International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)

ISSN:2347-6567

IJAMSCR | Volume 9 | Issue 4 | Oct - Dec - 2021
www.ijamscr.com

Review article *Medical research*

Solid dispersion and its types a short review

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ABSTRACT

Solid dispersion has been a preferred method to enhance the certain drugs solubility. To improve dissolution of some low water-soluble drugs and then enhancing their bioavailability after the solid dispersion of one or more active pharmaceutical ingredient in a carrier at solid state is shall along with the suitable medium or polymer. It has been immersed significant interest as a method by which dissolution rate can be increased. It takes place as the dispersions of poorly water-soluble drugs with some water-soluble carriers for enhancing the dissolution of the drugs. The one of the most difficult aspects in formulation and development of a dosage form is the solubility performance of drugs. The poorly water soluble compounds has radically increased those are required a special attention to enhance the solubility of such compounds. The solid dispersions preparation needs to consider some aspects like, selection of carrier and methods of physicochemical characterization. In this review article a short notice has been given on solid dispersion its characterization, advantages, disadvantages and the application of the solid dispersions in various formulations.

Keywords: Solubility, Dissolution, Solid Dispersion, Carrier, Bioavailability.

INTRODUCTION

Oral route of drug delivery has always been the most favored route of administration due to the simplest and easiest way of administering. The oral dosage forms have many advantages over other formulations as accurate dosage, less bulk, better stability and easy of being produced.

Poorly water soluble compounds have been a challenge for oral drug delivery system to the most of the formulation scientists in the pharmaceutical industry. About 50 % of new drug molecules are poorly water soluble. For the Poorly water soluble compounds a large dose is required for showing desirable effects.

Poorly water soluble drugs show decreased release rate and reduced bioavailability as big dose may leads to toxicity of the drug loading. For improving the bioavailability the solubility need to be increased.3

FACTOR THOSE AFFECTS THE DRUG ABSORPTION:[3]

These are the physiological properties of drug substances and formulation factors as given below;2

The physiological properties	Formulation Factors	Gastro-Intestinal motility
• Particles size & effective surface area	• Disintegration time	• Membrane physiology:
• Polymorphism	• Manufacturing variables	• Nature of cell membrane
• Solvates & hydrates	• Method of granulation	• Transport processes
• Salt form of drug	• Compression force	• Gastric emptying rate
• Ionization state	• Nature & type of dosage form	• Intestinal motility

• Drug pka & lipophilicity	• Pharmaceutical ingredients • Product age & storage conditions	• Drug stability in GIT • pH of GIT • Surface area of GIT • Intestinal transit • Blood flow to GIT. • Effect of food

WHAT IS SOLUBILITY![5]

The amount of drug that has passed into solution when equilibrium is attained between the solution and excess, undissolved substance, at a given temperature and pressure.

The substance that is to dissolved is called as 'solute' and the dissolving liquid in which the solute is dissolved is called as 'solvent', which together form a monophasic 'solution'.

DEFINITION OF DIFFERENT SOLUBILITY TERMS [3]

Description forms (solubility definition)	Parts of solvent required for one part of solute	Solubility range (mg/ml)	Solubility assigned (mg/ml)
Very soluble (VS)	<1	>1000	1000
Freely soluble (FS)	1 to 10	100 -1000	100
Soluble	10-30	33-100	33
Sparingly soluble (SPS)	30-100	10-33	10
Slightly soluble (SS)	100-1000	1-10	1
Very slightly soluble (VSS)	1000-10000	0.1-1	0.1
Practically insoluble (PI)	>10000	<0.1	0.01

METHODS /TECHNIQUES/APPROACHES FOR THE SOLUBILITY IMPROVEMENT OF POORLY WATER SOLUBLE DRUG: [9,11,14]

Chemical Modifications	Physical Modifications	Others
• Salt Formation • Co-crystallization • Co-solvency • Hydrotropic • Solubilizing agent • Nanotechnology	• Particle size reduction • Modification of the crystal habit • Complexation • Solubilization by surfactants • Drug dispersion in carriers i.e., Solid dispersions	• Supercritical fluid method • Spray freezing into liquid and Lyophillization • Evaporative precipitation into aqueous solution • Hot melt extrusion • Electrostatic spinning method • Direct capsule filling • Polymeric Alteration • High- Pressure Homogenization • Inclusion Complexes

For the solubility and dissolution rate incensement of the class II drug in the gastro-intestinal fluids the bioavailability may be improved.16,17,18

SOLID DISPERSIONS

The Solid dispersion is a process by which one or more active ingredients in an inert carrier or matrix at solid state are prepared by using different techniques like the melting (fusion), solvent evaporation and melting-solvent method.9

DIFFERENT TYPES OF SOLID DISPERSIONS:[5,9]

They can be distinguished as;

- As carrier used
- As drugs molecular arrangement

AS CARRIER SHALL

On the basis of carrier shall in the formulation of the solid dispersions can be classified into the three given generations:

1ST GENERATION

In this method crystalline carriers are shall such as urea and carbohydrates specially sugars, first generation solid dispersions can be prepared which were the first carriers to be employed in solid dispersions. There are some disadvantages like crystalline solid dispersions and did not release the drug as fast as amorphous ones can do.5

2ND GENERATION

The Second generation solid dispersions which includes the amorphous carriers instead of crystalline carriers which are mainly polymers. These includes the synthetic polymers like poly vinyl povidone (PVP), polyethyleneglycols (PEG) and polymethacrylates as well as some natural products based polymers like hydroxylpropylmethyl-cellulose (HPMC), ethyl cellulose, and hydroxypropylcellulose or starch derivatives

like cyclodextrins.8

3RD GENERATION

The dissolution profile can be improved if the shall carrier in solid dispersion has surface activity or self-emulsifying properties. That's why the 3rd generation solid dispersions has been occurred. 11

AS DRUG MOLECULAR ARRANGEMENT

Solid dispersions can have such categories as following types:

EUTECTICS SYSTEMS

In this type of mixture two compounds which in the liquid state are completely miscible but in the solid state only to a very limited extent. A very quick solidification of the fshall melt of two components these are arranged and that show complete liquid miscibility and small solid-solid solubility.19

AN AMORPHOUS PRECIPITATION IN A CRYSTALLINE CARRIER

The crystalline carrier has the drug that can also precipitate in an amorphous form instead of concurrent crystallization of the drug and the carrier (eutectic system). The amorphous solid state. The high energy state of the drug in this system generally produces much greater dissolution rates than the corresponding crystalline forms of the drug.17

GLASS SOLUTIONS AND SUSPENSIONS

These homogeneous glassy systems are in which solute is dissolved in glass carrier. Glass suspensions are the mixtures in which precipitated particles are suspended in glass solvent. The Lattice energy is much lower in glass solutions and suspensions.14

SOLID SOLUTIONS

A homogeneous one phase system is formed here when the two components crystallize together. The particle size of the drug is abridged to its molecular size in the solid solution. So a faster dissolution rate is achieved in a solid solution than the corresponding eutectic mixture. Solid solutions can be classified as continuous or discontinuous according to the extent of miscibility of the two components. In continuous solid solutions, the two component are miscible in the solid state in all proportions.13

CONTINUOUS SOLID SOLUTIONS

The components are miscible in all proportions in a continuous solid solution. Hypothetically, this means that stronger the bonding strength between the two components than the bonding strength between the molecules of each of the individual components.19

DISCONTINUOUS SOLID DISPERSIONS

Here the solubility of each of the components in the other component is limited in the case of discontinuous solid solutions. One of the solid components is completely dissolved in the other solid component in these regions. The joint solubility's of the two components start to decrease below a certain temperature.

SUBSTITUTIONAL CRYSTALLINE SOLID SOLUTIONS

A substitutional crystalline solid dispersion is depicted in which the solute molecules substitute for the solvent molecules in the crystal lattice. Substitution is only possible when the size of the solute molecules differs by less than 15% or so from that of the solvent molecules.13

TECHNIQUES FOR SOLID DISPERSIONS: [14, 16]

- Solvent evaporation
- Hot-melt extrusion
- Fusion method
- Solvent melt method
- Kneading technique
- Inclusion complexes
- Direct capsule filling
- Surface active carriers
- Particle size reduction
- Adsorption on insoluble carriers/fluidized bed system
- Solid deposition on super disintegrants
- Melt agglomeration method
- Dropping method

SOME ADVANTAGES OF SOLID DISPERSION: [1]

The solid dispersions technique have the following pharmaceutical advantages.

- Solid dispersion technique is useful to enhance solubility and bioavailability of poorly water soluble drugs**.**
- It is ease to produce and is more applicable
- It leads to increase in extent and rate absorption of a drug, hence rapid dissolution rate occurs.
- Transformation of liquid form of drug into solid form.
- Control of various parameters like molecular weight, composition, particle porosity and wettability can enhance the bioavailability of poorly water soluble drugs.
- It is ease to produce rapid disintegration oral tablets by solid dispersion.
- It is shall to mask the bitter taste of drug.
- It is shall to improve porosity of drug.

DISADVANTAGE OF SOLID DISPERSION: [13]

The disadvantages of solid dispersion are enlisted below:

- It leads to the poor scale-up for the purpose of manufacturing.
- The polymers shall in solid dispersion can absorb

moisture and cause phase-separation, crystal growth and convert amorphous form into crystalline form. Thus result in decrease solubility and dissolution rate.
- It is laborious method ofpreparation.
- It causes reproducibility of physicochemical characteristics.

APPLICATIONS OF THE SOLID DISPERSION:[11]

- The Solid dispersion systems were shown to provide the bio available oral dosage forms for the anti-cancer drugs, which could be substituted for the standard injections to improve the patient compliance & comfort.
- Solid dispersion also act as the functional carriers that offer the added benefit of the targeting the release of the highly soluble forms of the poorly water soluble drugs for absorption to an optimum site.
- The solid dispersion systems were also found to reduce the food effects on the drug absorption, thus by increasing the convenience of the drug therapy as it is the need for some drugs to be taken with food was eliminated.
- The solid dispersion formulations were demonstrated to accelerate the onset of action for the drugs such as NSAIDS [non-steroidal anti-inflammatory drugs] where immediate action is crucial in relieving acute pain and inflammation.
- The improved absorption efficiency was demonstrated for the solid dispersion systems that allows for the reduction in the content of the active agent per dose thus it decreases the cost associated with these drug therapies.
- The dry powder formulation consisting of the solid dispersion for use as inhalation is prepared in improving the immunosuppressive therapy in the lung transplant patients. Many problems can be avoided which includes use of local anaesthesia & irritating solvents.

DISADVANTAGES OF SOLID DISPERSIONS:[3]

- Laborious and expensive methods of preparation.
- Reproducibility of physicochemical characteristics.
- Difficulty in incorporating into formulation of dosage forms.
- Scale-up of manufacturing process.
- Stability of the drug and vehicle

CARRIER SELECTION:[4]

A carrier shall be,
- Non-toxic and pharmacologically inert.
- Heat stable with a low melting point for the melt method.
- Soluble in a variety ofsolvents.
- Able to preferably increase the aqueous solubility of the drug and
- Chemically compatible with the drug and not form a strongly bonded complex with the drug.

FIRST GENERATION CARRIERS

Example: Crystalline carriers: Urea, Sugars, Organic acids.

SECOND GENERATION CARRIERS:7

Example: Fully synthetic polymers include povidone (PVP), polyethyleneglycols (PEG) and polymethacrylates. Natural product based polymers are mainly composed by cellulose derivatives, such as hydroxypropylmethylcellulose (HPMC), ethylcellulose or hydroxypropylcellulose or starch derivates, like cyclodextrins.

THIRD GENERATION CARRIERS:1

Example: Surface active self emulsifying carriers: Poloxamer 408, Tween 80, and Gelucire 44/14

SOLVENTS SELECTION: 2

Solvent shall be,
- Both drug and carrier must be dissolved.
- Toxic solvents to be avoided due to the risk of residual levels after preparation e.g. chloroform and ichloromethane.
- Ethanol can be shall as alternative as it is less toxic.
- Water based systems are preferred.
- Surfactants are shall to create carrier drug solutions but as they can reduce glass transition temperature, so care must be taken in to consideration.

Common solvent shall.

CHARACTERIZATION OF SOLID DISPERSION:5

Solid dispersion is characterised by using different techniques such as; Differential Scanning Calorimetry, Differential Thermal Analysis, Thermo-Microscopic Methods, X- ray Diffraction, Fourier Transform Infra Red Spectroscopy (FT- IR), Scanning Electron Microscopy (SEM) and dissolution studies.

Different techniques are:

DIFFERENTIAL SCANNING CALORIMETRY (DSC):

Differential Thermal Analysis (DTA)
Thermo-Microscopic Methods:
X- ray Diffraction:
Dissolution Studies:
Fourier Transform Infra Red Spectroscopy (FT-IR):
Scanning Electron Microscopy (SEM):

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How to cite this article: Dr. Mayank Bansal, Mr. Jitendra Kumar, Mr. Ashutosh Sharma, Ms. Afreen Khan Solid dispersion and its types a short review .Int J of Allied Med Sci and Clin Res 2021; 9(4): 661-665.

Source of Support: Nil. **Conflict of Interest:** None declared.