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A Review on Solid Dispersion and Techniques

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ABSTRACT

Solid dispersions have attracted considerable interest as an efficient means of improving the dissolution rate and hence the bioavailability of a range of poorly water-soluble drugs. Solid dispersions of poorly water-soluble drugs with water-soluble carriers have been reduced the incidence of these problems and enhanced dissolution. The focus of this review article on advantages, disadvantages and the method of preparation, and characterization of the solid dispersion. Solid dispersion is an effective way of improving the dissolution rate of poorly water soluble drugs and hence its bioavailability. The water soluble carriers used in preparation of solid dispersion enhance the dissolution rate of the poorly water soluble drug. The review article focuses on the methods of preparation, advantages, disadvantages and characterization of the solid dispersions.

Keywords: bioavailability, Solid dispersions, dissolution rate, methods of preparation.

1. INTRODUCTION

Due to solubility issues, improving oral bioavailability of medications delivered in solid dosage forms remains a challenge for formulation experts. The rate-limiting mechanism in the absorption of a drug from a solid dosage form of relatively insoluble medicines could be the dissolving rate. As a result, the formulation scientists face a problem in increasing the solubility of poorly soluble medications using the solid dispersion approach. Solid dispersion techniques have piqued interest as a means of enhancing dissolving rates, wettability, and the formation of amorphous particles. A solid dispersion is a collection of solid goods made up of at least two components, usually a hydrophilic inert carrier or matrix and a hydrophobic medication. [1]

Orally administered medications are only entirely absorbed when they have a good solubility in the stomach media and have a high bioavailability. More than 40% of new chemical entities (NCEs) generated in the pharmaceutical industry are nearly water insoluble. These medications' weak water solubility, combined with their sluggish absorption, result in insufficient and unpredictable bioavailability, as well as gastrointestinal mucosal toxicity. As a result, improving drug solubility and hence oral bioavailability remains one of the most difficult parts of the drug development process, particularly for oral drug delivery systems. There are a variety of methods for improving the solubility of poorly water soluble drugs that have been documented in the literature. The approaches are chosen based on factors such as the qualities of the medicine in question, the nature of the excipients to be used, and the nature of the planned dosage form. [2]

Poor solubility and low dissolution rates of poorly water soluble drugs in aqueous gastro-intestinal fluids frequently result in insufficient bioavailability rather than limited permeation through the epithelia, and the formulation of poorly soluble drugs for oral delivery is now one of the major challenges facing formulation scientists in the industry. In quantitative terms, solubility is defined as the concentration of the solute in saturated solution at a certain temperature. In qualitative terms, solubility is defined as the spontaneous interaction of two or more substances to form a homogeneous molecular dispersion. [1]

2. Mechanism of action

The precise method through which Oxcarbazepine works as an anticonvulsant is uncertain. Oxcarbazepine's pharmacological effect is thought to be predominantly mediated by its 10-monohydroxy metabolite (MHD). MHD-induced blockage of voltage-sensitive sodium channels has been seen in vitro, resulting in the stabilisation of hyperexcited neuronal membranes, suppression of repeated neuronal discharges, and a reduction in synaptic impulse propagation. Anticonvulsant effects may also be aided by enhanced potassium conductance and regulation of high voltage activated calcium channels. [1,3]

3. Solid Dispersion

Summarizes the various formulation and chemical approaches that can be taken to improve the solubility or to increase the available surface area for dissolution.

Solid dispersions (SDs) have long been used to increase the solubility characteristics and bioavailability of medications that are poorly water soluble. Since the year 1960. Many researchers have investigated SDs of weakly water-soluble medicines in combination with various pharmacologically inert carriers to improve dissolution and oral absorption; however, only a few systems are commercially viable. [2]

Different types of drug–carrier interactions in solid-state dispersions have been suggested by Chios and Riegeman:

Solid solutions, glass solutions and glass suspensions, amorphous precipitates in a crystalline carrier, and compound or complex formation are all examples of simple eutectic mixes. When compared to crystalline material, a medication may exist in an amorphous state in polymeric carriers in SD's systems, which may result in better solubility and dissolving rates. Solid dispersion is a phrase used to describe a collection of solid goods made up of at least two separate components, usually a hydrophilic matrix and a hydrophobic medication. The matrix might be crystalline or amorphous in nature. Amorphous particles (clusters) or crystalline particles can be used to spread the medication molecularly. [3]

Several researchers have proposed ways for improving the dissolving rate of SDs. Drug molecular dispersion in polymeric carriers can reduce particle size and increase surface area, resulting in faster dissolving rates. Furthermore, during the dissolution process, no energy is required to break up the crystal lattice of a medication, and drug solubility and Wettbility are improved due to the presence of surrounding hydrophilic carriers. Increased dissolving may also be aided by reduced or absent aggregation and agglomeration. The melting process, the solvent method, and the solvent wetting method are all utilised to make SDs. Solid Dispersion has proven to be effective among the different techniques used to improve the dissolving of poorly soluble medicines. [4]

Due to increased wettbility, improved dispersibility of drug particles, and the presence of the drug in amorphous form with improved solubility and absence of drug particle agglomeration, fast or instantaneous drug dissolution from Solid Dispersions has been reported.[3]

3.1 Polymers used in solid dispersions

3.1.1 Polyethylene Glycol (PEG):

These chemicals are created by combining ethylene glycol with ethylene oxide. Polyethylene oxides are PEGs with a molecular weight more than 300,000. [4]

3.1.2 Phospholipids

Modification of the terminal hydroxyl with phosphate linked head groups to generate phospholipids increases the complexity of glycerides; popular phospholipid head groups include choline, ethanolamine, serine, inositol and inositol phosphate, and glycerol esters. Many species are possible by varying combinations of different head groups and fatty acyl substitution at the first and second positions of the glycerol backbone, and fluidity differences are visible as a function of the gel to liquid crystalline transition temperatures, just as they are with triglycerides. Rather than being merely a chemical function of the molecule, phospholipid solubility is inextricably tied to the confirmation of the aggregation material. Monoacyl phospholipids are frequently more soluble in aqueous solutions because they tend to form micelles. [5]

3.1.4 Polyvinyl Pyrrolidone (PVP)

The molecular weight of PVP varies between 2500 and 3000000. It is soluble in water, ethanol, chloroform, and isopropyl alcohol, among other solvents. At high temperatures, PVP decomposes. As a result, because melting occurs at a very high temperature, it is not suited for the formation of solid dispersions prepared by the melt method. [5]

3.1.5 Cyclodextrins:

By converting liquids into solids via entrapment, cyclodextrins are generally utilised to improve solubility, chemical protection, taste masking, and improved handling. [5]

3.1.6 Advantages of Cyclodextrins [6,7]

- Increasing the stability of the drug
- Release profile during gastrointestinal
- Transit through modification of drug
- Release site and time profile
- Decreasing local tissue irritation
- Masking unpleasant taste.

4. Applications of solid dispersion [6,7,8]

- It improves the solubility of poorly soluble medicines, increasing the dissolution rate and hence the drug's absorption and bioavailability.
- To protect unstable pharmaceuticals against decomposition processes such as hydrolysis, oxidation, and others.
- To lessen the negative effects of certain medications.
- The masking of a drug's undesirable taste and odour.
- To avoid incompatibilities that aren't desirable.
- To provide a uniform dispersion of a little amount of medication in solid form.
- In a solid dose, liquid (up to 10%) or gaseous chemicals are dispensed.
- Formulation of a long-acting dose form
- Pre-systemic circulation inactivation of medications like morphine and progesterone is reduced.

5. Ideal candidates for solid dispersion:

Drugs with low water solubility and permeability via biological membranes are used in solid dispersion technologies. Because of their low solubility, dissolving is difficult, and absorption and bioavailability suffer as a result. Solid dispersions are appropriate for BCS class II medicines, which have low water solubility but strong membrane permeability. [9,10]

6. Commercial solid dispersion products

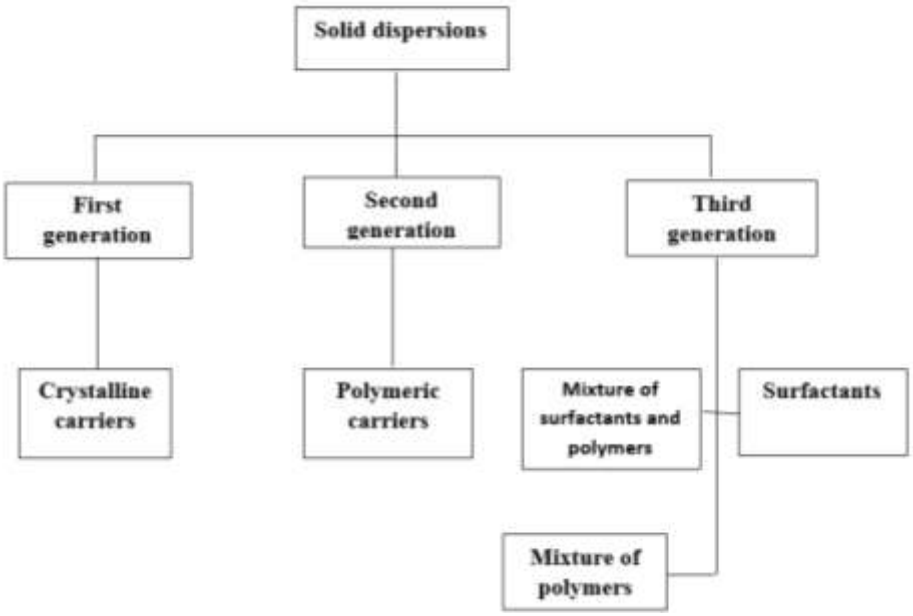
Griseofulvin, nifidipine, carbamazapine, albendazole, nimodipine, ofloxacin, prednisone, lamotrigine, diazepam, paracetamol etc. [8,9,10]

7. Marketed solid dispersion products

Some of the marketed solid dispersions are as follows:

- Troglitazone solid dispersion is marketed by Parke Davis
- Sporanox , a solid dispersion of itraconazole
- Gris-PEG®, solid dispersion of griseofulvin marketed by Novartis

8. Classification of solid dispersion [1]



Classification of solid dispersion

Depending on the molecular arrangement, solid dispersions can be of the following types:

- **Eutectic mixtures** - The physical mixture of very small crystals of the two components is usually obtained by rapidly cooling the co-melt of the two components.
- **Solid solutions** - Depending on the miscibility, the two types of solid solutions are:

- Continuous solid solutions - The components in continuous solid solutions are miscible in all proportions, meaning that the bonding strength between them is stronger than the bonding strength between the individual components. [3]
- Discontinuous solid solutions - The solubility of each component in the other component is limited in nature in discontinuous solid solutions. [4]
- Depending on the distribution of the solvates in the solvendum, solid solutions can be of two types:
  - Substitution crystalline solution- These are solid solutions with a crystalline structure in which the solute molecules in the crystal lattice replace the solvent molecules.
  - Interstitial crystalline solid solution – These are solid solutions in which the dissolved molecules fill the interstitial spaces in the crystal lattice between the solvent molecules.
- **Amorphous solid solutions**- The solute molecules in amorphous solid solutions are scattered molecularly yet irregularly inside the amorphous solvent.
- **Glass solutions and glass suspension**– The solute dissolves in the glassy solvent in a glass solution, which is a homogeneous system. Below the glass transition temperature, the glassy state is characterised by transparency and brittleness. A pure chemical or a mixture of pure chemicals in the glassy form is referred to as glass. Solid dispersion classification based on recent developments: [8] 1. Solid dispersions of the first generation - These solid dispersions are made with crystalline carriers. The earliest crystalline carriers utilised in the manufacture of

solid dispersions were urea and sugars. These have the disadvantage of being thermodynamically unstable and not releasing the medication as quickly. [9]

- **Second generation solid dispersion –** Instead of crystalline carriers, amorphous carriers are used to make these solid dispersions. In the polymeric carrier, the medication is molecularly distributed. Two types of polymeric carriers are available:
- **Synthetic polymer** – povidone, polyethylene glycols and polymethacrylates.
- **Natural polymers –** hydroxypropylmethylcellulose, ethyl cellulose, starch derivatives like cyclodextrin.[8,9]
- **Third generation solid dispersion –** Surfactant carriers or a mixture of amorphous polymers and surfactants serve as carriers in these solid dispersions. For medications with low solubility, these provide the highest level of bioavailability. Inulin, poloxamer 407, and other surfactants are utilised in the third generation solid dispersion. [8,9,10]

9. Advantages of solid dispersion [11,12]

1. Particles with reduced particle size.
2. Particles with improved wettability.
3. Particles with higher porosity.
4. . Drugs in amorphous state.

10. Disadvantages of solid dispersion [11,12]

1. Their instability is a significant disadvantage. They display crystallinity changes and a decrease in dissolving rate as they age.
2. Solid dispersions are more susceptible to temperature and moisture than physical mixes.
3. Tackiness makes it difficult to handle.

11. Characterization of solid dispersion [13,14,15]

Various characterization methods to assess the solid dispersion are as follows

11.1 Drug -carrier miscibility[14]

- Hot stage microscopy
- Differential scanning calorimetry
- Powder X-ray diffraction
- Spectroscopic methods like Raman spectroscopy, FT-IR spectroscopy

11.2 Physical Structure [13,14]

- Scanning electron microscopy
- Surface area analysis
- Surface properties
- Dynamic vapour sorption
- Inverse gas chromatograph
- Atomic force microscopy
- Raman microscopy

11.3 Amorphous content [15]

- Polarized light optical microscopy
- Hot stage microscopy
- Humidity stage microscopy
- DSC (MTDSC)
- Powder X-ray diffraction

11.4 Stability [14]

- Humidity studies
- Isothermal Calorimetry
- DSC (Tg, Temperature recrystallization)

- Saturated solubility studies.

11.5 Dissolution enhancement [13]

- Dissolution
- Intrinsic dissolution
- Dynamic solubility
- Dissolution in bio-relevant media.

12. Preparation methods of solid dispersions. [15,16,17,20]

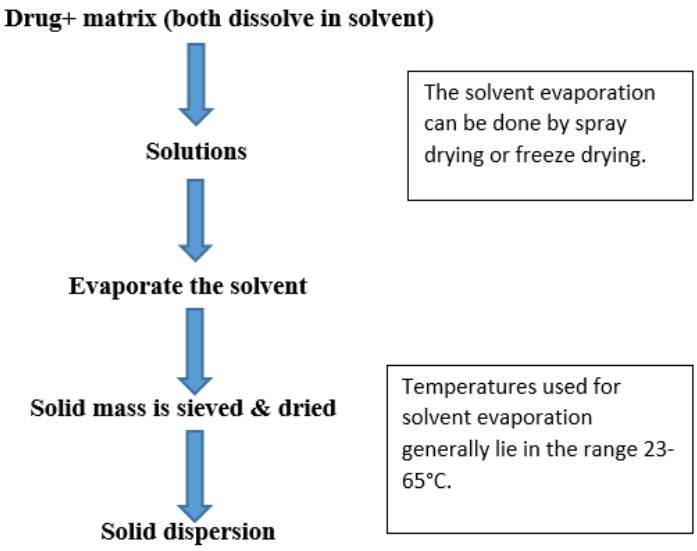
1. Solvent evaporation method
2. Fusion method/melting method.
3. Hot melt extrusion.
4. Supercritical fluid technology (SCF).
5. Dropping method.
6. Electrostatic Spinning Method.
7. Lyophilization techniques.
8. Materials and methods.

1. Solvent evaporation method [15]

This approach involves dissolving the physical mixture of drug and carrier in a common solvent, which is then evaporated until a clear, solvent-free film is left. After that, the film is dried to a consistent weight. The fundamental advantage of the solvent approach is that due to the relatively low temperatures necessary for the evaporation of organic solvents, thermal degradation of medications or carriers can be avoided. However, there are several drawbacks to this strategy, including as

1) The higher cost of preparation.
2) The difficulty in completely removing liquid solvent.
3) The possible adverse effect of traces of the solvent on the chemical stability
4) The selection of a common volatile solvent.
5) The difficulty of reproducing crystal form.
6) In addition, a super saturation of the solute in the solid system cannot be attained except in a System showing highly viscous properties.

Solvent evaporation method [14]

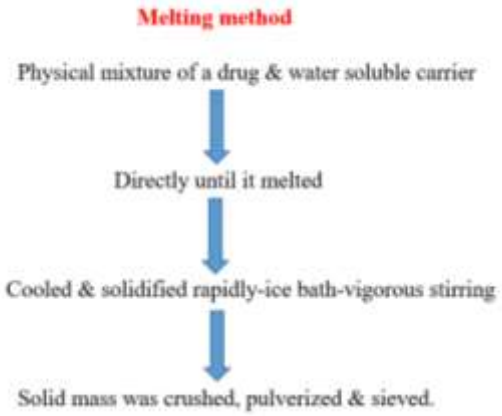


Overview of some organic solvents

Solvent	Melting point (°C)	Boiling point (°C)	Vapour pressure at 25°C (kPa)
Water	0	100	3.16
Methanol	-93.9	65	16.9
Ethanol	-117	78.5	5.75
1-propanol	-85.8	97.4	2.27
2-propanol	-127	82.4	5.85
Chloroform	-63	62	26.1
Dimethylsulphoxide(DMSO)	19	189	0.08
Acetic acid	17	118	1.64
1,4-dioxane	12	102	4.92
2-methyl-2-propanol (TBA)	25	82	5.49

2. Fusion method/melting method. [13,14]

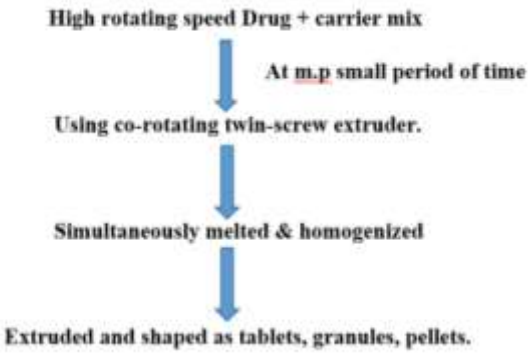
A physical mixture of the medicine and a water soluble carrier is generated by heating it directly until it melts in the melting or fusion process. Crushed, pulverised, and sieved solid mass is obtained at the end of the process. However, excessive temperatures during the melting process may cause the medicine or the carrier to degrade. Heating the combination in a sealed container, under vacuum, or in the presence of inert gases like nitrogen could be one way to solve this problem. Its simplicity and cost-effectiveness are advantages.



Despite its widespread use, the fusion process has significant drawbacks. To begin with, one significant drawback is that the approach may only be used when the medication and matrix are compatible and combine well at the heating temperature.

Two liquid phases or a suspension can be seen in the heated mixture when drug and matrix are incompatible (Greenhalgh et al., 1984; Timko and Lordi, 1984), resulting in an inhomogeneous solid dispersion. Surfactants can be used to avoid this (Damian et al., 2002 and Vippagunta et al., 2002) ’

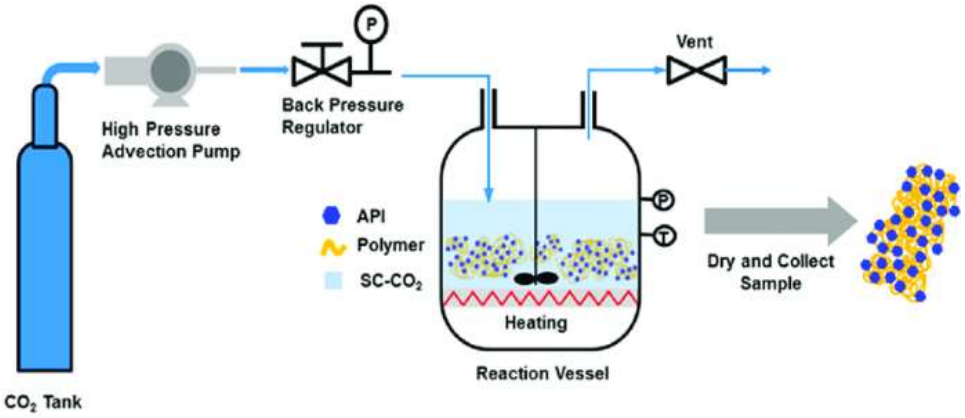
3. Hot melt extrusion. [14,15]



Melt extrusion is similar to fusion with the exception that the extruder causes intensive mixing of the components. The product stability and dissolution are comparable to melting in a vessel (Forster et al., 2001), but melt extrusion allows the heated drug-matrix mixture to be shaped into implants, ocular inserts, or oral dosage forms (Breitenbach, 2002).

Miscibility of medication and matrix, just like in the traditional fusion method, can be a concern. To forecast solidstate miscibility and identify matrices suited for melt extrusion, solubility characteristics are explored. For heat-sensitive materials, strong shear forces resulting in high local temperatures in the extruder can be an issue (Langer et al., 2003 and Forster et al., 2001). In comparison to the classic fusion approach, however, this technology allows for continuous production, making it appropriate for large-scale production. Furthermore, the product is easier to handle because the shape can be modified to the next processing stage without grinding at the extruder's outlet.

4. Supercritical fluid technology (SCF).[15]



A chemical that is over its critical temperature and pressure is known as SCF. The critical point is the temperature and pressure at which the substance is in equilibrium as a vapour and a liquid. SCF is employed in this process to create a solid dispersion of insoluble material/polymer with the medication, resulting in an increase in dissolving property.

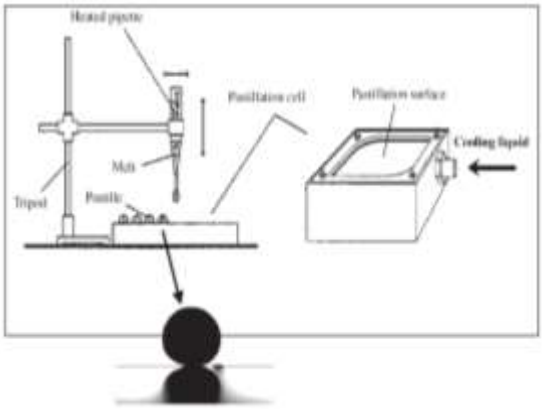
It outperforms traditional techniques (spray drying, hot melt, etc.). In this process, SCF carbon dioxide is primarily used, resulting in very rapid solid mixture precipitation, with no time for drug and polymer separation in the creation of solid dispersion. It forms a tiny, stable particle with a large surface area for good flow and low organic solvent residue.

Using SCF carbon dioxide in a precipitation tank, solid dispersion of carbamazepine with PEG-4000 has recently been achieved. As a result, carbamazepine is formed with an increased rate and extent of dissolution and a low solvent residual.

Carbon dioxide is employed as an antisolvent for the solute but as a solvent for the organic solvent in supercritical fluid antisolvent techniques. Various writers used different acronyms to describe micronization processes: aerosol solvent extraction system, compressed fluid antisolvent precipitation, gas anti-solvent, solution improved dispersion by supercritical fluids, and supercritical antisolvent. The SAS procedure entails spraying a solution containing the solute and an organic solvent into a continuous supercritical phase that is flowing at the same time. Although a small quantity of carbon dioxide remains trapped inside the polymer after the process is complete, using supercritical carbon dioxide is advantageous since it is much easier to extract from the polymeric materials when the process is complete; it provides no harm to the patient. Furthermore, carbon dioxide's ability to plasticize and swell polymers can be used, and the process can be carried out at room temperature. Furthermore, supercritical fluids are utilised to reduce the melting temperature of the dispersed active ingredient, lowering the temperature of the melt dispersion process. The solubility of the lighter component (dense gas) in the forming phase is the cause of this decrease (heavier component).

5. Dropping method[18]

Preparation of a Solid Dispersion by a Dropping Method



Equipment used in the dropping method with solid drops (Bülau & Ulrich, 1977)

(Contact angle of the drop: 174 ± 0.1°).

5.1 Solidification in Drops[19,20]

Bülau and Ulrich (1977) created the dropping method to aid in the crystallisation of various chemicals. It is a new method for creating spherical particles from melted solid dispersions. Preparation on a Lab Scale. A melting drug–carrier mixture is dispersed into a solid dispersion and put onto a cooling plate, where it hardens into spherical particles (Figure 1). Factors such as the viscosity of the melt and the size of the pipette can have an impact on the particle size and form. Due to the fact that viscosity is very temperature sensitive, it is critical to regulate the temperature so that the melt solidifies into a spherical shape when dropped onto the plate. Because the dropping method does not use organic solvents, it avoids the issues that come with solvent evaporation. The process also avoids the pulverisation, sieving, and compressibility issues that other melt procedures can cause, as well as the plug formation that can occur when using the direct capsule-filling method. The downside is that only thermally stable medications can be utilised, as well as the physical instability of solid dispersions. The process also avoids the pulverisation, sieving, and compressibility issues that other melt procedures have, as well as the plug formation that occurs with the direct capsule-filling method. The drawback is that only thermally stable medications can be utilised, and the physical instability of solid dispersions adds to the difficulty.

5.2 Materials used in dropping method [22,23]

EGIS Ltd was the source of the ME sample (Budapest, Hungary). Hungaropharma Ltd provided the polyethylene glycol (PEG) 4000. (Budapest, Hungary). The rest of the reagents and solvents were all of analytical quality.

5.3 Methods used in dropping method [24]

Preparation of Physical Mixture

ME and PEG 4000 were weighed and combined for 5 minutes in a pestle and mortar before sieving through a 400-m mesh to make a ME–PEG 4000 physical mixture. For further research, a firm gelatin capsule (size no. 2) was filled with 60 mg of ME–PEG 4000 powder mixture (containing 15 mg of ME and 45 mg of PEG 4000).

5.4 Tablet-Making [25,26]

A Korsch EKO eccentric tablet machine was used to make ME–PEG 4000 tablets (Emil Korsch Maschinenfabrik, Berlin, and Germany). Single, flat punches with a diameter of 10 mm and strain gauges were used as compression tools. The ME–PEG 4000 physical mixture was crushed at a pressure of 10 1 kN, a temperature of 24°C, and a relative humidity of 45 percent in the air. A Heberlein instrument was used to test the tablets' crushing strength (Flisa, Le Locle, Switzerland). A screw micrometre was used to measure the geometrical characteristics (Mitutoyo, Tokyo, Japan). The tablets were calibrated to a weight of 60 mg. Each tablet had 15 milligrammes of ME and 45 milligrammes of PEG 4000.

5.5 Preparation of Solid Dispersion by Dropping Method [27]

PEG 4000 was weighed and melted in a double-layered beaker at 58°C (1°C), and a measured amount of ME was added and swirled to make the ME–PEG 4000 solid dispersion by the dropping method. The levels of ME and PEG 4000 measured equated to a 1:3 drug–carrier ratio (each solid drop contained 5 mg of ME and 15 mg of PEG 4000). To maintain the temperature consistent, the melted drug–carrier mixture was pipetted and placed into an adjustable heating unit. On a stainless steel plate, the molten drug–carrier combination hardened into spherical particles. The stainless steel plate had a temperature of 20°C (-1°C). For further research, three round particles (60 mg) were inserted in hard gelatin capsules (size #2).

5.6 Investigation of Particle Size [28]

Laser diffraction was used to determine the particle size distribution of the ME sample (Malvern Mastersizer 2000, Malvern Ltd., Worcestershire, UK). The materials were dispersed in air and deagglomerated at a pressure of 1 bar for the measurements. The particle size was determined to be between 0.02 and 2,000 m, and the measurements were carried out three times. A screw micrometre was used to determine the particle size of the product obtained using the dropping method (S3) (Mitutoyo)

5.7 Dissolution Studies [28,29]

For dissolution studies, tablets, physical mixtures, pure ME, and spherical particles were created. Hard gelatin capsules were filled with the physical mixture, spherical particles, and pure ME as a control sample (size no. 2). Each capsule has 15 milligrammes of ME and 45 milligrammes of PEG 4000. Dissolution experiments were carried out using a Pharmatest dissolution tester (Hainburg, Germany) at a paddle speed of 100 rpm. At 37°C (0.5°C), artificial enteric juice (900 mL) with a pH of 7.5 (0.1) was utilised. After filtering, samples were taken at 5, 10, 20, 30, 60, and 90 minutes and spectrophotometrically measured at 361 nm (Helios; Spectronic Unicam, Cambridge, UK).

Langenbucher's Kinetic Calculation The modified Langenbucher model can be used to characterise the dissolving profiles of samples and pure me (Langenbucher, 1972).

Where m0 is the drug's mass at time t = 0 and mt is the drug's mass at time t. The rate constant (k value) and the intercept value were obtained as a result of the linear transformation (n).

5.8 Differential Scanning Calorimetry[31,32]

A differential scanning calorimetry (DSC) device was used to conduct the thermal analysis (Mettler-Toledo GmbH, Schwerzenbach, Switzerland). In a non-hermetically sealed aluminium pan, 10 mg of samples and 2.5 mg of pure ME were weighed. The samples were heated at a rate of 30°C/min from 25 to 300°C. Indium was used to calibrate the instrument.

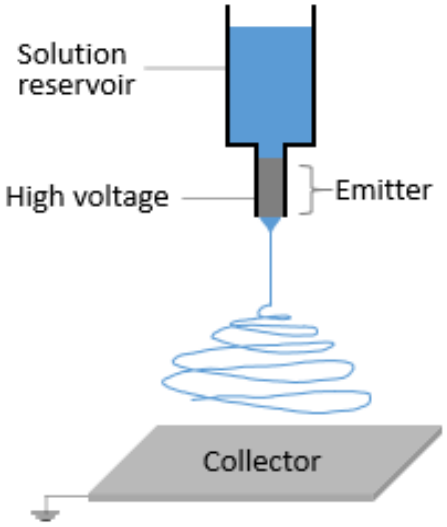
5.9 X-Ray Powder Diffractometry [34,35]

X-ray powder diffractometry (XRPD) was performed with a Philips X-ray diffractometer (PW 1050/70 PW 1710). The measurement conditions were radiation source, CuKα; scan speed (2θ/s), 0.035; step size (2θ/s), 0.035; and time per step, 1.0 s.

5.10 Chemometric Method [38,39]

For the XRPD study of mixtures of components, Fiala (1980) devised a process called correlation analysis. For the same reason, Nassab, Rajkó, and Szabó-Révész (2006) proposed a multivariate curve resolution approach, but without mentioning the Joint Committee on Powder Diffraction Standards (JCPDS). With the use of particular restrictions, the chemometric approach of multivariate curve resolution with alternative least squares (MCR-ALS) (Tauler, 1995; Tauler, Casassas, & Izquierdo-Ridorsa, 1991) can break the data matrix into profiles (composition profiles and pure diffractogram profiles) (De Juan & Tauler, 2003; De Juan, Vander Heyden, Tauler, & Massart, 1997; Tauler, 2001). Due to rotational and intensity (scaling) uncertainties, this decomposition is frequently not unique (Tauler, Smilde, & Kowalski, 1995). Van Benthem, Keenan, and Haaland (Van Benthem, Keenan, and Haaland, 2002). If convenient limits are employed, rotational ambiguity can be mitigated or even avoided (De Juan & Tauler, 2003; De Juan et al., 1997; Tauler, 2001). Tauler et al. (1995) created a Matlab code for MCR-ALS that included several limitations. Lawton and Sylvestre (1971) introduced the self-modeling curve resolution (SMCR) method for two-component systems to deconvolve raw spectroscopic data into the product of two physically interpretable profile matrices provided both concentrations and absorbances are nonnegative, accepting both as minimal constraints. Unfortunately, the approach is not unique: the method can only provide feasible regions for pure component profiles without any further constraints. Borgen and Kowalski (1985), as well as Borgen, Davidsen, Mingyang, and yen (1986), extended the LS approach to three-component systems with the same basic constraints. Borgen's method was reviewed recently by Rajkó and István (2005), who provided a clearer understanding and employed computational geometry methods to find inner and outer polygons. The SMCR approach for evaluating XRPD data is now presented.

6. Electrostatic Spinning Method.[41,42]



A nano-sized fibre thread is withdrawn from a polymer sol/polymer melt using electric force in this process. In the polymer business, this is a combination of solid dispersion and nanotechnology. Electric force (5 to 30kv) is applied to a stream of polymer solution/melt, causing the liquid's body to become charged and electrostatic repulsion to counterbalance surface tension. This created a strong cohesive force between the particles and droplets of polymer, resulting in the formation of a stream of fibre. Then, using a whipping process known as electrostatic repulsion, the fibre is thinned and stretched to nano diameter, resulting in the development of uniform nano diameter fibre. The rate of feeding surface tension and the amount of electric force employed are

both important factors in this operation. Solid fibres are created by electro spinning from a polymeric fluid stream solution or melt fed through a millimeter-scale nozzle.

A high electrostatic field is applied to a conductive capillary attached to a reservoir containing a polymer solution or melt and a conductive collection screen in this method. Charge species accumulating on the surface of a pendant drop collapse the hemispheric shape into a conical shape when the electrostatic field intensity is increased up to but not surpassing a critical value (commonly known as Taylor s cone). When the critical value is exceeded, a charged polymer jet is expelled from the cone's apex (as a way of relieving the charge built-up on the surface of the pendant drop). The electrostatic force carries the ejected charged jet to the collection screen.

The charged jet's thinning during its course to the collection screen is due to the Coulombic repulsion force. The charged jet's thinning down is limited. The charged jet is dried as the viscosity rises. This approach has a lot of potential for making nanofibers and controlling the release of medicines because it is the easiest and cheapest. It can also be used to make solid dispersions in the future.

7. Lyophilization technique [43,44]

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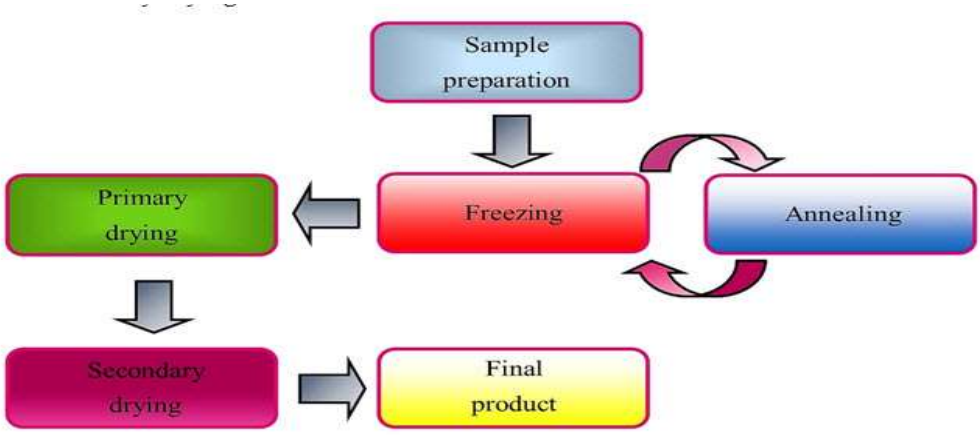

It is a phenomenon in which heat and mass are transferred from and to the product. The molecular mixture technique is an alternative to solvent evaporation in which the medication and carrier are dissolved in a common solvent, frozen, then sublimed.

8. Melt Agglomeration Process[44,45]

This method has been used to make solid dispersion in which the binder serves as a carrier. Furthermore, solid dispersions are made by heating the binder, drug, and excipient to a temperature above the binder's melting point (melt-in process) or spraying a drug dispersion in molten binder on the heated excipient (spray-on procedure) with a high shear mixer. Because it is easier to control the temperature and a higher binder content can be integrated in the agglomerates, the rotary processor may be preferred to the high melt agglomeration. In the preparation of solid dispersion by melt agglomeration, the effect of binder type, manufacturing method, and particle size are crucial parameters. With PEG 3000, poloxamer 188, and gelucire 50/13, it was discovered that the melt in process yields higher dissolving rates than the spray-on procedure, which was linked to the immersion mechanism of agglomeration formation and growth. In addition, the melt in method ensures that the medication is distributed uniformly throughout the agglomeration. Larger particles induce agglomerates to densify, but fine particles cause total adherence to the mass to the bowl immediately after melting due to fine particle distribution and coalescence.

Conclusion:

Increasing the Bioavailability of a poorly soluble drug is a challenging aspect of drug development. Because of the poor aqueous solubility the drug possess dissolution problems due to which the in vivo absorption of the drug is reduced and thus the bioavailability is reduced, making the drug inappropriate for oral consumption and therefore solubility enhancement become necessary for such drug candidate. Solid dispersion is a most simple and efficient technique for increasing the aqueous solubility of a drug.

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