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SOLID DISPERSION: A REVIEW ON NOVEL APPROACHES FOR SOLUBILITY ENHANCEMENT OF HYDROPHOBIC DRUGS

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ABSTRACT

Solid dispersion is a strategy for improving drug solubility by encapsulating weakly water-solvent medicines in an inert hydrophilic carrier in a solid-state, which may be achieved via several methods such as melting, solvent, or solvent melting. In the assessment of solid dispersion, only a few characterization techniques have been described. This is a comprehensive review article on preparation methods for lyophilization, spray drying solvent evaporation method, hot-melt extraction, supercritical fluid, and its characterization for SEM, TEM, DSC, FTIR, XRD, and NMR in Solid Dispersion. To use solid dispersion practically and successfully, comprehensive knowledge of certain characterization techniques, its rapid release principles, methods of production, selection of appropriate transporters, and assurance of physical characteristics will be required.

KEYWORDS: Solubility, Hydrophobic, Hydrophilic carrier, Polymer, Solid dispersion, Lyophilization.

1. INTRODUCTION

Tachibana and Nakamaru in 1965 developed a new technique for producing watery colloidal scatterings of β-carotene applying water-solvent polymers for example polyvinyl pyrrolidone. They broke up the medication as well as the polymer-carriers in a solvent system, then totally vaporized the solvent.[1] At the point when the co-accelerate was presented to water, it formed a colloidal dispersion. Mayersohn and Gibaldi showed that dispersing griseofulvin in polyvinyl pyrrolidone using the same solvent technique significantly increased the dissolving

rate.[2] The solid dispersion was also used in the fast-release formulation of griseofulvin.[3] It is thought that this relatively new area of pharmaceutical technology needs thorough characterization to achieve desired properties.[4] In the assessment of solid dispersion, only a few characterization techniques have been published and applied. To use solid dispersion practically and successfully, comprehensive knowledge of certain characterization techniques, its rapid discharge standards, techniques of production, selection of appropriate carriers, and determination of physical characteristics will be required. This article presents a summary of the preparatory phase for lyophilization, spray drying solvent evaporation method, hot-melt extraction, supercritical fluid, and its characterization for SEM, TEM, DSC, FTIR, XRD, and NMR in solid dispersions.

2. PREPARATION METHODS FOR SOLID DISPERSIONS

Solid Dispersions (SD) is made using a variety of techniques, including Melting Method/Fusion Method, Melting Solvent Method (Melt Evaporation), Melt Agglomeration Process, Lyophilization Techniques/Freeze-Drying, Electrospinning Method, Spray-Drying Method, Kneading Method, Solvent Evaporation Method, Hot Melt Extraction, Supercritical Fluid (SCF) Technology discussed as below.

- **Melting Method/Fusion Method:** Sekiguchi and Obi in 1961[5] were the first to utilize the melting method. This method comprises heating both a physical combination of the drug as well as a hydrophilic carrier to the temperatures just above their eutectic composition till they dissolve. Though being agitated, the melting is immediately frozen & chilled inside an ice bucket.
- **Solvent Melting Process (Melt Evaporation):** This process was 1stinvestigated by Goldberg et al.[6] To increase the solubility of griseofulvin, researchers applied succinic acid as carriers as well as methanol as solvents. Melting solvents are a process that merges melted as well as evaporated solvents. The drug is the 1st that dissolved in a solvent until being combined with carriers melted as well as dried.
- **Process of Melt Agglomeration**: This is a procedure wherein binders act like carriers. In this method, the drug, binders, as well as other excipients are transformed into heat with high temperatures over the binding material melting point. The drug is also poured like a dispersal over the heating binder.[7]
- **Lyophilization Techniques/Freeze-Drying:** Lyophilization refers to a method for obtaining a lyophilized molecular dispersal that substitutes evaporation of the solvent via diluting the drug as well as carriers in a solvent and afterward chilling the solutions with

liquid nitrogen.[8] This method is most commonly used with thermolabile chemicals, which are volatile throughout aqueous solutions yet robust for long durations throughout the dried form. Soluplus has used PEG 6000 as a carrier during prior studies to manufacture nifedipine as well as sulfamethoxazole SD to estimate physicochemical and also in vitro properties.[9]

- **Electrospinning Method:** Throughout the electrospinning process, SD technologies, as well as nanotechnology, get merged. Throughout this process, solid fibers are formed from the polymeric flowing fluid or melt given by a millimeter-scale nozzle.[10]
- **Spray-Drying Technique:** This technique is among the oldest forms of drying goods, particularly for those who are thermally delicate, including foodstuffs as well as medications. The drug is dissolved in an appropriate solvent, and also the carriers get diluted in an aqueous solution containing the feed solution. Therefore, both fluids are combined through sonic or some other appropriate methodologies until the answer is apparent. These feed solutions first were blasted with the rising nozzles in a drying medium to create small droplets. Dried fluid (hot gas) is used to make the droplets, which are nano as well as micro-sized particulates.[11] In the healthcare profession, spray-drying has been routinely utilized to enhance the concentrations of SD and BA of weakly water-soluble medicines for example nilotinib[12], spironolactone[13], valsartan[14], rebamipide[15], and artemether.[16]
- **Kneading Technique:** The carriers are disseminated with distilled water and processed into a solution in this technique. The medication is then carefully administered and rubbed. The final kneaded material is allowed to dry before being sieved as needed. Cefixime SD was synthesized using -CD as carriers as well as the kneading procedure in a prior study by Dhandapani and El-gied.[17]
- **Solvent Evaporation Technique:** This technique is one of the most common methods used in the industry of pharmaceutical to make a rise in the liquidity of drugs that are not sufficiently soluble in water. Due to the combination of medicines as well as the carriers with a solvent instead of heat, like in the melting, such strategy was particularly developed for thermal instability elements. Accordingly, this method permits the use of extremely high melting point supports. The basic principle of this technique is to dissolve the drug and carriers in a volatile solvent to give a homogeneous mixture.SD is created by evaporating solvents while stirring them continuously. Afterward when the solid SD gets crushed and sieved. In 1965, Tachibana & Nakamura[18] were among the first to apply

such an approach. To manufacture the formulations, a medicine (-carotene), as well as a carrier (PVP), got dissolved in a suitable solvent (chloroform).

- **Hot Melt Extraction:** This is a common technique in enhancing the solubility as well as orally BA of drugs that are poorly water-soluble.[19] This amorphous SD is made even without a solvent since there is no leftover solvent inside the formulations. A uniform medicine, polymer, as well as plasticizer mixture is melted and afterward extruded into the apparatus, combining the melting procedure with extrusion. The items' shapes can be modified at the extruder's output, therefore they do not have to be polished throughout the final phase.
- **The technology of Supercritical Fluid (SCF):** The introduction of SCF was seen between the 1980s and 1990s. Hannay & Hogarth described SCF as a platform for particle generation during 1897.[20] SCF generates a formulation with restricted particle size distributions (microparticles and nanoparticles) without solvents. Whenever the pressure and temperature of material exceed its vital point, it is said to be in supercritical condition. With SD, SCF may behave as solvents or an antisolvent.

3. CHARACTERIZATION METHODS

Characterization methods can identify solid solutions (medicine that is distributed molecularly), solid dispersions (wherein the medicine is only partly distributed molecularly), as well as physical combinations of medicines as well as carriers. Several instances of analytical procedures are provided below.

- **SEM**: The production technique and chemical composition may provide information about drug crystal characteristics such as particle size and morphological surface. Furthermore, the form and granulometric characteristics of powder particles may be described using a set of parameters acquired automatically by using an image processor to connect a scanning electron microscopy (SEM).[21]
- **TEM**: The goal of using TEM-based methods was to increase the detection limit of crystallinity in amorphous solid dispersions ASDs when identifying the position, size, as well as structure of every crystallization which happened during storage, it also provides some insight into transition pathways. This offers up the potential of gaining a better knowledge of the stability and performance of a medicinal product.[22]
- **DSC**: The most reliable thermoanalytical method is differential scanning calorimetry (DSC). It's a thermal tool for calculating the flow of heat as well as temperatures as just a function of temperature or time with a connection to material changes. Through DSC, we

may determine melting temperatures antrack and evaluate various materials' thermal behaviorls. Systems that use creative energy can be statistically measured through DSC. Drug-polymer interactions are thought to be the source of variations in exothermic and endothermic peaks.[23]

- **FTIR**: Since it considers the specific absorbance of atomic vibrations in the example for quality assessment of biomedical materials, FTIR spectroscopic imaging is believed to be more useful than different strategies. IR might be used to distinguish varieties in the energy dissemination of medication grid associations. Crystallinity is shown by sharp vibrational groups. Fourier Transformed Infrared Spectroscopy (FTIR) has been utilized to gauge crystallinity in unadulterated substances, which goes from 1 – 99 percent. It tends to be utilized to screen varieties in the limiting of useful gatherings.[24]
- **XRD**: FTIR spectroscopic checking is respected to turn out to be more helpful than a few different methodologies for evaluating the viability of biomedical materials since it looks at the particular receptiveness of sub-atomic vibrations inside the examples. Powder X-beam diffraction might be utilized to distinguish glasslike eases in blended arrangements. Fragility is brought about by an excess of crystallinity. The crystallinity parts produce tight, sharp diffraction tops, though the nebulous part creates a wide pinnacle. The proportion of these forces might be used to decide how much crystallinity is available in the material.[25]
- **NMR**: Strong state atomic attractive reverberation spectroscopy could be utilized to look at polymorphism by investigating the environmental factors of particles as in strong structure. Nonequivalent cores reverberate with differing frequencies, and this multitude of synthetic movements are generally connected with adjustments in the compound's construction or substance surroundings. It's additionally valuable since it can ascertain the number of crystallographic focuses in a unit cell. Despite powdered x-beam diffraction, strong state atomic attractive reverberation spectroscopy is appropriate to investigating shapeless plans of drugs and solvates which are commonly too little to even think about being detected. Obtaining spectroscopy at different temperatures is important to know polymorphism varieties just as sub-atomic versatility in materials.

4. CONCLUSION

Solid dispersions (SD) are presently commonly viewed as among the best techniques for expanding the dissolvability or BA of water-insoluble medications. Even though challenges with pharmaceutical formulations, consistency, as well as storage formulation could reduce

the number of commercial SD items offered, Solid Dispersions (SD) items are slowly becoming more prevalent in healthcare situations, due to improved manufacturing techniques as well as carriers which discuss the aforementioned problems. In conclusion, the manufacturing technique used has a significant impact on the formulation's success. On a lab scale, the melting point and thermal stability are used to choose which melting technique to use. The characteristics of the medication, the carrier, and an organic solvent are all essential elements to consider when choosing a solvent evaporation technique. Only a few manufacturing methods are used to produce SD on an industrial basis. The most frequent melting method for producing SD is hot-melt extrusion. The dissipation technique's chosen criteria are also dependent on solvent toxicity and loading capacities. According to a literature review of solid dispersion assessment parameters, the precise nature and/or behavior of pure drug and drug carriers must be known to produce solid dispersion with optimal features. All of the characterization techniques mentioned above had a significant influence on solid dispersion.

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