Ultrasound-Assisted Melt Sonocrystallization: Innovations in Particle Engineering and Drug Solubility Enhancement

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Abstract- Aqueous solubility, drug permeability, and dissolution rate are those factors that influence an oral bioavailability of drug. Poor solubility and inadequate permeability are the most prevalent reasons of low oral bioavailability. A poorly water-soluble medicine needs large dosages in order to achieve therapeutic plasma concentrations following oral delivery. In accordance with the Biopharmaceutics Classification System, class II pharmaceuticals go through a preventive process in which the drug is released from the dosage form and solubilizes in stomach fluid but is not absorbed; as a result, for BCS class II drugs, bioavailability rises as solubility increases. Greater the surface area higher is the rate of disintegration which further leads to enhancement in dissolution rate of the drug. As a result, several methods to increase drug bioavailability are being revealed. It has been shown that the majority of the newly identified chemical entities have poor water solubility, which reduces their medicinal effectiveness. Melt sonocrystallization is a more recent particle engineering technology that uses ultra sound energy to produce small particles of drug that aid to increase their bioavailability and water solubility.

Index-Terms: Sonocrystallization, Melt Sonocrystallization, BCS, Ultra sound.

I. INTRODUCTION

The term "solubility" describes the ability of a substance to dissolve in a solvent and form a solution at a certain temperature and specific gravity. Solubility plays a crucial role in the dissolution process in order to carry out a movement and achieve the desired pharmacological response and drug solubility for better bioavailability [1]. Due to the ease of administration, high patient compliance, cost efficiency, absence of sterility restrictions, and flexibility in dosage form formulation, oral ingestion is the most practical and extensively utilised form of drugs delivery. Because of this, it's more probable that numerous generic drug companies will create bioequivalent drug formulations [2]. The most important design flaw is the low bioavailability of oral dose forms. Aqueous solubility, drug permeability, dissolution rate, first-

pass metabolism, pre-systemic metabolism, and the susceptibility to efflux mechanisms are some of the variables that affect oral bioavailability. Low solubility and inadequate permeability are the two main reasons of low oral bioavailability. Other dosage forms, such as parenteral formulations also heavily rely on solubility [3]. Solubility is one of the key elements in achieving the required drug concentration in the systemic circulation for the intended pharmacological effect. After oral administration, poorly water-soluble medications may need high doses to obtain therapeutic plasma concentrations. Formulating novel chemical entities as well as generics is fundamentally challenging due to low water solubility. Any medication that is to be absorbed at the absorption site must be there in the form of an aqueous solution. Liquid pharmaceutical compositions are best suited to a solvent like water. The majority of medications are either mildly basic or moderately acidic, and thus are poorly soluble in water [4]. The pharmaceutical sector produces more than 40% of new chemical entities (NCEs) that are inherently insoluble in water. These poorly water-soluble medicines sluggish drug absorption which causes inconsistent and inadequate bioavailability as well as damage to the gastrointestinal mucosa. Although the solubility permits the medication to reach the necessary concentration in the systemic circulation for pharmacological response, solubility is the most significant rate limiting factor for pharmaceuticals given orally. Formulation scientists have a significant hurdle with the solubility issue. In especially for oral drug delivery systems, enhancing drug solubility and, as a result, oral bioavailability, is one of the most challenging parts of drug development. There are several techniques for improving the solubility of weakly water-soluble substances that have been published in various literatures [5]. The techniques are chosen based on a number of factors, such as the characteristics of the medicine being considered, the kind of excipients to be used, and the preferred dose form. Poorly water-soluble medications often have weak solubility and a slow rate of dissolution in aqueous gastrointestinal fluids, which leads to insufficient bioavailability [6]. Bioavailability may be enhanced through increases in the medication's solubility and rate of dissolution in gastrointestinal fluids, particularly for class II (low solubility and high permeability) medications. Therefore, increasing solubility increases bioavailability of BCS class II pharmaceuticals because solubility in stomach fluid and drug release from the dosage form are the rate-limiting mechanisms for BCS class II medications rather than absorption. The majority of medications in development come from the high-capacity Screening approach, which results in larger molecular weights and subsequent bioavailability issues [7]. Insufficient solubility or permeability may be the cause of the bioavailability problem. The majority of chemicals struggle with solubility. Consequently, when chemical science develops, there is a greater requirement for pharmaceutical technology development. Comparing pharmaceutical techniques to improving bioavailability is time- and money-consuming, and undoubtedly more cost-effective. Therefore, a number of solubility-enhancing techniques are being explored [8]. A group of methods known as solubility enhancement strategies can facilitate the formulation process. In physical and chemical research, such as pharmacokinetics treatment, the concept of solubility is unique and is more helpful in the medical and biopharmaceutical fields. Solubility enhancement methods for assessing drug solubilization include Micronization, solid dispersion, pH modification, Micelle solubilization, cosolvency Complexation, and hydrotropic [9]. Additionally, for the aim of establishing the drug's solubility parameter, the solubility enhancement approach distinguishes between physical and chemical alterations of

the drug component. This technique is employed to increase the solubility and dissolution of medications for parenteral and oral delivery [10]. Traditional approaches include particle size distribution, PH, co-solvency, micelle solubilization, micro-emulsion complexation, supercritical fluid process, solid dispersion, and hydrotrophy. For improving the solubility of pharmaceuticals that are poorly water-soluble, a variety of procedures are now available, including Micronization, nano-suspension, homogenization, salt creation, spray drying, hot-melt extrusion, solvent evaporation, and conventional solid dispersion [11].

Biopharmaceutical Classification System: It is classified into four classes according to the solubility and permeability depending on the nature of the drug.

Table No. 1: Biopharmaceutical Classification System

Class	Permeability	Solubility	Examples
I	High	High	Propranolol, Diazepam, Acyclovir, Levodopa, Metoprolol.
II	High	Low	Nifedipine, Naproxen, Amlodipine, Itraconazole
III	Low	High	Cimetidine, Naphazoline, Metformin
IV	Low	Low	Taxol, Chlorothiazide, Colistin

The development of pharmaceutical goods would greatly benefit from a better understanding of the physicochemical and biological characteristics of medicines. From a biopharmaceutical perspective, the Biopharmaceutics Classification System (BCS) is a valuable tool for formulation development decision-making. The BCS categorizes drug substances into four categories based on their solubility and intestinal permeability, and these four categories are defined as follows: Class I (high solubility/high permeability), Class II (low solubility/high permeability), Class III (high solubility/low permeability), and Class IV (low solubility/low permeability). When a pharmacological substance is shown to absorb 90% or more of a dosage provided to human, it is said to be "highly permeable". In vitro permeability experiments utilising Caco-2 or MDCK cells or synthetic membranes are widely used at an early stage of research to predict drug ingredient permeation from the gastrointestinal lumen into the circulation. The greatest dosage strength of a pharmaceutical ingredient is considered as "highly soluble" if it is dissolved in 250 mL or less of aqueous medium with a pH range of 1-7.5 at 37 °C. Another method of classifying a medication's solubility in the early stages of drug development is to utilise the greatest predicted human dosage [12].

BCS class I drugs

Drugs classified as BCS class I must also be extremely soluble and permeable. For instance, this class includes theophylline, propranolol, and metoprolol. There wouldn't be a rate-limiting step for oral absorption for BCS class I medicines. Traditional tablet or capsule formulations, for instance, are frequently made in IR solid oral dose forms to ensure quick breakdown in the gastrointestinal system [13].

BCS class II drugs

Low solubility and high permeability are the known molecular properties of BCS class II medicines. For instance, this class includes itraconazole, griseofulvin, and cyclosporine. A

BCS class II drug's bioavailability is often rate-limited by how quickly it dissolves, therefore even a minor increase in dissolving rate can occasionally result in a significant increase in bioavailability. As a result, increasing the dissolution rate of the drug has been considered to be a crucial component in raising the bioavailability of BCS class II medications. The rate at which pharmaceuticals dissolve is governed by a number of physicochemical parameters [14]. The effective surface area, diffusion coefficient, diffusion layer thickness, saturation solubility, amount of dissolved drug, and volume of dissolution medium are the variables that influence the rate of drug dissolution, according to a modification of the Noyes-Whitney equation. The dissolving rate of pharmaceuticals is positively impacted by increases in the saturation solubility and the effective surface area, and these characteristics may be enhanced through preformulation research and formulation design. For enhancing the dissolving behaviour of BCS class II pharmaceuticals, crystal modification, particle size reduction, self-emulsification, pH manipulation, and amorphization are thought to be useful [15].

BCS class III drugs

BCS class III drugs are those with high solubility and poor permeability. For instance, this class includes medications like metformin, cimetidine, and atenolol. The membrane permeability in the gastrointestinal system rate-limits the bioavailability of BCS class III medicines. Theoretically, there are three transepithelial routes for medications to get from the intestinal lumen to the bloodstream: paracellular transport, transcellular carrier-mediated active or facilitated transport, and transcellular passive transport [16]. Transcellular passive transport is used to absorb most medicines taken orally. Drugs having a relatively high intrinsic lipophilicity would have high membrane permeability in this situation, where the intrinsic lipophilicity of the medication is a determinant of drug transport through the enterocytes. It is required to go back to the lead optimisation phase in order to improve the permeability via the transcellular route since a drug's inherent lipophilicity is governed by its chemical structure. Drugs that are hydrophilic typically enter the intestinal barrier through paracellular pathways. Drug permeability is increased via the paracellular route by permeability enhancers such fatty acids, bile salts, surfactants, and polysaccharides; however, some of these substances are known to damage membranes. Although the absorption may be constrained by membrane penetration, IR solid dosage forms should be practically created for clinical usage because there is much less knowledge about the effective and safe dose alternatives for BCS class III medications [17].

BCS class IV drugs

BCS class IV medicines have difficult molecular characteristics including limited permeability and solubility. It would be deemed that physiological parameters, such as stomach emptying time and gastrointestinal transit time, greatly impact the absorption of BCS class IV drugs since solubility and permeability are both rate-limiting processes for absorption. As a result, there may be significant inter- and intra-subject variability in the absorption of medicines of BCS class IV. The formulation design of BCS class IV medications may become difficult as a result of this variation in absorption. For BCS class II medicines, there are feasible formulation alternatives that emphasise improving the dissolving behaviour. However, the methods for increasing their permeability are still in the early stages of development, and it is unclear how safe they are. In this situation, formulation techniques comparable to those for BCS class II

medications might be effectively used to BCS class IV pharmaceuticals, despite the possibility that poor gastrointestinal tract permeability would impede absorption [18].

II. KEY CONSIDERATIONS AFFECTING DRUG SOLUBILITY

1) Nature of Solvent and Solute

Solubility is determined by the chemical reactions that occur among the solvent molecules and the solute particles. The "like dissolves like" principle governs this relationship, where compounds with similar intermolecular forces and polarity tend to dissolve well in each other. Polar solvents, such as water, have a strong affinity for polar solutes like salts and sugars because of their ability to form hydrogen bonds and dipole-dipole interactions. On the other hand, non-polar solvents, such as hydrocarbons, are more effective at dissolving non-polar solutes like oils and fats, as they lack significant polar interactions.

2) Temperature

Solubility is significantly influenced by temperature. In general, as the temperature rises, so does the solubility of solid solutes in a solvent. This is because the solute particles may disperse more easily in the solvent at higher temperatures since they have greater kinetic energy. For many solid solutes, the dissolution process is endothermic, requiring energy input to overcome the forces holding the solute together. As temperature rises, more solute particles acquire the energy needed to break these intermolecular forces, leading to increased solubility. However, for some compounds, such as gases in liquids, the solubility may decrease with increasing temperature due to changes in thermodynamic factors [19].

3) Pressure (for Gases)

Pressure, especially at high pressures, has an impact on the solubility of gases in liquids. Henry's law states that a gas's solubility in a liquid is directly proportionate to its partial pressure in the gas phase. More gas molecules are pushed into the liquid when the partial pressure of a gas above it rises, increasing the gas solubility. This principle is essential in various applications, such as carbonation in beverages and gas exchange in biological systems.

4) Particle Size

The surface area of a solute significantly affects its solubility. Finely divided particles have a larger surface area compared to larger particles, providing more contact points with the solvent. As a result, finer particles offer more opportunities for solvent molecules to interact with the solute, leading to faster dissolution rates and increased solubility. Conversely, larger particles have fewer contact points with the solvent, leading to slower dissolution and lower solubility.

5) pH and Ionization (for Ionic Compounds)

The pH of the solution may have an impact on the solubility of ionic substances. Ionic substances break down into their individual ions in watery solutions. The solubility of salts is affected by the degree of ionization and the solubility product constant. When the pH of the solution is adjusted, the ionization of the solute may change, leading to altered solubility. For example, changes in the equilibrium of the dissolving process might cause salts that are partially soluble to become more soluble in acidic or basic conditions [20].

6) Pressure (for Solids)

The impact of pressure on the soluble state of solids is complicated and less commonly observed than the effect on gases. Some solid compounds, particularly those with polymorphic forms or crystal structures sensitive to pressure changes, may exhibit variations in solubility with pressure. High-pressure conditions can lead to changes in the packing arrangement of solid particles, affecting their solubility in certain solvents.

7) Chemical Interactions

Solubility can be significantly influenced by specific chemical interactions between the solute and solvent molecules. Hydrogen bonds, interactions between dipoles, ion-dipole interactions, and other intermolecular forces are examples of these interactions. The molecule becomes more soluble when solute-solvent interactions are favourable. On the other hand, if the interactions between the solute and solvent are weak or repulsive, the solubility may be reduced.

8) Common Ion Effect

Le Chatelier's principle, which asserts that when an equilibrium condition is disrupted, a system will adjust to counterbalance the disturbance, governs this phenomenon. The common ion alters the equilibrium of the dissolution reaction when a solute with a common ion is introduced to a saturated solution of another solute, resulting in a decrease in solubility. This effect is commonly observed in precipitation reactions and is essential for controlling solubility in various chemical processes [21].

9) Complexation

Solubility can be influenced by the formation of complexes between the solute and solvent molecules. Complexation involves the reversible association of solute and solvent species to form stable complexes. These complexes can either maximize or minimizes the solubility, based on the nature of the complex formed. For instance, in metal ion complexation, certain ligands can enhance the solubility of metal ions, making them more available for reactions.

10) Temperature-Dependent Solubility

Some compounds exhibit solubility behaviour that is inversely related to temperature, leading to a reverse solubility trend. This phenomenon is often observed in certain salts and compounds with unique crystal structures. As temperature increases, the dissolution process may become less favourable, leading to reduced solubility.

Understanding these factors and their impact on solubility is crucial in various scientific fields and practical applications. In pharmaceutical development, knowledge of solubility is fundamental for designing drug formulations with optimal drug delivery and bioavailability, ensuring effective therapeutic outcomes for poorly water-soluble drugs. Additionally, in chemistry, environmental sciences, and material sciences, the understanding of solubility is vital for studying chemical reactions, designing industrial processes, and predicting the behaviour of materials in different environments [22].

III. STRATEGIES FOR ENHANCING DRUG SOLUBILITY

Drug discovery process begins with formulation methods when chemical solubility is lower in aqueous media, and it is necessary for the choice of the lead material and the formulation of commercial pharmaceutical products. Poorly water-soluble medications can be made to dissolve and dissolve more quickly in a number of methods, including the ones described below: [23].

Physical Modification Technique				
1. Reduction in particle size	2. Drug dispersion in carrier	3. Modification of crystal habit	4. Complexation	5. Solubilization by surfactant
a. Micronization b. Nanosuspension c. Sonocrystallization d. Supercritical fluid technology e. Spray Drying	a. Solid solution b. Eutectic Mixture c. Solid dispersion	a. Polymorph	a. Use of complexing agent • Inorganic • Coordination • Chelates • Metal Olefin • Inclusion • Molecular complexes	a. Microemulsion b. Self-emulsifying drug delivery system
Chemical Modification Technique				
a. Co-solvency	b. Co-crystallization	c. Salt formation	d. Solubilising agent	e. Hydrotrophy
Other Technique				
a. Hot melt extrusion	b. Supercritical fluid method	c. Solvent evaporation	d. Lyophilisation technique	e. Polymorphic alteration

Table No. 2: Strategies for Enhancing Drug Solubility

IV. ULTRASOUND ASSISTED SONOCRYSTALLIZATION

Sonocrystallization is an innovative particle engineering technique that encourages the solubility and dissolution of hydrophobic medications while simultaneously examining how it affects the drug's crystal characteristics. In response to improvements in ultrasonic technology, sonocrystallization saw a rise in industrial application through the 1980s. Today, the pharmaceutical and fine chemical industries frequently utilise sonocrystallization to produce crystals. Sonocrystallization is a method based on the application of ultrasound (US) to achieve the appropriate morphology and reduced particle size and particle size distribution (PSD) [24]. An oscillating sound pressure wave with a frequency range of 15 kHz to 10 MHz is known as an ultrasound (US). When ultrasonic vibrations travel through a liquid with enough amplitude, the negative pressure is greater than the liquid's local tensile strength, which causes bubbles formation. In the area of pre-existing impurities bubbles are produced, and these

bubbles oscillate and expand throughout cycles of compression and expansion. In a single compression expansion cycle, when the growing bubbles have reached their resonant size, they effectively absorb energy from ultrasonic waves. The resonant size is roughly 170 m for an ultrasound that is being emitted at a frequency of 20 kHz. Due to effective energy absorption at the resonant size, bubbles expand quickly after a single cycle of ultrasonic waves. Although the bubbles cannot continue to grow without energy absorption, they implosively deflate once they reach the resonant size. Acoustic cavitation is the term used to describe this phenomenon [25].

In heterogeneous systems as compared to homogeneous systems, ultrasound has a wider range of physical effects. When a bubble collapses close to a bigger surface or particle, it no longer collapses spherically, and as a result, a high-velocity liquid stream with a velocity more than 100 m/s is produced. The solid substance is deformed or undergoes chemical change as the liquid advances towards its surface. Furthermore, acoustic cavitation shockwaves result in high-velocity collisions between solid particles with a diameter of less than a micron (interparticle collisions). Additionally, shockwaves can cause breaking by directly interacting with particles. Sonofragmentation is another name for this phenomenon [26].

The thickness of the diffusion layers near to the crystal surfaces is reduced as a result of the stirring effect, which is brought on by high-energy shockwaves impinging on the particle surface. The sonocrystallization-produced small particle has the most frequently accepted explanation. The size and form of the particles may be considerably altered by high-velocity particle-particle collisions. According to some studies, even metal particles have a propensity to melt together as a result of these interparticle collisions due to their extreme intensity. The actual processes of ultra sound-assisted crystallisation are yet unclear; hence the following ideas tend to be the most frequently accepted.

1. The effect of Ultra Sound is indirectly caused by vibrations of the Ultra Sound waves but directly caused by formation of the cavitation bubbles by the Ultra Sound field.
2. Quantity and the size of the cavitation bubbles both affects the nucleation rate.
3. Production of more cavitation bubbles and increased nucleation is a result of higher ultra sound intensities.
4. Larger Ultra Sound frequencies, smaller are the cavitation bubbles. Which leads smaller effect on the nucleation rate.
5. Size of the cavitation bubbles link to the nucleation rate by the segregation and cavitation bubble theories [27].

V. VARIABLES AFFECTING SONOCRYSTALLIZATION

1. Frequency of Ultrasound

The bubble behaviour is affected by changes in ultrasonic frequency. The lifespan of the cavity is decreased at low ultrasonic frequencies (200 kHz) and the ultrasound wavelength shortens. In all situations, there are often thick clouds of cavitation bubbles, and the strength of each bubble's collapse depends on its size: large bubbles collapse more powerfully at low frequencies, whereas small bubbles collapse less powerfully at high frequencies. Researchers formulated the liposomes with various ultrasonic irradiation frequencies and studied how the irradiation frequency create impact on the size of the liposomes. Three

different frequencies (43, 143, and 480 kHz) were employed at a constant intensity of 8 W/cm2. It was found that variations in bubble size caused the liposome size to reduces as the sonication frequency dropped [28].

2. Intensity of Ultrasound

When the ultrasonic intensity is increased, the size of the crystals formed decreases, and vice versa. The increased microscale mixing and turbulence caused by higher sonication intensity causes solutes to diffuse more quickly. Because of the quicker solute diffusion, the induction time and metastable zone width (MZW) are reduced, and the nucleation rate is raised. The strong microscale mixing and turbulence prevents crystals from forming agglomerates. The effect of ultrasonic intensity on roxithromycin during sonocrystallization was investigated. During a 10-minute sonication, the intensity was changed from 5 to 15 W/cm2, and the crystal length was reduced from 60 to 15 m [29].

3. Sonication Time

As the sonication period increases, the crystal sizes decrease and also become more uniform. Short sonication times result in crystals with asymmetrical sizes and shapes, which hinder solution and precipitants from mixing uniformly. Longer sonication periods improve mixing and prevent crystal aggregation formation [30].

4. Ultrasound generator varieties

Different experimental settings for sonocrystallization are available with various types of ultrasonic generators. Typically, ultrasonic baths, horns/probes, and plate transducers are used as ultrasound generators. Typically used to disperse particles in liquid, sonicating baths are a staple piece of scientific equipment [31]. Sonocrystallization is another process that is carried out using ultrasonic horns, also known as probe sonicators, which provide batch or flow through configurations. Ultrasound frequencies are produced across a broad frequency spectrum by the plate transducer. When high frequencies are required (>100 kHz), it is crucial for sonocrystallization. batch arrangement often utilised for crystallisation with an ultrasonic plate transducer [32].

VI. MELT SONOCRYSTALLIZATION

Melt sonocrystallization is an innovative process used for particle engineering, involving the application of ultrasound energy to a molten mass dispersed in an immiscible liquid. This technique facilitates the solidification or crystallization of the emulsified melt. Initially used for producing sintered crystals and porous glassy beads, it allows precise control over the resulting particle properties by adjusting ultrasound energy input, frequency, and melt solidification rate. The solidification rate is influenced by both the material's glass transition temperature and the surrounding medium. By employing ultrasound at temperatures above the transition temperature, crystallization is promoted, while processing at temperatures below the transition temperature results in an amorphous form. The crystals or porous beads are formed due to mechanical stress induced by ultrasonication. Melt sonocrystallization is versatile, aiding in enhancing the solubility of poorly soluble drugs by producing both crystalline and amorphous particles. Notably, this technique does not require solvents or carriers, making it possible to create small fragments with improved water solubility [33].

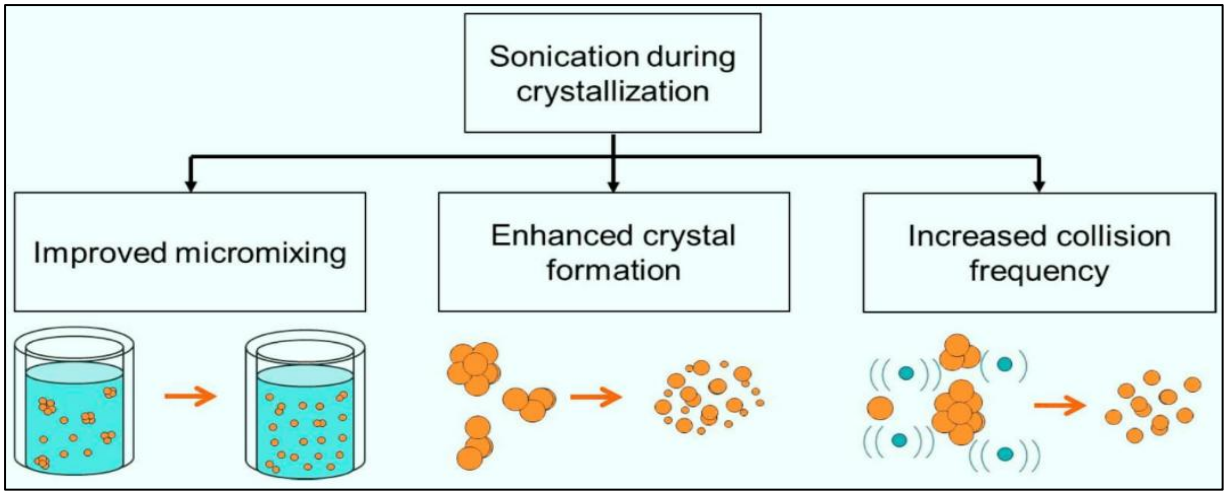

Figure No. 2: Process During Crystallization

To execute the melt sonocrystallization process, the desired amount of drug is melted in a glass container using a paraffin oil bath at a controlled temperature. The molten drug is then placed into a container filled with deionized water at a specific temperature range. Ultrasonication is applied for a designated period using various amplitudes of probe ultrasonicator. The final product is obtained when the dispersed droplets solidify, which can be separated through filtering and subsequently dried at room temperature.

VII. APPLICATIONS OF MELT SONOCRYSTALLIZATION

Melt sonocrystallization is a versatile and innovative particle engineering process with a wide range of applications in various industries. This technique harnesses the power of ultrasound energy to control crystal formation and solidification of a molten mass, resulting in improved product properties and performance. The following are some of the key applications of melt sonocrystallization:

A. Pharmaceutical Industry

The pharmaceutical industry often faces challenges with poorly water-soluble drugs, leading to limited bioavailability and therapeutic efficacy. Melt sonocrystallization addresses this issue by producing both crystalline and amorphous particles. The process optimizes the crystal size and morphology, resulting in increased drug surface area, which significantly improves dissolution rates and, consequently, enhances drug solubility and bioavailability. This advancement opens new possibilities for formulating drugs that were previously challenging to administer effectively.

B. Food and Nutraceutical Industries

In the food and nutraceutical industries, sensitive bioactive compounds, such as vitamins, antioxidants, and essential oils, are prone to degradation when exposed to air, heat, or light. Melt sonocrystallization provides an efficient way to encapsulate these delicate compounds into solid matrices, such as lipids or polymers. The resulting encapsulated particles protect the bioactives from environmental factors, ensuring their stability and enhancing their bioavailability upon consumption. The functional properties of food ingredients are crucial for product quality and consumer acceptance [34]. Melt sonocrystallization can tailor the crystal

structure and morphology of food components, leading to improvements in texture, mouthfeel, and solubility. For example, in the confectionery industry, sonocrystallization can enhance the crystalline structure of sugar, resulting in smoother and creamier chocolates.

C. Materials Science

Melt sonocrystallization plays a crucial role in the development of advanced materials with tailored properties for diverse applications. By precisely controlling the crystal growth and nucleation, researchers can engineer materials with specific properties, such as enhanced electrical conductivity, improved mechanical strength, and unique optical characteristics. These advanced materials find applications in electronics, optics, and catalysis, contributing to technological advancements.

D. Chemical Industry

In the chemical industry, controlling the polymorphic form of a compound is critical for ensuring consistent product quality and performance. Melt sonocrystallization offers a precise method to produce specific polymorphic forms of chemicals, allowing manufacturers to select the most suitable crystal structure for their intended applications. This technique offers a more efficient and cost-effective alternative to traditional separation methods, contributing to the development of high-purity chemical products.

E. Cosmetics and Personal Care Products

Melt sonocrystallization finds applications in cosmetics and personal care products, where controlled release of active ingredients is desired. By manipulating the crystallization process, manufacturers can design products that release active compounds gradually over time, providing prolonged benefits to the skin or hair. This controlled release ensures the active ingredients are delivered effectively and maintained at the target site for extended periods, enhancing the efficacy of the cosmetic formulations.

F. Energy Storage and Conversion

Energy storage technologies, such as lithium-ion batteries, rely on crystalline materials for efficient energy storage and conversion. Melt sonocrystallization has been explored to produce crystalline battery electrodes with enhanced performance. By carefully controlling the crystal growth and morphology, researchers aim to improve the capacity, cycling stability, and overall efficiency of energy storage devices. These advancements have the potential to revolutionize the energy storage sector and accelerate the adoption of renewable energy sources [34].

VIII. CONCLUSION

A popular technique for formulating organic crystals with the required size and size distribution is sonocrystallization. The pharmaceutical sector is particularly interested in the micro- and nanometer-sized crystals produced through modifying the crystallisation because of the increased bioavailability based on the smaller particle sizes. Melt sonocryatallization is a more recent particle engineering approach that involves applying ultrasonic energy to soft or viscous molten material to produce small particles that aid to increase their bioavailability and solubility in water.

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