Original Article
ISSN (Online): 2582-7472

ShodhKosh: Journal of Visual and Performing Arts
July 2024 5(7), 1716–1725

A REVIEW ON SOLID DISPERSION TO ENHANCE TECHNIQUE FOR POORLY WATER-SOLUBLE DRUGS AND ITS POLYMERS

Dr. Neelu Basant [1]

[1] Assistant Professor Department of Chemistry, Nalanda College of Engineering, Chandi (Nalanda) Bihar- 803108, India

DOI
10.29121/shodhkosh.v5.i7.2024.6376

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ABSTRACT

During the formulation development process, one of the most demanding factors is still the solubility behavior of pharmaceuticals. These days, there is a sharp rise in the quantity of novel chemical entities with intermittent problems with low permeability and solubility. For medications with low water solubility, solid dispersion has been shown to be a better dosing form. The use of solid dispersions in water-soluble carriers to increase the rate of drug dissolution and bioavailability for hydrophobic medications has attracted a lot of attention. Because of solubility issues, formulation scientists continue to face challenges in improving the oral bioavailability of medications administered in solid dosage forms. The rate-limiting mechanism in the drug absorption process from a solid dosage form of relatively insoluble medicines may be the dissolving rate. Thus, one of the challenges facing formulation scientists is the rise in the solubility of poorly soluble pharmaceuticals by the use of solid dispersion techniques. Solid dispersion techniques, which reduce drug particle size, improve wettability, and produce amorphous particles, have received significant interest in enhancing the dissolving rate of highly lipophilic medicines and, consequently, improving their bioavailability. The several synthetic, natural, semisynthetic, and modified natural hydrophilic carriers that are utilized to formulate solid dispersions are summarized in this article. We will talk about it in this essay. A review of solid dispersion as an improved approach for medicines and their polymers that are poorly soluble in water.

Keywords: Solid Dispersion, Poorly Water-Soluble Drugs, Polymers, Poor Permeability, Dosage Form, Hydrophobic Drugs, Bioavailability, Biopharmaceutical Classification System, Components, Hydrophilic Matrix, Binary Solid Dispersion

1. INTRODUCTION

Due to its convenience and ease of ingestion, the oral route of medication administration is the most popular and recommended mode of delivery. From the patient's point of view, taking medication by swallowing a dose form is a known and pleasant method. Because of this, oral medication delivery generally results in better patient compliance and, thus, more effective drug treatment than alternative administration routes, such as parenteral. [1]

When giving patients medication, the oral route is typically chosen. However, the use of many medications in oral administration is limited due to their poor solubility. Drug bioavailability and dissolution rate are mostly impacted by poor solubility. Based on solubility and permeability, the medications were divided into four categories by the Biopharmaceutical Classification System (BCS). [2] Drugs that belong to BCS classes II and IV have poor solubility issues. Enhancing the solubility of these medications that belong to BCS II and IV presents the greatest hurdles. Many techniques are employed for this, including solid dispersion, particle size reduction (Micronization and Nanonization), salt production, pH adjustment, formation of polymorphs and pseudo polymorphs, complexation procedure, and the use of surfactant and co-solvent. However, solid dispersion is the most straightforward of these methods and produces highly accurate solubility improvement results. [3]

2. SOLID DISPERSION

There are several methods for improving solubility. One of the finest methods to improve solubility is solid dispersion. The phrase solid dispersion refers to a category of solid products comprising of at least two separate components, often a hydrophilic matrix and a hydrophobic medicament. The matrix may be crystalline or amorphous; generally speaking, amorphous materials are more soluble than crystalline ones since they dissolve drugs more quickly and require less energy to break up the drug's crystal lattice. Surrounding hydrophilic carriers may improve drug wettability and solubility. [4]

3. TYPES OF SOLID DISPERSION

- Binary Solid Dispersion: It consists of medication and a polymeric carrier.
- Ternary Solid Dispersion: A polymeric carrier, a surfactant, and a medication make up this mixture. [5]
- Surface Solid Dispersion: To increase its solubility, surface solid dispersion is made with polymers such polyethylene glycol, polyvinyl pyrrolidone, and polyvinyl pyrrolidone-vinyl acetate copolymer through fusion process. [6]

Different solid dispersion systems can be categorized according to their primary fast release mechanisms. solid dispersions into the six illustrative categories listed below. [7]

Based on their molecular arrangement,

- **Type1:** Simple eutectic mixture
- **Type2:** Amorphous precipitations in crystalline matrix.
- **Type3:** Solid solutions
- **Type4:** Glass suspension Type6-Glass solution. [8]

4. CLASSIFICATION OF SOLID DISPERSION ON THE BASIS OF RECENT ADVANCEMENT

1) **First generation solid dispersion:** Crystalline carriers are used to create these solid dispersions. The earliest crystalline carriers utilized in the creation of solid dispersions were urea and sugars. These have the drawback of not releasing medication more quickly and being thermodynamically unstable. [9]
2) **Second generation solid dispersion:** Rather than employing crystalline carriers, amorphous carriers are used to create these solid dispersions. The polymeric carrier allows the medicine to be molecularly distributed. There are two categories for the polymeric carriers:

Synthetic polymer: povidone, polyethylene glycols and polymethacrylates.

Natural polymers: hydroxypropyl methylcellulose, ethyl cellulose, starch derivatives like cyclodextrin. [10]

3) **Third generation solid dispersion:** A surfactant carrier or a combination of amorphous polymers and surfactants as carriers is present in these solid dispersions. For medications with low solubility, these provide the maximum level of bioavailability. The third-generation solid dispersion contains surfactants like poloxamer 407 and inulin, among others. [11]

5. POLYMERS USED IN SOLID DISPERSIONS

These substances are known as polyethylene glycol (PEG), and they are produced when ethylene glycol and ethylene oxide combine. PEGs are generally referred to as polyethylene oxides when their molecular weight is greater than 300,000. [12]

Phospholipids: Choline, ethanolamine, serine, inositol and inositol phosphate, and glycerol esters are examples of frequent phospholipid head groups. Phospholipids are created by modifying the terminal hydroxyl of glycerides with phosphate linked head groups. [13] Fluidity differences are apparent as a function of the gel to liquid crystalline

transition temperatures. As with triglycerides, a variety of species are achievable by various combinations of different head groups and fatty acyl substitution at the first and second positions of the glycerol backbone. Phospholipid solubility is not just a chemical property of the molecule; it is closely related to the validation of the aggregate material. Since they frequently form micelles, monoacyl phospholipids are typically more soluble in aqueous solutions. [14]

The molecular weight of polyvinylpyrrolidone, or PVP, varies between 2500 to 3000000. It is soluble in ethanol, water, chloroform, and isopropyl alcohol, among other solvents. PVP disintegrates in hot weather. Melting occurs at a very high temperature; thus it is not appropriate for preparing solid dispersions made by the melt method.

Cyclodextrins: By entrapping liquids and turning them into solids, cyclodextrins are mainly employed to improve solubility, chemical protection, taste masking, and improved handling. [15]

6. REVIEW OF LITERATURE

One important physicochemical component influencing drug absorption and therapeutic efficacy is solubility. Failure in formulation development would result from a medication with low water solubility. Inadequate bioavailability is sometimes caused by the medication ingredients' low solubility and slow rate of dissolution in water in aqueous GIT fluid. Enhancing the solubility and dissolution of hydrophobic pharmaceuticals continues to be one of the most challenging endeavors in the drug development process. Numerous strategies have been proposed to overcome this issue (Ford, 1986). [16]

Numerous commercially feasible techniques, such as liquisolid, in which the medication is adsorbed upon insoluble carriers while in solution, are available to improve the solubility and rate of dissolution of poorly soluble pharmaceuticals (Nokhodchi et al., 2005). [17] Surfactants can also be added to formulations to increase the wettability and solubility of certain lipophilic compounds (Bakatselou et al., 1991). [18] Drug micronization is not the best option because the product has a tendency to clump together, reducing the amount of useful surface area available for dissolving. However, formulators find that solid dispersion is the most promising approach due to its repeatability, ease of preparation, and ease of optimization (Leuner et al., 2000). [19] A class of dosage forms known as "solid dispersions" are those in which the medication is dissolved in a matrix that is physiologically inert, typically to increase oral bioavailability (Nernst, 1994). [20]

The number of poorly soluble drug candidates has sharply increased with the advent of high throughput screening for potential therapeutic agents, and one of the most frequent and pressing challenges facing formulation scientists in the pharmaceutical industry today is the formulation of poorly soluble compounds for oral delivery (Noyes et al., 1997). [21] There are very few solid dispersion options available on the market. Their inadequate physical characteristics for dosage form formulation are the cause of this. Solid dispersions made with a water-soluble carrier are a mushy, sticky mass that is difficult to work with, especially when developing tablet formulations and capsule filling processes that require pulverization, screening, and mixing.

For formulation scientists, the paradigm of solubility issues remains basically unaltered. A major obstacle in the design and development of formulations is the drug's poor water solubility and consequent dissolving rate. Over the past twenty years, combinatorial screening technologies such combination high throughput screening have been used in the drug development and new chemical entity (NCE) selection process to undertake a thorough examination approach (Lipinski et al., 2001; Baird & Taylor, 2012). [22]

The use of innovative polymers and scalable manufacturing processes is the primary focus of recent research on solid dispersions. The focus is on improving the solubility and bioavailability of pharmaceuticals with high melting points and intractable solids by creating a molecular dispersion using specifically designed polymers. Alternatively, the amphiphillic polymer Polyvinyl caprolactam-polyvinyl acetate-PEG graft copolymer (Soluplus) was employed by Enose A et al. [23] to improve the solubility of telmisartan, a medication that is not very soluble in water. By using powder X-ray diffractometry and DSC to characterize the generated solid dipersions, it was discovered that they were more stable and had a greater drug release than free drug. But Zawar et al. [24] shown that a unique microwave-induced solid dispersion technology is a more efficient, solvent-free, and superior substitute for existing preparation techniques for improving the solubility of a medication that is poorly soluble in water. In contrast to synthetic polymers, Singh et al.'s recent study [25] demonstrated the efficacy of employing natural polymers to increase medication solubility. Using a particle size analyzer to measure the generated dispersions' particle size revealed that they were nanometric in size and extremely soluble when locust bean gum was used as a carrier, improving the analysis of the results.

In addition to improving the solubility of poorly soluble medications, studies are being conducted to ascertain the potential uses of solid dispersions in other domains. Using PEG as a polymer, Usmanova et al. [26] created magnetically active solid dispersions for the efficient and focused delivery of phenacetin. Atomic force and magnetic force microscopy were used to demonstrate the development of the solid dispersion formed by the supermagnetic nanoparticles that had been mixed and distributed in a polymeric matrix. Because it combines the benefits of targeted distribution and increased solubility, this may be more effective. On the other hand, Duarte and colleagues synthesized nano solid dispersions by a unique microfluidization-based solvent-controlled precipitation method. In comparison to micron-sized amorphous powder, they created both crystalline and amorphous nanosolid dispersions, which were found to have better bioavailability and faster rates of dissolution. They came to the conclusion that, in the case of solid dispersions, the drug's amorphization is less significant than the reduction of particle size into the nanometric range. By employing these cutting-edge methods, the widely publicized mechanism of amorphization of a crystalline medication has been defeated in favor of improved solubility. In a similar vein, a study conducted during the manufacture of carvedilol solid dispersions shown that transforming a crystalline medication into an amorphous form is not always necessary to improve its solubility. However, by utilizing innovative surface attached spray-dried solid dispersion technology, we are able to transform the hydrophobic medicine into a hydrophilic form without altering the crystalline structure by attaching the hydrophilic carriers to the drug's surface. The drug solubility and dissolution rate of the produced solid dispersions were found to be 11 500-times and 2 fold higher, respectively. [27]

(DW Shahid, 2021). [28] Particle size reduction in SD increases porosity, wettability, and polymorphism changes, which improve drug aqueous solubility. Techniques for melting, evaporating, and wetting solvents are a few ways to make solid dispersions. By decreasing the effective drug particle size to the smallest possible size, increasing the drug surface area, decreasing its crystallinity, and increasing wettability by surrounding hydrophilic carriers due to their special morphology, solid dispersions, which are two-component systems, can significantly improve drug wettability and bioavailability. (S. Tereza, 2019) [29]

The ability of a chemical substance, known as a solute, to dissolve in a solid, liquid, or gaseous solvent and create a homogenous solution in the solvent is known as solubility. A substance's solubility is mostly dependent on the solvent employed, temperature, and pressure. (Savjani K, 2012) [30] The saturation concentration, which is reached when adding more solute without increasing its concentration in the solution, is used to quantify the degree of solubility of a material in a particular solvent.

Nonetheless, the primary obstacle in the development of oral dose formulations is their low bioavailability. Aqueous solubility, drug permeability, dissolving rate, first-pass metabolism, pre-systemic metabolism, and sensitivity to efflux mechanisms are some of the variables that affect oral bioavailability. Low permeability and poor solubility are the most common causes of low oral bioavailability. Another important factor in various dosage forms, such as parenteral formulations, is solubility. (K. Edward, 2008) [31]

7. OBJECTIVES

- A Review on Solid Dispersion to enhance technique for Poorly Water-Soluble Drugs and its Polymers
- Type of Solid Dispersion.
- Techniques for solubility enhancement of poorly water-soluble drugs

8. RESEARCH METHODOLOGY

All the literature was accessed from four most popular search engines i.e. PubMed, Scopus, Web of Science and Google Scholar. The papers from the standard scientific journals were only included, in which the research on clinical trials were mainly focused on the present review.

9. RESULT AND DISCUSSION

Solubility is an important physicochemical property that affects both medication absorption and therapeutic effectiveness. Inadequate solubility in water can result in formulation development failure. The drug's poor solubility

and slow rate of dissolution in aqueous media are the primary causes of its insufficient bioavailability. [32] Today, a great deal of hydrophilic carriers are being investigated, and they have demonstrated noteworthy improvements in solubility.

The majority of medication substances on the market today are innovative, but one of the most challenging jobs in drug research is still trying to make hydrophobic drug substances more soluble and dissolve. For oral medications, dissolution of the drug in an aqueous medium such as stomach fluid is crucial for improved absorption and bioavailability. Thus, polymer matrix of different origin can be used to advance the bioavailability of weakly water-soluble substances such as biopharmaceutical categorization system class II and IV medications. To overcome this issue, a number of solubility augmentation techniques have been devised.1. There are various methods for improving solubility, which can be divided into three categories: chemical modifications for the drug material, physical modifications, and other methods2, all of which are mentioned in Table 1. [33]

Table 1 Techniques for solubility enhancement of poorly water-soluble drugs:

Techniques for solubility enhancement [2-5]	
Physical modification	A) Reduction Particle size
	a) Micronization
	b) Nanosuspension,
	B) Modification of the crystal habit
	C) Solid dispersions
	a) Eutectic mixtures
	b) Solid solutions
	c) Amorphous solid solutions
	d) Glass solutions and glass suspension
	e) Cryogenic techniques.
Chemical modification	A) Change of pH,
	B) Use of buffer,
	C) Derivatization,
	D) Complexation,
	E) Salt formation.
Miscellaneous methods	A) Supercritical fluid process,
	B) Use of adjuvant like surfactant, solubilizers, cosolvency, hydrotropy, and novel excipients.

Solid dispersion formulation is one of the most effective and promising methods for improving solubility. "The dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by the melting [fusion], solvent, or melting-solvent method" is the definition given by Chiou and Riegelman to solid dispersion systems. [34]

The former is the main topic of this article, specifically the application of solid dispersion technologies to enhance the oral bioavailability of medications that dissolve poorly in water. It has been shown in the pharmaceutical literature that a variety of solid dispersion techniques can enhance the dissolving characteristics of medications that are not very water soluble. To enhance the dissolution characteristics of poorly water-soluble drugs, various techniques have also been employed, including salt formation, complexation with cyclodextrins, drug solubilization in solvent(s), and particle size reduction. Nevertheless, each of these approaches has significant drawbacks. However, medication formulation is solid. [35]

When creating oral delivery systems for medications that are not very water soluble, dispersions provide a range of processing and excipient alternatives that allow for versatility (table 2). medications that are highly permeable to biological membranes and weakly soluble in water are the focus of a large portion of the research that has been published on solid dispersion technologies (Table 3). For these medications, absorption is slowed down by the process of dissolution. Therefore, the theory has been that an increase in the rate of drug dissolution will coincide with an acceleration in the rate of absorption in vivo. Drugs classified as Class II in the Biopharmaceutical Classification System

(BCS) have high membrane permeability and poor water solubility (Amidon et al., 1995). As a result, solid dispersion technologies hold great promise for enhancing BCS Class II medication bioavailability and oral absorption. [36]

Table 2 List of Poorly Soluble Drugs with Hydrophilic Carriers

Sr. No.	Carrier	Drug
1.	Polyethylene glycol (PEG)	Griseofulvin
2.	Polyvinylpyrrolidone (PVP)	Flufenamic acid
3.	Hydroxypropylmethylcellulose (HPMC)	Albendazole, Benidipine
4.	Sorbitol	Predinisolon
5.	Urea	Ofloxacin

Table 3 Different materials used as carriers for solid dispersions [37]

Class	Example of carriers
Sugars	dextrose, Sucrose, Galactose, Sorbitol, Maltose, Xylitol, Mannitol, Lactose
Acids	Citric acid, Succinic acid
Polymeric materials	Polyvinylpyrrolidone (PVP), Polyethylene glycols (PEG), Hydroxypropyl-methylcellulose, Methylcellulose, Hydroxyethylcellulose, Hydroxypropylcellulose, Cyclodextrins, Pectin, Galactomannan
Insoluble or enteric polymers	Hydroxypropylmethylcellulosephthalate, Eudragit L-100, Eudragit S-100, Eudragit RL, Eudragit RS
Surfactants	Polyoxyethylene stearate, Polyoxyethylene stearate, Poloxamer 188, Deoxycholic acid, Tweens, Spans
Miscellaneous	Pentaerythritol, Pentaerythrityltetracetate, Urea, Urethane, Hydroxyalkylxanthins

10. TYPE OF SOLID DISPERSION

1) Eutectics
2) Amorphous solid solutions
3) Solid solution
   - Continuous solid solution
   - Discontinuous solid solution
   - Substitutional solid solution d
   - Interstitial solid solution
4) Glass solution and suspension

1) Eutectics Mixtures: Two compounds that are entirely miscible in the liquid state but only very little so in the solid state make up a basic eutectic mixture. It's made by quickly solidifying a fused melt of two ingredients that exhibit perfect liquid miscibility but very little solid-solid solution.

Figure 1

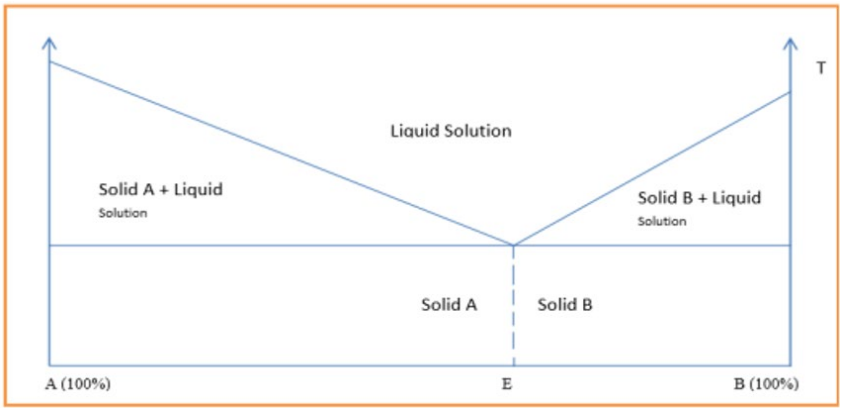

Figure 1 Eutectics Mixtures

2) Amorphous solid solution: The sole distinction between this and basic eutectic mixes is that the drug precipitates out in an amorphous form [38].

Figure 2

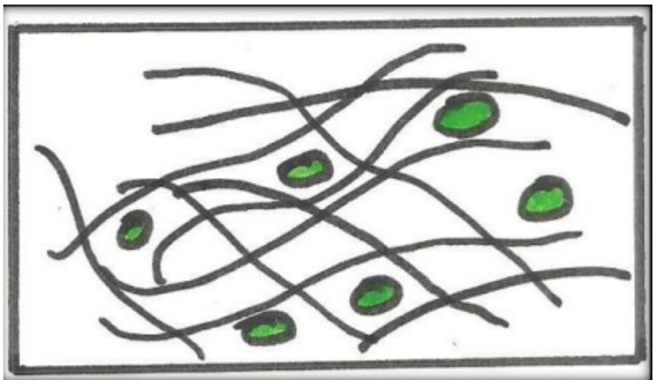

Figure 2 Amorphous Solid Solution

3) **Solid solution:** Regardless of the quantity of components, solid solutions are similar to liquid solutions in that they are composed of a single phase. In solid solutions, the drug's molecular dimensions have been lowered to the bare minimum, and the dissolving rate is dictated by the carrier's rate of dissolution. divided into two categories: first, based on their miscibility (continuous versus discontinuous solid solutions); second, based on the distribution of solvate molecules within the solvendum (interstitial, amorphous, substitutional).

- **Continuous solid solution:** All proportions of the constituents in a continuous solid solution are miscible. This indicates, in theory, that there is a stronger bond between the two components than there is between the molecules of each individual component.
- **Discontinuous solid solutions:** There is a limited amount of solubility between each component in a discontinuous solid solution. Goldberg et al. have proposed that the term "solid solution" should only be used when the mutual solubility of the two components is greater than 5% due to practical issues.

Figure 3

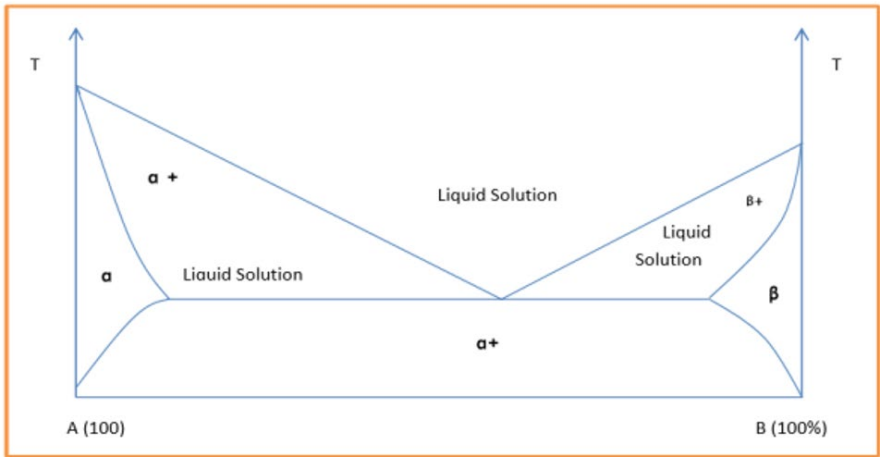

Figure 3 Discontinuous Solid Solution

- **Substitutional solid dispersions:** Only in cases where the size difference between the solute and solvent molecules is less than 15% is substitution feasible15. The solute molecules in classical solid solutions can either fit into the spaces between the solvent molecules or act as a stand-in for the solvent molecules in the crystal lattice [39].

Figure 4

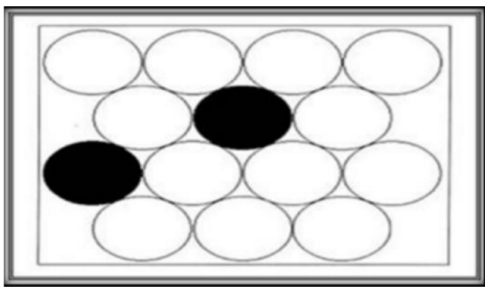

Figure 4 Substitutional Solid Solution

- **Interstitial solid solutions:** In an interstitial solid solution, the dissolved molecules fill the voids created in the crystal lattice by the solvent molecules. The diameter of the solute molecule should be less than 0.59 times that of the solvent molecule. [40]

Figure 5

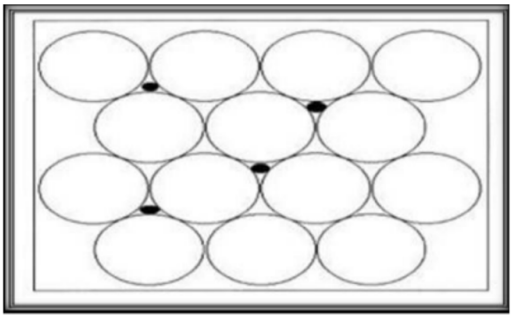

Figure 5 Interstitial Solid Solution

4) **Glass solutions and suspensions:** Solutes dissolve in glass carriers in glass solutions, which are homogenous glassy systems. Glass suspensions are mixtures in which glass solvent is used to suspend precipitated particles. The lattice energy in suspension and glass solution is substantially lower.

Solid Dispersion: The dispersion of one or more active ingredients in a solid state through an inert carrier or matrix is known as solid dispersion. [41]

Figure 6

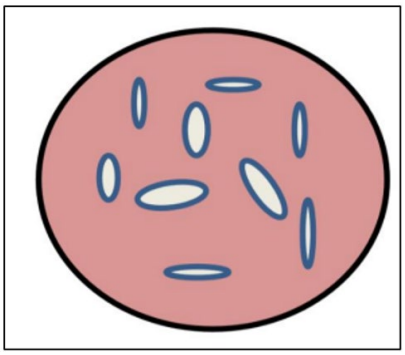

Figure 6 Solid Dispersion of Polymer Matrix.

11. CONCLUSION

The drug's solubility and bioavailability are the primary determinants of its therapeutic efficacy. The function of the solid dispersion in enhancing the solubility of poorly water-soluble pharmaceuticals is strongly supported by the growing number of drug candidates that are poorly water-soluble as well as advancements in the production procedures

for solid dispersions. The fact that many of the used carriers for solid dispersions are already widely utilized as excipients in the pharmaceutical sector and do not require safety studies gives them an additional benefit over alternative methods. In order to enhance the biological profile, solid dispersions are prepared using innovative technologies, which are discussed in this article. Nevertheless, issues including medication instability, cost-effectiveness, and scale-up must be resolved before this technology can be commercially developed. Solid dispersion is one technique that has been utilized to increase solubility among many others. For the past ten years, solid dispersion has been used to increase solubility. But in order to commercialize this technique, problems including medication instability, cost-effectiveness, and scale-up must be resolved. Although solid dispersion technology works well for making medications that are poorly soluble more soluble, further research is required before it can be applied more widely in the industrial sector.

CONFLICT OF INTERESTS

None.

ACKNOWLEDGMENTS

None.

REFERENCES

Prasad D, Lande J, Chauhan H, Chauhan H. Ternary amorphous solid dispersions. J Dev Drugs. 2017;6(3):181. doi: 10.4172/2329-6631.1000181.

WadkeDA, Serajuddin A, Jacobson H, "Preformulation testing". In: Lieberman HA, Lachman L, Schwartz JB, eds. Pharmaceutical Dosage Forms: Tablets. New York, NY: Marcel Dekker; 1989.

Brahmankar DM, Jaiswal SB. Biopharmaceutics and Pharmacokinetics, Vallabh Prakashan, 1st Edn. 1995:347-352.

Patel PB, Prajapati ST, Patel NR, Patel NN, Patel CN. Solid Dispersion: A Method of Improving Bioavailability and Taste Masking. Inventi Rapid: Pharm Tech Vol. 2012; Issue 4.

Varshney HM, Chatterjee, A. Solubility enhancement of poorly hydrophilic drugs by using different newer techniques: A Review. International Journal of Therapeutic Applications,2012; 6:8-138.

Wairkar SM, Gaud RS. Solid Dispersions: Solubility enhancement technique for poorly soluble drugs. International Journal of Research in Pharmaceutical and Biomedical Sciences,Jul– Sep 2013; 4 (3):847-854.

Pawar AR, Choudhari PD. Novel techniques for solubility, dissolution rate and bioavailability enhancement of class II and IV drugs. Asian Journal of Biomedical and Pharmaceutical Sciences,2012; 2 (13):9-14.

Bhise SB, Rajkumar M. Effect of HPMC on Solubility and Dissolution of Carbamazepine Form III in Simulated Gastrointestinal Fluids. Asian Journal of Pharmaceutics 2008; 2(1):38-42.

Christensen KL, Design of Redispersible Dry Emulsion: A Potential Oral Drug Delivery System. PhD Thesis 2000: 35-45

Patidar Kalpana et al. Drug Invention Today Vol.2.Issue 7. July 2010, 349-357.

Birdar V. S.,Arpana R. Patil, Guditi V. Sudarshan and Varsha B. Pokharkar, A comparative Studies of approaches improve solubility of roxithromycin, Int. J.Pharm., 2006; 22-32.

Chaudhari P.D., Current trend in solid dispersion techniques, www.pharmainfo.net, 2006; 2-12.

Dhirendra k, solid dispersions: a review, pak. j. pharm. sci., vol.22, no.2, April 2009, pp.234-246.

Dixit AK., Singh RP; solid dispersion – A strategy for improving the solubility of poorly soluble drugs; IJRPBS; 2012; 3(2); 960-966

Huda N.H., Saffoon N., Sutradhar K.B., Uddin R; Enhancement of Oral Bioavailability and Solid Dispersion: A Review; Journal of Applied Pharm Sci; 2011; 1; 13-20.

Ford JL. The current status of solid dispersions. Pharmaceutica Acta Helvae, 1986; 61:69-88.

Nokhodchi A, Javadzadeh Y, Siahi-Shadbad MR, Barzegar-Jalali M. The effect of type and concentration of vehicles on the dissolution rate of a poorly soluble drug (indomethacin) from liquisolid compacts. J Pharm Pharm Sci 2005; 8:18-25.

Bakatselou V, Oppenheim RC, Dressman JB. Solubilization and wetting effects of bile salts on the dissolution of steroids. Pharm Res, 1991;8:1461-9

Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm 2000; 50:47-60.

W. Nernst, Theorie der Reaktionsgeschwindigkeit in heterogenen Systemen, Zeitschrift f. Physik. Chemie 1994; 4:752-5.
Noyes AA, Whitney WR., The rate of solution of solid substances in their own solutions, J. Am. Chem. Soc 1997;19:930-4.
Enose AA, Dasan P, Sivaramakrishanan H, Kakkar V. Formulation, characterization and pharmacokinetic evaluation of telmisartan solid dispersions. J Mol Pharm Org Process Res 2016; 4:1-8.
Zawar L, Bari S. Microwave induced solid dispersion as a novel technique for enhancing dissolution rate of repaglinide. AdvPharmacol Pharm 2013; 1:95-101.
Singh G, Sharma S, Gupta GD. Extensive diminution of particle size and amorphization of a crystalline drug attained via eminent technology of solid dispersion: A comparative study. AAPS PharmSciTech2017; 18:1770-84.
UsmanovaLS, ZiganshinMA, GorbatchukV, ZiganshinaSA, BizyaevDA, BukharaevA, et al. A study of the formation of magnetically active solid dispersions of phenacetin using atomic and magnetic force microscopy. J Adv Pharm Tech Res 2017; 8:2-7.
Duarte I, Corvo ML, Serodio P, Vicente J, Pinto JF, Temtem M, et al. Production of nano-solid dispersions using a novel solvent-controlled precipitation process-Benchmarking their in vivo performance with an amorphous micro-sized solid dispersion produced by spray drying. Eur J Pharm Sci 2016; 93:203-14.
Lee SN, Poudel BK, Tran TH, Marasini N, Pradhan R, Lee YI,etal.A novel surface-attached carvedilol solid dispersion with enhanced solubility and dissolution. Arch Pharm Res 2013; 36:79-85.
Shahid DW, Vasundhra K, Surya PG, Gangadharappa HV, Mohammad A, Mubashir HM, Afrasim M. Enhancing therapeutic potential of poor aqueous soluble herbal drugs through solid dispersion-An overview. Phytomedicine Plus, 2021,1(4), 1-6.
Tereza S, Michaela S, Andrea S, Alena KR, Jan P and Petr Z. Investigation of Dissolution Mechanism and Release Kinetics of Poorly Water-Soluble Tadalafil from Amorphous Solid Dispersions Prepared by Various Methods. Pharmaceutics,2019;11(383),1-25.
Savjani K, Gajjar A, Savjani J. Drug solubility: Importance and enhancement technique. ISRNP. 2012; 1-10.
Edward K, Li D. Solubility in druglike properties: concept, structure, design and methods, from ADME to Toxicity Optimization. Elsevier. 2008; 56.
Jain C.P., Sharma A; Solid dispersion: A promising technique to enhance solubility of poorly water-soluble drug; Int. J of Drug Delivery; 2011; 3; 149-170.
Das S.K., Roy S., Kalimuthu Y., Khanam J., Nanda A; Solid Dispersions: An Approach to Enhance the Bioavailability of Poorly Water-Soluble Drugs; Int. J of Pharmacology and Pharmaceutical Technology; 1; 37 – 46.
praveen kumar; solid dispersion – A review; Journal of pharmaceutical and scientific innovation; 2012; 1(3); 27-34 8. Jaskirat et al; solubility enhancement by solid dispersion method: A review; Jornal of drug delivery & therapeutics; 2013; 3(5); 148-155
Adamer V, Krekeler A, Sedlmayr M. (2019). Solid dispersion comprising an orexin receptor antagonist. US10206880B2.
Adeli E. (2016). The use of supercritical anti-solvent (SAS) technique for preparation of irbesartan-Pluronic®F-127 nanoparticles to improve the drug dissolution. Powder Technol 298:65–72. [Google Scholar]
Ali W, Williams AC, Rawlinson CF. (2010). Stoichiometrically governed molecular interactions in drug: poloxamer solid dispersions. Int J Pharm 391:162–8. [PubMed] [Google Scholar]
Alshehri S, Imam SS, Altamimi MA, et al. (2020). Enhanced dissolution of luteolin by solid dispersion prepared by different methods: physicochemical characterization and antioxidant activity. ACS Omega 5:6461–71. [PMC free article] [PubMed] [Google Scholar]
Alshehri S, Shakeel F, Elzayat E, et al. (2019). Rat palatability, pharmacodynamics effect and bioavailability of mefenamic acid formulations utilizing hot-melt extrusion technology. Drug Dev Ind Pharm 45:1610–6. [PubMed] [Google Scholar]
Alshehri S, Shakeel F, Ibrahim M, et al. (2017). Influence of microwave technology on solid dispersions of mefenamic acid and flufenamic acid. PLoS One 12: E0182011. [PMC free article] [PubMed] [Google Scholar]
Alshehri SM, Shakeel F, Ibrahim MA, et al. (2019). Dissolution and bioavailability improvement of bioactive apigenin using solid dispersions prepared by different techniques. Saudi Pharm J 27:264–73.