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ORAL BIOAVAILABILITY IMPROVEMENT USING SOLID DISPERSION TECHNIQUES: A REVIEW

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ABSTRACT: A solid dispersion is the dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by melting, solvent, or melting-solvent Method. The poor solubility of drug substances in water and their low dissolution rate in the aqueous gastro-intestinal fluids often lead to insufficient bioavailability. If the dissolution rate of the active ingredient in the gastrointestinal liquid is the rate-limiting factor for the absorption of the drug, the objective of the formulation will have to be an increase in the dissolution rate. From many years, variety of solubility techniques have been used & studied for increasing solubility of poorly soluble drugs. Around 40% of chemical entities discovered by pharmaceutical industry are poorly soluble in nature. Solid dispersion is one of these methods, which was most widely and successfully applied to improve the solubility, dissolution rate & bioavailability of the poorly soluble drugs. This article reviews historical background of solid dispersion technology, limitations, classification, and various preparation techniques with its advantages and disadvantages. This review also discusses the recent advances in the field of solid dispersion technology and gives rise to reasoning and suggested choices of carrier or matrix and solid dispersion procedure.

Keywords: Melting-solvent method, Dissolution rate, Bioavailability, Solid dispersion, Solubility enhancement

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INTRODUCTION: Oral drug delivery is the more preferable route of drug administration due to the ease of administration, patient conformity, flexibility in formulation, *etc.* However, in case of the oral route there are several challenges such as limited drug absorption resulting in poor bioavailability and poor pharmacological response resulting in inadequate and erratic oral absorption [1].

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When delivering an active agent orally, it must first dissolve in gastric and intestinal fluids before it can then permeate the membranes of the GI tract to reach the systemic circulation. Therefore, a drug with poor aqueous solubility will typically exhibit dissolution rate limited absorption, and a drug with poor membrane permeability will typically exhibit permeation rate limited absorption.

Hence, two areas of pharmaceutical research that focus on improving the oral bioavailability of active agents include enhancing solubility and dissolution rate of poorly water-soluble drugs and enhancing the permeability of poorly permeable drugs. Hence, solubility enhancement method is used for poorly soluble drugs [2].

TABLE 1: TECHNIQUES FOR SOLID DISPERSION

Chemical Modifications	Physical Modifications	Other
Salt Formation	Particle size reduction	Supercritical fluid method
Co-crystallization	Modification of the crystal habit	Spray freezing into liquid and Lyophilization
Co-solvency	Complexation	Evaporative precipitation into aqueous solution
Hydrotropic	Solubilization by surfactants	Hot melt extrusion
Solubilizing agent	Drug dispersion in carriers	Electrostatic spinning method
Nanotechnology	Solid solution, Eutectic mixtures, Solid dispersion	Direct capsule filling

For increasing solubility, various solubility enhancement techniques summarized in the following table are used, such as following [3, 4].

Solid Dispersions:

Definition: The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles (clusters) or crystalline particles. Therefore, based on their molecular arrangement, six different types of solid dispersions can be distinguished. Moreover, certain combinations can be encountered, *i.e.*, in the same sample; some molecules are present in clusters while some are molecularly dispersed [5, 2]

Types of Solid Dispersion: [6]

First Generation Solid Dispersions: Solid dispersions were first described by Sekiguchi and Obi in 1961 in which they used the concept of eutectic mixtures. They mentioned that the formulation of eutectic mixtures improve the rate of drug release and thus increase the bioavailability of the poorly soluble drug. Thus the first generation solid dispersions were prepared using crystalline carriers. Eutectic mixtures are binary systems comprising of poorly water-soluble drug and highly water-soluble carrier and at eutectic point drug crystallizing out simultaneously only in the specific composition. When the eutectic mixture is dissolved in an aqueous medium, the carrier part will dissolve quickly, and the drug will be released in the form of fine crystals. The main disadvantage of the first generation Solid dispersion is crystalline nature, which leads to less solubility as compared to amorphous form, however, they possess good thermodynamic stability. First generation solid dispersion were generally prepared using crystalline carriers like urea, mannitol.

Second Generation Solid Dispersions: In second generation instead of crystalline carriers, amorphous carriers were used to diffuse drugs which are generally polymers. Polymeric carriers can be of fully artificial origin like povidone, polyethylene glycols and polymethacrylates whereas natural product based polymers comprises of cellulose derivatives like hydroxypropyl methylcellulose, ethylcellulose or starch derivatives, like cyclodextrins. Amorphous solid dispersions are further classified as solid solutions, solid suspension or mixture of both as per molecular interaction of drug and carrier. Amorphous carriers: Polyethyleneglycol, Povidone, Polyvinylacetate, Polymethacrylate, cellulose derivatives.

Third Generation Solid Dispersions: In the third generation, solid dispersion surfactants carrier or a mixture of the polymer are used as a carrier. If a carrier has surface active or self-emulsifying properties, the dissolution profile of poorly soluble drug can be enhanced and hence result in increased bioavailability. Typically used surfactants as solid dispersion carriers are poloxamer 407, gelucire 44/14, compritol 888 ATO27, inulin.

Advantages of Solid Dispersion: [7] The major advantage of solid dispersions is that it improves the dissolvability of a poorly water-soluble drug in a pharmaceutical composition and results in rapid dissolution rates, thereby improving the bioavailability of the drug. Along with this, the approach may also offer other advantages, which include:

Rapid Disintegration of Oral Tablets: The drug is formulated with the hydrophilic carrier (*e.g.*, PEG) as a solid dispersion to increase its aqueous solubility and dissolution. Then superdisintegrant (*e.g.*, croscarmellose sodium) is used in a tablet formulation to achieve rapid disintegration of

tablets prepared by wet granulation method. These rapidly disintegrating tablets can be used as an alternative to parenteral therapy, enabling patient for self-medication even lacking the aid of water.

As a Formulation Vehicle: Solid dispersions can be used as a formulation vehicle for ease of preclinical safety and early clinical studies on new chemical entities with very low aqueous solubility. It provides a means to rapidly assess the safety and efficacy profile of the drug substance that may be otherwise complicated to obtain.

Particles with Reduced Particle Size: Solid dispersions characterize the last state on particle size reduction, and after carrier dissolution, the drug is molecularly dispersed in the dissolution medium. Solid dispersions apply this principle to drug release by creating a mixture of a poorly water-soluble drug and very soluble carriers, thus a high surface area is formed, resulting in an increased dissolution rate and therefore enhanced bioavailability.

Particles with Improved Wettability: Improvement of drug solubility is related to drug wettability. It was observed that even carriers without any surface activity, such as urea improved drug wettability. Carriers with surface activity, such as cholic acid and bile salts when used, significantly increase the wettability of drug. Moreover, carriers can influence the drug dissolution profile by direct dissolution or co-solvent effects.

Particles with Higher Porosity: Particles in solid dispersions have been found to have a higher degree of porosity. Solid dispersions containing linear polymers produce larger and more porous particles than those containing reticular polymers and, therefore, results in a higher dissolution rate. The increased porosity of solid dispersion particles also increases the drug release rate.

Drugs in the Amorphous State: The improvement of drug release can usually be achieved if the drug in its amorphous state because no energy is required to break up the crystal lattice during the dissolution process. In solid dispersions, drugs are presented as supersaturated solutions after system dissolution, and it is speculated that if drugs precipitate it is as a metastable polymorphic form with higher solubility than the most stable crystal form

Disadvantages of Solid Dispersion: [8] Disadvantages of solid dispersions are mainly related to their instability. Changes occur in several systems in crystallinity, and a decrease in dissolution rate with aging and system may be destabilized through physical treatment such as pulverization and aging. There is the more deteriorating effect of moisture and temperature on solid dispersions than on physical mixtures. Usually, solid dispersions are prepared with water-soluble low melting point synthetic polymers such as polyvinyl pyrrolidone, mannitol or polyethylene glycol. These polymers show superior results in drug dissolution enhancement, but the amount of these polymers required is relatively large, around 1:2 to 1:8 (drug/ polymer) ratio.

An obstruction of solid dispersion technology in pharmaceutical product development is that a large amount of carrier, *i.e.*, more than 50% to 80% w/w, is required to achieve the desired dissolution. Solid dispersion is a high energy metastable form. Phase separation, crystal growth or conversion from the amorphous to the crystalline form during storage decrease solubility and dissolution rate and result in variable oral bioavailability.

Selection of the Carrier: [2] The selection of the carrier effect on the dissolution characteristics of the dispersed drug, since the dissolution rate of one component from the surface is affected by the other component in a multiple component mixtures. Therefore, a water-soluble carrier results in a faster release of the drug from the matrix. A poorly soluble or insoluble carrier leads to the slower release of a drug from the matrix. If the active drug present is a minor component in the dispersion, faster release of a drug can be achieved from matrix.

Pharmaceutical Application of Solid Dispersion Technique: [2, 9]

1. To improve the solubility of poorly soluble drugs, thereby improve the dissolution rate, absorption, and bioavailability.

2. To obtain a uniform distribution of a small amount of drug in a solid state.

3. To stabilize unstable drugs and protect against decomposition by processes such as hydrolysis, oxidation, racemization, photo-oxidation etc.

4. To dispense liquid or gaseous compounds;

5. To formulate a fast release priming dose in a sustained release dosage form;

6. To formulate sustained release preparation of soluble drugs by dispersing the drug in the poorly soluble or insoluble carrier;

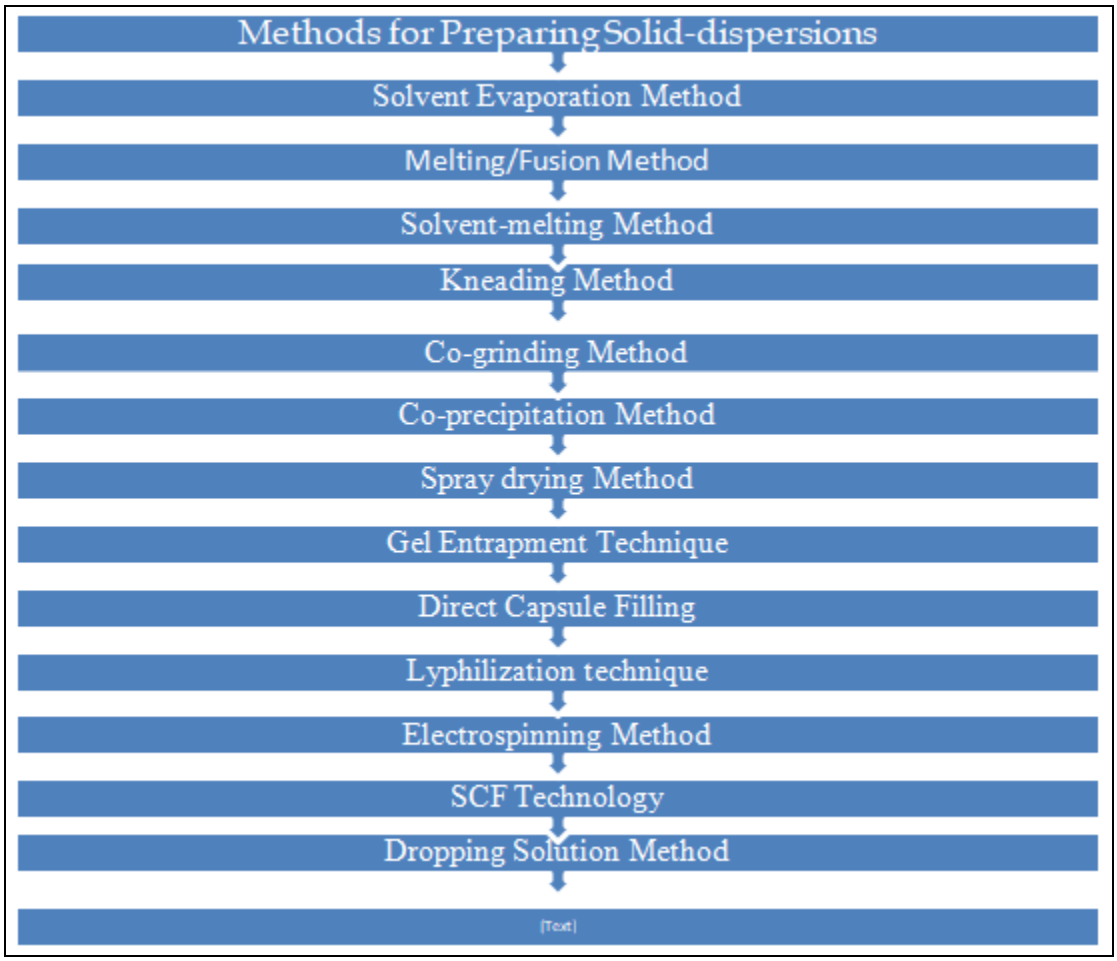
7. To reduce side effects-(a) the binding ability of drugs for example to the erythrocyte membrane is decreased by making its inclusion complex, (b) the damage to the stomach mucous membranes by certain non-steroidal anti-inflammatory drugs can be reduced by the administration as an inclusion compound;

8. To mask the obnoxious taste and smell and avoid undesirable incompatibilities.

9. To convert liquid compounds into formulations. Liquid drugs can be manufactured as solid drug formulations such as powders, capsules or tablets, *e.g.,* unsaturated fatty acids, essential oils, nitroglycerin, benzaldehyde, prostaglandin, clofibrate, *etc.*

10. To reduce pre systemic inactivation of drugs like morphine and progesterone.

Flow Chart:



FLOW CHART 1: METHODS OF PREPARATION OF SOLID DISPERSION

Methods of Preparation of Solid Dispersion: [10, 11]

Melting Method: The melting or fusion method is the preparation of a physical mixture of a drug and a water-soluble carrier and heating it directly until it melted. The melted mixture is then solidified rapidly in an ice-bath under vigorous stirring. The final solid mass is crushed, pulverized, and sieved. Appropriately this has undergone many changes in pouring the homogenous melt in the form of a thin layer onto a Petri plate or a stainless steel plate and

cooled by flowing air or water on the opposite side of the plate. Also, a super-saturation of a solute or drug in a system can often be obtained by quenching the melt rapidly from a high temperature.

Under such conditions, the solute molecule is in confinement state in the solvent matrix by the immediate solidification process. The quenching technique gives a much finer dispersion of crystallites when used for simple eutectic mixtures. However, many substances, drugs, or carriers, may deteriorate during the fusion process, which employs high temperature. It may also cause evaporation of volatile drug or volatile carrier during the fusion process at high temperature. Some of the means to overcome these problems could be heating the physical mixture in a sealed container or melting it under vacuum or in the presence of inert gas like nitrogen to prevent oxidative decay of drug or carrier.

Solvent Method: In this method, the physical mixture of the drug and carrier is dissolved in a common solvent, which is evaporated until a clear, solvent free film is left. The film is further dried to constant weight. The main advantage of the solvent method is the thermal decomposition of drugs or carriers can be prevented because of the relatively low temperatures required for the evaporation of organic solvents. However, some disadvantages are associated with this method, such as:

- The higher cost of preparation.
- The difficulty in completely removing the liquid solvent.
- The possible undesirable effect of traces of the solvent on the chemical stability
- The selection of a common volatile solvent.
- The difficulty of reproducing crystal form.
- Also, supersaturation of the solute in the solid system cannot be attained apart from in a System showing highly viscous properties.

Melting Solvent Method (Melt Evaporation): It involves preparation of solid dispersions by dissolving the drug in a proper liquid solvent and then add the solution directly into the melt of polyethylene glycol, which is then evaporated until a clear, solvent free film is left. The film is further dried to constant weight. The 5-10% (w/w) of liquid compounds can be added into polyethylene glycol 6000 without significant loss of its solid property. It is possible that the selected solvent or dissolved drug may not be miscible with the melt of the polyethylene glycol. Also, the liquid solvent used may affect the polymorphic form of the drug, which precipitates as the solid dispersion. This technique possesses unique advantages of both the fusion and solvent evaporation methods. From a practical standpoint, it is only limited to drugs with a low therapeutic dose, *e.g*., below 50 mg.

Melt Extrusion Method: The drug/carrier mix is typically processed with a twin screw extruder. The drug / carrier mix is simultaneously melted, homogenized, and then extruded and shaped as tablets, granules, pellets, sheets, sticks, or powder. The intermediates can then be further processed into conventional tablets. An important advantage of the hot melt extrusion method is that the drug/carrier mix is only subjected to a higher temperature for about 1 min, which enables drugs that are somewhat thermo labile to be processed.

Solid dispersion by this method is composed of active ingredient and carrier, and prepare by hostage extrusion using a corotating twin-screw extruder. The concentration of drug in the dispersions is always 40% (w/w). The screw-configuration consist of two mixing zones and three transport zones distribute over the entire barrel length, the feeding rate is fixed at 1 kg/h, and the screw rate is set at 300 rpm. The five temperature zones are set at 100, 130, 170, 180, and185C from feeder to die. The extrudes collect after cooling at ambient temperature on a conveyer belt. Samples are milled for 1 min with a laboratory cutting mill and sieve to exclude particles >355μm.

Lyophilization Technique: Lyophilization involves the transfer of heat and mass too and from the product under preparation. This technique was planned for as an alternative technique to solvent evaporation. Lyophilization has been thought of a molecular mixing technique where the drug and carrier are co-dissolved in a common solvent, frozen and sublimed to obtain a lyophilized molecular dispersion.

Vial Freeze-Drying: Dissolve the drug in the solvent at a fixed concentration. Dissolve the carrier in water. Mix both the solution in a ratio of 40/60 v/v. afterward immerses the mixture in liquid nitrogen until it gets fully frozen. Various concentration of drug in the resulting solid dispersions is obtained by adjusting carrier concentrations while maintaining drug concentration constant. Then lyophilize the frozen solution by lyophilizer. Lyophilization is performed according to a two-step procedure,

- Firstly set the pressure at 0.22 mbar & the shelf temperature at (-35 °C) for 1 day.
- Subsequently release the pressure to 0.05 mbar, while raising the shelf temperature up to 200. Maintain these conditions for another day. After removing the samples from the freeze dryer, place them in a vacuum desiccator over silica gel at room temperature for at least 1 day.

Spray Freeze Drying: Dissolve the drug in a solvent at a fixed concentration and carrier in water. Mix the solution in a ratio of 40/60 v/v. spray the solutions through the nozzle into liquid nitrogen. Set the liquid feed rate and atomizing air flow. Position the outlet of the nozzle at about 10cm above the liquid nitrogen. Hot water is pumped through the jacket of the nozzle to avoid freezing of the solution inside the nozzle. Shift the resulting suspension (frozen droplets of the solution in liquid nitrogen) to the lyophilizer. Lyophilization procedure is started as soon as all liquid nitrogen is evaporated.

Melt Agglomeration Process: This technique has been used to prepare solid dispersion wherein the binder acts as a carrier. Also, solid dispersion is prepared either by the heating binder, drug, and excipient to a temperature above the melting point of the binder (melt- in procedure) or by spraying a dispersion of drug in a molten binder on the heated excipient (spray-on procedure) by using a high shear mixer.

The rotary processor might be preferable to the high melt agglomeration because it is easier to control the temperature and because a higher binder content can be incorporated in the agglomerates. The effect of binder type, method of manufacturing, and particle size are critical parameters in preparation of solid dispersion by melt agglomeration. It has been found that the melt in procedure gives higher dissolution rates than the spray-on procedure with PEG 3000, poloxamer 188, and gelucire 50/13 credited to immersion mechanism of agglomerate formation and growth. Also, the melt in procedure also results in the homogenous distribution of the drug in agglomerate. Larger particles result in the densification of agglomerates while fine particle causes complete adhesion to the mass to bowl shortly after melting attributed to distribution and coalescence of the fine particles.

Electrospinning: Electrospinning is a process in which solid fibers are produced from a polymeric fluid stream solution or melt delivered through a millimeter-scale nozzle. This process includes the application of a strong electrostatic field over a conductive capillary attaching to a reservoir containing a polymer solution or melt and a conductive collection screen. Upon increasing the electrostatic field strength up to but not more than critical value, charge species accumulated on the surface of a hanging drop destabilize the hemispherical shape into a conical shape.

Beyond the critical value, a charged polymer jet is expelled from the apex of the cone (as a way of relieving the charge built-up on the surface of the pendant drop). The expelled charged jet is then carried to the collection screen via the electrostatic force. The Columbia repulsion force is responsible for the thinning of the charged jet during its route to the collection screen. The thinning down of the charged jet is limited. If the viscosity increases, the charged jet is dried.

This technique has significant potential for the preparation of nanofibers and controlling the release of biomedicine, as it is simplest, the cheapest this technique can be used for the preparation of solid dispersions in the future.

Super Critical Fluid Technology: The supercritical fluid antisolvent techniques, carbon dioxide, are used as an antisolvent for the solute but as a solvent concerning the organic solvent. Different acronyms were used by various authors to denote micronization processes: aerosol solvent extraction system, precipitation with a compressed

fluid anti-solvent, gas anti-solvent, and solution enhanced dispersion by supercritical fluids and supercritical anti-solvent. The SAS process includes the spraying of the solution containing a solute and of the organic solvent into a continuous supercritical phase flowing simultaneously. Use of supercritical carbon dioxide is profitable as it is much easier to remove from the polymeric materials when the process is complete, even though a small amount of carbon dioxide remains trapped inside the polymer; it poses no hazard to the patient.

Also, the capability of carbon dioxide to plasticize and swell polymers can also be subjugated, and the process can be carried out near room temperature. Moreover, supercritical fluids are used to lower the temperature of the melt dispersion process by lowering the melting temperature of the dispersed active agent. The reason for this depression is the solubility of the lighter component (dense gas) in the forming phase (heavier component).

Spray Drying: Dissolve the various amounts of carriers in water. Then disperse the 10gm of the drug, pre-sieved through a 60-mesh screen in the solution. The resulting scattering is subjected towards the nozzle at a flow rate previously fixed using a peristaltic pump & spray dry it at an inlet temperature of about 120 °C & an outlet temperature of about 65-70 °C. Fix the spray pressure. Maintain the flow rate of drying air at the aspirator. After spray-drying, collect each resulting powders by cyclone separation and transferred to glass vials.

High- Pressure Homogenization: The high-pressure homogenization involves dispersing a drug powder in an aqueous surfactant solution and passing through a high-pressure homogenizer; afterward, nanosuspensions are obtained. The cavitation force experienced is sufficient to split up the drug from microparticles to nanoparticles. The particle size is dependent on the hardness of the drug substance, the processing pressure, and the number of cycles applied. However, only fragile drug candidates might be broken up into nanoparticles by this technique.

Polymeric Alteration: Different crystalline forms of a drug that may have different properties are known as Polymorphs. Polymorphs may differ in physicochemical properties such as physical and chemical stability, shelf-life, melting point, vapor pressure, intrinsic solubility, dissolution rate, morphology, density, and biological activities as well as bioavailability. It is convenient to develop the most thermodynamically stable polymorph of the drug to assure reproducible bioavailability of the product over its shelf-life under a variety of real-world storage conditions

Inclusion Complexes:

A) Kneading Technique: Mix drug and polymer with the small amount of the solvent, *i.e.* water to form a thick paste by kneading and hence it is dried at 45 C in an oven. Pass the mass through the sieve no. 30 and store in the desiccators.

B) Co-precipitation: Add the required amount of drug to the solution of β- cyclodextrins. Keep the system under magnetic agitation with controlled process parameters and protect from the light. Separate the formed precipitate by vacuum filtration and then dry at room temperature to avoid the loss of the structured water from the inclusion complex.

C) Neutralization: Add drug in an alkaline solution like sodium hydroxide, ammonium hydroxide. Then add a solution of β- cyclodextrin to dissolve the join drug. The clear solution is obtained after a few seconds under agitation. Then neutralize it using HCl solution until the equivalence point is reached. At this moment, the appearance of a white precipitate could be esteemed, corresponding to the formation of the inclusion compound. Finally, filter and dry the precipitate.

D) Co-grinding: Weigh the calculated amounts of drug and carriers and mix with one ml of water. Pass the damp mass obtained, through a 44-mesh sieve; scatter the resultant granules in Petri dishes and dried at 60°C under vacuum, until a constant weight is obtained. Store the granules in desiccators until used for further studies.

E) Spray-Drying Method: Dissolve drug in a suitable solvent and the required stoichiometric amount of carrier material like β- cyclodextrin in water. Mix the solutions by sonication or another

appropriate method to produce a clear solution. Dry it using spray dryer.

F) Microwave Irradiation Method: Drug and cyclodextrin mixture is reacted in a microwave oven to form inclusion. It is a novel method for industrial-scale preparation due to its major advantage of shorter reaction time and higher yield of the product.

Characterization of Solid Dispersions: [3, 11, 12] Several dissimilar molecular structures of the drug in the matrix can be encountered in solid dispersions. Several techniques have been available to examine the molecular arrangement in solid dispersions. However, most effort has been put in to differentiate between amorphous and crystalline material.

TABLE 3: MARKETED PRODUCTS PREPARED BY SOLID DISPERSION TECHNIQUE [13]

Product/ Substance	Dispersion Polymer or Carrier	Technology used	Company
Gris-PEG® (Griseofulvin)	Polyethylene glycol	Melt process	Novartis
Sproramax capsules (Itraconazole)	HPMC	Spray layering process	Janssen pharmaceutical
Cesamet® (Nabilone)	Polyvinylpyrrolidone	process unknown	Lilly
Kaletra (lopinavir and ritonavir)	HPMC acetate succinate	Melt-extrusion	Abbott Laboratories
Torcetrapib, Ibuprofen	PVP	Spray drying	Pfizer
Isoptin SRE-240 (Verapamil)	HPMC	Melt-extrusion	Soliqs
Rezulin (Troglitazone)	HPMC	Melt-granulation	Life Cycle Pharma

Various methods include Thermal analysis, DSC, Powder X-ray diffraction method, Spectroscopic methods (FTIR, NMR, Raman spectroscopy) microscopic method (Hot-stage microscopy) and *in-vitro* dissolution studies.

Recent Advances & Future Aspects: [14] Solid dispersion having great strength both for increasing the bioavailability of drug and developing controlled release preparations. Thus, to solve bioavailability issues concerning poorly water-soluble drugs, solid dispersion technology has grown rapidly.

The dosage form can be developed and prepared using small amounts of drugs substances in early stages of the drug development process; the system might have an advantage over such other commonly used bioavailability enrichment techniques as micronization of drugs and soft gelatin encapsulation. There are some most important research areas where concentration must be given in context to solid dispersion, which includes:

Identification of New Surface-Active Carriers and Self-Emulsifying Carriers: [15, 16] A major spotlight of future research will be the identification of new surface-active carriers and self-emulsifying carriers for solid dispersions. Only a small number of such carriers are currently available for oral use. Some carriers that are used for topical application of drug only may be capable for oral use by conducting appropriate toxicological testing. Two new surface active carriers were planned for

- Gelucire 44/14: It is a mixture of glycerol & PEG-1500 esters of long chain fatty acid
- Vitamin E TPGS NF (D-α-tocopheryl PEG 1000 succinate)

Identification of Vehicles: Research should also be intended toward recognition of vehicles or excipients that would delay or prevent crystallization of drugs from supersaturated systems. Concentration should also be given to any physiological and pharmacological effects of carriers used. Many of the surface-active and self-emulsifying carriers are lipidic, so important roles of such carriers on drug absorption, especially on their pglycoprotein-mediated drug efflux, require careful consideration

Bioavailability Enhancement: Solid dispersions have shown potential future for both rising the bioavailability of drugs and for developing controlled-release preparations. Few successful developments of solid dispersion systems for preclinical, clinical and commercial use have been practicable in recent years due to the availability of

surface-active and self-emulsifying carriers with relatively low melting points.

Extended-Release Dosage Forms: To enlarge, the release rate dosage form has been reinvigorated by the availability of surface-active and self-emulsifying carriers and the development of new capsule filling processes. Since the formulation of solid dispersion for bioavailability improvement and extended release of drugs may employ essentially similar processes, except for the use of slower dissolving carriers for the later use, it is expected that the research in these two areas will progress concurrently and be corresponding to each other.

CONCLUSION: Solid dispersion technique has emerged as an extremely important tool in improving the dissolution properties of poorly water-soluble drugs. Most of the promising NCEs are poorly water-soluble drugs, which may present a lack of therapeutic effect, because of their low bioavailability. Solid dispersions are one of the most attractive processes to improve drugs' poor water solubility. The third generation solid dispersions can improve their stability and performance by increasing drug-polymer solubility, amorphous fraction, particle wettability, and particle porosity. Moreover, new, optimized manufacturing techniques that are easily scalable are also coming out of academic and industrial research

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