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Solid Dispersion: Promising Approach to Enhance the Solubility

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ABSTRACT

The majority of the time, oral administration of medications to patients is chosen. However, many drugs' limited usage in oral administration is a result of their poor solubility. In the pharmaceutical industry, improving a drug's water solubility is a primary goal. One of the most crucial factors affecting bioavailability and dissolution rate is solubility. Therefore, the creation of solid dispersion with carriers with strong water solubility is advantageous to overcome such issues and promote dissolution. Therefore, it is discovered that using solid dispersion methods is a successful way to increase the drug's solubility when it has a low solubility in water. The review emphasises the many types of solid dispersion, their justifications, benefits, and drawbacks, as well as the production procedures for their limited commercialization.

INTRODUCTION:

Due to its simplicity and convenience, the oral route is the most practical and preferred way to administer medication. Because it is familiar to the patient, taking medication orally is a comfortable and convenient method[1]. As a result, oral medicine delivery is superior to alternative methods of administration. Due to sluggish release, slow dissolving, and poor bioavailability, at least 40% of innovative drugs produced by the pharmaceutical companies have a poor ability to dissolve in water, necessitating the administration of high doses in order to achieve desired pharmacological effects[2,3]. The greatest answer to these issues is improving solubility and increasing the rate of dissolution of poorly soluble medications using the solid dispersion method. Therefore, solid dispersion is among the finest methods. for improving the oral bioavailability, solubility, and dissolution rate of poorly water-soluble drugs[4,5].'The dispersion of one or more active components in an inert carrier or matrix at a solid state created by the melting [fusion], solvent, or melting-solvent process,' according to Chiou and Riegelman, is the definition of solid dispersion systems. The matrix is hydrophilic, whereas the medication is hydrophobic [6].

Importance of Solubility

Due to its simplicity, high patient compliance, cost effectiveness, lack of sterility restrictions, and flexibility in dosage form design, oral consumption is the most practical and frequently used method of drug delivery. Many generic medicine manufacturers are therefore more likely to produce bioequivalent oral drug products[7]. The poor bioavailability of oral dose forms, however, presents the biggest design problem. Aqueous solubility, drug permeability, dissolving rate, first-pass metabolism, pre-systemic metabolism, and sensitivity to efflux mechanisms are some of the variables that affect oral bioavailability. Poor solubility and inadequate permeability are the two most common causes of low oral bioavailability. Other dose forms, such as parenteral formulations, are significantly influenced by solubility as well[8]. One of the key factors in attaining the desired drug concentration in the systemic circulation and the necessary pharmacological response is solubility[9]. When taken orally, poorly water soluble medications may need high dosages to attain therapeutic plasma concentrations. The main issue in developing formulations for new chemical entities as well as generics is low water solubility. Any medicine that is to be absorbed must be present at the absorption site in the form of an aqueous solution. The preferred solvent for liquid medicinal compositions is water. Most medications have poor aqueous solubility and are either weakly

basic or mildly acidic. Over 40% of the NCEs (New Chemical Entities) created by the pharmaceutical industry are essentially water insoluble. These medicines' delayed drug absorption and poor water solubility cause inadequate and inconsistent bioavailability as well as gastro intestinal mucosal damage. The most crucial rate limiting factor for medications taken orally is solubility, which allows for the achievement of the desired concentration of the drug in the systemic circulation for pharmacological response. For formulation scientists, the solubility problem presents a significant challenge [10]. One of the most difficult areas of drug development, particularly for oral-drug delivery systems, continues to be the enhancement of drug solubility and, consequently, its oral bioavailability. The solubility of medications that are poorly water-soluble can be improved using a variety of techniques that have been published in the literature. The methods are chosen based on a number of factors, including the qualities of the medicine under consideration, the kind of excipients to be chosen, and the kind of dosage form intended. Insufficient bioavailability is frequently caused by the poor solubility and slow dissolution rate of poorly water soluble medications in aqueous gastrointestinal fluids. Increases in the drug's solubility and rate of dissolution in gastrointestinal fluids, particularly for class II (low solubility and high permeability) compounds, may improve bioavailability. Since the rate-limiting step for BCS class II medications is drug release from the dosage form and solubility in stomach fluid rather than absorption, boosting solubility also increases the drugs' bioavailability[11,12].

Advantages of Solid Dispersion [13]:

- To reduced particle size.
- To improve wet ability.
- To improve porosity of drug.
- To decrease the crystalline structure of drug in to amorphous form.
- To improve dissolvability in water of a poorly water-soluble drug in a pharmaceutical.
- To mask the taste of the drug substance.
- To prepare rapid disintegration oral tablets.
- To obtain a homogenous distribution of small amount of drugs at solid state.
- To stabilize unstable drugs.

- To dispense liquid or gaseous compounds.
- To formulate a faster release priming dose in a sustained release dosage form.
- To formulate sustained release dosage or prolonged release regimens of soluble drugs using poorly soluble or insoluble carriers.

Disadvantages of Solid Dispersions [14]:

- Poor soundness is a problem of strong scattering since medication may experience crystalline state in an unclear condition.
- Handling issue show up because of thickness of some strong scatterings.
- In nearness of dampness and extraordinary temperature strong scattering might be disintegrated, that can result in precious stone development.
- Shelf life forecast of indistinct material is troublesome.
- Hygroscopicity of polymers utilized in strong scattering retains dampness that can result in change of nebulous structure into crystalline form.
- The main drawback of the solid dispersion is its instability. The physical mixture is more affected by the degrading effects of solid dispersions, such as moisture and temperature, because tackiness makes handling harder.

Type of Solid Dispersion [15,16]:

1 Eutectics Mixtures: Two compounds that are entirely miscible in the liquid state but only to a very small extent in the solid state make up a straightforward eutectic combination. It is made by quickly solidifying two components that were fused together and exhibit total liquid miscibility but minimal solid-solid solution.

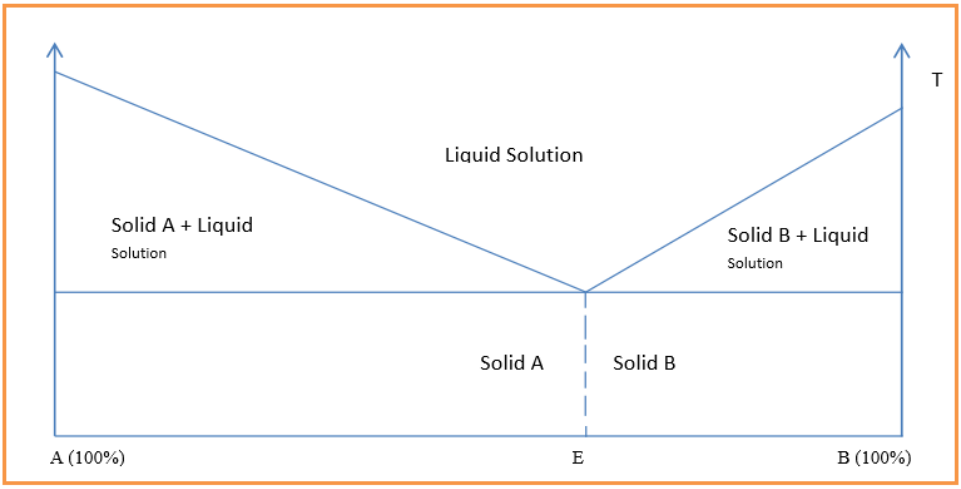

Figure No 1: Eutectics Mixtures

2 Amorphous Solid Solution: The sole distinction between this and simple eutectic mixes is that the medication precipitates out in an amorphous form.

a. Solid Solution: Solid solutions are similar to liquid solutions in that they only include one phase, regardless of the number of constituents. The drug's molecular dimensions14 and dissolution rate are defined by the carrier's rate of dissolution in the case of solid solutions, where the drug's particle size has been reduced to its smallest possible level. the way the solvate molecules are distributed in the solvendum (interstitial or amorphous, substitutional) or second, according to their miscibility (discontinuous solid solutions versus continuous).

b. Continuous Solid Solution: The components are miscible in all ratios in a continuous solid solution. This implies, theoretically, that the molecules of the two components' individual molecules have stronger bonds than the molecules of the other two components combined. Such solid solutions have not previously been documented in the pharmaceutical industry.

c. Discontinuous Solid Solutions: The solubility of one component in the other component is constrained in the case of discontinuous solid isolutions. According to Goldberg et al., the phrase "solid solution" should only be used when the mutual solubility of the two components surpasses 5% due to practical issues.

d. Subsitutional Solid Dispersions: Only when the size of the solute molecules differs from the size of the solvent molecules by around 15% or less is substitution possible. The solute

molecules in traditional solid solutions can either replace the solvent molecules in the crystal lattice or fit into the spaces created by the solvent molecule.

e. Interstitial solid solutions: The dissolved molecules occupy the interstitial spaces between the solvent molecules in the crystal lattice in interstitial solid isolutions. The difference in molecular diameter between the solvent and the solute should not exceed 0.59.

3. Glass solution and suspensions: Glass isolutions are uniform glassy systems where the solute dissolves in the glass carrier. Glass suspensions are mixtures in which glass solvent is suspended with precipitated particles. In suspension and solution glass, the lattice energy is significantly smaller.

Mechanisms of Incorporation of Drug into Polymer

Polymers are the carriers utilised in solid dispersions. When a drug and a polymer are in close proximity, the drug fills the voids left by the polymer's chain and makes it more pliable. For instance, in the hot melt extrusion technique, the polymer is allowed to heat up to a point where the heat is what causes the polymer chain to loosen and include the drug molecule. In contrast, the solvent utilised in the spray drying process causes weak cohesive intra- and intermolecular contacts of polymer chains, which leads to the creation of solvent polymer interactions. The drug molecules are then added to the loosened polymer chains after being dissolved in a solvent.

When a substance is combined with another, the antiplasticization effect is seen when the mechanical properties of the original substance become stiff and brittle. Another way to put it is that the mixture's low Tg compound would fall somewhere between the Tgs of the two compounds. The medication in this instance goes through antiplasticization. As the Tg of a polymer drops, however, plasticization occurs[17].

Drug Release Mechanism from Solid Dispersion

Following oral administration of a solid dispersion in the form of a tablet, capsule, etc., the dissolution performance will provide an accurate indication of the final outcome. Converting the drug's crystalline form to an amorphous form is one of the effective methods for increasing the solubility of poorly soluble drugs. Supersaturation state maintenance and amorphous form stabilisation are essential components for effective solid dispersion formulation. The issue with solid dispersions is the supersaturated drug's precipitation, which

will ultimately impact its bioavailability.[17]. Due to decreased particle size and agglomeration, it is noticed that the medication is more stable and soluble in the medium[18]. Due to an increase in drug dissolving rate, a spring-like phenomenon is seen in supersaturating drug delivery systems such solid dispersion. Drug precipitation causes a decrease in dissolution rate at the supersaturation stage. Furthermore, when precipitation inhibitors are added to such a system, a parachute-like effect is seen on the drug dissolution profile. Two different sorts of mechanisms are involved in drug release from instant release solid dispersions: drug controlled release and carrier controlled release. While in the case of CRSD, drug release mechanisms based on polymer properties and the miscibility of the drug and carrier are seen to diffuse and erode. If the carrier is soluble in the dissolution medium then the release of ASD is dissolution controlled mechanism while in case of insoluble carrier diffusion controlled mechanism is observed[19].

Methods Of Preparation Of Solid Dispersion [20-23]**:**

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

1. Melting method
2. Solvent method
3. Melting solvent method (melt evaporation)
4. Melt extrusion methods
5. Lyophilization techniques
6. Melt agglomeration Process
7. The use of surfactant
8. Electrospinning
9. Super Critical Fluid (SCF) technology

Melting method:

In the melting or fusing procedure, the medication and a water-soluble carrier are heated directly until they melt in order to create a physical combination. The obtained final solid

mass is crushed, pulverised, and sieved. However, because to the high temperature during the melting process, components such as the medicine or the carrier may degrade. The combination could be heated under vacuum or in the presence of inert gases like nitrogen as a way to get around this issue. The benefit is that it is straightforward and inexpensive.

Solvent method:

The physical mixture of the drug and the carrier is dissolved in a common solvent and evaporated until a clear solvent-free film is formed. This process is also known as the solvent evaporation method. The key benefit is that because organic solvents need a low temperature to evaporate, thermal degradation of the medicine or carrier can be avoided. The difficulty in removing the solvent and increased preparation costs are the drawbacks of this procedure.

Melting solvent method:

In this procedure, the medication is dissolved in a suitable liquid solvent, and the solution is then added directly to the polyethylene glycol melt before being evaporated to produce a transparent film free of solvent. Fusion and solvent evaporation methods are combined in this process.

Melt extrusion method:

The drug/carrier mixture is concurrently melted, homogenised, extruded, and formed into various forms, such as tablets, granules, pallets, powder, etc. using a twin screw extruder. The approach can be used with medications that are thermolabile since the drug and carrier mixture is heated for roughly a minute.

Lyophilization:

It involves the movement of mass and heat away from and towards the product. The medication and carrier are dissolved in a common solvent, frozen, then sublimed in a molecular mixture process as an alternative to solvent evaporation.

Melt Agglomeration technique:

Binder is used as the carrier in this approach. There are two ways to prepare solid dispersions: the first involves spraying the drug onto melted excipients and binder, and the second involves melting the drug and excipients above the melting point of the binder being employed. The rotary technique may be advantageous for managing temperature when

employing a high binder content. This method helps to evenly mix drugs, however bigger particle sizes produce densification and fines cause mass adhesion.

Electrosipinnig method:

In this method, a nano-sized fibre thread is removed from the polymer sol/polymer melt using electric force. This is a combination of solid dispersion and polymer industry application of nanotechnology. Electrostatic repulsion balances off surface tension when a stream of polymer solution or melt is subjected to electric force (5 to 30 kv). This causes the liquid's body to become charged. This created a powerful cohesive force between the polymer particle or droplets and a stream of fibre. Then, using a whipping process known as electrostatic repulsion, the fibre is thinned and stretched to a nano diameter, resulting in the development of uniform fibre. The rate of feeding, surface tension, and applied electric force are all factors in this process.

Supercritical fluid technology:

Over its critical temperature and pressure, SCF is a material. The critical point is the greatest temperature and pressure at which a substance can coexist in equilibrium as a liquid and a vapour. This method increases the drug's ability to dissolve solid insoluble materials or polymers by using SCF to create the solid dispersion. It is superior to traditional methods (spray drying, hot melt, etc.). SCF carbon dioxide is primarily employed in this method, which results in very rapid solid mixture precipitation, leaving no time for the separation of medicine and polymer in the formation of solid dispersion. With a greater surface area for good flow and minimal remaining organic solvent, it forms very stable tiny particles. Recently, SCF carbon dioxide has been used to create solid carbamazepine and PEG-4000 dispersion in a precipitation vessel. Resulting in formation of carbamazepine with increase rate and extent of dissolution with low solvent residual.

CONCLUSION:

It can be difficult to improve a drug's bioavailability when it is poorly soluble. Because of the drug's poor aqueous solubility, this causes dissolution issues that reduce in vivo absorption and, in turn, bioavailability, making the drug unsuitable for oral consumption. As a result, solubility enhancement is required for such drug candidates. The most straightforward and effective method for improving a drug's aqueous solubility is solid dispersion. An alternate and superior option for increasing the solubility of the inadequately water-soluble BCS-II

medication is a solid dispersion with a synthetic or natural carrier that is less toxic, biocompatible, and more widely accessible.

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