were typically manufactured as solid dispersions using a solvent or melt. Methods of evaporation. Cooling caused the materials, which were often waxy and semisolid in nature, to become harder. low temperatures. They were then ground up, sieved, combined with sizable volumes of excipients, and taken as tablets or enclosed in firm gelatin capsules. Increasing the size of these operations for the preparing dosage forms for use. The availability of resources has, however, led to a recent shift in the situation. self-emulsifying carriers that are surface-active.

REFERENCES

[10] Giliyar C, Fikstad DT, Tyavanagimatt S. Challenges and opportunities in oral delivery of


