Solid dispersion: application and limitations

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Abstract

Solubility and dissolution rate are essential factors in the bioavailability of a drug. The drug must be well-soluble in water to have good bioavailability. Solid dispersion is among the most widely used and effective methods for increasing solubility and releasing inadequately water-soluble medications. Solid dispersion requires the choice of a suitable carrier for the right active pharmaceutical ingredients and the proper techniques for preparing solid dispersions. The reliable dispersion system is designed in various ways to achieve the goal and avoid the accompanying obstacles.

Keywords: solid dispersion, solubility, solvent evaporation, lyophilization, generation, methods

Introduction

During drug discovery and development, it is estimated that a 40% to 70% rate of new chemical entities are delayed or failed. The main reason behind this is biopharmaceutical properties. Poor pharmacokinetics Examples of challenges that can arise include low solubility, poor permeability, and inadequate absorption. Chemical stability 1. In addition to permeability, Solubility and dissolution rate are essential factors in the bioavailability of a drug. There have always been pharmacists whose solubility has been troubling in developing a formulation suitable for oral administration. The therapeutic effect of the formulation depends on the amount of the drug at the site of action, which depends on the bioavailability of the drug 2. The drug must be well-soluble in water and have good permeability to have good bioavailability. Dissolution might be the stage that influences the rate at which therapeutic action is onset. Solubility is the amount of drug solute present in a given volume of the solvent system at a given temperature, pressure, and pH. 3. Possible causes of inadequate oral bioavailability are typically 4: 1. Aqueous solubility less than 2. Poor dissolution: intrinsic dissolution rate less than 0.1 mg/cm²/min 3. High molecular weight (greater than 500 Daltons), self-association, and aggregate 4. High crystal energy. The Biopharmaceutical Classification System (BCS) was developed in 1995 to classify drugs by absorption conductivity. Drugs, according to BCS, are classified into four groups based on solubility and permeability 5, as shown in Figure 1. The BCS is considered highly permeable if its absorption rate in humans is 90% or more of the administered dose. It is defined as a product with high solubility, the maximum dose that can be dissolved from pH 1 to 7.5 in 250 ml or less of an aqueous medium 6. BCS links drug release in vitro to bioavailability in vivo. It is a beneficial method for in vitro-in vivo correlations (IVIVC) that satisfies the requirements of the physicochemical properties of a compound, such as solubility and permeability 6. When the modified Noyes-Whitney equation is considered, some indications demonstrate how very poorly soluble drugs can reduce their limitations on oral availability by increasing their dissolution rate 7,8.

\[
\frac{dc}{dt} = \frac{AD}{Cs - C}
\]

In this equation, C is the concentration of the drug in the solution at time t; Cs is the solubility of the drug in the dissolution medium; h, the thickness of the diffusion boundary, and the dissolution rate of dissolution are all variables. Low solubility is a problem for BCS class II and IV medicines. The primary difficulty is improving the solubility of BCS II and IV medications. Different approaches to expanding the dissolution/bioavailability of poorly soluble drugs are shown in Table 1. Due to the solubility challenge, the pharmaceutical industry has been compelled to investigate chemical, physical, and carrier-based procedures for increasing drug solubility. 9. By changing the drug’s molecular structure, additive or new chemical salt conjugates with distinct pharmacological and pharmacokinetic
characteristics can be created with different pharmacokinetic and pharmacological aspects. The solubility is enhanced because the physical technique decreases the size and increases the contact surface. Various formulation approaches to increase solubility include producing liquid systems based on lipid carriers and/or surfactants or carrier-based solid formulations. Each has its advantages and limitations. (SDs) are a promising technology because of their appealing properties—including solubility, small particle size, high wettability, high porosity, and enhanced drug stability—solid dispersions. Increased solubility can be easily achieved through reliable distribution, yielding high precision.

### Aim

This article examines the history of solid dispersion technology, including its categorization, various preparation procedures, benefits, and drawbacks. Applications. This study also reviews the numerous medications for which this approach has been employed.

### Table 1: Solubility enhancement techniques

<table>
<thead>
<tr>
<th>Physical modification</th>
<th>Chemical modification</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>- A smaller overall particle size</td>
<td>- Salt Formation</td>
<td>- Homogenization at High Pressure</td>
</tr>
<tr>
<td>1. Micronization</td>
<td>- The use of buffering agents</td>
<td>- Utilizing Hydrotropy</td>
</tr>
<tr>
<td>2. Complexation by use of nanosuspension</td>
<td>- A shift in the pH level</td>
<td>- The technique of solvent evaporation</td>
</tr>
<tr>
<td>- Alterations to the crystal structure</td>
<td>- Complexification</td>
<td>- Conversion of Polymers</td>
</tr>
<tr>
<td>- Dispersion of the drug in various carriers</td>
<td>- Physical Mixture</td>
<td>- Supercritical fluid technique</td>
</tr>
<tr>
<td>1. The procedure is known as fusion melt</td>
<td>- Technique of co-grinding</td>
<td>- Technique based on electrostatic spinning</td>
</tr>
<tr>
<td>2. The process of using a solvent</td>
<td>- Process of kneading</td>
<td>- Spray freezing into liquid</td>
</tr>
<tr>
<td>3. Dropping technique</td>
<td>- Neutralization</td>
<td>- Lyophilization method</td>
</tr>
<tr>
<td>4. The method is known as spray drying</td>
<td>- The Process of Spray-Drying</td>
<td>- Evaporative precipitation into aqueous solution</td>
</tr>
<tr>
<td>5. Method of Irradiation using Microwaves</td>
<td>- Technique of Irradiation using Microwaves</td>
<td>- Filling of capsules directly</td>
</tr>
<tr>
<td>6. lyophilization and freeze drying</td>
<td>- Soluble prodrug approach</td>
<td></td>
</tr>
</tbody>
</table>

### Figure 1: Biopharmaceuticals classification system.
**Solid solution:**

The SD technique is widely used and effective for increasing solubility and releasing inadequate water-soluble medications. In 1960, Sekiguchi and Obi were the first to successfully demonstrate the solid dispersion method. To improve the bioavailability of drugs with poor water solubility, such as sulfathiazole, they suggested creating a eutectic combination with a water-soluble and physiologically inert carrier, like urea. This would allow the pharmaceuticals to be absorbed more quickly. Due to the uniform medication distribution in the solid eutectic, the active ingredient released into fluids consists of tiny, scattered particles that showed in Fieger 2.

![Solid dispersion Solution](image)

**Figure 2:** A schematic shows how solid dispersion improves the bioavailability of weakly soluble in-water drugs compared to a traditional tablet or capsule.

They are defined as "the dispersion of one or more active ingredients in an inert carrier matrix at solid-state produced via melting (fusion), solvent, or melting-solvent method" by Chiou and Riegelman, authors of a classic review. In his seminal work, Corrigan (1985) defined solid dosage forms as "products formed by converting a fluid drug-carrier combination to the solid state." Chiou and Riegelman (1971) were the first to define these systems as 'solid dispersion' 19. Patients are more therapeutically compliant with SD compared to other solubilization products. In contrast to the milling process or micronization, in which the particles of the size are confined to a range of 2-5 μm, the SD effectively lowers the size of the particle, which in turn leads to an improvement in the medicament discharge. One further definition of further dispersion is "product formed by converting a fluid medicament-carrier combination to the solid-state." Therefore, the SD of medications satisfies the active agent bioavailability and solubility of a poor water solubility medication, which increases the medication’s efficacy and decreases adverse effects. Physically stable SD are formed when solid dispersions are combined with high conformational entropy and low molecular mobility 20. By using polymers that increase the physical strength of amorphous pharmaceuticals, it is possible to reduce molecular mobility 21. To fabricate a commercially viable product, it is necessary to consider several essential factors. Once these things are considered, considering the variable parameters for the assessment and the variable production procedure, a concept demonstration is made. The technique has several disadvantages, including difficulties in scaling up to an industrial level, achieving consistent results when assessing physicochemical properties in a laboratory setting, and the instability of the body. As SDs age, they lose crystallinity and dissolve more slowly. SD is unstable at room temperature and humidity due to its thermodynamic nature. These factors can increase the overall molecular mobility.
lower the glass transition temperature (Tg), or disturb interactions between the drug and carrier. These all promote phase separation and crystallization of SD, reducing its solubility and dissolving rate. The SD method frequently experiences problems with phase separation and drug stability. The recrystallization of the drug from a supersaturated solution and the incompatibility of the drug with the solvent are possible explanations. Polarity and temperature dependence of supersaturation are two factors that contribute to this mismatch. Products including NorvirVR, IncivekVR, and RezulinVR (all from the Abbott Laboratories in Chicago, Illinois) were taken off the market. The medicine recrystallized (changes in crystallinity resulted in a lower dissolving rate) from a supersaturation solution as it aged, which explains why it was taken off the market. Avoiding problems requires a solid grounding in the physicochemical properties of the medication, solvent, and matrix. 

Table 2: Carrier Excipients

<table>
<thead>
<tr>
<th>Nature used carriers</th>
<th>Example</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugars</td>
<td>Dextrose, Mannitol, Glucose, Lactose, Sorbitol, Sucrose</td>
<td>Possess the ability to influence drug absorption compatible with thermosensitive medications.</td>
</tr>
<tr>
<td>Organic acid</td>
<td>Tartaric acid, succinic acid, phosphoric acid, and Succinic acid.</td>
<td>Water solubility is compatible with the melt method. Not applicable for acid-labile API.</td>
</tr>
<tr>
<td>Polymer</td>
<td>polyvinyl pyrrolidone (PVP),PEG400, Poloxamer 188, PVP K30, Bicyclodextrin, Eudragit L100 sodium salt,</td>
<td>Able to inhibit recrystallization.</td>
</tr>
<tr>
<td>Surfactant</td>
<td>Pluronic F68, Tween 80, Gelucire 44/14, vitamin E TPGS, docusate sodium, polyoxyethylene stearate, sodium lauryl sulfate.</td>
<td>Capable of enhancing drug dissolution and absorption.</td>
</tr>
<tr>
<td>Hydrotropy</td>
<td>Sodium acetate, Sodium benzoate, resorcinol, ascorbic acid, sodium citrate</td>
<td>compatible with thermosensitive medications</td>
</tr>
</tbody>
</table>

Carriers:

It is crucial in SD formation; Carriers are shown in Table 2. A wide variety of physicochemical factors can influence the process of making SDs. When developing SD, the characteristics, including molecular weight carrier, pore volume, type (amorphous, crystalline, semi-crystalline) carrier, Micrometric properties, specific surface area, carrier concentration, and transport hygroscopicity have been taken into account. These factors significantly impact the drug's soluble, dissolvable states, absorption, and SD stability. SD carrier excipients are categorized as polymeric, low-molecular-weight, and surfactant carriers. The following conditions must be met for a vehicle to optimize a drug dissolution rate: Rapid dissolution is characteristic of water-soluble substances and water-insoluble in carriers used to produce sustained release solid dispersion. Nontoxic and inactive from a pharmacological standpoint, temperature resistance for the melting procedure, Solubility in an assortment of solvents, rather than enhancing the medicine's aqueous solubility. Only make weakly linked complexes with the drug that is chemically compatible with it. It was an attempt to use low-molecular-weight carriers like urea, saccharides, and organic acids. The medicine and liquid used set High standards for these carrier excipients. Polymeric carriers have a higher molecular weight than carriers with a low molecular weight, allowing for greater drug dispersibility and recrystallization inhibition. PEG, PVP, PVPVA, HPMC, and hydroxypropyl cellulose (HPC) are examples of polymers utilized in commercial formulations. A high glass transition temperature is essential for a suitable carrier to get sufficient kinetic stability in supersaturated glass solutions. Functional groups that are either donors or acceptors of hydrogen bonds are also helpful since specific interactions make it easier for the solid drug to dissolve in its carrier. These interactions also seem to play a significant role in stopping a medication from separating into phases and crystallizing from a glass solution. Polymeric carriers without surfactants have insufficient absorption-enhancing effects for poorly permeable pharmaceuticals, which only require dispersibility. Pages with surfactants can help the body absorb drugs better by interacting with the absorptive epithelium and stopping drug efflux transporters.
Classification of solid dispersion:

Solid dispersions were first classified by Chiou and Riegelman, who separated them into six different types: glass solutions and glass suspensions; solid solutions, simple eutectic mixtures, amorphous precipitations in a crystalline carrier; compound or complex formation; and combinations of the above five types.\textsuperscript{19} Table 3 displays the molecular and physical configurations of API. Such as active pharmaceutical ingredients (API) scattered as crystalline particles, API dispersed as amorphous groups, or API molecularly dispersed within the carrier.\textsuperscript{25} This classification was used for a significant amount of time and had widespread acceptance and citation. Nevertheless, several adjustments to the classification system have been made during the past several years. Proposed. Vasconcelos et al, who also classified solid dispersions into three generations\textsuperscript{35}, accounted for recent advancements in the solid dispersion approach. Furthermore, it modified this categorization by including control release solid dispersion, as Table 3 displays API’s molecular and physical configurations. Such as active pharmaceutical ingredients (API) scattered as crystalline particles, API dispersed as amorphous groups, or API molecularly dispersed within the carrier. Fourth generation.\textsuperscript{36} Solid dispersions can be divided into crystalline solid dispersions and amorphous solid dispersions, depending on the physical condition of the carrier, which may be crystalline or amorphous. Solid dispersions can also be classified into four generations, as shown in Figure 3:

- **1st generation**
  - Crystalline carriers like urea and sugar can be used to make the beginning solid dispersions. However, crystalline are more stable than amorphous ones and don’t release the drug as fast.

- **2nd generation**
  - Instead of using crystalline carriers, which are often polymers, amorphous carriers are employed. Natural polymers such as hydroxypropyl cellulose or starch derivatives such as cyclodextrins as well as synthetic polymers such as polyvinyl pyrrolidone (PVP), polyethylene glycols (PEG).  
  - Rate of dissolution; Supersaturation precipitation; Weak stability

- **3rd generation**
  - Surface activity or self-emulsifying capabilities in the carrier have recently been identified to further enhance the dissolving profile. As a result, we now have strong dispersions of the third generation. Surfactants like inulin, and poloxamer 407 have been proven to improve in vivo bioavailability and generate high polymorphic purity, lowest stability due to supersaturation-induced precipitation, high rate dissolution

- **4th generation**
  - The term "controlled-release solid dispersions" (CRSD). It has medications that have a short biological half-life yet aren’t very water-soluble. Both water-soluble and water-insoluble carriers can be utilized. The goals of CRSD are to improve drug solubility and to allow for the controlled, prolonged release of medications. In CRSD, we employ ethyl cellulose, Eudragit RS, and other water-soluble carriers. increase dissolution rate

Figure 3: Generations of solid dispersion \textsuperscript{37,38,39,40}
Table 3: Classification of Active Pharmaceutical Ingredients and Carriers by Physical State and Molecular Structure.

<table>
<thead>
<tr>
<th>Class</th>
<th>The physical and molecular arrangement of API</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalline-Crystalline</td>
<td>Dispersion of crystalline API in a crystalline carrier</td>
</tr>
<tr>
<td>Crystalline-Amorphous</td>
<td>Dispersion of crystalline API in an amorphous carrier</td>
</tr>
<tr>
<td>Amorphous-Crystalline</td>
<td>Dispersion of Amorphous API in crystallin carrier</td>
</tr>
<tr>
<td>Amorphous-Amorphous</td>
<td>Dispersion of Amorphous API in an amorphous carrier</td>
</tr>
<tr>
<td>Molecularly dispersed-Crystalline</td>
<td>Dispersion API molecularly in crystallin carrier</td>
</tr>
<tr>
<td>Molecularly dispersed Amorphous.</td>
<td>Dispersion API molecularly in an amorphous carrier</td>
</tr>
</tbody>
</table>

Techniques/Methods for Solid Dispersion:

Methods for preparing solid dispersions: The reliable dispersion system is designed in various ways. These procedures are listed below.

1. Kneading technique.
2. Lyophilization.
3. Melt Agglomeration technique.
5. Electrospinning method.
7. Melt extrusion method.
8. Supercritical fluid technology
10. Solvent method.

Solvent method:

Solvent evaporation is one of the most often utilized procedures in the pharmaceutical business for enhancing the solubility of poorly water-soluble medicines. This method was developed specifically for heat-unstable components instead of opposed to melting, in which the medication and carrier are mixed using solvent rather than heat. Therefore, this method enables using pages with very high melting points. 41. The basic principle of this method is to dissolve the drug and carrier in a volatile solvent so that they combine evenly. The solvent evaporates to achieve SD while the mixture is constantly stirred. The next step is to crush and sift the solid SD. In 1965, Tachibana and Nakamura were the first to use this strategy. The primary advantage of this method is that it prevents drug and carrier degradation due to the low temperature required for evaporation. Due to the low evaporation temperature, this method is beneficial for preserving the medication’s and carrier’s integrity. 42. This approach has many disadvantages, including the increased expense of preparation, the difficulty in extracting the liquid solvent completely, the potential negative impact of solvent traces on chemical stability, Choosing a common volatile solvent, the challenge of replicating crystal form and supersaturation of the solute in the solid system is only possible in a system with very viscous characteristics. 43. This method has been used to enhance the solubility of many medicines, including tectorigenin 44, flurbiprofen 45, azithromycin 46, cilostazol 47, piroxicam 48, ticagrelor 49, indomethacin 50, abietic acid 51, loratadine 52

Fusion/melting technique:

The medication and the carrier are combined and melted at a temperature above their eutectic point in this procedure. Then, other methods are used to cool or solidify the liquid, such as spreading it out on stainless steel sheets exposed to air conditioning, placing a Petri dish in a desiccator filled with water, shaking an ice bath, or submerging the container in liquid nitrogen. After extraction, the solid is broken down, sieved, diced, and crushed. High-temperature fusion poses a risk of drug and carrier degradation. Fusion at high temperatures can cause the loss of volatile drugs or carriers. To avoid this issue, the physical mixture can be heated in a sealed container or melted under a vacuum or inert gas such as nitrogen. 53. The advantage of this method is that no solvent is necessary, and it is simple and economical. Sekiguchi and Obi first used the dissolve technique in 1961 38. This method has been used to enhance the solubility of many medicines, such as Sulfathiazole 39, clotrimazole 54, albendazole 55, tacrolimus 56, fenofibrate 57, paclitaxel 58, manidipine 59, olanzapine 60, furosemide 61.

Lyophilization:

Alternative to solvent evaporation, lyophilization dissolves the drug and carrier. Lyophilized molecular dispersion is created by freezing the solution in liquid nitrogen. This approach has often employed the drug and carrier, dissolved in a common solvent and thermolabile compounds unstable in aqueous solutions but stable in dry form for lengthy storage. 62. This method has enhanced the solubility of many medicines, such as Nifedipine and sulfamethoxazole 63, celecoxib 64, meloxicam 65, and docetaxel 66.

Supercritical fluid technology SCF:

It exceeds its temperature and pressure thresholds. Vapour and liquid in equilibrium are essential at the highest possible temperature and pressure. SCF solidifies insoluble material/polymer with medication to improve solubility. It outperforms spray drying, hot melt, etc. Because SCFs are midway between liquid and gas 67,68, it is possible to fine-tune the mixture of structures needed for product processing. SCF processing long used in the food sector, has been adapted for medical purposes. Most solvents are carbon dioxide, The liquid that is used the most. It is cost-effective, safe, and ecologically friendly. SCFs appeal in clinical research because they have low operating conditions (temperature and pressure) 69, nitrous oxide, ethylene, and propylene. Drug particles scattered in the SCF can be recyled into smaller particles. Due to their flexibility and precision, SCF techniques can gradually create medication particles below micron levels. SCF methods can make nanosuspensions of 5-2,000 nm particles. Nektar Therapeutics and Lavipharm use SCF technology to reduce particle size and enhance melt 70,71. By lowering the melting temperature of the dispersed active
ingredient, supercritical fluids reduce the melt dispersion process temperature. The solubility of the lighter component (dense gas) in the developing phase (heavier part) is the cause of this depression 72. This method has been used in drugs such as irbesartan 73, apigenin 74, carbamazepine 75, glibenclamide 76.

**Mechanism of drug release from SD:**

The dissolution rate of a pharmaceutically active agent prepared by solid dispersion technique after oral administration in tablets, capsules, etc., will indicate its eventual success. One of the best ways to make poor soluble drugs more soluble is by transforming crystalline medicine into an amorphous structure. Maintaining a supersaturated state and stabilizing an amorphous form are two of the most important aspects of solid dispersion formulations. A problem with solid dispersions is the precipitation of supersaturated medications, which reduces their bioavailability 77. The stability and solubility of the drug in the medium are improved by supersaturating drug delivery systems and particle size reduction, such as solid dispersion, and a spring-like action is observed due to the increased dissolving rate of the medication. The dissolving rate decreases during the supersaturation phase due to drug precipitation. Furthermore, when precipitation inhibitors are introduced to reduce aggregation, a parachute-like effect is observed in the dissolving profile of medicines in such a system. 78. Two significant mechanisms mediate the release of medication from SDs. The drug was released after (1) drug-controlled release in the first mechanism and (2) carrier-controlled release in the second. Due to its hydrophilic characteristics, the designed drug carrier matrix readily dissolves or absorbs water. A concentrated gel layer or carrier layer may form in some cases. Because of the high viscosity of this gel matrix, drug diffusion is complicated when the medication dissolves. It is a rate-limiting stage in which the carrier is distributed into the bulk phase. After interaction with the dissolution medium, the sparingly soluble or insoluble medication is released into the concentrated layer and released intact. The release profile is also affected by particle size, drug solubility, and polymorphism 78.

**Solid dispersions Characterization:**

There are numerous methods for contributing data on the physical characteristics of solid dispersion systems. The enhanced dissolution of inadequately water-soluble pharmaceuticals in solid dispersions can be demonstrated using standard dissolution techniques. Other attributes of solid dispersions should be evaluated, including the drug-carrier interaction, the physical states of medicines, and the chemical stability of drugs. As a result, numerous instrumental and analytical techniques are used to confirm these properties. The crystalline condition and degree of pharmaceuticals are uniquely characterized. Indirectly, the quantity of amorphous narcotics can be deduced from the sample’s degree of crystallinity 79.

**Drug-carrier miscibility**

Differential scanning calorimetry, hot-stage microscopy, and Raman Spectroscopic and FT-IR spectroscopy.

**Drug carrier interactions**

Raman spectroscopy, FT-IR spectroscopy, Solid-state NMR

**Physical Composition**

Atomic force microscopy, Raman microscopy, dynamic vapour sorption, surface characteristics, scanning electron microscopy, surface area analysis, and Inverse gas chromatography.

**Amorphous content Studies**

polarized light optical microscopy, powder X-ray diffraction, humidity stage microscopy, hot-stage microscopy, DSC (MDTSC), stability

isothermal calorimetry, Humidity studies, saturated solubility study, DSC (Tg, Temperature recrystallization).

**Enhancement of dissolution**

dissolution, dissolution in media of biological relevance. Intrinsic dissolution, dynamic solubility,

**Thermal Analysis Approaches:**

Thermal analysis is a collection of methods in which a substance is put into a controlled temperature program to measure a physical attribute as a function of temperature. The technique will provide helpful data on the physical and chemical processes in SD and the carriers and stability of the medicine, which may be used to determine the best processing and preparation settings for SD formulation 80.

**X-Ray Diffraction (XRD):**

This technique calculates a sample's XRD (or reflection) intensity of a sample as a function of the diffraction angles. The diffraction technique helps identify compounds and the formation of complexes. As complexes’ spectrum or lattice parameters are notably different from those of purified components, the inability of dispersion systems to distinguish between amorphous precipitation and molecular dispersion if the lattice parameters of the solvent component are not altered is the primary challenge when employing the diffraction technique 81.

**Differential scanning calorimetry (DSC):**

Determining the heat flow and temperature associated with substance transitions as a function of time and temperature is a thermal process. Using DSC, we can define the melting temperatures of various substances and monitor and analyze their thermal behaviour. DSC allows for the quantitative...
observation of energy-consuming or energy-producing processes. It is commonly believed that interactions between pharmaceuticals and polymers alter the exothermic and endothermic peaks. DSC is the most reliable thermoanalytical technique for determining chemical transitions' temperature and heat flux. DSC permits the evaluation and monitoring of melting temperatures and the investigation of the thermal behaviour of various compounds. DSC can be used to observe quantitatively the methods by which energy is produced or required. Interactions between medications and carriers modify the exothermic and endothermic maxima. DSC is also a common technique for determining the quantity of crystalline material. In DSC, samples are continuously heated, and the required energy is measured. DSC can observe the temperatures at which thermal events occur. Thermodynamic processes include transforming glass to rubber, (re)crystallization, dissolution, and degradation. In addition, it is possible to quantify melting and (re)cry stallization energies. The melting point can be used to determine the number of crystallized substances.

**Fourier Transformed Infrared (FTIR) spectroscopy:**

Infrared spectroscopy (IR) can detect variations in the energy distribution of drug-matrix interactions. Sharp vibrational bands signify crystalline structure. FTIR was used in purified material to detect crystallinity ranging from 1% to 99.9%.

**Applications of solid dispersion:**

The following are the most critical applications of the solid dispersion technique in formulating pharmaceutically active compounds.

- Formulation of a sustained-release dosage form
- Decreased systemic inactivation of drugs such as morphine and progesterone.
- It increases the solubility of inadequately soluble medications and, as a result, the dissolution rate, thereby enhancing dissolution, which improves the absorption and bioavailability of the drug.
- To stabilize problematic pharmaceuticals against various decomposition processes, including hydrolysis, oxidation, etc.
- To reduce the side effects of medications.
- They mask the unpleasant flavour and odour of narcotics.
- To avoid undesirable incompatibilities.
- To accomplish a uniform distribution of a limited number of solid-form pharmaceuticals.

Solid-liquid dosage (up to 10 percent) or gases.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nifedipine</td>
<td>Elan Corp, Ireland</td>
</tr>
<tr>
<td>Cesamet® Nabilone</td>
<td>Lilly, USA</td>
</tr>
<tr>
<td>Cesamet® Nabilone</td>
<td>Valeant Pharmaceuticals, Canada</td>
</tr>
<tr>
<td>Certican® Everolimus</td>
<td>Novartis, Switzerland</td>
</tr>
<tr>
<td>Gris-PEG® Griseofulvin</td>
<td>Novartis, Switzerland</td>
</tr>
<tr>
<td>Gris-PEG® Griseofulvin</td>
<td>VIP Pharma, Denmark</td>
</tr>
<tr>
<td>Fenoglide® Fenofibrate</td>
<td>LifeCycle Pharma, Denmark</td>
</tr>
<tr>
<td>Nivadil® Nivaldipine</td>
<td>Fujisawa Pharmaceuticals Co., Ltd</td>
</tr>
<tr>
<td>Nimotop® Nimodipine</td>
<td>Bayer</td>
</tr>
<tr>
<td>Torcetrapib® Torcetrapib</td>
<td>Pfizer, USA</td>
</tr>
<tr>
<td>Ibuprofen® Ibuprofen</td>
<td>Germany</td>
</tr>
<tr>
<td>Incivek® Telaprevir</td>
<td>Vertex</td>
</tr>
<tr>
<td>Sporanox® Itraconazole</td>
<td>Janssen Pharmaceutica, Belgium</td>
</tr>
<tr>
<td>Onmel® Itraconazole</td>
<td>Stiefel</td>
</tr>
<tr>
<td>Prograf® Tacrolimus</td>
<td>Fujisawa Pharmaceuticals Co., Ltd</td>
</tr>
<tr>
<td>Cymbalta® Duloxetine</td>
<td>Lilly, USA</td>
</tr>
<tr>
<td>Noxafil® Posaconazole</td>
<td>Merck</td>
</tr>
<tr>
<td>LCP-Tacro® Tacrolimus</td>
<td>LifeCycle Pharma, Denmark</td>
</tr>
<tr>
<td>Intelic® Etravirine</td>
<td>Tibotec, Yardley, PA</td>
</tr>
<tr>
<td>Incivo® Etravirine</td>
<td>Janssen Pharmaceutica, Belgium</td>
</tr>
<tr>
<td>Rezulin® Troglitazone</td>
<td>Pfizer, USA</td>
</tr>
<tr>
<td>Isoptin SRE-240® Verapamil</td>
<td>Germany</td>
</tr>
<tr>
<td>Isoptin SR-E® Verapamil</td>
<td>Abbott Laboratories, USA</td>
</tr>
<tr>
<td>Crestor® Rosuvastatin</td>
<td>AstraZeneca</td>
</tr>
</tbody>
</table>
Conclusion:
Solid dispersion is a valuable technique for achieving better or controlled release profiles of pharmaceutically active compounds; the method is fast, simple, and cost-effective in many cases and could provide a solution for poorly soluble compounds.

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References:


70. Manna L, Banchero M, Sola D, Ferri A, Ronchetti S, Scaridi S. Impregnation of PVP microparticles with ketoprofen in the