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SOLID DISPERSION: AN OVERVIEW OF DIFFERENT METHODOLOGY AND TECHNIQUES

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Abstract

Formulation scientists continue to face challenges in improving the oral bioavailability of medications administered in solid dosage forms due to limited solubility of drug molecules. The rate-limiting mechanism in the drug absorption process from a solid dosage form of relatively insoluble medicines may be the dissolving rate. Therefore, formulation scientists have a difficulty as more poorly soluble medications dissolve using the solid dispersion technique. Solid dispersion techniques, involves reduction of drug particle size, improve wettability, and produces amorphous particles, and have received significant interest in enhancing the dissolving rate of highly lipophilic medicines and, consequently, improving their bioavailability. A collection of solid products with at least two distinct components—typically a hydrophilic inert carrier or matrix and a hydrophobic drug—are referred to as solid dispersions. This article consists of the origins, categorization, procedures and advantages and drawbacks of several preparation methods for solid dispersion technology. The latest developments in the realm of solid dispersion technology are also included in this overview.

Keywords: Solubility, rate of solubility, solubility enhancement, need of solubility enhancement, solid dispersion.

1. Introduction

An estimated 35–40% of pharmaceuticals are thought to have poor aqueous solubility, which impacts drug absorption from the gastrointestinal tract and causes high inter- and intra-subject variability, poor oral bioavailability, increase in doses, decreased therapeutic efficacy, and ultimately, formulation development failure. Various formulation techniques, such as the production of solid solutions or solid dispersions with hydrophilic carriers, complexation, Micronization, solubilization, and drug solubilization using dendrimers, as well as self-micro emulsifying drug delivery systems (SMEDDS) are implemented in order to overcome the formulation development challenges. For the purpose of improving solubility, pro-drug strategies, spray drying, salt synthesis, and nanoparticulate techniques have all been tried. Using many hydrophilic carriers in a straightforward solid dispersion approach would be an appealing option. By lowering particle size to almost molecular levels, this approach offers a range of processing and excipient alternatives that facilitate the formulation of cost-effective oral delivery systems for low water-soluble drug substance, hence indicating an improved formulation [1].

1.1 Solubility and Dissolution

One of the most significant variables influencing a drug's oral bioavailability is its solubility behaviour. There have always been some drug substances, whose solubility has made it difficult to create an oral administration formulation having high bioavailability. The number of poorly soluble drug moieties has abruptly increased with the introduction of high throughput screening of potential therapeutic agents. As a result, one of the biggest and most frequent challenges facing formulation scientists in the pharmaceutical industry today is the formulation of poorly soluble compounds for oral delivery [2].

The term "solubility" refers to the amount of a substance that enters solution to create a saturated solution at constant pressure and temperature. Using the modified Noyes-Whitney equation (1) can offer some guidance on how to maximise the oral bioavailability of a substance by improving the dissolution rate of even extremely poorly soluble compounds. Noyes-Whitney equation:

$$dC/dt = AD (Cs - C)/h$$

Where A is the surface area available for dissolution, D is the compound's diffusion coefficient, Cs is the compound's solubility in a dissolution medium, C is the drug concentration in the medium at a time t, and h is the thickness of the diffusion boundary layer next to the surface of the dissolving compound [4].

As a result, the rate of dissolution is expressed as dC/dt. The total amount of energy that the system has available to carry out work is measured as free energy, or G. When no more energy can be produced, the process's value declines until equilibrium is reached, or when $\Delta G=0$ at equilibrium, as stated in reference [3]. A saturated solution is created when there is a balance between the dissolved and undissolved solute components during the dissolution process.

The primary techniques employed to improve dissolution are to: reduce the thickness of the boundary layer; ensure sink conditions for dissolution; increase the surface area available for dissolution by decreasing the size of the particles present in the solid compound by optimising the wetting phenomenon of the compound surface; and, last but not least, improve the apparent solubility of the drug molecules under physiologically relevant conditions. A number of factors can hinder a drug's capacity to be absorbed from the gastrointestinal (GI) tract, but the two most significant ones are the drug's poor water solubility and/or membrane permeability.

When administering an active drug orally, it is crucial that it dissolves in the stomach and/or intestinal fluids in order for the GI membrane permeability to allow systemic circulation. Therefore, a medication with low aqueous solubility will show limited absorption by dissolving rate, and a medication with low membrane permeability will essentially show limited absorption by permeation rate. Therefore, increasing the permeability of poorly permeable medications and boosting the solubility and dissolution rate of poorly water-soluble drugs are two fields of pharmaceutical research that concentrate on improving the oral bioavailability of the active ingredients [5].

The rate at which the relative amount of a drug supplied dose enters the systemic circulation from the site of administration is known as bioavailability (American Pharmaceutical Association, 1972). The drug's physiochemical characteristics, drug formulation type, gastric emptying rate, enzyme induction/inhibition by other drugs/foods, circadian variations, transporters, disease state, gastrointestinal tract health, etc. are some of the factors that affect the drug's bioavailability. Given that the GI tract's contents are aqueous in nature, a medication with low saturation solubility will also have a low dissolving rate, which will lead to a poor oral bioavailability. Solubility of medicines originating from synthetic sources is less than 0.1 mg/ml for about 60% of them [7].

Numerous methods are available for improving poorly soluble drugs solubility and dissolution. Some of them are listed below:

1.1.1 Physical Modifications

- Particle size
- Micronization
- Nanosuspensions
- Modifications of the crystal habit
- Polymorphs
- Pseudo polymorphs (including solvates)
- Complexation/solubilization
- Utilization of surfactants
- Utilization of cyclodextrins
- Dispersion of Drug in a carrier
- Implication of Eutectic mixtures
- Solid dispersions (non-molecular)
- Solid solutions

1.1.2 Chemical Modifications

- Soluble prodrug approach
- Salt formation
- Co-solvency
- Co-crystallization
- Nanotechnology

Among all these methods, one of the technologies- Solid dispersion method is explained further.

2. Solid Dispersion

In 1961, Sekiguchi and Obi published the first description of solid dispersions. Till date, formulation of solid dispersion remains one of the widely used methods for enhancing the solubility of poorly soluble drugs, mainly of BCS class II and IV. One of the key tactics for addressing the oral absorption of poorly soluble substances that is limited by the rate of dissolution is solid dispersion. According to the physical state of the solid dispersion, formulating poorly soluble compounds as solid dispersions may result in reduced agglomeration, enhanced wetting, altered drug molecule physical state changeability, and perhaps even a dispersion at the molecular level. A collection of solid products made up of two or more distinct components, usually a hydrophilic matrix and a hydrophobic pharmaceutically active moiety, are referred to as solid dispersions. There are two forms of solid: Crystalline and Amorphous. The drug might be distributed molecularly as crystalline or amorphous particles (clusters) in the crystal lattice. This distribution is one of the major reasons that contribute to the solubility of drug in solid dispersion formulation.

2.1 Classification of Solid Dispersion

Solid dispersions are categorised in a number of ways, depending on the carrier employed as well as their solid-state structure. It is important to categorise different solid dispersion systems according to how quickly they release particles. Solid dispersions were categorised by Riegelman and Chiou into the following six representative types: Simple eutectic mixtures, glass solutions and suspensions, solid solutions, amorphous precipitations in a crystalline carrier, compound or complex formation, and mixtures of the preceding five categories [8].

It is anticipated that if a drug substance and a polymer are immiscible when the fluid mixture is solidified, they will not show signs of miscibility. Because of this, such systems may be thought of as being similar to their corresponding physical mixtures. Any decrease in dissolution performance could result in changes to the drug's or the polymer's morphology as a result of physical transformations (i.e., solid to liquid state and back), increased surface area, and/or close drug-polymer mixing.

- ✓ **Drug and Polymer Exhibiting Miscibility in Fluid State**

  The mixture may or may not experience phase separation during solidification if the medication and polymer are miscible in their fluid form. This could have an impact on the solid dispersion's structure.

- ✓ **Eutectic Mixtures**

  Sekiguchi & Obi first defined eutectic mixtures as solid dispersions in 1961. When a polymer and a medicine are miscible when they are molten, but crystallise into two different components with very little miscibility when cooled, this is known as a eutectic combination.

- ✓ **Crystalline Solid Dispersion**

  When the pace at which the drug crystallises from the drug-polymer miscible mixture is higher than the rate at which the drug-polymer fluid mixture solidifies, a crystalline solid dispersion is produced.

- ✓ **Amorphous Solid Dispersion**

  The drug is kinetically trapped in its amorphous or "solidified-liquid" state if the drug-polymer fluid mixture is cooled at a pace that prevents drug crystallisation. There is a significant chance that these kinds of dispersions could change into a more stable, less soluble crystalline form.

- ✓ **Solid Solution**

  A solid dispersion that is miscible in both solid and fluid states is referred to as a solid solution. These solid solutions could be crystalline or amorphous in nature. Since the drug is molecularly scattered in the carrier matrix in the case of amorphous solid solutions, its effective surface area is primarily greater, increasing the drug's rate of dissolution. When a crystalline medication gets stuck inside a crystalline polymeric carrier, crystalline solid solution could happen.

  - The solid solutions can be classified as continuous or discontinuous based on how well the two components mix. The two substances are miscible in the solid state in all ratios in continuous solid solutions. Discontinuous solid solutions are made up of components that are immiscible at intermediate compositions but miscible at extremes.

  - The solid solutions are categorised as interstitial and substitutional based on the molecular sizes of the two constituents. An interstitial solid solution is created when the solute (guest) molecule occupies the interstitial space in the solvent (host) lattice. In a substitutional solid solution, the solute molecule replaces the solvent molecule in the crystal lattice.

Based on the choice of the polymer employed in the preparation of the solid dispersions, it is divided into four different classes: First generation solid dispersions, second generation solid dispersions, third generation solid dispersions and fourth generation solid dispersions.

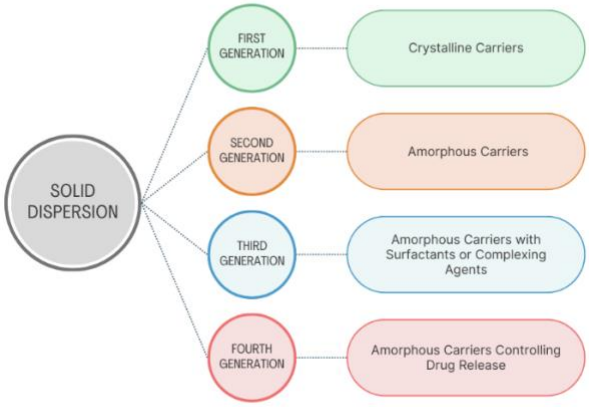

Figure 1: Different generation of solid dispersion

A. First generation: Crystalline carriers, such as sugar and urea, were the first to be added to solid dispersions and can be used to create first-generation solid dispersions. They cannot release the medication as quickly as amorphous ones and have the drawback of creating crystalline solid dispersions, which were thermodynamically more stable.

B. Second generation: Instead of crystalline carriers, which are often polymers, amorphous carriers are employed in second generation solid dispersions. Some examples of these polymers are starch derivatives like cyclodextrins, natural product-based polymers like hydroxylpropylmethyl-cellulose (HPMC) and hydroxypropyl cellulose, and synthetic polymers like poly vinyl pyrrolidone (PVP), polyethylene glycols (PEG), and ethyl cellulose polymethacrylates.

C. Third generation: It has been noted recently that if the carrier exhibits self-emulsifying or surface activity, the dissolving profile can be further enhanced. Third generation solid dispersions were therefore created. It has been demonstrated that using surfactants as carriers—such as inutec SP1, inulin, compritol 888 ATO, gelucire, and poloxamer are useful in producing high polymorphism purity and improving the solubility of the drug thereby enhancing the dissolution profile.

D. Fourth generation: These are also known as controlled release solid dispersions. Drugs having short biological half-life and hydrophobic properties are formulated as controlled release solid dispersions. Some of the polymers employed in these dispersions are hydroxypropyl cellulose (HPC) and Eudragit variants.

3. Manufacturing methods for preparing amorphous solid dispersions

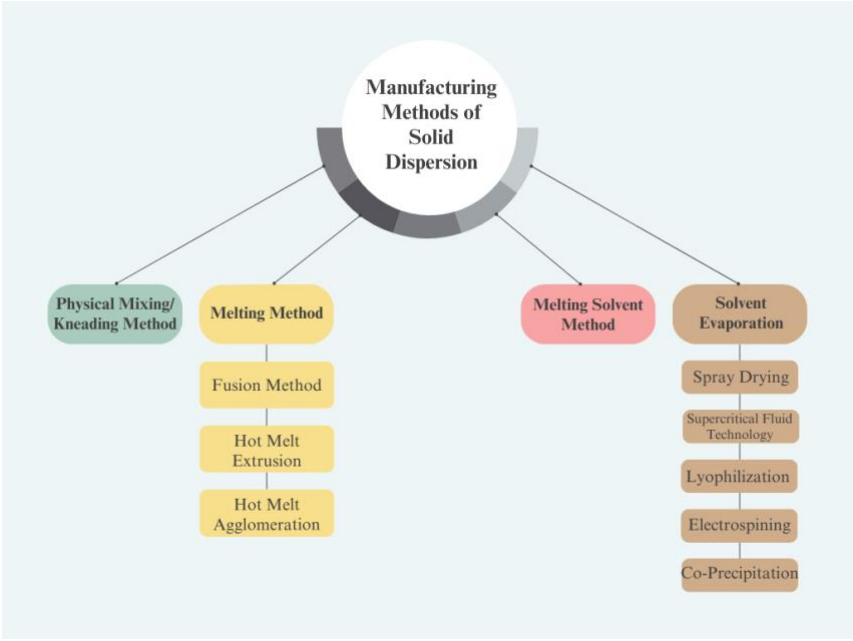

Figure 2: Different manufacturing methods of SD

3.1 Melting Method/ Fusion Method

The melting technique was initially applied by Sekiguchi and Obi in 1961 [9]. The fundamental idea behind the melting approach is to directly heat a physical mixture of a medication and a hydrophilic carrier until the mixture melts at a temperature marginally higher than its eutectic point. After that, the melt is quickly cooled and frozen in an ice bath while being stirred. After being crushed, the resulting solid mass is sieved. This method's simplicity and economy are its advantages. This approach has been used to create a number of drugs SDs, including paclitaxel [13], furosemide [11], fenofibrate [10], albendazole [12], and sulfathiazole [9]. Solid dispersion was made using the melting process utilising PEG 4000 and mannitol as the carriers in order to increase the solubility of prednisolone [14]. The findings demonstrated that drug release from the SD (~85%) was higher than drug release from the pure drug (~50%) for weight ratios of drug: PEG 4000 (1:4) and drug: mannitol (1:7). The solubility of anticancer medications that are poorly soluble has also been improved by the melting approach. In an investigation aimed at enhancing paclitaxel release from poly(ε-caprolactone) (PCL)-based films, paclitaxel SD was synthesised by the melting technique, employing poloxamer 188 and PEG as carriers, and was subsequently integrated into PCL films. Over 90% of the drug was released from the SD after one hour at a weight ratio of poloxamer 188 (1:3), which was more drug released from the SD than from the pure drug.

3.2 Solvent Evaporation Method

One of the most used techniques in the pharmaceutical business for increasing the solubility of poorly water-soluble medications is solvent evaporation. Since the medication and carrier are combined using a solvent rather than heat, as in the melting process, this method was primarily developed for heat-sensitive components. Consequently, the employment of carriers with an abnormally high melting point is permitted by this approach. This method's fundamental idea is to dissolve the medicine and carrier in a volatile solvent to enable homogenous mixing. The solvent is evaporated while being constantly stirred to produce solid dispersion. The dispersion is then crushed and sieved. Tachibana and Nakamura used this technique for the first time in 1965 [15]. An organic solvent (chloroform) was used to dissolve a medication (β-carotene) and a carrier (PVP) to create the formulation. Subsequently, the solvent was totally evaporated, resulting in a solid mass that underwent sieving and drying. The primary benefit of this approach is that it prevents the medicine and carrier from decomposing because evaporation requires a low temperature. Mayersohn and Gibaldi created an SD of griseofulvin in 1966 by employing chloroform as the solvent and PVP as the carrier [16]. At a griseofulvin:PVP ratio of 1:20, the SD's griseofulvin disintegration was 11 times higher than the pure drug's. Numerous medications, including azithromycin [17], tectorigenin [18], flurbiprofen [19], cilostazol [20], ticagrelor [21], piroxicam [22], indomethacin [23], loratadine [24], diclofenac [25], abietic acid [26], efavirenz [27], and repaglinide [28], have been made more soluble using this technique.

3.3 Melting Solvent Method (Melt Evaporation)

Goldberg et al. conducted the initial research on the melting solvent approach [29]. In their investigation, methanol was used as the solvent and succinic acid as the carrier to create a solid dispersion that improved griseofulvin solubility. The solvent evaporation method and the melting process are combined in the melting solvent method. After dissolving the medication in an appropriate solvent and adding it to the carrier melt, the combination is dried off by evaporating it completely. For medications with a high melting point, this technique is quite helpful practically. A unique monolithic osmotic tablet was demonstrated by Chen et al. [30]. It was formulated with 10-hydroxycamptothecin (HCPT) that employed the melting solvent method, with methanol serving as the solvent and PEG 6000 acting as the carrier. The optimised formulation was able to deliver HCPT at a constant rate of 1.21 mg/h for 12 hours in simulated intestinal fluid (SIF; pH 6.8), and at that point, the cumulative release of the drug was over 90%.

3.4 Melt agglomeration Process

A binder functions as a carrier during the process of melt agglomeration. This technique involves heating the medication, binder, and additional excipients above the binder's melting point. As an alternative, the heated binder is sprayed with a drug dispersion [31, 32, 33, 34]. To increase the rate of dissolution, a diazepam solid dispersion was formulated using the melt agglomeration method in a high shear mixer. Lactose monohydrate was employed as the binder in this mixture, while PEG 3000 or Gelucire 50/13 was utilised to melt agglomerate it. One of the two methods used to add the binder was pump-on or melt-in. A high dissolution rate at a lower drug concentration was obtained by using melt agglomeration. The rates of dissolution for melt-in and pump-on techniques were comparable. Furthermore, compared to the SD containing PEG 3000, the diazepam-containing Gelucire 50/13 SD demonstrated a greater degree of disintegration.

3.5 Hot-melt Extrusion Method

Hot-melt extrusion, in which the amorphous solid dispersion is made without solvent and hence avoids residual solvents in the formulation, is a popular technique for enhancing the solubility and oral bioavailability of poorly water-soluble drug substance[35]. This process involves melting a homogenous mixture of the active drug, polymer, and plasticizer, then extruding it through the apparatus using a combination of the melting method and an extruder. Products at the extruder's outlet can have their physical forms altered employing the roller crusher at the end, pulverising the end product. For example, oleanolic acid's solubility and oral bioavailability were improved by using the melt extrusion method [36]. It was successful to produce a solid dispersion of oleanolic acid using PVP VA 64 as the carrier. The dissolution of this dispersion was superior to that of a physical mixture (45% after 2 hours) and pure drug (37% after 2 hours), with almost 90% of the drug from the solid dispersion released in the first 10 minutes. Furthermore, the drug from the oleanolic acid-solid dispersion showed an enhancement of 2.4 and 5.6 times for $AUC_{0–24h}$ and C_{max} (761.8 ± 272.2 ng·h/mL and 89.1 ± 33.1 ng/mL respectively), as compared to the pure drug's $AUC_{0–24h}$ (1840 ± 381.8 ng·h/mL) and C_{max} (498.7 ng/mL). In another work by Sathigari et al., [37], efavirenz solid dispersion was prepared via hot-melt extrusion process using Eudragit EPO or Plasdone S-630 as carriers to increase the dissolving rate of efavirenz. In the dissolution test, due of very low water solubility (3–9 µg/mL), sodium lauryl sulphate (SLS) was introduced in the dissolution medium. The outcomes demonstrated that efavirenz's solubility rose significantly (to 197 µg/mL) as compared to the drug's pure form. Using Eudragit EPO

and Plasdone S-630 as carriers, roughly 96% and 82% of the drug was released from SD after 30 minutes, respectively, a 2- and 1.7-fold increase over the drug alone. After nine months, the solid dispersion was also stable.

3.6 Lyophilization Techniques/Freeze-Drying

By dissolving the drug and carrier in a solvent and freezing the mixture in liquid nitrogen, lyophilization is an alternate method to solvent evaporation that produces a lyophilized molecular dispersion [38]. This method is typically applied to products that are thermolabile, or unstable in aqueous solutions but stable in the dry state over long periods of storage. In an earlier effort, nifedipine and sulfamethoxazole solid dispersion were synthesised using Soluplus and PEG 6000 as carriers in order to evaluate physicochemical and in vitro properties [39]. The rate of drug dissolution was increased, and the solid dispersion for the two drugs were made efficiently. In a study on the anticancer drug exemestane[40], a phospholipid/ sodium deoxycholate solid dispersion loaded with exemestane was created to improve the drug's solubility and oral bioavailability. When compared to its pure form, exemestane from solid dispersion showed greater solubility and dissolution rate. Absorbent transport increased 4.6 times when the solid dispersion was compared to the conventional drug. Additionally, the drug's AUC_{0-72h} in the solid dispersion was 2.3 times greater than its AUC_{0-72h} on its own. The carriers used in a second study [41] on a flutamide solid dispersion made by lyophilization to increase the dissolving rate were PVP K30, PEG 6000, and poloxamer 407. When employing poloxamer 407 as the carrier, the dissolution of SD after 30 minutes was higher than when using other carriers (PVP K30, 66.5%, and PEG 6000, 78.2%), as well as higher than when using the pure drug (13.5%).

3.7 Electrospinning Method

An electrospinning technique combines nanotechnology and solid dispersion technologies. This method creates solid fibres by transmitting a polymeric fluid stream or melt through a millimetre-scale nozzle [42]. One advantage of this strategy is that it's a simple and reasonably priced process. This method is effective for controlling biomedical release and producing nanofibers. A polyvinyl alcohol (PVA): ketoprofen (1:1, w/w) nanofiber was produced by electrospinning [43]. The dissolution of this nanofiber was significantly ($p < 0.05$) higher than that of ketoprofen alone. An amorphous formulation of griseofulvin and indomethacin was also created by electrospinning using PVP as the carrier. This formulation held up well for eight months in a desiccator [44].

3.8 Co-Precipitation

Using this procedure, a solution is made by dissolving the carrier in the solvent and then adding the medicine while stirring to create a homogenous mixture. To create precipitation, water is then added to the homogenous mixture dropwise. The precipitate is then dried and filtered. Sonali et al.'s study [45] involved the preparation of a silymarin solid dispersion using HPMC E15LV as the carrier and a number of techniques, including co-precipitation, spray-drying, and kneading. In comparison to the other two approaches, the silymarin solid dispersion produced through co-precipitation exhibited a considerably ($p < 0.05$) increased solubility. Additionally, compared to the conventional medication, the solubility of silymarin from the solid dispersion generated by co-precipitation increased by a factor of 2.5.

3.9 Supercritical Fluid (SCF) Technology

In the late 1980s and early 1990s, SCF was first released. SCF was described as a medium for particle formation by Hannay and Hogarth in 1897 and yields a formulation with a restricted particle size range (microparticles or nanoparticles) without the need for a solvent [46]. When a substance's critical point is exceeded by both temperature and pressure, it is said to be in the supercritical condition. In solid dispersion, SCF can function as an antisolvent or solvent. The fundamental idea behind SCF is dissolving the medication and carrier in a supercritical solvent (such CO2) and then spraying the mixture through a nozzle into a lower pressure expansion vessel. Rapid expansion causes the dissolved medications and carriers to nucleate quickly, which produces solid dispersion particles with the right size distribution quickly. Currently, there are a number of ways to carry out SCF, including gas antisolvent (GAS) [48], supercritical antisolvent (SAS) [49], rapid expansion from supercritical solution (RESS) [47], and solution enhanced dispersion by SCF (SEDS) [50]. Here is how the RESS procedure is carried out: To create an SD, drug and carrier are dissolved in SCF and sprayed through an atomizer in an expansion vessel that is kept at low pressure. This method's benefit is that it can reduce the amount of organic solvent needed to prepare the solid dispersion. Due to its low critical temperature (31.04 °C) and low critical pressure (7.38 MPa), as well as its lack of toxicity and inflammability, CO2 is an appropriate solvent in SCF technology for the synthesis of solid dispersion of insoluble medicines [51]. Adeli created an SD by the SAS approach with poloxamer 407 as the carrier to enhance irbesartan dissolution [49]. A 1:1 ratio between the medication and the carrier was ideal. Consequently, the irbesartan-SAS sample's dissolution was 13 times greater than the drug's pure concentration. In a different work, apigenin nanocrystals were made using the SAS approach to increase the solubility and bioavailability of apigenin [52]. As compared to the medication alone, the final formulation's C_{max} and AUC increased 3.6 and 3.4-folds, respectively, according to the data, indicating enhanced BA. SCF technique holds promise for improving the solubility and bioavailability (BA) of medicines with low water solubility in drug development. The fact that the majority of medications are insoluble in CO2 is one method's drawback.

3.10 Spray-Drying Method

One of the earliest techniques for drying materials is spray drying, particularly for heat-sensitive goods like food and medicine. This approach prepares the feed solution by dissolving the carrier in water and the medication in an appropriate solvent. After that, the two solutions are combined using sonication or other appropriate techniques until the mixture becomes transparent. Using a high-pressure nozzle, the feed solutions were first sprayed into a drying chamber to create tiny droplets. The drying fluid (hot gas) that forms the droplets forms nano- or micro-sized particles [53]. In the field of medicine, the spray-drying technique is frequently employed to prepare SD that enhances the solubility and bioavailability of medications that are poorly soluble in water, including nilotinib [54], spironolactone [55], valsartan [56], rebamipide [57], and artemether [58]. For instance, an SD of nilotinib was created

by spray-drying to improve solubility in a study conducted by Herbrink et al. [54]. On the basis of in- vitro dissolving experiments, Soluplus was determined to be the optimal carrier. When compared to the pure drug, nilotinib's solubility increased 630-fold at a drug: Soluplus (1:8) ratio. To increase solubility and dissolution, an artemether SD was synthesised by spray-drying in a different investigation conducted by Pawar et al. [58]. The outcomes demonstrated that a 1:3 medication-to-carrier ratio (artemether: Soluplus) was ideal. Compared to the standard medication (20%), artemether release from SD was 4.1 times higher, at 82% after 1 hour. An effective method for preparing solid dispersion to increase the solubility of hydrophobic medications is spray-drying.

4. Conclusion

The classification of solid dispersion, preparation techniques, and contemporary developments in the formulation to increase the solubility of poorly soluble medications, such as anticancer treatments, were the main topics of this review. When treating cancer, intravenous (IV) injection is recommended. However, because this approach requires patients to attend a hospital in order to obtain treatment, it causes inconveniences for them. As a result, researchers are developing oral dose formulations of anticancer medications. Due to patient convenience, oral administration is currently the most popular method of drug administration.

In order for a drug to be absorbed in the GI tract during oral administration, it must dissolve in water. However, about 40% of NCEs, including anticancer medications, are insoluble in water, which results in poor absorption, poor blood concentration variability within and between individuals, and poor BA. Enhancing the solubility of medications that are poorly soluble in water is therefore a significant task for the pharmaceutical industry. Many techniques, including complexation, lipid-based systems, solid dispersions, micronization, nanonization, and co-crystallization, were created for therapeutic application in order to address this issue. Among them, solid dispersion is one of the most effective techniques and is frequently applied to the creation of new medications. It is seen as a potentially effective method for resolving issues with low BA and poor aqueous solubility. The solubility and dissolution of pharmaceuticals were enhanced by increasing their wettability and surface area. Understanding the characteristics of the drug and carrier during the manufacture of SD, as well as choosing an appropriate procedure, are critical to the formulation's success.

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