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Improving Dissolution Rates of Low Solubility Pharmaceuticals Through Solid Dispersion Techniques

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ABSTRACT:
The ability of a solute to dissolve in a solvent and produce solution. The original intent of the solid dispersion procedure was to distribute Water-soluble carriers for weakly water-soluble medicines, which enhanced the pharmaceuticals 'dissolving characteristics and bioavailability. Strongly water-soluble drugs have poor dissolving qualities, which presents problems for pharmaceutical companies because the rate at which these drugs dissolve may also be the speed at which a drug's absorption in a solid dosage form is restricted. There are several methods for getting over low solubility one of them solid dispersion technique. This review aims to improve poorly soluble drug solubilization and bioavailability by using solid dispersion techniques. This review covers classification, carriers for solubility enhancement, and solid dispersion technique.

1. Introduction

. Pharmaceutical companies have challenges due to the poor dissolution properties of weakly water-soluble medications, as the rate at which these pharmaceuticals dissolve could be the speed at which a drug's absorption than a solid dosage form is limited [1][2].

One of the biggest problems formulation scientists today face is formulating poorly soluble chemicals for oral administration. This is due to the recent development of large-scale screening for possible medicinal drugs, which has produced a sharp increase in the number of medication candidates with low solubility. The increased apparent soluble state of a medicine that dissolves inadequately in water is achieved by a process called solubilization. Techniques for solubilization include complexation, using surface active agents (micellization), adding a cosolvent, forming salt, designing prodrugs, and reducing particle size [3].

Various physio-chemical techniques such as solubilizing vehicles, polymorphs, absorbents, solvate and hydrates, hydro trophy, pH modification, etc. can be employed to improve inadequate solubility medication absorption through the mouth [4-6].

It has been demonstrated that the method of solid dispersion is the most efficient for enhancing bioavailability and dissolving, especially for medications with low water solubility. Its ease of use, affordability, and advantages over alternative methods have led to its growing popularity [7]. Particle size can be decreased by solid distribution, and the medicines can be disseminated molecularly in either crystalline or amorphous particulate [8]. It provides improved surface qualities and wetness by enabling the distribution of the carrier component around and in between the medication.

One of the biggest issues that may occur from giving an active substance orally and result in poor medication absorption and inadequate bioavailability. This means that two areas of investigation in pharmaceuticals that are on enhancing the degree to which active ingredients are bioavailable orally are raising the permeability of poorly permeable medications and accelerating the rate of solubility and dissolution of inadequately soluble in

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water medications [9]. Various techniques, including salt creation, cyclodextrin complexation, medication solubilization in solvent(s), as well as reduction of the size of the particles, have been used to enhance the dissolving characteristics of pharmaceuticals with low water solubility [10][11][12]. Drugs classified as class II have an increased permeability of the membrane. and a low aqueous solubility with reference to the Biopharmaceutical Classification System. Consequently, bioavailability as well as oral BCS Class II absorption medications can be enhanced with solid dispersion technology is employed [13].

2. Biopharmaceutical Classification System: If a medication dissolves in digestive juices, penetrates the intestinal wall, goes through the liver without becoming inactivated, and reaches the circulation system, it is deemed to be orally active. Solubility is a serious challenge for new chemical entities that are highly lipophilic and water-insoluble. Amidon et al. categorized active chemicals of four kinds based on how soluble and permeable they are. The system for classifying biopharmaceuticals (BCS) [14].

- **Class I** Due to the compound's high permeability and solubility, the rate at which the stomach empties are the only factor affecting its bioavailability.
- **Class II** For molecules with poor water dissolution is the process that sets the rate limit, together with solubility and enough permeability.
- **Class III** substances that are soluble but permeability is low will be absorbed mostly through the gut wall.
- **Class IV** When a molecule has limitedthe step that limits the rate the permeability and solubility vary depending on the circumstance [15].

Class I increased solubility, increased permeability [Example – Levofloxacin]	Class-III insufficient solubility, Increased permeability [Example- Ibuprofen]
Class-III increased solubility, reduced permeability [Example-Cimetidine]	Class-IV Insufficient solubility, minimal permeability [Example-Ciprofloxacin hydrochloride]

3. Factor affecting solubility:[16][20]

Particle size: Particle solubility is dependent on their size. While the particle size gets smaller, the surface area to volume ratio rises. The interaction of a particle with the solvent intensifies as its surface area increases [20].

Temperature: Solubility is impacted by temperature. Since the process of solution absorbs energy, solubility increases. while also warming up. Energy generated during the solution process results in a decrease in solubility with increasing temperature [21].

Molecular size: The impossibility of solvating compounds with bigger molecular weights and sizes by surrounding larger molecules with solvent molecules is the cause of this drop in solubility.

Nature of solvent and solute: The concentration and mixing temperature of solutes and solvents affect how they interact with one another. At ambient temperature, 100 ml of water dissolves one gram of lead (II) chloride, yet with the same water concentrations, 200 grams of zinc chloride dissolved in 100 ml of water [19].

Pressure: Rising pressure causes gaseous solutes to become more soluble, whereas falling pressure causes them to become less soluble. Pressure variations have little effect on solubility for either liquid or solid.

Polarity: The polarity of the solvent and solute molecules has an impact on solubility. It is the property of polar solvents to dissolve solute molecules and the property of non-polar solvents to dissolve non-polar solute molecules.

Polymorphs: Polymorphism is the property that allows a substance's ability to exist in several crystalline states. An agent's capacity to crystallize in multiple forms is known as polymorphism. A solid may assume many different forms if it crystallizes in different ways. There can be variations in a polymorph's melting point. Due to the relationship between solubility and melting point of a solid, polymorphs will differ in their solubility [19].

Technique to overcome low solubility: [22-29]

Chemical Modifications:

- Salt Formation
- Co-crystallization
- Co-solvency
- Hydrotropic
- Use of novel solubilizer
- Nanotechnology

Physical Modifications:

- Particle size reduction

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- Conventional method
- Micronization
- Nanosuspension
- Polymorphs

Modification of the crystal habit:

- Pseudo polymorphs
- Complexation
- Physical mixture
- Kneading method
- Co-precipitate method

Inclusion Complex Formulation Based Techniques:

- Kneading method
- Lyophilization/Freeze-drying Technique
- Microwave irradiation method

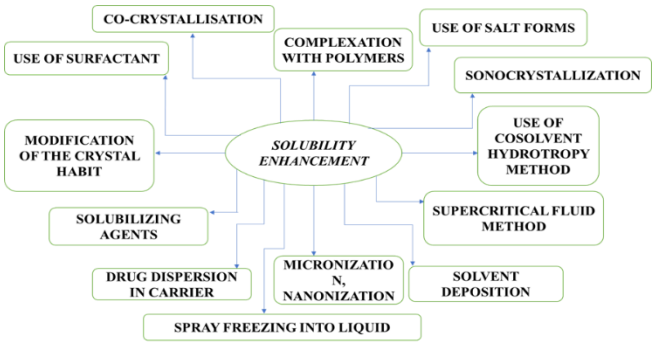
Solubilization by surfactants:

- Microemulsions
- Self-micro emulsifying drug delivery system

Drug dispersion in carriers:

- Solid solutions
- Solid dispersions
- Fusion Process
- Solvent Method
- Fusion solvent method
- Spray drying
- Lyophilization
- Hot melt Extrusion
- Dropping Method
- pH adjustment
- Supercritical fluid process
- Liquisolid technique
- Polymeric alteration

Figure-1: Technique of solubility enhancement [30][31][32]



4. Solid dispersion technique:

Chiou and Riegelman claim that solid dispersion is the process of forming eutectic mixes of pharmaceuticals and water-soluble transporters through melting [33]. A solid-state mixture of a single or more active components within an inert matrix or carrier is known as solid dispersion, achieved through melting, solvent or the procedure of melting and solvent. According to Sekiguchi et al., the substance was found in a microcrystalline, eutectic condition [34]. Goldberg et al. found that all drugs are not microcrystalline in solid form. Some drugs may be molecularly dispersed throughout the matrix, producing a stable solution [35]. Fine colloidal particles containing the medicine were discharged. when the solid dispersion became visible. to diluted liquids and the carrier disintegrated. Raising the surface area speeds up the rate at which drugs with poor water solubility dissolve and become more bioavailable. The commercial use of solid dispersion systems has been restricted due to manufacturing problems. However, carriers that are self-emulsifying and surface active can help overcome these challenges. At very high temperatures, the carriers melt, dissolving the drugs in between. When we talk about solid products, we usually mean products that contain two or more elements, usually a medication that is hydrophobic and a hydrophilic matrix. Crystalline or amorphous matrix are both possible. Molecular, amorphous cluster, or crystalline particles can all be used to disperse the drug. When active ingredients are dispersed solidly utilizing fusion, solvent, or melting solvent techniques, they are placed within a matrix or inert carrier. Medicines dissolved in solid diluents using conventional mechanical mixing techniques are excluded from this category. Solid dispersion is a concept that Meyerson and Gibaldi introduced.

Organizing Solid Dispersions by Class: Depending on the carrier used to create them, solid dispersions can be categorized.

1st Generation Solid Dispersions: These are made utilizing crystalline polymers. Examples: Organic acids, sugars, and urea [36].

2nd Generation Solid Dispersion: Polymers, either natural or synthetic, are used to make them. Examples include cyclodextrins, hydroxypropyl methylcellulose, ethyl cellulose, polyvinyl pyrrolidines, polyethylene glycols, and polymethacrylates [37].

3rd Generation Solid Dispersion: Polymers that self-emulsify on the surface are used to make them. Glucire

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44/14, Tween 80, and Poloxamer 408 are a few examples [38].

Types of Solid Dispersion: The medication may be dissolved using a solvent or melting process, resulting in crystalline, amorphous, or cluster-shaped particles. Therefore, different forms of solid dispersions can be distinguished using their molecular organization (**Table 1**) [39].

Table 1: Types of Solid Dispersions

S.no	Types of SD	Matrix	Drug	Remarks	Number of phases
I.	Eutectic	C	C	Initial SD type produced	2
I.	Amorphous precipitations inside a crystalline structure	C	A	Encountered infrequently	2
I.	Continuous	C	M	Unprepared and incompatible with all compositions	1
	Discontinuous	C	M	Partially miscible	2
	Substitutions	C	M	The drug's molecular diameter and the carrier diameter differ by less than 5%. This means that in such a case, the medication and matrix are synonymous. Continual or sporadic	1 or 2
	Interstitial	C	M	The drug's (solution) molecular diameter is less than 59% different from the carrier diameter. Can only be sporadic	2
V.	Glass suspension	A	C	The rate of evaporation and cooling affects the particle size in the dispersed phase. obtained after the medication has crystallized in an amorphous matrix.	2
V.	Glass suspension	A	A	The pace of cooling and evaporation affects the dispersed phase's particle size; this type of dispersion is typical for solids.	2
I.	Glass solution	A	M	needs fast cooling, difficult formation evaporation, or solid solubility OR miscibility throughout manufacture; many (recent) examples, especially with PVP	1

Advantages of solid dispersion Technology:

Pharmaceutical dosage forms containing poorly water-soluble medications become more soluble when solid dispersions are used, leading to faster dissolution and higher bioavailability. Furthermore, the strategy provides additional benefits, suchas [40].

I. Parenteral therapy can be substituted with fast-dissolving tablets., allowing patients to self-medicate without requiring water.

II. Compared to ordinary grinding, this method reduces particle size to a high degree, making it suited for waxy materials. It generates no dust and poses no risk of discharge.

III. Controlled medication release can be achieved with the use of appropriate excipients, such as cellulose derivatives.

IV. Capable of converting liquid pharmaceuticals to solidified dosage forms by mixing them using liquefied carriers, then cooling and pulverizing quickly. This approach worked well by using liquid medications like clofibrate and methyl salicylate.

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V.Solid dispersions can precipitate pharmaceuticals in an amorphous state, which is better more quickly and with greater solubility than in the stable crystalline condition.

Drawbacks of solid dispersion Technology:

I. Polymers employed can absorb moisture in solid dispersions,leading to crystal formation and phase separation development, or transformation from metastable to stable, crystalline to amorphous structures when being stored. This may lead to lower solubility and dissolution rates [41].
II. Inadequate scaling up for production [41].
III. Stability problems: Younis [42] found that as solid dispersions age, their dissolution rate decreases due to polymorphic transitions and the amorphous drug's recrystallization in the system.

Applications of solid dispersion in the pharmaceutical field:

The solid dispersion method may have several medicinal uses in addition to improving absorption; these should be investigated further. It is conceivable to employ this method:

- To attain an even distribution of a minimal quantity of medication in a solid condition.
- In order to regulate the erratic medication [43]
- To administer gaseous or liquid substances in a solid dose (up to 10%).
- Developing a sustained-release dosage form for a primary dose that releases quickly.
- To lessen the medicines' pre-systemic inactivation such as progesterone and morphine [44].
- It is possible to transform transforms intoeutectic, within a given system, solid solution, isomorphous etc [45].

Materials used As Carriers	Examples
Sugar	Succinic acid, Citric acid, Mannitol,
Acid	Sorbitol, Polyvinyl Pyrrolidone
Polymeric materials	(PVP-K90, PVP-K30 PVP) Polyethylene Glycols (PEG-6000, PEG-4000) Eudragit, HPMC phthalate (S100, L100, RS, RL)
Enteric or insoluble polymers	Spans, Tweens
Surfactants	
Surfactant Polymers	Gelucire, Poloxamer 188 Lutrol F-127, Solu plus, 44/14
Miscellaneous	Urea

Table2: Materials Used as Carrier

Preparation techniques for dispersing solids:

There are several methods for creating solid dispersions, ranging from manual procedures to complex techniques that require specialized equipment for the pharmaceutical business. A few of these tactics are discussed in brief below.

Co-melting method: This method entails physically combining a medication having a carrier that dissolves in water, heating it up to the desired temperature of melting, and then cooling it down. In a vigorously stirred ice bath, the molten slurry soon solidifies. Pulverized, crushed, and sieved is the final solid bulk.To modify the process, pour uniform melt applied in a ferrite or stainless-steel plate in a thin coating, and the other side cooled using water or air. To achieve solute super-saturation or medication of a system, quickly quench melting at a high temperature. Solute molecules are detained in the solvent matrix due to immediate solidification under certain conditions. The quenching approach improves crystallite dispersion in simple eutectic solutions. The co-melting approach is cost-effective and solvent-free. However, it may not be suited for unstable drugs or carriers that evaporate at higher temperatures. In order to stop oxidative damage of the medicine or carrier, consider Utilizing an inert gas like nitrogen, melting the combination under vacuum, or heating it in a sealed container [46].

Fusion technique: That's a co-melting process variant. Melt the carrier by placing it in a ceramic dish and heating it over a steam bath. Use a glass rod to gradually spread the correctly weighed medication into the molten medium. Once the medicine is evenly distributed within the carrier, after being removed from the steam bath, the dish is let to cool at room temperature until it solidifies. After being crushed, the solid dispersion is sieved. This approach can reduce the heat degradation of pharmaceuticals [47].

Solvent evaporation technique: Following a common volatile solvent's dissolution, the medication and carrier are removed under vacuum. A sieve and crusher are used to produce the solid dispersion [48].

Kneading technique:It involves making a paste out of the carrier by soaking it in water. Next, for a predetermined amount of time, the medication is kneaded and added. Once the mixture has been kneaded,

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it is dried and sieved as required. This approach is appropriate for thermolabile medicines, but not for those moisture-sensitive[49].

Co-precipitation technique: To the carrier solution, add the necessary dosage of medication.The system is kept under magnetic agitation and shielded from light. Vacuum filtration is used to separate the precipitate, which is then dried at room temperature [50].

Co-grinding technique: It is combined using a blender the medicine and carrier at a specific speed for a set amount of time. The slurry is charged into a ball mill chamber that vibrates. The powder combination is crushed. Until it is needed, the product is collected and stored in a glass vial with a screw cover at room temperature [51].

Gel entrapment technique: To create a translucent gel, the carrier (hydroxyl propyl methyl cellulose) is dissolved in a solvent that is organic. Sonication is used for a few minutes to dissolve the drug in the gel. Under vacuum, the organic solvent evaporates. To prepare solid dispersions, use a mortar and pestle to minimize their size before sieving [52].

Spray drying technique: The necessary quantity ofthe carrier dissolves in the liquid, and the medication is dissolved in an appropriate solvent. To produce a fine, free-flowing particle dispersion that is solid, a clear solution is mixed using sonication or other suitable methods before being spray-dried with a spray dryer.

Electrospinning technique: Electrospinning involves delivering a millimeter-scale nozzle, a polymeric fluid stream to generate solid fibres. Using an electrostatic field, a high-conducting capillary connected to a reservoir containing a polymer melt or solution and a conductive collection screen are applied during the process. Charge accumulation on the surface of a pendant drop occurs when the electrostatic field intensity reaches a certain value. causes it to collapse into a conical form, sometimes referred to as a Taylor cone. An electrically charged polymer jet is propelled beyond the critical value. from the cone's apex and transported to the collection screen by electrostatic force [53]. This technology offers the ability to prepare nanofibers and control them [54].

Freeze-drying technique: The technique includes putting the drug and carrier into a solvent to dissolve them., then freezing it with liquid nitrogen. Finally, the lyophilized frozen solution is used. Although the literature suggests that this technology is effective for incorporating drugs into stabilizing matrices, it is underutilized for preparing solid dispersions causing cost constraints. Freeze drying has advantages such as minimizing heat stress during solid dispersion formation and reducing the possibility of phase separation [55].

Supercritical fluid technique: Carbon dioxide (CO2) is commonly employed in supercritical fluid technologies as both a solvent for drugs and an anti-solvent. A common solvent is used to dissolve the medication and carrier and then poured using a nozzle into a particle-forming chamber. Following that, the gas is heated above its temperature and pressure critical points. Upon spraying the solution, the SCF rapidly extracts the solvent, leaving behind solid dispersion particles on the vessel's walls and bottom. This method's advantages are its high yield, low particle size, and residual solvent content [56].

Direct capsule filling [57]: During the process, a liquid combination of drug and carrier is filled into hard gelatine capsules. Once cooled to room temperature, the molten dispersion solidifies inside the capsule. Advantages include avoiding grinding-induced changes in drug crystallinity decreasing operator exposure and cross-contamination in a dust-free environment while increasing fill weight and consistency.

Characterization of solid dispersion:

The drug in the matrix may have a spectrum of solid dispersions' molecular structures. There are many ways to analyze the positioning of molecules in solid dispersions. However, the majority of research has been on differentiating between crystalline and amorphous materials. The amount of crystalline material in a dispersion can be ascertained in a variety of ways[58].

Infrared spectroscopy (IR)

It is possible to identify changes during drug-matrix interactions, in terms of energy distribution by using infrared spectroscopy (IR). Vibrant bands with sharp

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edges show crystallinity. With pure material, Crystallinity in the range of 1 to 99% was properly measured using Fourier Transformed Infrared Spectroscopy (FTIR)[59].

Water vapor sorption

When the hygroscopicity varies, Materials can be distinguished between crystalline and amorphous using water vapor sorption[60]. Precise information regarding for this approach, completely crystalline and entirely amorphous samples must be hygroscopic.

Isothermal Microcalorimetry

Isothermal microcalorimetry is utilized to calculate the energy required for amorphous materials to crystallize when heated above the temperature at which glass transitions (temperature gradient) [61]. There are certain restrictions on this method. First off, this technique can only be applied in situations where crystallization only happens during the measurement due to physical stability. Second, any amorphous material must be considered to crystallize. Thirdly, when two amorphous substances are mixed together, it can be difficult to discern between the energy of crystallization for the medication and matrix.

Dissolution calorimetry

Dissolution calorimetry is used to measure the dissolving energy, which depends on the sample's crystallinity[62]. Crystalline materials often dissolve endothermically, whereas amorphous materials dissolve exothermically.

Macroscopic techniques

A macroscopic method of evaluating the crystalline and amorphous materials' mechanical properties can give an indication of the degree of crystallinity. The degree of crystallinity affects the modulus of elasticity for viscosity, which is determined by dynamic mechanical analysis (DMA) and density measurements. Nevertheless, these methods also necessitate an understanding of the characteristics' additivity in firmly blended binary solids.

Calorimetry using Differential Scanning

Differential scanning calorimetry is one method that is often used to calculate the amount of crystalline material [63]. Samples are heated steadily while the energy needed to do so is measured using DSC. DSC may be used to find the temperatureswhere thermal events take place. Melting, degradation, and the shift from glass to rubber are examples of thermal events.

Furthermore, it is possible to quantify the energy required for melting and (re)crystallization.The amount of crystalline material can be determined using the melting energy.

Calorimetry using Temperature-Modulated Differential Scanning

One technique to evaluate the level of drug mixing in an included substance is calorimetry using temperature-modulated differential scanning. One can distinguish between reversible and irreversible actions because of the modulation. For example, reversible glass transitions in amorphous materials are differentiated from irreversible crystallization or relaxation. Moreover, the value of the Tg is determined by the content of the uniformly dispersed solid dispersion. Research has demonstrated that TMDSC has a higher sensitivity than traditional DSC [64]. Consequently, the amount of medication that has been molecularly disseminated can be determined using this technique [65]. From there, it is determined what percentage of the medication is distributed as distinct molecules[66].

In Vitro Dissolution Studies

To ascertain the behavior of dissolution, in vitro dissolution experiments are conducted. Via in vitro-in vivo correlation (IVIVC), the bioavailability or bioequivalence of the medicinalsubstance can be shown via the in-vitro dissolution study. On the other hand, if the rate at which a medication dissolves limits the amount of absorption that occurs the medication in the gastrointestinal fluid dissolves or is liberated from the dose form faster than it can flow freely through the biomembranes. To determine the absorption rate in a solid dispersion system, as well as its bioavailability and ultimately its bioequivalence, a specially designed in-vivo dissolution research will be necessary. For testing dissolution, the US Pharmacopoeia uses the following equipment.

Solubility Studies

Studies on solubility are conducted to determine the behavior of solubility that the solid dispersion mechanism found in many solvent systems and bodily fluids.

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Conclusion:

It is evident from this review that among the most advanced techniques for dealing with the problem of a medication that is not very soluble in water Solid dispersion technology is called solubility. Therefore, before creating a novel solid dispersal mechanism for a certain medication, it is imperative to investigate the physiochemical drug's and carrier's characteristics that can coexist harmoniously. Furthermore, enhancing the medication's solubility and rate of dissolution depends critically on the manufacturing method and the carrier-to-drug ratio.In order to accomplish this goal, we have tried to organize all of the information in this post so that it may be tailored to each individual element.

Thus, solid dispersion technology will advance further in the future of issues related to the delivery of soluble poorly medicines in novel drug delivery applications.

References:

1. Kalpana P, Manish S, Dinesh SK, Surendra JK. Solid Dispersion: Approaches, Technology involved, Unmet need & Challenges. Drug Invention Today. 2010 Jul 1;2(7).
2. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. European journal of Pharmaceutics and Biopharmaceutics. 2000 Jul 3;50(1):47-60.
3. James S, James CB. Encyclopedia of Pharmaceutical Technology. 2nd ed. New York Basel: Marcel Dekker Inc.; 2002. pp.1676-1685.
4. Ahuja S, Scypinski S, editors. Handbook of modern pharmaceutical analysis. Academic press; 2001 Jul 26.
5. Al Masum MA, Islam SA, Reza MS. Enhancement of solubility and dissolution characteristics of ibuprofen by solid dispersion technique. Dhaka University Journal of Pharmaceutical Sciences. 2012 Nov 4;11(1):1-6.
6. Rasool AA, Hussain AA, Dittert LW. Solubility enhancement of some water-insoluble drugs in the presence of nicotinamide and related compounds. Journal of pharmaceutical sciences. 1991 Apr 1;80(4):387-93.
7. Tiwari R, Tiwari G, Srivastava B, Rai AK. Solid dispersions: an overview to modify bioavailability of poorly water-soluble drugs. International Journal of PharmTech Research. 2009 Oct 1;1(4):1338-49.
8. Pouton CW. Lipid formulations for oral administration of drugs: non-emulsifying, self-emulsifying and 'self-microemulsifying'drug delivery systems. European journal of pharmaceutical sciences. 2000 Oct 1;11:S93-8.
9. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. European journal of Pharmaceutics and Biopharmaceutics. 2000 Jul 3;50(1):47-60.
10. Kalpana P, Manish S, Dinesh SK, Surendra JK. Solid Dispersion: Approaches, Technology involved, Unmet need & Challenges. Drug Invention Today. 2010 Jul 1;2(7).
11. Biradar SV, Patil AR, Sudarsan GV, Pokharkar VB. A comparative study of approaches used to improve solubility of roxithromycin. Powder Technology. 2006 Oct 24;169(1):22-32.
12. Sharma PK, Chaudhari PD, Badagale KD, Kulkarni PA, Barhate NS. Current trends in solid dispersion techniques. Drug Delivery Technology. 2006 May;6(5):2-12.
13. GL A. Theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res. 1995;22:11-23.
14. Galia E, Nicolaides E, Hörter D, Löbenberg R, Reppas C, Dressman JB. Evaluation of various dissolution media for predicting in vivo performance of class I and II drugs. Pharmaceutical research. 1998 May;15:698-705.
15. Janssens S, De Armas HN, Roberts CJ, Van den Mooter G. Characterization of ternary solid dispersions of itraconazole, PEG 6000, and HPMC 2910 E5. Journal of pharmaceutical sciences. 2008 Jun;97(6):2110-20.
16. Awuchi CG, Amagwula IO, Priya P, Kumar R, Yezdani U, Khan MG. Aflatoxins in foods and feeds: A review on health implications, detection, and control. Bull. Environ. Pharmacol. Life Sci. 2020 Aug 9;9:149-55.
17. Akhgari A, Shakib Z, Sanati S. A review on electrospun nanofibers for oral drug delivery. Nanomedicine Journal. 2017 Oct 1;4(4):197–207.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 36-46 | ISSN:2251-6727

18. Koda-Kimble MA. Koda-Kimble and Young's applied therapeutics: the clinical use of drugs. Lippincott Williams & Wilkins; 2012 Feb 1.
19. Alubaidy A, Venkatakrishnan K, Tan B, Nanofibers reinforced polymer composite microstructures. Adv Nanofiber 2013;7:165–184.
20. Bhanja S, Ellaiah P, Martha S, Sahu A, Padhy S. Preparation and evaluation of solid dispersions of poorly soluble drug repaglinide. Asian Journal of Biochemical and Pharmaceutical Research. 2011;3(1):201–221.
21. Buckton G, Beezer AE (1992) The relationship between particle size and solubility. International journal of pharmaceutics 1992; 82:R7–R10.
22. Broadhead J, Edmond Rouan S, Rhodes C, the spray drying of pharmaceuticals. Drug development and industrial pharmacy 1992; 18: 1169–1206.
23. Buckton G, Beezer AE (1992) The relationship between particle size and solubility. International journal of pharmaceutics 1992; 82:R7–R10.
24. Sahana S. Purabisaha, Roshan kumar, Pradipta das, Indranil Chatterjee, Prasit Roy, Sk Abdur Rahamat. A Review of the 2019 Corona virus (COVID-19) World Journal of Pharmacy and Pharmaceutical science. 2020;9(9):2367-81.
25. Chavan RB, Thipparaboina R, Kumar D, Shastri NR, Co amorphous systems: A product development perspective. International journal of pharmaceutics 2016; 515:403–415.
26. Chiou WL, Riegelman S (1971) Pharmaceutical applications of solid dispersion systems. Journal of pharmaceutical sciences 1971; 60:1281–1302.
27. Davis ME, Brewster ME, Cyclodextrin-based pharmaceutics: past, present and future. Nature reviews Drug discovery 2004; 3:1023–1035.
28. Dengale SJ, Grohganz H, Rades T, Löbmann K, Recent advances in co-amorphous drug formulations. Advanced drug delivery reviews 2016; 100:116–125.
29. Bind A, Das S, Singh VD, Kumar R, Chourasia A, Saha P. Natural bioactives for the potential management of gastric ulceration. Turkish Journal of Physiotherapy and Rehabilitation. 2020;32(3):221-6.
30. Thorat YS, Gonjari ID, Hosmani AH. Solubility enhancement techniques: a review on conventional and novel approaches. International journal of pharmaceutical sciences and research. 2011 Oct 1;2(10):2501.
31. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. Philadelphia: Lea &Febiger; 1976:221.
32. 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):13.
33. Chiou WL, Riegelman S. Pharmaceutical applications of solid dispersion systems. Journal of pharmaceutical sciences. 1971 Sep 1;60(9):1281-302.
34. 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. Chemical and Pharmaceutical Bulletin. 1961 Nov 25;9(11):866-72.
35. Hancock BC, Zografi G. Characteristics and significance of the amorphous state in pharmaceutical systems. Journal of pharmaceutical sciences. 1997 Jan;86(1):1-12.
36. GL A. Theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res. 1995;22:11-23.
37. Kawabata Y, Wada K, Nakatani M, Yamada S, Onoue S. Formulation design for poorly water-soluble drugs based on biopharmaceutics classification system: basic approaches and practical applications. International journal of pharmaceutics. 2011 Nov 25;420(1):1-10.
38. Sharma D, Soni M, Kumar S, Gupta GD. Solubility enhancement–eminent role in poorly soluble drugs. Research Journal of Pharmacy and Technology. 2009;2(2):220-224.
39. Vasconcelos T, Sarmento B, Costa P. Solid dispersions as strategy to improve oral bioavailability of poor water-soluble drugs. Drug discovery today. 2007 Dec 1;12(23-24):1068-1075.
40. Dalvi PB, Gerange AB, Ingale PR. Solid dispersion: strategy to enhance solubility. Journal of Drug Delivery and Therapeutics. 2015 Mar 13;5(2):20-28.
41. Singh S, Baghel RS, Yadav L. A review on solid dispersion. International journal of pharmacy & life sciences. 2011 Sep 1;2(9):1078-1095.
42. Mahmoud A. Younis. Development and evaluation of new dosage forms of domperidone. Master thesis, Faculty of Pharmacy. Assiut University, Egypt, 2016.

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43. Kamalakkannan V, Puratchikody A, Masilamani K, Senthilnathan B. Solubility enhancement of poorly soluble drugs by solid dispersion technique–A review. J. Pharm. Res. 2010 Sep;3(9):2314-21.
44. McKelvey CA. Solid Dispersions: New Approaches and Technologies in Oral Drug Delivery. Controlled Release Society. 2009.
45. Liu R, editor Water insoluble drug formulation. Library of Congress Cataloging-in- Publication Data; 2007.
46. Kalaiselvan R, Mohanta GP, Manna PK, Manavalan R. Studies on mechanism of enhanced dissolution of albendazole solid dispersions with crystalline carriers. Indian J Pharm Sci. 2006 Sep 1;68(5):599-607.
47. Akiladevi D, Shanmugapandiyan P, Jebasingh D, Basak S. Preparation and evaluation of paracetamol by solid dispersion technique. Int J Pharm Pharm Sci. 2011;3(1):188-91.
48. Alaziz DM, Sammour OA, Elshamy AE, Neseem DI. Formulation and evaluation of binary and ternary solid dispersions of domperidone by solvent evaporation method 2014;8(3):66-80.
49. Ghareeb MM, Abdulrasool AA, Hussein AA, Noordin MI. Kneading technique for preparation of binary solid dispersion of meloxicam with poloxamer 188. AapsPharmscitech. 2009 Dec;10:1206-1215.
50. Shah N, Iyer RM, Mair HJ, Choi D, Tian H, Diodone R, Fahnrich K, Pabst-Ravot A, Tang K, Scheubel E, Grippo JF. Improved human bioavailability of vemurafenib, a practically insoluble drug, using an amorphous polymer-stabilized solid dispersion prepared by a solvent-controlled coprecipitation process. Journal of pharmaceutical sciences. 2013 Mar 1;102(3):967-81.
51. Nokhodchi A, Talari R, Valizadeh H, Jalali MB. An investigation on the solid dispersions of chlordiazepoxide. International journal of biomedical science: IJBS. 2007 Sep;3(3):211-216.
52. Bhise SB, Rajkumar M. Effect of HPMC on solubility and dissolution of carbamazepine form III in simulated gastrointestinal fluids. Asian Journal of Pharmaceutics (AJP). 2008;2(1):38-42.
53. Hohman MM, Shin M, Rutledge G, Brenner MP. Electrospinning and electrically forced jets. II. Applications. Physics of fluids. 2001 Aug 1;13(8):2221-36.
54. Neamnark A, Rujiravanit R, Supaphol P. Electrospinning of hexanoyl chitosan. Carbohydrate polymers. 2006 Nov 2;66(3):298-305.
55. Van Drooge DJ, Hinrichs WL, Visser MR, Frijlink HW. Characterization of the molecular distribution of drugs in glassy solid dispersions at the nano-meter scale, using differential scanning calorimetry and gravimetric water vapour sorption techniques. International journal of pharmaceutics. 2006 Mar 9;310(1-2):220-229.
56. Majerik V, Charbit G, Badens E, Horváth G, Szokonya L, Bosc N, Teillaud E. Bioavailability enhancement of an active substance by supercritical antisolvent precipitation. The Journal of supercritical fluids. 2007 Feb 1;40(1):101-10.
57. Serajuddin AT, Mufson D, Bernstein DF, Sheen PC, Augustine MA. Effect of vehicle amphiphilicity on the dissolution and bioavailability of a poorly water-soluble drug from solid dispersions. Journal of pharmaceutical sciences. 1988 May 1;77(5):414-417.
58. Kaushal AM, Gupta P, Bansal AK. Amorphous drug delivery systems: molecular aspects, design, and performance. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2004;21(3):133-193.
59. Taylor LS, Zografi G. Spectroscopic characterization of interactions between PVP and indomethacin in amorphous molecular dispersions. Pharmaceutical research. 1997 Dec;14:1691-1698.
60. Buckton G, Darcy P. The use of gravimetric studies to assess the degree of crystallinity of predominantly crystalline powders. International Journal of Pharmaceutics. 1995 Sep 12;123(2):265-71.
61. Sebhatu T, Angberg M, Ahlneck C. Assessment of the degree of disorder in crystalline solids by isothermal microcalorimetry. International Journal of Pharmaceutics. 1994 Apr 11;104(2):135-44.
62. Pikal MJ, Lukes AL, Lang JE, Gaines K. Quantitative crystallinity determinations for β-lactam antibiotics by solution calorimetry: Correlations with stability. Journal of pharmaceutical sciences. 1978 Jun 1;67(6):767-73.
63. Kerc J, Srcic S. Thermal analysis of glassy pharmaceuticals. Thermochimica acta. 1995 Jan 2;248:81-95.
64. De Meuter P, Rahier H, Van Mele B. The use of modulated temperature differential scanning calorimetry for the characterisation of food systems.

International Journal of Pharmaceutics. 1999 Dec 1;192(1):77-84.

65. Cilurzo F, Minghetti P, Casiraghi A, Montanari L. Characterization of nifedipine solid dispersions. International journal of pharmaceutics. 2002 Aug 21;242(1-2):313-317.
66. Vasanthavada M, Tong WQ, Joshi Y, Kislalioglu MS. Phase behavior of amorphous molecular dispersions I: Determination of the degree and mechanism of solid solubility. Pharmaceutical research. 2004 Sep;21:1598-1606.