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A REVIEW ON SOLID DISPERSION TECHNIQUE FOR ENHANCING SOLUBILITY OF POORLY SOLUBLE DRUGS

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ABSTRACT

Solid dispersion, defined as the dispersion of one or more active pharmaceutical ingredients in a carrier in the solid state, is an efficient technique for improving the dissolution and bioavailability of poorly water-soluble drugs. Solid dispersion has attracted considerable interest as an efficient means of improving the dissolution rate and hence bioavailability of a range of hydrophobic drugs Oral route is mostly preferred for administrating drug to patients. But due to the poor solubility many drugs have limited used in oral administration. Enhancement of water solubility of poor water-soluble drugs is in main target in a pharmaceutical field. Solubility is one of the most important factors which affect dissolution rate and bioavailability. Solid dispersion is widely employed technique in pharmaceutical science to enhance solubility of poorly soluble drugs this review article delves into the various aspect of solid dispersion, highlighting its significance and application in drug formulation and development.

KEYWORDS: Classification; Solid dispersion; Solubility; Dissolution; Bioavailability.

INTRODUCTION

Oral administration of most preferable for drug delivery because of minimal Invasiveness, ease of use, smaller unit, ease of production.[1,2] limited drug absorption resulting in poor bioavailability is paramount amongst the potential problems that can be encountered when delivering an active agent via the oral route. 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 permeability of poorly permeable drugs. Solid dispersion, defined as the dispersion of one or more active pharmaceutical ingredients in a carrier in the solid state, is an efficient technique for improving the dissolution and bioavailability of poorly water- soluble drugs. Poor water solubility is one of the major problems for various types of drugs, and various approaches have been introduced to improve the solubility of such drugs. Drug dissolution behaviour remains one of the most challenging aspects of formulation development. The number of compounds that are poorly soluble in water increased dramatically. Currently, only 10-12% of 4,444 drug candidates exhibit both high solubility and high permeability, 60-65% of over 4,444 active drugs have low water solubility. Solid dispersions have attracted great interest as an efficient means to improve the dissolution rate and thus the bioavailability of various hydrophobic drugs. Compared to traditional formulations such as tablets and capsules, solid dispersions, which can be prepared using a variety of methods, have many advantages. When producing solid dispersions, only a few aspects need to be considered, such as the choice of carrier and the method of physicochemical characterization. This review focuses on the different types of solid dispersions, their manufacturing processes, characterization, advantages, disadvantages, and applications of solid dispersions, as well as the challenges in formulating dosage forms of solid dispersions. An overview of the body in general. Types of commercially available preparations.

Solid Dispersion

The term of solid dispersion means a group of solid products composing of at least one or more different components mainly a hydrophilic matrix and hydrophobic drug. The matrix used can be crystalline or amorphous. The drug can be dispersed in amorphous particle or crystalline particles. Since its introduction by Sekiguchi and Obi in 1961, solid dispersion (SD) has been the most widely used solid-state reforming technology and has achieved great commercial success. Since his first FDA-approved SD, Cesamet® (Bausch Health Companies Inc., Laval, QB, Canada) in 1985, there are now over 30 amorphous solid dispersions in Class II and IV. It is commercially available as an oral dosage form using this technology. A solid dispersion (SD) can be defined as a solid mixture of one or more hydrophobic drugs and one or more hydrophilic carriers. The process involves the distribution of drug molecules in a hydrophilic carrier matrix at the molecular or colloidal level by melting (fusion), quenching, solvent evaporation, spray drying, freeze drying, or hot melt extrusion. In SD, the particle size of the drug decreases, increasing the surface area of

the drug in contact with the solvent, or the crystalline pure drug is converted to an amorphous form, increasing solubility. Based on the miscibility of the drug in the carrier, the final solid-state form (crystalline or amorphous), and the molecular arrangement, SD can be classified as (a) a simple eutectic mixture, (b) a solid solution, or (c) a glass. Can be prepared as a solution., (d) glass- suspension, or amorphous precipitate in a crystalline support.[3,4]

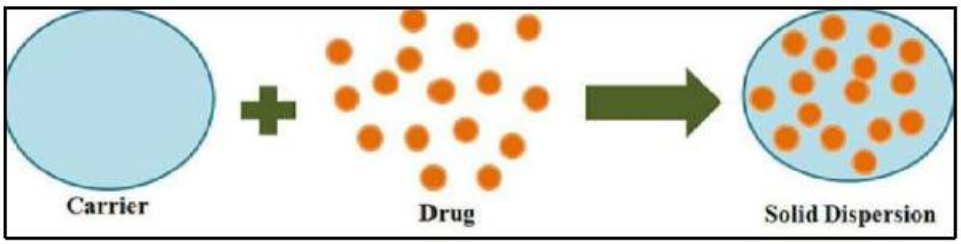

Fig. 1: Solid dispersion.

Solubility and it's types

Solubility is the property of a solid, liquid or gaseous chemical substance called solute in a solvent to form a homogenous solubility of a substance fundamentally depends on the solvent used as well as on temperatures and pressure. The extent of solubility of a substance in a specific solvent is measured as the saturation concentration where adding more solute does not increase its concentration on a solution.[5]

- **Intrinsic/absolute solubility:** The maximum amount of solute dissolve in a given solvent under slandered conditions of temperatures, pressure and pH is called as absolute or intrinsicsolubility.

- **Saturated solubility:** maximum amount of solute dissolve in a given solvent up to its Saturated level. Additionally solute will not dissolve in solvent table 1.

Table 1: USP and BP solubility criteria.

Descriptive term	Part of solvent required per part of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10000
Practically insoluble	10000 and over

Biopharmaceutical classification system (BCS)

Amidon et al, developed the biopharmaceutical classification system (BCS). The BCS classification of a drug depends upon its three key parameters that control absorption solubility, dissolution rate and permeability. BCS classified the drugs into one of the 4 groups which is as follow table 2.[6]

Table 2: BCS classification of drugs.

Class	Permeability	Solubility	Example
Class I	High	High	Diltiazem, Metoprolol, Propranolol
Class II	High	Low	Nifedipine, 4carbamazepine, Azilsartsn, Naproxen
Class III	Low	High	Insulin, metformin, cimetidine
Class IV	Low	Low	Taxol, chlorthiazide, furosemide

Table 3: Materials used as carrier for solid dispersion.[7,8]

Sr. No	Material used as carrier	Carriers
I.	Sugars	Dextrose, sucrose, galactose, sorbitol, maltose,
II.	Acid	Citric acid, succinic acid
III.	Polymeric material	Polyvinyl pyrimidine (PVP), polyethylene glycol (PEG), hydroxypropyl methyl cellulose (HPMC), methyl cellulose (MC), hydroxy ethyl cellulose, cyclodextrin, hydroxy propyl cellulose, pectin, galactomannan
IV.	Insoluble or enteric polymer	Hydroxy propyl methyl cellulose phthalate
V.	Surfactant	Polyoxyethylene stearate, poloxamer 188, deoxycholic acid,tweens, spans
VI.	Miscellaneous	Pentaerythritol, pentaerythrityl tetraacetate, urea, urethane,hydroxy alkyl xanthins

Types of solid dispersion[8,9]

1) Eutectics mixture
2) Amorphous solid solutions
3) Solid solution

a) Continuous solid solution
b) Discontinuous solid solution
c) Substitutional solid solution
d) Interstitial solid solution

1) Eutectics mixture

A simple eutectic mixture consists oftwo compounds Which are completely immiscible in the liquid but only to a very limited extent in the solid state. It is prepared by Rapid solidification of fused melt oftwo components that Show complete liquid miscibility but negligible solid

Solutions.[8,9,10] when a mixture of poor watersoluble and water-soluble carrier is dissolved in aqueous medium, the carrier is dissolved rapidly, realisingvery fine crystal of drug.

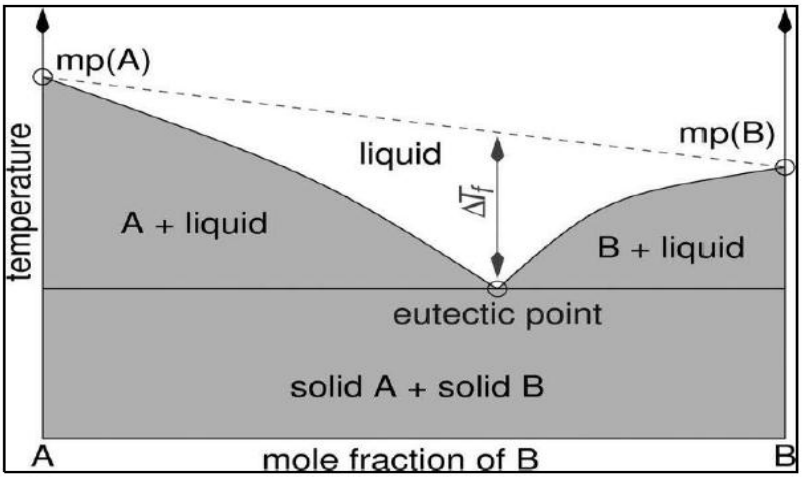

Fig. 2: Eutectics mixture.

2) Amorphous solid solution

This is same as simple eutectic mixtures but only Difference is that the drug is precipitated out in an amorphous Form.[8,11,12] ASD is a solid dispersion in which the active Ingredient is dispersedwithin an excipient matrix in a substantially Amorphous form.[29,30] Drug solubility and dissolution rate of Poorly water-soluble drugs can be successfully improved by formulating themas ASDs[32,33] With the drug in an amorphous Form, no energy is required to break the drug crystal lattice. For this Reason, relative to the crystalline form, the amorphous form of many Poorlywater-soluble drugs can achieve substantially higher apparent Solubility and markedly faster dissolution[34] ASDs are also known to Result in higher membrane flux due to a higher supersaturation and thus, improve bioavailability in crystalline carriers, drug may precipitate in an amorphous form instead of drug, resulting in simultaneous crystallization of drug and carrier (Eutectic system). The amorphous solid state of is shown in Figure 3. This high energy state of the drug in the system generally results in much higher dissolution rates than the corresponding in the crystalline form of the drug.[35]

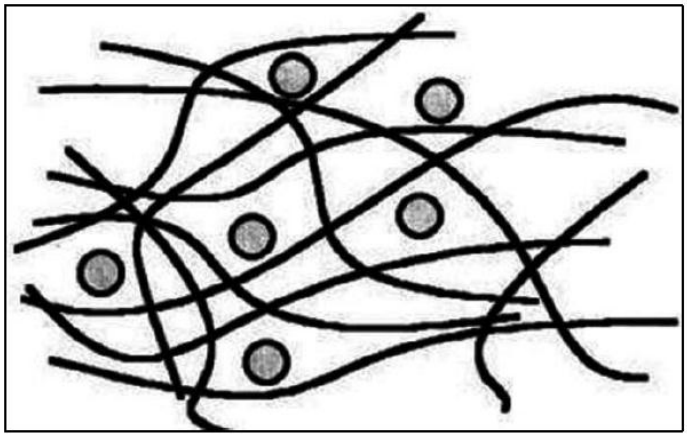

Fig. 3: Amorphous solid solutions.

3) Solid solution

A solid solution is equivalent to a liquid solution and consists of only one phase, regardless of the number of components in solid solution, the particle size of the drug is reduced to an absolute minimum. The rate of dissolution is determined by the rate of dissolution of the carrier. They are classified according to their immiscibility (discontinuous solid solution vs. Continuous) and secondly according to the way the isolated molecules are distributed in the solvent (interstitial or amorphous, substituted).[8]

a) Continuous solid solutions

In a continuous solid solution, the components are miscible in all proportions. In theory, this means that the bond strength between the two components is stronger than the bond strength between each component's molecules This type of solid-state separation has not been previously reported in thepharmaceutical industry.[8,13]

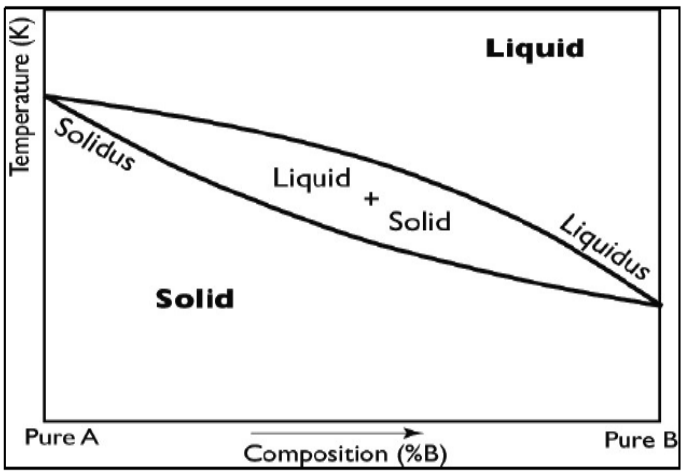

Fig. 4: Continuous solid solution.

b) Discontinuous solid solutions

In a discontinuous solid solution, the solubility of each component in the other components is limited. Due to practical considerations, Goldberg et al. Proposed that the term "solid solution" should only be used when the mutual solubilityof the two components is greater than 5%.[8,13]

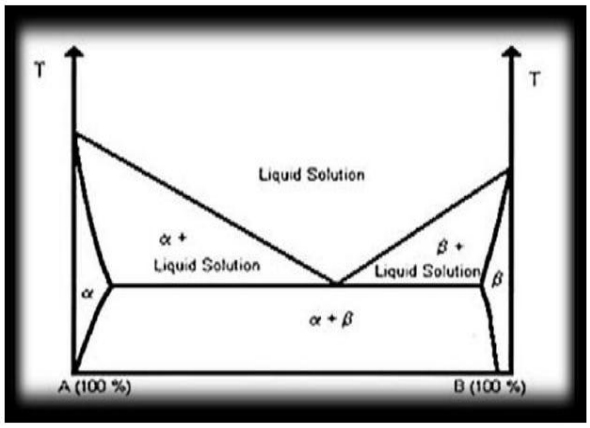

Fig.5: Discontinuous solid solutions.

c) Substitutional solid solution

Substitution is possible only if the difference between the size of the solute and the size of the solvent molecule is less than about 15%. A classical solid solution has acrystalline structure in which dissolved molecules replace solvent molecules in the crystal lattice or fit inside between solvent molecules.[8]

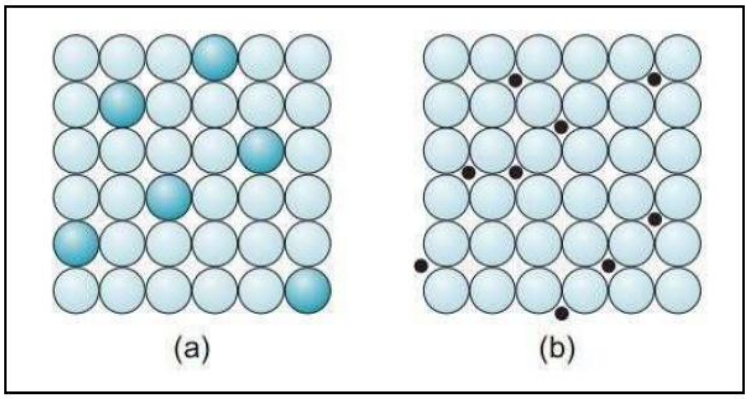

Fig. 6: Substitutional solid solutions.

d) Interstitial solid solutions

In an interstitial solid solution, dissolved molecules occupy the spaces between solvent molecules in the crystal lattice. The diameter of the dissolved molecules must be less than 0.59 times the diameter ofthe solvent molecules.[8,13]

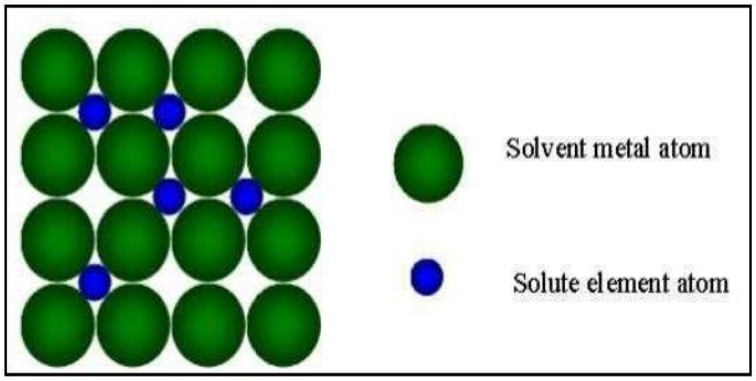

Fig.7: Interstitial solid solution

4) Glass solution and Suspension

The glass is a homogeneous glassy system in which solute dissolve in the glassy system. a glass suspension refers to a mixture in which precipitate particle is suspended in glassy solvent. Characterization of the glassy state is transparency and brittleness below the glass transition temperature

Methods of preparation[14]

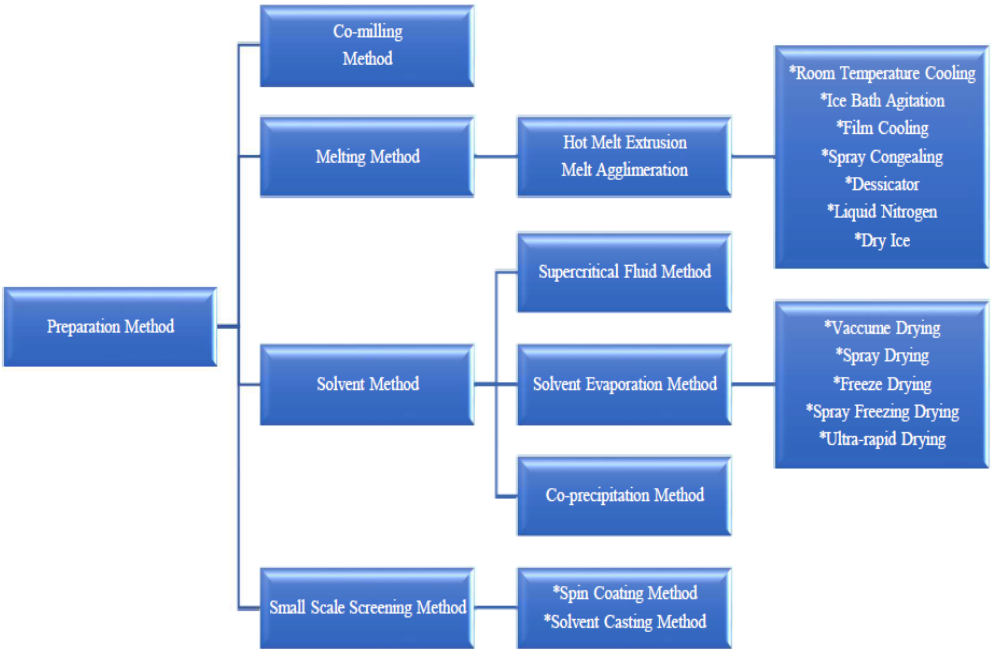

Fig. 4: Preparation methods of solid dispersion.

1. Melting method
2. Solvent evaporation method
3. Lyophilization technique
4. Melting solvent method

5. Hot Melt extrusion methods
6. Melt agglomeration process
7. Spray drying
8. Effervescent method
9. Electrospinning
10. Super critical fluid (SCF) technology

1) Melting method

Mix the drug and carrier in a mortar and pestle to achieve uniform dispersion, heat the mixture above the melting points of all ingredients. This is then cooled to obtain a solidified mass. Grind it and sift it. Example: A solid dispersion of Albendazole and urea was prepared using this method.[15]

2) Solvent evaporation methods

In this method, both the active ingredient and the carrier are dissolved in an organic solvent. Aftercomplete dissolution, evaporate the solvent. Grind the solid mass, sieve and dry. Example A solid dispersion of furosemide was prepared by solvent evaporation.[15] Tachibana and nakumra wherefirst to dissolve both drug and carrier in common solvent and then evaporate the solvent under vacuum to produce a solid solution this enable them to produce a solid solution of highly lipophilic beta carotene in highly water-soluble carrier polyvinylpyrrolidone.

However, this method has some drawbacks

1. Requires significant preparation effort.
2. It is difficult to completely remove liquid solvents.
3. Potential negative effects of trace amounts of solvent on chemical stability.
4. Selection of common volatile solvents.
5. Difficulty in reproducing crystal shapes.
6. Furthermore, supersaturation of solutes in solid systems can only be achieved in highlyviscous systems.

3) Lyophilisation method

This method involves the transfer of heat and mass from the product being manufactured This technique has been proposed as an alternative to solvent evaporation. This is a molecular mixing technique in which the carrier and drug are co-dissolved using a common solvent. It is

then frozenand sublimated to obtain a molecular lyophilized dispersion.[14,16]

4) Melting solvent method

In this method, a fixed amount of solvent is added and this solution is introduced into molten polyethylene glycol at a temperature below 70°C. This method is also used for Thermolabile drugs with high melting points. However, when therapeutic doses are low (less than 50 mg), limited drugis needed.[12,14]

5) Hot melt extrusion method

In the early 1930s, the HME process was most commonly used in the plastics, rubber, and food industries. Subsequently, with the advancement of technology, the suitability of his HME processin the development of various pharmaceutical formulations was investigated in the early 1980s.[17,18,19] Initially, single screw extruders (SSE) were introduced to the pharmaceutical industry. However, SSE results in non-uniform distribution of formulation ingredients and increases the requirements for twin screw extruders (TSE) and multi-screw extruders (MSE). By implementingTSE and MSE, the limitations of uneven distribution were overcome. In today's world, HME is the most widely used method to develop his ASD from poorly water-soluble drug substances.[20,21,22] A schematic diagram of the hot melt extruder is shown in Figure 10. HME is a one- step, continuous manufacturing process that requires controlled feeding of a physical mixture intobarrels. A cylinder of screws rotating in the same or opposite directions along with a mechanical shearer provides distributive and dispersive mixing of the treated material. The configuration of screw is mainly conveying and mixing elements, and can be adjusted according to your needs. Theprimary purpose of the conveying element is to convey the material between mixing zones and hasno mixing properties. Mixing elements exert mechanical shear on the material being processed but have no conveying properties. Mixed elements can be configured with offset angles of 0°, 30°, 60°, and 90°. As the angle increases, the shear force on the material increases and the residence time of the material in the cylinder decreases. The material in the cylinder is exposed to mechanical and thermal energy greater than the lattice energy of the drug crystals, resulting in the formation of an amorphous solid dispersion. The molten mass within the cylinder is conveyed over the lengthof the cylinder and pumped as a cylindrical filament through the nozzle connected to the exit points the collected extrudates can be cut into pellets, ground, encapsulated, or compressed into tablets using suitable diluents. The various process parameters involved in the extrusion process include feed rate, screw speed, barrel and die temperature, process

torque, and melt pressure. To date, various researchers have evaluated the suitability of his HME method in the development of BCS class II and IV ASDs for immediate release, modified release, sustained release, chronotherapy, colon targeting, gastro retentive substances,Formulas that mask taste. Additionally,his ASD filaments from the HME process can also be used as raw materials for manufacturing patient- centred dosage forms using three- dimensional (3D) printing with fused dep -position modelling (FDM).[22]

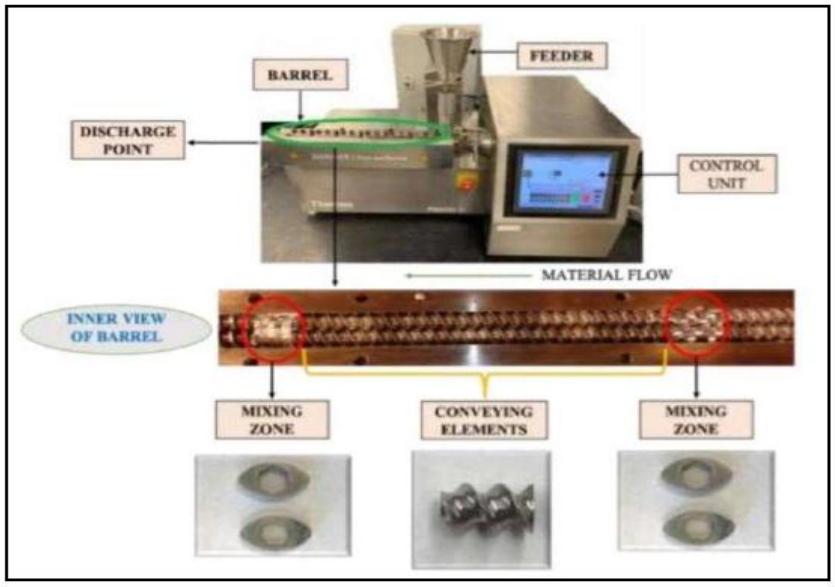

Fig.9: Schematic representation of hot melt extrusion.

6) Melt agglomeration process

This process produces a solid dispersion in which the binder acts as a carrier. Additionally, solid dispersions can be prepared by heating the binder, drug, and excipients to a temperature above themelting point of the binder (Meltdown process), or by heating a dispersion of drug in a molten binder. It can be prepared by spraying onto the formulation (Spray-on). Process) using a high shearmixer. Rotary processors are an alternative device for melt agglomeration. Rotary processors are particularly suitable for high melting point agglomerations. Because temperature control is easy and higher binder content can be incorporated into the agglomeration.[8,14]

7) Spray drying

In recent years, spray drying has been most widely investigated for the development of ASD for poorly water-soluble drug substances. This approach is advantageous for processing heat sensitive and high-melting point drug substances. Spray drying requires the supply of heated gas, but the contact time between particles and heated gas is much shorter in seconds

compared to his HME process. The spray drying process mainly involves spraying a formulated solution or suspension into a drying chamber using a nozzle supplied with heated gas. The dried particles are transported to a cyclone separator and filter where they are separated from the gas. A schematic diagram of the spray drying system is shown in Figure 10. Spray drying processes are still expensive compared to HME because they require large amounts of solvent to produce the raw materials.[23,24] In addition, special recovery units are required for solvent recovery. Particle size mainly depends on the spray nozzle and atomization pressure The smaller the particle size, the better the surface and therefore more solvent will evaporate. However, this process uses solvents and thermal energy, so great care must be taken as there is a risk of explosion. The spherical morphology of the particles improves the flow behaviour of the formulation. The discharge speed and type of pump are determined primarily by the viscosity of the discharged liquid being sprayed. The higher the concentration of active ingredient, the faster the drying time because less solvent is incorporated. Spray drying can also be used for taste masking of bitter medicines, modified release formulations, and the production of inhalation formulations. It can also be used to prepare sterile formulations that have a longer shelf life than liquid intravenous formulations.[35,36,37]

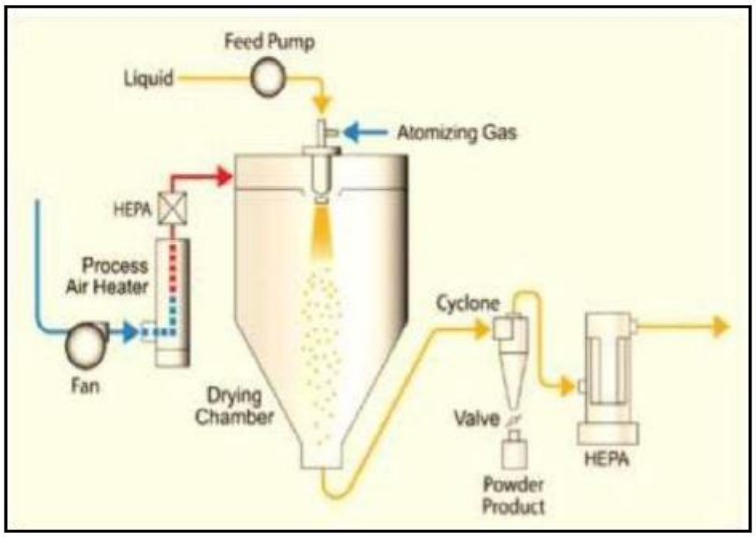

Fig. 10: Spray drying.

8) Effervescent method

This is a method of foaming by reacting sodium bicarbonate with an organic acid such as citric acid or succinic acid. However, combining both increases the rate of dissolution and absorption ofpoorly soluble drug.[15,16] The carrier (Mannitol) was dissolved in a glass beaker (175-180°C) and the organic acid (Citric acid) was added to the dissolved mannitol. This

mixture of mannitol and organic acid was melted and mixed uniformly by continued stirring. Powder of poorly soluble drug (Atorvastatin calcium or cefuroxime acetyl or clotrimazole or ketoconazole or metronidazole benzoate) was added to this molten mixture with continuous stirring. Sodium bicarbonate (Carbonate base) was added to the molten mixture of carrier, organic acid, and drug with rapid stirring. The ratio of carbonate base to organic acid depended on their molar reactivity. One molecule of citric acid can react with three molecules of sodium bicarbonate, so the amount of citric acid is a 1: 3 molar ratio of sodium bicarbonate. After the addition of sodium bicarbonate, foaming (Microbubbles) was generated due to the acid-base reaction, and the molten mixture became a white foam (except for cefuroxime acetyl). The foamy molten mixture was continuously stirred until foaming subsided (and nearly stopped). The foam was cooled and solidified at low temperature (freezer). The cooled solid dispersion was ground and carefully ground in a mortar and pestle. Powdered EASD was stored in a desiccator.

9) Electrospinning

The name "electrospinning" indicates that this process requires the application of an electric field. Electrospinning processes can be used to develop nanofibers with sizes less than 100 nm. Nanofibers offer the benefit of surface improvement. This is a solvent-based approach in which drug and polymer solutions are injected through the opening of a needle (spinneret) using an injection pump.[25,26,27] An electric field is generated between the needle and the sample collector using a high voltage power supply. When the electric field energy exceeds the surface tension, the solution droplet on the needle tip deforms and forms a Taylor cone. Taylor cones run as thin nanofibers and coils on a rotating collector drum. This approach does not require external heat and the solvent evaporates as the nanofibers move from the needle tip to the collector drum or plate. The quality of nanofibers is influenced by solution viscosity, feeding rate, needle size, tension, and distance between needle tip and collector. The commercial viability of this technology for large-scale manufacturing of ASD remains questionable, as this process requires low solution feed rates.[28,29] Single-needle and high-speed electrospinning have been considered to scale up the process, but throughput remains below the required commercial-scale batch volumes. A detailed overview of the electrospinning process is shown in Figure 11.

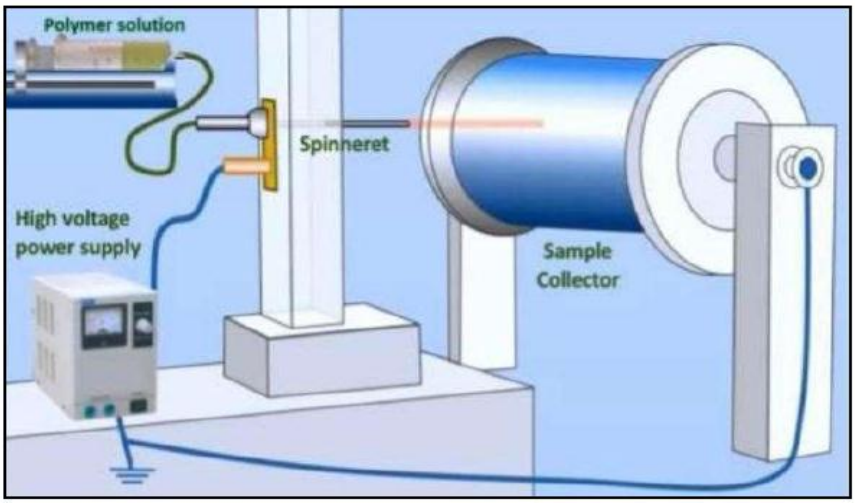

Fig. 11: Electrospinning.

10) Super critical fluid (SCF)

This is a supercritical fluid antisolvent technology that uses carbon dioxide as an antisolvent for the solute. After drug particles are solubilized in supercritical fluids, they can be recrystallized to significantly reduce particle size. The flexibility and precision afforded by supercritical fluid processes allows drug particles to be micronized within a narrow size range down to the submicron range. Current supercritical fluid processes have the ability to demonstrate and produce nanoparticle suspensions of particles ranging from 5 to 2000 in diameter. Nebulization of a solution consisting of solute and organic solvent occurred in a continuous supercritical phase thatfollowed simultaneously.[13]

Mechanism of bioavailability enhancement

The increase in dissolution rate due to the formation of solid dispersions compared to pure drug varies from 400-fold to less than two folds. Although there is a myriad of possible factors that canincrease dissolution rate, it is very difficult to demonstrate experimentally that any one factor is more important than another. Solid dispersions enhance the dissolution rate of poorly water-solubledrugs by one of the following mechanisms.[38]

- Reducing particle size
- Improving wettability and dispersibility
- Conversion of the drug from crystalline to amorphous form
- Reducing agglomeration and agglomeration of drug particles.

Characterization of solid dispersion

Many methods are available that can contribute information regarding the physical nature of

solid dispersion system. A combination of two or more methods is required to study its completepicture.[3]

- Thermal analysis.
- Spectroscopic method.
- X-ray diffraction method.
- Dissolution rate method.
- Microscopic method.
- Thermodynamic method.
- Modulated temperature differential scanning calorimetry
- Environmental scanning electron microscopy
- Dissolution testing

Advantages

1. Improving drug bioavailability by changing Their water solubility has been possible by Soliddispersion.
2. Solid dispersions are more efficient than These particle size reduction techniques, since the latter have a particle size reduction limit Around 2-5 mm which frequently is not Enough to improve considerably the drug Solubility or drug release in the small Intestine.
3. Improving drug bioavailability by changing the aqueous solubility of drugs has become possible through solid dispersion.
4. Solid dispersions are more efficient than these particle size reduction techniques. The particle size reduction limit of the latter is approximately 2–5 mm, which is often insufficient to significantly improve drug solubility or drug release in the small intestine.
5. Increases dissolution rate and extent of absorption and decreases systemic metabolism.
6. Conversion of drugs from liquid form to solid form.
7. Parameters such as carrier molecular weight and composition, drug crystallinity, particle porosity and wettability, if well controlled, can lead to improved bioavailability

Disadvantages

1. Most polymers used in solid dispersions can absorb moisture, resulting in phase separation, crystal growth, or conversion from an amorphous state to a crystalline state or from a metastable crystalline form during storage. Conversion to a more stable structure may occur. This can reduce solubility and dissolution rate.
2. A disadvantage of solid dispersions is that they are poorly scaled up for manufacturing

purposes.

Application

Apart from improving absorption, solid dispersion technology may have many pharmaceuticalapplications that should be further investigated. Such techniques may be used.

1. Obtain uniform distribution of small amounts of drug in solid state.
2. To stabilize unstable drugs.
3. For dispensing liquid or gaseous compounds in fixed quantities.
4. Formulate an immediate release initial dose in a sustained release dosage form.
5. Formulation of sustained release regimens of soluble drugs using poorly soluble or insolublecarriers.
6. Reduces systemic pre-inactivation of drugs such as morphine and progesterone. Polymorphisms within a given system can be converted into isomorphic, solid solution eutectic, or molecular compounds.

Marketed products

- Gris-PEG, a solid dispersion using a fusion process of griseofulvin and PEG, was originally manufactured by Dorsey/Sandoz and appeared on the market in the mid-1970s. Gris-PEG was developed as a tablet product and two of his USP monographs on griseofulvin tablets were created. Griseofulvin solid dispersion tablets are currently sold by many manufacturers and contain corn starch, lactose, magnesium stearate, PEG, and sodium lauryl sulphate as inactiveingredients.[39]

- Cesamet is a nabilone-PVP solid solvent dispersion manufactured by Eli Lilly and Co. and sold internationally since 1982. Eli Lilly has discontinued sales of his Cesamet, which containsPVP and cornstarch as inactive ingredients and is offered as a capsule product42. A solid dispersion formulation of troglitazone (Rezulin) is sold by Parke-Davis.[40]

- Polyvinylpyrrolidone - a solid solution of lopinavir and ritonavir in vinyl acetate. Copolymers have made it possible to reformulate Kaletra (Abbott Laboratories, Abbott Park, IL). In additionto reducing the dosage load from six softgel capsules to four tablets, tablets prepared in solid solution eliminate the need for refrigeration.

- "Sporanox" (Janssen Pharmaceutica, Titusville, NJ) is a solid dispersion of itraconazole in hypromellose coated onto sugar beads.The most recently approved product is the non-

nucleoside reverse transcriptase inhibitor Intelence (Tibotec, Yardley, PA).It is an amorphous,spray-dried solid dispersion of etravirine, hypromellose, and microcrystalline cellulose.

Summary

Certainly! Solid dispersion refers to a technique used to enhance the solubility of poorly water- soluble drugs by dispersing them in a solid matrix. The article likely covers the methods, benefits, and applications of solid dispersion in improving drug dissolution and bioavailability. It might discuss different formulation approaches, such as melting, solvent, or melting-solvent methods, as well as the impact of solid dispersion on drug delivery systems. There are almost six to seven types of solid dispersion viz are eutectic mixture, amorphous solid solution, solid solution, continuous solution, discontinuous solution, interstitial solution, substitutional solution and methods ofpreparation of solid dispersion such as melting method, solvent evaporation method, Lyophilization process, hot melt extrusion, electrospinning, super critical fluid technology, spraydrying, effervescent method, melt agglomeration method etc.

CONCLUSION

The solubility property of drugs remains one of the most Challenging aspects in formulation development. Dissolution of Drug is the rate determining step for oral absorption of the poorly Water-soluble drugs and solubility is the basic requirement for the Absorption of the drug from GIT. The various techniques Solid Dispersion described above can be used to enhance the solubility of the drugs.

Types of solid dispersion: eutectic mixture, amorphous solid solution, solid solution, continuoussolution, discontinuous solution, interstitial solution, substitutional solution etc.

Method of preparation: melting method, solvent evaporation method, Lyophilization method, hot melt extrusion, electrospinning, super critical fluid technology, spray drying, effervescent method, melt agglomeration method etc.

REFERENCES

1. Sosnik, A.; Augustine, R. Challenges in oral drug delivery of antiretrovirals and the innovativestrategies to overcome them. Adv. Drug delivery. Rev, 2016; 103: 105–120.
2. Vasconcelos T, Costa, P. Solid dispersions as strategy to improve oral bioavailability of

poorwater-soluble drugs. Drug Discovery Today, 2007; 12: 1068–1075.

3. Leunar, C. and Dressman, J, improving drug solubility for oral Delivery using solid dispersions. European journal of pharmaceutics and biopharmaceutics, 2000; 50: 47-60.
4. Dhirendra k, solid dispersions: a review, pak. J. pharm. Sci, 2009; 22, 2: 234-246.
5. Savjani K, Gujjar A, Savjani J. Drug solubility: Importance and enhancement Technique.ISRNP, 2012; 110.
6. Sharma D, Soni M, Kumar S, Gupta G. Solubility enhancement-eminent role in poorly solubledrugs. RJPT, 2009; 2: 220-224.
7. Dhirendra K, Lewis S, Udupa N and Atin K: Solid dispersion: A Review, Pakistan journal ofpharmaceutical sciences, 2009; 22(2): 234-246.
8. Singh J, Walia M, HariKumar SL, Solubility enhancement by solid Dispersion method: A Review, Journal of drug delivery & Therapeutics, 2013; 3(5): 148-155.
9. Sekiguchi K, Obi N, Studies on Absorption of Eutectic Mixture. I. A comparison of the behaviour of eutectic mixture of Sulfathiazole and that of ordinary sulfathiazole in man, Chem.Pharm, 1961; 9: 866-872.
10. Goldberg AH, Gibaldi M, Kanig JL, Increasing dissolution rates and gastrointestinal absorption of drugs via solid solutions and Eutectic mixtures II – experimental evaluation of aeutectic Mixture: urea-acetaminophen system, J. pharm. Sci, 1966; 55: 482-487.
11. Castellan GW, Addison-Wesley, Menlo Park, CA, Umar. B, Solid dispersion- A review, Pharmatutorial, 2017; 5(2): 24-29.
12. Dixit ND, Niranjan SK. "A review: Solid dispersion" World journal of pharmacy and pharmaceutical science, 2014; 3(9): 238-257.
13. Singh S, Baghel RS and Yadav L, "A review on solid dispersion "International journal of pharmacy & life science, 2011; 2(9): 1078-1095.
14. Yadav B and Tanwar YS, Application of solid dispersion: Journal of chemical and pharmaceuticals Research, 2015; 7(2): 965-978.
15. Shaikh SN, Hifzurrahman S, Athar MD, Dr. Khan GJ, Raza S, Mohd AA, "Review on solid dispersion of poor water-soluble drug by using natural polymers" The Pharma innovation Journal, 2019; 8(1): 631-636.
16. Butreddy A, Nyavanandi D, Narala S, et al. Application of hot melt Extrusion technology in the development of abuse-deterrent Formulations: An overview. Current Drug Delivery, 2021;18(15): 4–18.
17. Mamidi H, Rohera B. Application of thermodynamic phase Diagrams and Gibbs free energy of mixing for screening of Polymers for their use in amorphous solid dispersion

Formulation of a. J Pharm Sci, 2021; 110(7): 2703–2717.

18. Mamidi H, Rohera B. Material-Sparing Approach using Differential Scanning Calorimeter and Response Surface Methodology for Process Optimization of Hot-Melt Extrusion. J pharm Sci, 2021; 110(12): 3838– 3850.
19. Repka MA, Kumar Battu S, Upadhye SB, et al. Pharmaceutical Applications of hot-melt extrusion: Part II. Drug Development and Industrial Pharmacy, 2007; 33(10): 1043–105.
20. Maniruzzaman M, Boateng JS, Snowden MJ, et al. A review of hot-Melt extrusion: process technology to pharmaceutical products. ISRN Pharm, 2012; 340-351.
21. Lang B, McGinity JW, Williams RO. Hot-melt extrusion-basic principles and pharmaceuticalapplications. Drug delivery Ind pharma, 2014; 40(9): 1133-1155.
22. Duarte Í, Santos JL, Pinto JF, et al. Screening methodologies for the development of spray- dried amorphous solid dispersions. Pharm Res, 2015; 32(1): 222–237.
23. Ding Z, Wang X, Wang L, et al. Characterization of spray dried Microcapsules with amorphous lutein nanoparticles: Enhancement of process ability, dissolution rate, and storage Stability. Food Chem, 2022; 383: 132-200.
24. Vasconcelos T, Marques S, Naves J, et al. Amorphous solid Dispersions: Rational selection ofa manufacturing process. Adv. drug Deliv Rev, 2016; 100: 85–10.
25. Marano S, Barker S, Raimi-Abraham BT, Missaghi S, Rajabi Siabhoomi A, Craige DQ. Development of Micro-fibrous solid dispersions of poorly water-soluble drugs in Sucrose using temperature-controlled centrifugal spinning. European Journal of Pharmaceutics and Biopharmaceutics, 2016; 103: 84–94.
26. Pandi P, Bulusu R, Kommineni N, et al. Amorphous solid: an update for preparation, characterization, mechanism of bioavailability, stability and regulatory consideration and marketed products. Int J pharma, 2020; 119-560.
27. Paudel A, Geppi M, van den Mooter G. Structural and dynamic Properties of amorphous solid dispersions: the role of solid-state nuclear magnetic resonance spectroscopy and relaxometry.J Pharm Sci, 2014; 103(9): 2635–2662.
28. Yu D, Yang J, Branford-White, C, et al. Third Generation Solid Dispersions of ferulic acid inelectro spun composite nanofibers. Int J Pharm, 2010; 400(1–2): 158–164.
29. Jatwani S, Rana AC, Singh G, Aggarwal G. An overview on solubility enhancement techniquesfor poorly soluble drugs and solid Dispersion as an eminent strategic approach. Int J Pharma Sci Res, 2012; 3: 9-42.
30. Di L, Fish PV, Mano T. Bridging solubility between drug discovery and development. Drug discov today, 2012; 17: 86-95.

31. Brough C, Williams R. Amorphous solid dispersions and nano-crystal technologies for poorlywater-soluble drug delivery. Int J pharm, 2013; 453: 57-66.
32. Van den Mooter G. The use of amorphous solid dispersions: a Formulation strategy to overcome poor solubility and dissolution rate. Drug Discov Today Technol, 2012; 9: 79-85.
33. Vaka SRK, Bommana MM, Desai D, Djordjevic J, Phuapradit W, Shah N. Excipients for amorphous solid dispersions. In: Shah N, Sandhu H, Choi DS, Chokshi H, Malick AW, editors. Amorphous Solid dispersions. New York City: Springer, 2014; 61-123.
34. Kumari M, Kumar H, solid dispersion: its types and mechanism of enhancement of solubilityby solid dispersion. J pharma Res, 2019; 8(3): 65-71.
35. Patel K, Shah S, Patel J. Solid dispersion technology as a Formulation strategy for the fabrication of modified release Dosage forms: A comprehensive review. DARU, Journal of Pharmaceutical Sciences, 2022; 30(1): 165–189.
36. Li J, Zordan C, Ponce S, et al. Impact of Swelling of Spray Dried Dispersions in Dissolution Media on their Dissolution: An Investigation Based on UV Imaging. J Pharm Sci, 2022; 111(6): 1761–176.
37. Zaitone A, Al-Zahrani B, Ahmed O, et al. Spray Drying of PEG6000 Suspension: Reaction Engineering Approach (REA) Modeling of Single Droplet Drying Kinetics. Process, 2022; 10(7): 1365.
38. Arise MJ, Gines JM, Moyano JR, Perez M. Influence of preparation method of solid dispersions their dissolution rate; Study of triamterene d-mannitol system. Int J Pharm, 1995;123: 25-31.
39. Breitenbach J, Magerlein M. Melt Extruded Molecular Dispersion. In: Sellassie IG, Martin C,editors Pharmaceutical Extrusion Technology. Informa Health care, 2003; 246.
40. URL:http://www.pharmtech.findpharma.com/pharmtech/.../article/...529177