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Solid dispersions: A Technology for improving Bioavailability

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Abstract :

Drug solubility behavior is still one of the most difficult parts of developing formulations. Combinatorial chemistry and high throughput screening have significantly expanded the amount of molecules that are poorly soluble in water. Despite this, solid solutions offer enormous promise for enhancing medication solubility. This article examines the different practical preparation factors that should be taken into account while creating solid dispersions, including carrier selection and physicochemical characterization techniques. To lessen the shortcomings of the original method, new manufacturing techniques have also been developed to produce solid dispersion. The goal of this review is to go over the latest developments in the field of solid dispersions. For increasing the oral absorption and bioavailability of BCS Class II medications, solid dispersion technologies hold great promise. This review article focuses on the solid dispersion's use, benefits, drawbacks, characterization, carrier employed, and preparation process.

Keywords: carrier, bioavailability, solid solutions, solubility, and solid dispersions.

Introduction:

The maximum amount of solute that dissolves in a specified volume of solvent at a given temperature is known as solubility. [1] Due to low and irregular levels of absorption, oral bioavailability improvements for such poorly water-soluble medications frequently exhibit poor bioavailability. Because the particle size is reduced, drugs that experience dissolution rate limiting gastrointestinal absorption typically exhibit enhanced solubility and bioavailability. Drug micronization, however, frequently causes particle agglomeration and aggregation, which impairs wet ability. Using water-soluble carriers in solid dispersions of poorly water-soluble medications has improved dissolution and decreased the frequency of these issues. The drawbacks of earlier strategies, including salt formation, co-solvent solubilization, and particle size reduction, were overcome with the creation of solid dispersions as a workable way to increase the bioavailability of poorly water-soluble medications. Research has shown that medications in solid dispersion do not always have to be micronized. A solid dispersion may form if a portion of the medication molecularly disperses in the matrix. The carrier dissolves and the medicine is released as tiny colloidal particles when the solid dispersion is exposed to watery fluids. [2]

Descriptive term	Parts solvent to 1 part solute	Solubility range(mg/ml)
Very soluble	Less than 1	>1000
Freely soluble	1-10	100-1,000
Soluble	10-30	33-100
Sparingly soluble	30-100	10-33
Slightly soluble	100-1,000	1-10
Very slightly soluble	1,000-10,000	0.1-1
Practically insoluble	More than 10,000	<0.1

The rate and amount of drug absorption is known as bioavailability. The pharmacological effects of the medicine reflect any changes in its bioavailability. Distribution and excretion are additional mechanisms that contribute to a drug's therapeutic action. [3]

Class	solubility	Permeability	example
Class I	High	High	Diltiazem , propranolol
Class II	Low	High	Nifedipine , Naproxen
Class III	High	Low	Insulin , Metformin
Class IV	Low	Low	Taxol, hlorthiazide

Need of solubility enhancement :

Drug discovery is increasingly driven by improved characterisation of biochemical targets, which are typically cell-based and relatively easy to reach in these models. This has resulted in the much-discussed spread of highly active substances with physicochemical properties that make them unsuitable for transport to an entire organism; poor water solubility is at the top of this list of unwanted traits**.**

Solid Dispersion Definition:

Dispersion of one or more hydrophobic active substances in a hydrophilic inert carrier at a solid state made by melting (fusion), solvent, or melting solvent technique is known as solid dispersion. Two distinct components are present in the resultant product: a hydrophilic matrix and a hydrophobic medication.[**6]** Because of the low levels of absorption, medications with limited water solubility frequently exhibit poor oral bioavailability. Drugs that experience reduced absorption due to dissolution rate can have their dissolving rate increased by micronization or size reduction, although this results in particle agglomeration and poor wet ability. Salt production is one of the additional strategies for boosting the bioavailability of medications that are poorly soluble in water. Particle size reduction, complexation with cyclodextrin, and solubilization with a co-solvent all have drawbacks. The shortcomings of earlier methods were overcome with the development of solid dispersions of medicines with low bioavailability.[7]

Application of solid dispersion : [6,7,8]

1) To make poorly soluble medications more to protect unstable medications from degradation processes such as hydrolysis, oxidation, recrimination, isomerization, and photooxidation. to lessen some medications' adverse effects.
2) Concealing the bad taste and odour of narcotics.
3) Enhancement of medication release from gels and creams for ointments.
4) In order to prevent unwanted incompatibilities.
5) To achieve a uniform dispersion of a small quantity of solid-state medication.
6) To administer gaseous or liquid substances in a solid dose (up to 10%). to create a sustained-release dosage form with a fast-release primary dose.
7) To provide a prolonged release schedule for soluble medications employing insoluble or weakly

soluble carriers.

8) To lessen the presystemic inactivation of medications such as progesterone and morphine.

9) The drug's chemical characteristics remain unchanged.

Features include: [9]

Microscopy in a hot stage X-ray diffraction using powder and differential scanning calorimetry Spin lattice relaxation time in NMIR IH

Advantages :

Reduced particle size particles Improved wettability of the particles Greater porosity in the particles The amorphous state of drugs

Disadvantages :

The volatility of SDs is one of its main drawbacks. Temperature and moisture degrade solid dispersions more than they do physical mixtures.

Carriers for solid dispersion :[10]

a) Acids - Citric acid, Tartaric acid, Succinic acid.

b) Sugars – Dextrose, sucrose, sorbitol, Maltose, Galactose, Xylitol.

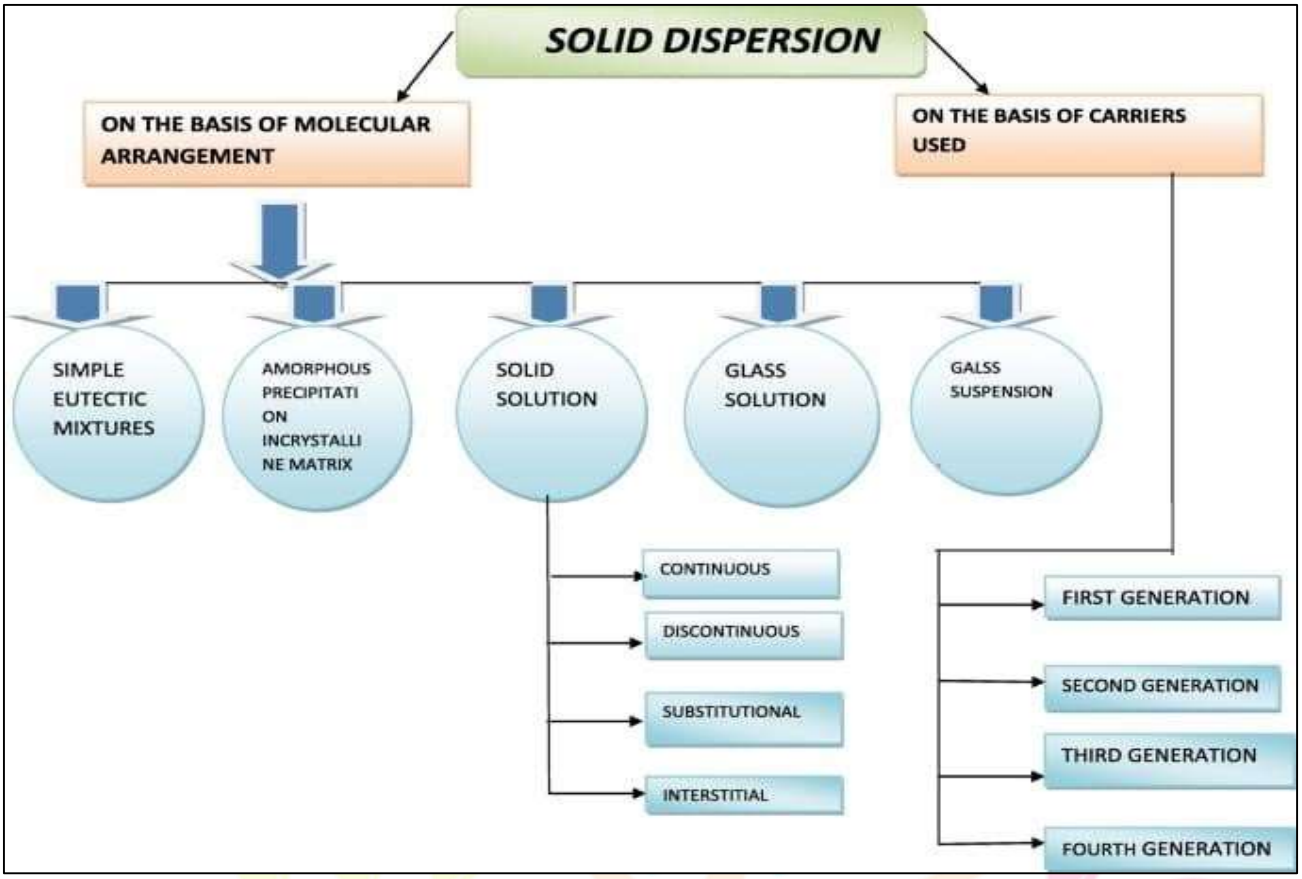
c) Polymeric materials – Polyvinylpyrollidone, PEG 4000, PEG 6000, HPMC, CMC, Guar gum, Sodium alginate, Cyclodextrin.

d) Surfactants – Poloxamer, Tween, Span, Gelucire 44/14, Deoxycholic acid, Polyoxyethelene stearate, Vitamin E TPGS NF.

Examples of surface active carriers improving dissolution rate of solid dispersions.[11]

carrier	Drug
Poloxamer 188	Ibuprofen
Poloxamer 407	Nifedipine
Poloxamer 188 and Gelucire 50/13	Nifedipine
Gelucire 44/14 or PEG 6000	Glibenclamide
Gelucire 44/14 and Soya lecithin	Ubidecarenone
PEG 8000, Gelucire 44/14, Vitamin E	Carbamazepine
Capmul MCM C10, Gelucire 44/14	Ceftriaxone

Classification:[11,12]



SOLID DISPERSION – METHODS OF PREPARATION.

a) Melt/Cool Method:
i) Melting Solvent Method
ii) Hot stage extrusion
b) Solvent Evaporation:
i) Hot Plate Drying
ii) Vacuum drying
iii) Slow evaporation at low temperature
iv) Rotary evaporation
v) Spray drying
vi) Freeze drying
vii) Spin drying
viii) Fluid bed coating
c) Co-precipitation
i) Addition of an anti-solvent
d) Dropping method

Hot Melt Extrusion:

In the pharmaceutical sector, melt extrusion was first employed as a manufacturing technique in 1971. In recent years, hot melt extrusion has become widely accepted as the preferred technique for creating solid dispersions. The physicochemical characteristics of the compounds and their miscibility in the molten state are crucial to the hot-melt extrusion process. If an overly high temperature is required during the melt extrusion process, particularly when the API's melting point is high, there is a chance that the polymer, the API, or both may degenerate. This study describes a unique process in which the API was melt-extruded with an appropriate polymer at a drug load of at least 20% w/w after initially being transformed into an

amorphous form by solvent evaporation. This made it possible to undertake melt extrusion at a temperature significantly lower than the drug's melting point. Content According to reports, when miscible components are melt-extruded, an amorphous solid solution is formed; nevertheless, when immiscible components are extruded, an amorphous drug is dispersed in crystalline excipients. In a single step, the method has proven helpful for creating solid dispersions.

Melting Solvent Method:

By directly filling hard gelatin capsules with semisolid ingredients as a melt that solidified at room temperature, Francois and Jones (1978) advanced the solid dispersion technique. According to Chatham, it is possible to create PEG-based solid dispersions by filling hard gelatin capsules with drug-PEG melts. The drug is first dissolved in an appropriate liquid solvent, and this solution is then added to the polyethylene glycol melt, which is accessible below 70C without the liquid solvent being removed. The polyethylene glycol melt may not be miscible with the chosen solvent or dissolved medication. Additionally, the liquid solvent utilized may have an impact on the polymorphic form of the medication that precipitated in the solid dispersion.[14]

SOLVENT EVAPORATION:

The solvent evaporation method involves dissolving the drug and carrier in an organic solvent. The solvent is evaporated once it has completely dissolved. The solid material is sieved, dried, and ground. For example, the solvent evaporation approach was used to create a solid dispersion of ofloxacin with polyethylene glycol.[15]

Co precipitation method :

The method of co-precipitation The necessary quantity of medication is added to the carrier solution. The system is shielded from light and maintained under magnetic agitation. To prevent the loss of the structural water from the inclusion complex, the precipitate is separated by vacuum filtration and allowed to dry at room temperature.[14,15]

Spray drying method:

The method of spray-drying The necessary quantity of carrier is dissolved in water, and the drug is dissolved in an appropriate solvent. After that, solutions are combined using sonication or another appropriate technique to create a transparent solution, which is subsequently spray-dried with a spray dryer.[16,17]

Dropping Method :

The dropping method is a novel technique for creating spherical particles from melted solid dispersions that was created to aid in the crystallization of various substances. Some of the issues with the other approaches might be resolved by this strategy. A solid dispersion of a melting drug-carrier mixture is pipetted and then deposited onto a plate for laboratory-scale production, where it hardens into spherical particles. The dropping process might be facilitated by the use of carriers that solidify at room temperature. In addition to streamlining the production process, the dropping approach increases the rate of dissolution. It has none of the issues related to solvent evaporation because it doesn't employ organic solvents[17,18,19]

Conclusion:

As the number of medication candidates that are poorly soluble rises, so does the demand for advancements in drug production technology. Thus, solid dispersion technology appears to be a viable way to enhance these medications' dissolving properties. More large-scale manufacturing advancements, improved forecasts of whether a given drug/carrier combination will result in a partially crystalline dispersion or a true solid solution, and whether the dispersion will maintain its physical stability through additional processing and storage are some of the issues that still need to be addressed in the upcoming years. Last but not least, even though the focus of this article has been on using solid dispersions to increase oral bioavailability and release rate, a drug's release pattern can also be delayed or slowed down by carefully selecting the carrier when creating a solid dispersion. Solid dispersions offer enormous potential in the field of controlled release dosage forms, as evidenced by the abundance of polymers that either swell in aqueous environments or are themselves poorly soluble. [20]

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