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# A Systemic Review on Method of Preparation and Characterization of Amorphous Solid Dispersions

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**ABSTRACT**

In today's pharmaceutical research pipelines, poor water solubility is still a common property of drug candidates. Various processes have been developed to improve the solubility, dissolution rate, and bioavailability of active ingredients classified as BCS II and IV by the biopharmaceutical classification system (BCS). Amorphous solid dispersions (ASDs) are widely employed in the drug product development process to improve the bio-distribution of lipophilic molecules by accelerating the amount and degree of dissolve. Amorphous products, especially ASDs, are the most rapidly growing region in the pharma industry right now. This pragmatic perspective has a substantial impact and gains on overall drug product performance in clinical settings, which leads to dosage form clearance through major regulatory bodies and market entry. The emphasis of this review article is on the amorphous solid dispersion's preparation process and characterization.

## INTRODUCTION:

As a result of its simplicity of treatment, high patient abidance, cost-efficient, decreased sterility limitations, and consistency in dosage form design, oral drug distribution is the most widely used route of administration. As a drug is taken orally, it must move through many biological thresholds, including dissolution into gastric fluid, penetration through the gut membrane, and first-pass digestion, until reaching its target position through the circulatory system. Any checkpoint is a possible bottleneck, with the dissolution of gastric fluid being the most critical. Indeed, for most medicines, enabling systemic circulation is the most important condition that defines bioavailability(1).

In the last two decennaries, new chemical entities (NCEs) in pharmaceutical science are poorly water-soluble, making solution formulations for such molecules/compounds virtually impossible. Between 2007 and 2017, the Food and Drug Administration (FDA) approved 19 commercial ASD drugs, according to reports(2). Amorphous solid dispersions (ASDs) are commonly utilized in support of medicinal compounds that are poorly soluble. In an ASD, a drug material's solubility is increased by disorganizing its translucent structure to produce an elevated vitality amorphous state(3).

By reacting with amorphous APIs, polymers help to boost their solubility and bioavailability. Beneath several advanced stabilization circumstances, such as raised temperature and respective humidity, the polymer may stabilize the ASD and avoid it from crystallizing, as well as have increased physical stability. An ASD may choose low-solubility active pharmaceutical ingredients to other recorded solubilization approaches (APIs)(4). Since ASD keeps its saturated solution in the GI tract, it has a better potential(5). A compound's absorption may be expanded to be better than either a saturated solution state when supersaturation is regulated. Moreover, when various crystalline structures are transformed to the amorphous state, solubility can be lost(6).

Poor aqueous solubility is a serious issue if a medication's medicinal dosage cannot be liquefied within the number of gastrointestinal fluids available. Danazol is a well-known example, with an aqueous solubility of 1 mg/mL at gastric pH and a dosage range of 200-600 mg/d(7). Nearly 200 liters of aqueous media will be required to dissolve the minimum medicinal dose of danazol at gastric pH but is completely unfair in vivo. Moreover, lipophilic medications are more likely to have lower absorption rates because they possibly will pass through the absorption site before completely dissolving. As a result, formulation scientists

are very interested in developing dependable, reliable, cheap, and ascendable techniques to improve the water solubility of BCS class II drugs(8).

A drug's crystal-like form has the benefits of high transparency and corporeal or compound stability. The grid power obstruction, on the other hand, is a significant stumbling block in the degradation of lucid drug molecules(9). In contrast to a crystalline form, the amorphous state has a disordered composition and has greater free energy, resulting in advanced visible water solubility, dissolution rate, and oral absorption(10).

Because of their intrinsic physical and chemical volatility, absolute amorphous drugs are seldom utilized in preparation production. By conceive useful methods to "kinetically stabilize" amorphous APIs, these systems' solubility advantage can be preserved. As a result, the manufacturing of amorphous solid dispersions (ASDs) products has accelerated.

**Amorphous solid dispersion**

**Amorphous state (solid-state)**

Amorphous medicinal products are thermodynamically metastable and easily transition to crystalline shape. The relatively nonthermodynamic perspective of the amorphous state has elevated solubility than the crystalline form because it has a significantly higher free energy than the lucid form(11).

Amorphous structures are seen to have a vitreous look that can be rapidly cooled into a super-cooled liquid. If the material cools, the molecular mobility reduces and the viscosity of the material grows at the same time. “The temperature at which the glass transition occurs is known as the glass transition temperature, and the state of the material is known as glassy”(12).

Glassy compounds, on the other hand, are metastable, and together the balance super-cooled liquid and the lucid phases of the material are metastable, so long-term physical stability testing was needed before the manufacture of pharmaceutical products(13). The glass transformation is linked to improvements in enthalpy, entropy, and phase length, among other thermodynamic properties. It's also known as a second-order thermodynamic change(14).

**Amorphous solid dispersion**

"A molecular dispersion of one or more active ingredients in an inert carrier in the solid-state prepared by the melting, solvent, or melt-solvent method," according to the most common definition(15). Since the energy necessary to disturb the grid composition of lucid drugs isn't necessary to disperse medications in an amorphous state, the dissolution rate and fugacious solubility of its API inside an amorphous state increase significantly(16).

"In a matter of kinetics, the interrelation between polymer and API molecules can cause nucleation and crystal growth in the dissolution medium to be delayed or inhibited. As a result, the drug's supersaturation could be sustained for a prolonged period, allowing for optimal drug absorption"(17).

**Types of solid dispersion based on the polymer used in their preparation**

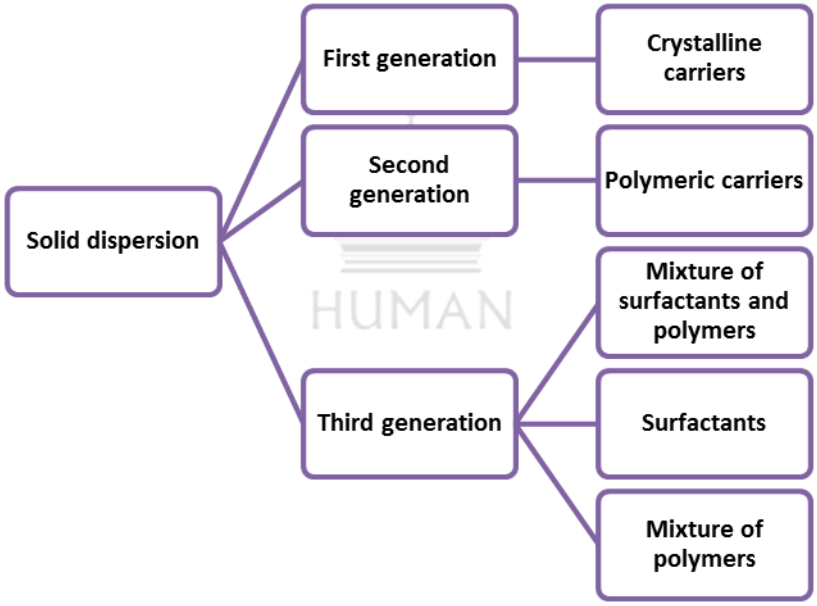


**Figure No. 1: Types of Solid Dispersion based on the polymer used in their preparation**

On a molecular basis, all elements of an ASD are combined. "The need to classify the relationship between the drug and the polymer, phase separation during storage, the dissolution mechanism and physical stability forecast are all challenges in ASD characterization"(18). There is an enhancement in bioavailability when drugs present in amorphous form with the help of solid dispersions. The ability of a drug to go into the solution form and solid-state stability can be enhanced due to the addition of appropriate polymer compliant with the formulation. "A polymer carrier that facilitates the conversion of

crystalline drugs to their amorphous counterparts while also stabilizing the ASD by lowering molecular mobility and enhancing the glass transition temperature (Tg)"(19).

**BCS classification**

Per-oral drug absorption is influenced by solubility and permeability. The BCS scheme is widely used in the pharma industry for drug production as well as discovery(20).

This proposal has been approved by the US Food and Drug Administration, the European Medicines Agency (EMEA), and the World Health Organization (WHO). In manufacturing quality control, the ICH also recommends the BCS method for in-vitro dissolution. "Aside from drug solubility and permeability, three dimensionless quantities, absorption, dissolution, and dosage, all play important roles"(21).

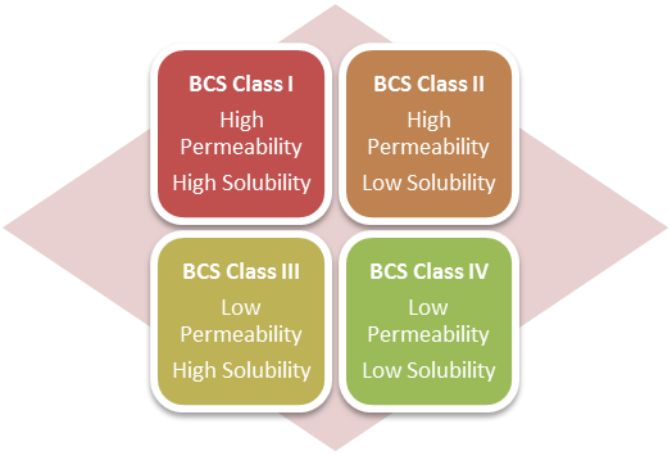


**Figure No. 2: Biopharmaceutical classification system**

**Selection of polymers in amorphous solid dispersion**

Although not many substances have a high glass formation potential and a low tendency to crystallize, their undifferentiated forms are thermodynamically precarious. Since they are thermodynamically fragile, amorphous forms are solid glass modifiers with poor crystallization behavior. "Amorphous solid dispersion is the absorption of an amorphous drug into a polymer of choice, altering the kinetics of crystalline transfer and molecule supersaturation"(22)(23).

The perfect polymer should i) be capable of preserving the drug in an amorphous state not just during processing but also during storage and shipping, ii) it must be readily soluble in the Gastrointestinal system and must retain the most concentrated solution state necessary for

drug absorption., iii) It should also be able to improve bioavailability by - drug permeation across GI membranes(24).

**Preparation methods of amorphous solid dispersion**

Various methods of preparation like nanotechnology, effects of very low-temperature methods, inclusion complex of cyclodextrins, and several other methods have all been documented in the literature for solid dispersions(25). Because of their straightforward formulation approach, simplicity of scale-up, and lower manufacturing costs, two-phase systems are widely employed for the preparation of ASDs(26).

"Based on composition and product stability requirements, most complicated ternary and quaternary structures were established. Polymers may help with ASD stabilization and solubility, but they would also make it more complicated and aren't easily absorbed in the body"(27). When selecting strategies, it's important to prevent demixing or phase separation. In general, phase separation or recrystallization of amorphous drugs and polymers can be avoided by limiting their molecular mobility during preparation(28).

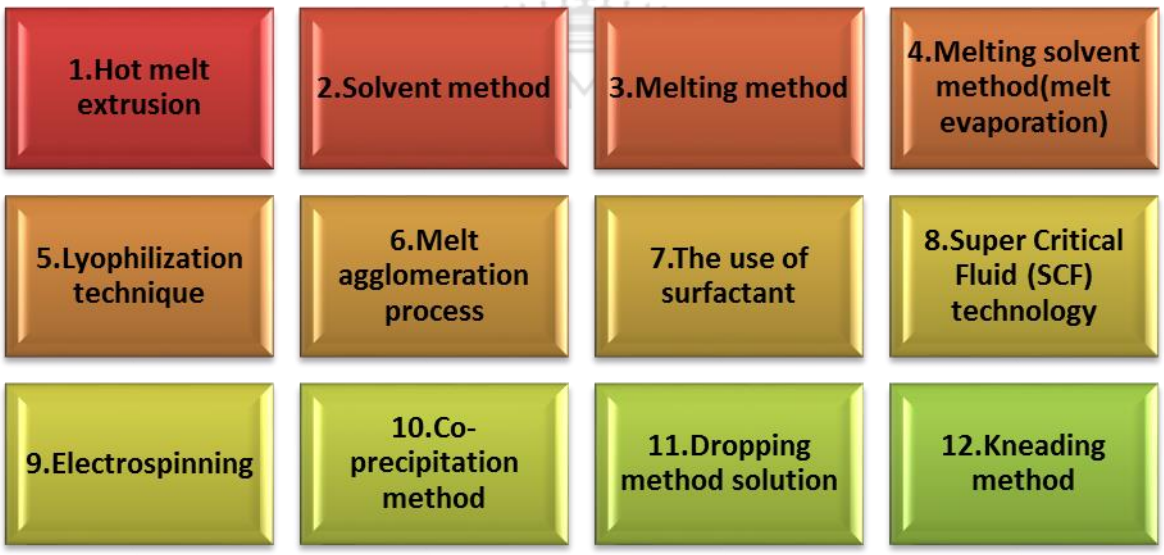


**Figure No. 3: Preparation methods of solid dispersion**

**Hot-melt extrusion**

"The drug/carrier combination is only exposed to a raised temperature for around 1 minute with the hot melt extrusion system, which allows for the handling of drugs that are very thermolabile"(29).

Warm-surface extrusion with a co-revolving twin-screw extruder achieves strong dispersion, which is made up of active ingredient and carrier. In the dispersions, the drug concentration is always 40% (w/w). In the pharmaceutical industry, the melt extrusion process is used to produce several drug formulations, such as sustained-release pellets(30).

**Solvent method**

This process involves dissolving small batches of medication and vector in a common solvent, which is then vaporized until a smooth, solventless film remains. After that, the film is dehydrated to a consistent mass. "The key benefit of the solvent process is that due to the comparatively low temperatures needed for the evaporation of organic solvents, thermal decomposition of drugs or carriers can be avoided"(31). Ex. "Solid dispersion of furosemide with eudragits was prepared by solvent evaporation method"(32).

**Melting method**

In an ice bath, a melted combination of medication and soluble in water carrier is solidified with intense stirring. The end product was obtained after grounding to the solid mass with mortar pestle and sieved. Various modifications have been made, such as gushing a homogeneous molten solution in the form of a thin sheet onto a ferromagnetic or brittle metal frame and cooling the plate with flowing air or water lying on the reverse side. When used with basic eutectic mixtures, the quenching procedure creates a much smoother dispersion of crystallites(33)(34).

**Melting solvent method**

In this method, the drug is dissolved in the organic solvent which is poured into the polyethylene glycol melt. The material is then dried to a uniform amount. After that, it's melted away to leave a smooth, solvent-free film. Liquid compounds in the range of 5–10% (w/w) can be mixed into polyethylene glycol 6000 without significantly reducing its stable properties. It's conceivable that the preferred solvent or dissolved drug will not mix with the polyethylene glycol melt. The liquid solvent can also influence the drug's polymorphic shape,

which precipitates as a solid dispersion. Practically, it is restricted to medications with a reduced dosage level, such as less than 50 mg(33). Ex. “Solid dispersion of furosemide with eudragits was prepared by solvent evaporation method”(32).

**Lyophilization technique**

Heat and mass are transported to and from the substance being prepared during Lyophilization. This method was suggested as a viable alternative to solvent evaporation. “Lyophilization is a molecular mixing procedure in which the agent and carrier are combined in a typical solvent, frozen, and sublimed to create a lyophilized molecular dispersion”(35)(36).

**Melt agglomeration process**

Such a method was employed to make Solid Dispersion, in which the binder serves as a transporter. “Warming the binder, drug, and excipient to a temperature above the binder's melting point, or sprinkling a drug dispersion in a liquefied binder on the hot excipient with a high pressure, produces SD(s)”(37). Because of the simplicity with which the temperature can be regulated and the higher binder material that can be integrated into the agglomerates, a rotary processor is a piece of optional machinery for this method(38)(39).

**The use of surfactant**

Surfactant processes play a critical function in solubilization. Adsorption of surfactants on solid surfaces can change their lipophilicity, electrical interaction, and several leftovers essential properties that control interfacial processes including accumulation, floatation, wetting, solubilization, detergency, enhanced oil recovery, and erosion inhibition. Surface active agents encompass drawn the interest of researchers for the manufacturing of solid dispersions due to their peculiar properties(40)(41).

**Supercritical fluid technology (SCF) technology**

Carbon dioxide is utilized as an anti-dissolvent for the solute as well as a solvent for the organic dissolvent in supercritical fluid antisolvent techniques. Various scholars used different acronyms to describe micronization processes: aerosol dissolvent extraction method, compressed fluid antisolvent precipitation, gas anti-solvent, solution evading dispersion by critical fluids, and critical antidissolvent. “The SAS method entails sprinkling a solution

containing the solute and an organic dissolvent into an uninterrupted critical stage that is flowing at the same time"(42).

While only a minute quantity of carbon dioxide is contained within the polymer before the procedure is completed, essential carbon dioxide is gainful and after the process is finished, it is much easier to strip from the polymeric materials. Carbon dioxide's tendency to plasticize and flourish polymers will be used in the count, and the procedure is being carried out at room temperature. "Furthermore, supercritical fluids are used to decrease the temperature of the melt dispersion process by lowering the melting temperature of the dispersed active agent. The solubility of the featherweight component (heavy gas) in the formation process is the cause of this decrease(massive component)"(43).

**Electrospinning**

Solid fibers are created by electrospinning with polymer melted solution supplied via a millimeter-scale nozzle(44). A liquid brook of a drug/polymer solution is exposed to a voltage within 5 and 30 kV in this process. The developed fibers can be together on a computer to make a non-woven cloth, or they can be collected on a rotating mandril to make yarn(45). This method has a lot of promise for making nanofibers and monitoring the release of biomedicine since it is the easiest and fastest. It can also be used to make solid dispersions in the future(46).

**Co-precipitation method**

The necessary volume of medication is applied to the carrier solution. The device is kept agitated by magnetic fields and is shielded from light. "The formed precipitate is vacuum filtered and dried at room temperature to avoid the removal of structure water from the inclusion complex"(47).

**Dropping solution method**

The dropping process is a modern method for making circular particles from molten rigid dispersions to speed up the crystallization of various chemicals. This approach could be able to solve some of the challenges that other techniques have. A dispersion of a molten drug-carrier mixture is poured onto a tray, where it solidifies into spherical particles for laboratory-scale preparation. Using carriers that solidify at room temperature would likely help with the falling procedure. The falling procedure does not merely make the production process

simpler, but it also raises the rate of dissolution. It doesn't use organic solvents, so it doesn't have any of the issues that come with solvent evaporation(48).

**Kneading method**

The carrier is permeated with water and converted into a paste in this process. The drug is then applied and kneaded for a certain amount of time. After that, the kneaded mixture is dried and, if possible, sieved(49)(50).

**Characterization of solid dispersion**

A variety of analytical methods can be used to classify ASDs in their solid-state state. No one approach can include all of an ASD's structural detail.

Based on the processes of analysis, solid-state characterization approaches are classified into three groups:

(1) Microscopic and Surface Analysis Methods

(2) Thermal Analysis Methods

(3) Spectroscopic Methods.

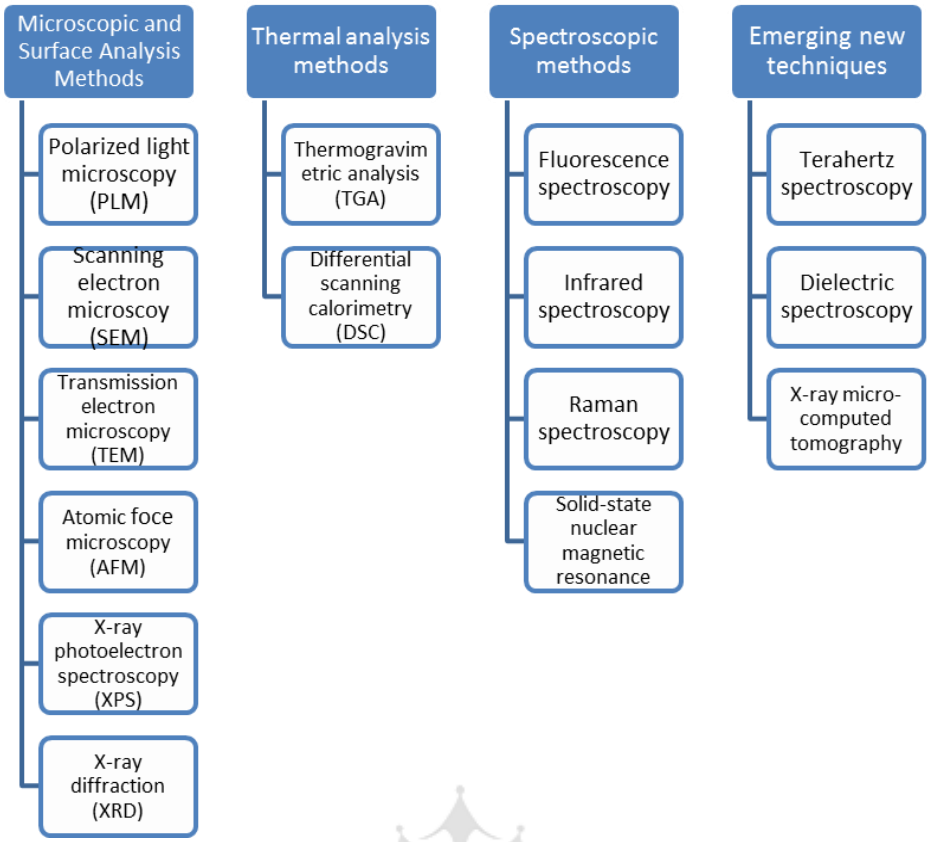


**Figure No. 4: various characterization methods of amorphous solid dispersion**

**Microscopic and surface analysis methods**

It's an adaptable, quick, and non-damaging method for examining little samples for physicochemical properties (26). It includes:

I. Polarized light microscopy (PLM),

II. Scanning electron microscopy (SEM),

III. Transmission electron microscopy (TEM),

IV. Atomic force microscopy (AFM), and

V. X-ray photoelectron spectroscopy (XPS).

**Polarized light microscopy (PLM) and hot stage polarized light microscopy (HSPLM)**

Telang utilized PLM to investigate the initiation of solidification in different ASDs and discovered that PLM is an extra responsive method for researching substance nucleation in

corporal stability studies than XRPD. PLM may be used in combination with other analytical tools to determine the kinetics of compound crystallization, polymorphic transformations, and crystallization(51)(52). Another fast and flexible approach for witnessing the thermal activity of specimens with a polarized light microscope is hot-stage polarized light microscopy (HSPLM).

**Scanning electron microscopy (SEM)**

SEM has the supremacy in followings:

(1) A higher amplification of about ×250,000,

(2) An immense deepness of pasture, and

(3) An edgewise perceptual precision of 3 nm or greater

The effects of manufacturing processes on particle sound structure can be investigated using SEM(53). "It is utilized to track improvements in the arrangement of the ASD sample after dissolution or to perform a physical stability test"(54).

**Transmission electron microscopy**

To isolate crystalline drugs in ASDs, it produces real-space images as well as electron diffraction architecture. Ricarte et al(55) "used TEM to detect average 3 percent crystallinity in a spray-dried ASD based on hydroxypropyl methylcellulose acetate succinate (HPMCAS), which is below the wide-angle X-ray scattering functional lower detection limit". "And used in combination with EDX, TEM can be utilized to determine drug-polymer integration position in ASD at the formulation and method growth phases"(56).

**Atomic force microscopy**

The core use of AFM is sub-nanometer resolution superficial chorography measurement. "A sharp probe tip on the underside of a flexible cantilever, usually made of silicon (Si) or silicon nitride (Si3N4), rasters scans over the sample surface during AFM testing"(57)(58).

Lamm(59) employed AFM to investigate the phase behavior and architecture of copovidone and TPGS 1000 stable dispersions produced by hot-melt extrusion under a variety of manufacturing conditions and compositions. In conclusion, AFM is a reliable approach for

investigating the phase action and molecular composition of ASDs, as well as a novel analytical technique for improving the ASD preparation procedure(60).

**X-ray photoelectron spectroscopy (XPS)**

X-ray photoelectron spectroscopy (XPS) is a superficial investigation tool that uses atomic concentrations to determine the chemical composition of a substance's surface. Interactivity in ASDs can be studied using the change in chemical bonding energy(61).

Dahlberg et al. (62) employed XPS to determine how much drug was available on the surface of ASDs that had been primed by spray drying and rotary evaporation. They noticed to the molecular exterior composition of ASDs affected wettability, which in turn influenced dissolution capacity and solid-state physical stability. In the early stages of ASD growth, XPS provides a rapid screening method for carrier and drug loading collection. In ASDs, Song et al (63) used XPS to look at the drug and the excipient has acid-base connections.

**X-ray diffraction**

It is widely utilized for ASD characterization other than single-crystal diffraction. It contains data on at least three main material characteristics(64). PXRD is originally often utilizing explore changes in the crystalline phase and polymorphic changes of ASDs after processing or stability checks. PXRD is especially useful for assessing the crystalline content of a batch of ASD using powders because it deals with vast quantities of details(65). In general, amorphization produces long, disperse separating signals, while lucent substances produce pointed Bragg reflections. The degree of lucidity of a combination of amorphous and lucid materials is calculated by the ratio of combined lucid strength to overall combined monolithic and crystallographic hardness. The normal identification constraints for lucid content seem to be in the 1–5percent (w/w) range, depending on the reflection techniques.

The secondary application of PXRD in ASD research is the cumulative scattering pair distribution function is used to directly characterize miscibility and amorphous structure (PDF). “The PDF is generated by performing an inverse Fourier transform on the reduced total scattering structure function F(Q), which is the background diffracted amplitude involving both Bragg and diffuse scattering and is then subtracted, corrected, and normalized”(66). Synchrotron radiation's production of high-energy X-rays allowed bringing into play little wavelengths to gain a wider recognition range. Synchrotron X-ray diffraction

and PDF were used by Araujo et al.(64) to look at the chemical and ionic composition of the area interactions between drugs and polymers in a lapatinib ASD hypromellose phthalate (HPMCP) and hypromellose phthalate (HPMCP) (HPMC-E3) (HPMC-E3) (HPMC-E3). "Recent developments in PXRD, such as PXRD with variable temperature and humidity control, will provide useful information in non-ambient settings, allowing for new insights into the crystallization kinetics of amorphous drugs in ASDs"(67). PXRD's ability to identify drug lucidity improves greatly when combined with other techniques, such as second-harmonic generation microscopy(68).

**Thermal analysis methods**

The thermal methods of analysis are a vital as well as a deep-rooted instrument for the identification of ASD. A high-temperature study is described as the measurement of a substance's reaction (e.g., variations in energy, temperature, and mass) to a variation in the material's temperature. Endothermic and exothermic processes (e.g., glass transformation, melting, solid-solid phase change) are typically monitored using thermal analysis techniques (e.g., crystallization, chemical degradation).

**Thermogravimetric analysis (TGA)**

In this step, the concentration of a material in a chosen atmosphere (air or nitrogen) is determined as a feature of temperature. TGA is commonly utilized in ASD identification to evaluate the temperature tolerance of drugs and polymers, as well as to analyze volatile materials. To prevent thermal oxidation in hot-melt extrusion, this knowledge may be used to establish the temperature window(69).

TGA was often utilized to learn the vaporization outline of supply solutions during spray drying. "According to TGA analysis, the drying kinetics of the discrete solvent has a significant influence on the surface chemistry and particle morphology of spray-dried ASDs"(70).

**Differential scanning calorimetry (DSC)**

The two common types of calorimetry are differential scanning calorimetry (DSC) and modulated differential scanning calorimetry (MDSC) for ASD characterization. Thermal transformations such as ebullition, glass transition, polymorphic appearance conversion, plus

recrystallization can be detected using these methods by measuring the energy contribution related to heating materials.

While DSC is a powerful analytical method, when thermal transitions are slow or overlap, it has some limitations. MDSC was created to fix these flaws(71). MDSC has greater sensitivity in calculating heat potential and can distinguish simultaneous thermal events. "MDSC has been used to assess drug crystallization potential, drug-polymer miscibility, glass transfer, crystallinity/crystallization (e.g., crystal growth rate, crystallinity degree), and molecular mobility (e.g., structural relaxation, viscosity)"(71)(72)(73).

**Spectroscopic methods**

Spectroscopic techniques are based on the molecular as well as nuclear changes that occur when a sample is exposed to electromagnetic emission. "Depending on the energy variance between the ground and excited states, spectroscopy processes are divided as fluorescence spectroscopy, infrared spectroscopy, near-infrared spectroscopy, Raman spectroscopy, and nuclear magnetic resonance. Terahertz-pulsed spectroscopy is a new technique for studying low-energy vibrations such as intramolecular torsional vibrations and intermolecular vibrations such as translations and liberations"(74).

**Fluorescence spectroscopy**

The physical characteristics and dissolution deportment of ASDs have been studied using fluorescence spectroscopy. It detects the fluorescence produced when UV–Visible radiation excites a material. Fluorescence spectroscopy can be carried out in a variety of ways, counting (1) emission searches with a fixed wavelength of excitation, (2) simultaneous searches with all monochromators, (3) excitation searches of a set emission wavelength, and (4) complete luminescence searches. Tian et al (75) investigated the relationship between drug-polymer miscibility and ASD physical stability using fluorescence spectroscopy. Drug mounting has a major effect on drug-polymer mixability, according to fluorescence spectroscopy results, with a close connection between weak mixability and decreased physical stabilization. The power and emission extremity of lucid Form I, a hypromellose-based ASD, were found to be substantially different from the povidone-based ASD. "The disparity in fluorescence spectra in these two solid dispersions was explained by variations in diflunisal mobility in the crystalline solid. Fluorescence spectroscopy was also utilized to investigate how ASDs dissolve in water"(76,77).

**Infrared spectroscopy**

Drug–polymer interactions in ASDs can be determined using IR spectroscopy by identifying differences in peak form or location. “Changes in wavelength, bandwidth, and band intensity will reveal molecular-level information regarding the solid-state formulations of drugs and polymers”(78). As a result, FTIR may be utilized to test the physical stability of ASDs and identify molecular interactions. In addition, FTIR can be used to determine drug delivery in polymer matrixes and phase severance.

“FTIR imaging was utilized to analyze moisture-induced phase severance in melt-extruded ASDs”(79). Furthermore, with the introduction of FTIR imaging technology, real-time drug release monitoring from ASDs is now possible. (80).

**Raman spectroscopy**

Raman spectroscopy is used in conjunction with infrared spectroscopy. Changes in the polarizability of a molecule are used in Raman spectroscopy, while changes in the dipole moment are used in Infrared spectroscopy. The relative wavelengths at which a specimen emits emissions are determined using Raman spectroscopy. Since shorter wavelength light is used, confocal Raman microscopy is a popular way to merge Raman with microscopic analysis(81).

“In the study of drug-polymer interactions, miscibility, and phase distribution, Raman spectroscopy has been widely used to describe ASDs”(82). In vivo, real-time ASD dissolution processes have also been studied using chemical imaging and Raman spectroscopy(83).

**Solid-state nuclear magnetic resonance (SSNMR)**

It has proved to be an effective method for collecting molecular-level data. Using dipolar correlation, spin diffusion, and other techniques, researchers can learn about the dynamics and phase compositions of ASDs(84).

SSNMR is a non-deleterious approach for assessing crystallization propensity, molecular stability(85), miscibility, drug-polymer interactions, crystallinity, and crystallization kinetics in ASDs(86).

SSNMR has also been employed to monitor the success of ASD remission. The enthalpy relaxation and H1 NMR relaxation times of amorphous compound crystallization rates and molecular mobility were shown to be highly correlated. The 2D cross-polarization heteronuclear coupling experiment was utilized to detect spin diffusion effects to investigate the relationship between the amorphous drug and the polymer.

**Emerging new techniques**

**Terahertz spectroscopy**

"Terahertz spectroscopy (TPS) is a non-deleterious approach that probes the long-range crystalline lattice motions, low-energy torsion, and hydrogen-bonding vibrations of pharmaceutical materials using spectral details in the far-IR region of the electromagnetic spectrum"(87).TPS has gotten a lot of coverage in the area of pharmaceutics science over the last few years. TPS and imaging technologies provide new ways to detect and characterize ASDs.

An amorphous material doesn't have any special distinct spectral bands. because it corresponds to intermolecular vibrations within the lattice system rather than intramolecular vibrations.TPS may be used to track and qualify any recrystallization in an ASD(88).

The distinct spectral variations that arise with rising temperature give important knowledge about relaxation and crystallization processes when temperature-dependent TPS is used in situ.TPS may also be used to assess the initiation and intensity of molecular mobility, which is needed for amorphous drugs to crystallize(88).

**Dielectric spectroscopy**

Dipoles with sufficient versatility respond to an exterior electric field in dielectric spectroscopy. At temperatures ranging from -170 to 300°C, this reaction allows the recognition of molecular movement with a composure time of 103–109 sec. (89).In materials research, dielectric spectroscopy is commonly utilized to analyze complex structures, and it is gaining traction as an important method for pharmaceutics material characterization(90).

**X-ray micro-computed tomography**

The use of X-rays in X-ray micro-computed tomography (X-ray micro-computed tomography) is a three-dimensional picture reconstruction technique for diagnostic imaging and materials science studies.

X-ray micro-computed tomography provides three-dimensional X-ray images based on electron density variations observed within various phases present within a sample, as opposed to X-ray diffraction methods, which reflect X-rays from an ordered series of atoms. “For ASD characterization, X-ray micro-computed tomography was used to photograph and quantify the shape of spray drying particles, such as wall thickness and internal structures”(91)(92).

## CONCLUSION:

The modern medicinal landscape has moved the bulk of newer medications away from hydrophilicity and lipophilicity. As a result, a substantial amount of drugs in production are hydrophobic, posing major challenges for formulation scientists. Amorphous solid dispersions have provided an appealing option for reducing solubility constraints, endowing high-energy and thermodynamic properties on the amorphous drug, while still driving them toward devitrification and limiting their economic utility by the use of altered "molecular design." For designing effective and safe amorphous drug delivery systems, a deeper understanding of thermodynamics and molecular level processes such as glass transformation, molecular mobility, fragility, devitrification, and molecular interactions of drug and polymer are needed. As polymers are being used as carriers in the molecular engineering of amorphous drugs, solid dispersion materials can be stabilized more effectively. Better regulation of solid-state stabilization, as well as the generation and preservation of supersaturation, will contribute to more attractive and stable distribution systems, as well as a feasible alternative for solubilizing "difficult to solubilizing" medicines.

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