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MORPHOLOGY AND SIZE COMPARISON OF CRYSTALLIZED MATERIALS USING IMAGE-BASED COUNTING TECHNIQUES: CONVENTIONAL VS. SUPERCRITICAL PROCESSES

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Abstract

Morphological characterization of aggregates or agglomerates using image analysis is a growing topic of research in a variety of industries, including chemical, environmental, food, and pharmaceuticals. The ultimate features of agglomerates are frequently related to their size and shape distribution, and aggregate morphology can have a considerable impact on the efficiency of industrial operations as well as their health and environmental impacts. Given the significant importance of the crystallized product's shape and size, it is critical to apply technologies that allow for measurement, characterization, and quantification, image analysis in particular. This article attempts to use image analysis to determine the size and kind of aggregates analyzed, which is one of the most active study fields. It is demonstrated that, whereas conventional procedures are best suited for quantitative production jobs, supercritical processes are feasible strategies for producing such materials with recrystallized structure based on morphological range and a specified size distribution. The topic covers image analysis methodologies, aggregate characterization, and the various imaging instruments employed. Furthermore, this study demonstrates experience in managing the supercritical recrystallisation process.

Keywords: supercritical fluid; crystallization; image; particle morphology; particle size distribution.

ПОРІВНЯННЯ МОРФОЛОГІЇ ТА РОЗМІРІВ КРИСТАЛІЗОВАНИХ МАТЕРІАЛІВ З ВИКОРИСТАННЯМ МЕТОДІВ ПІДРАХУНКУ НА ОСНОВІ ЗОБРАЖЕНЬ: ТРАДИЦІЙНИЙ *vs.* НАДКРИТИЧНИЙ ПРОЦЕСИ

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Анотація

Морфологічна характеристика агрегатів або агломератів за допомогою аналізу зображень є зростаючою темою досліджень у різних галузях промисловості, включаючи хімічну, екологічну, харчову та фармацевтичну. Кінцеві характеристики агломератів часто пов'язані з їхнім розміром і розподілом за формою, а морфологія агрегатів може мати значний вплив на ефективність промислових операцій, а також на здоров'я і навколишнє середовище. Враховуючи значну важливість форми і розміру кристалізованого продукту, дуже важливо застосовувати технології, які дозволяють вимірювати, характеризувати і кількісно оцінювати їх, зокрема, аналіз зображень. У цій статті зроблено спробу використати аналіз зображень для визначення розміру та типу аналізованих агрегатів, що є одним з найактивніших напрямів досліджень. Показано, що в той час як звичайні процедури найкраще підходять для кількісних виробничих завдань, надкритичні процеси є можливими стратегіями для отримання таких матеріалів з рекристалізованою структурою на основі морфологічного діапазону і заданого розподілу за розмірами. Тема охоплює методології аналізу зображень, агрегатні характеристики та різні інструменти для отримання зображень. Крім того, це дослідження демонструє досвід керування процесом надкритичної рекристалізації.

Ключові слова: надкритична рідина; кристалізація; зображення; морфологія частинок; розподіл частинок за розмірами.

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Introduction

Particle uniformity is crucial across industries for consistent product quality, efficient processes, and regulatory compliance. Achieving uniform size and shape in micrometric particles is critical for improving the efficacy, efficiency, and quality of goods and processes across a wide range of sectors. In fact, constant particle size in pharmaceuticals ensures homogenous dissolution, which increases drug bioavailability and efficacy [1]. In both the cosmetics and food industries, consistency in particle size distribution plays a crucial role in enhancing product quality. In cosmetics, it improves the texture, making products smoother and more uniform, while also aiding in better absorption and efficacy of active ingredients. Uniform particle distribution enhances mechanical properties in minerals, composite materials, and ceramics, while increasing optical and protective properties in coatings. Additionally, uniform particles in catalysis enhance the specific surface area for chemical reactions, which improves efficiency [2]. Thus, particle homogeneity improves experiment reproducibility and simplifies theoretical modeling. As a result, standard procedures such as grinding, spray drying, and solvent evaporation may not be appropriate for creating clean, fine particles that enable precision dosing. Consequently, ensuring uniform micrometric particles is critical for improving performance and quality across a wide range of industrial and scientific applications.

Conventional crystallization approaches frequently fail to provide exact control over particle size and shape, resulting in large size distributions and irregular morphologies. Maintaining uniform particle characteristics between batches may be difficult, particularly in procedures like milling and precipitation when external variables might fluctuate. While conventional particle-forming techniques are varied and well-established, with multiple ways for creating particles of varying sizes and shapes, they confront hurdles in terms of particle morphology control, environmental effect, and repeatability [3].

On the other hand, high-pressure fluid crystallization looks to be an appealing technological option. Several researchers have demonstrated the use of supercritical or near-critical fluids as solvents or anti-solvents in particle production over the last four decades, as well as their importance as a modifier of particle properties such as size, size distribution, crystalline appearance, and morphology [4–5].

The achievement of micronization techniques is largely dependent on various critical variables. Temperature and pressure have an essential effect in the solubility of the materials being micronized. The recovery system's design and efficiency, as well as the precipitator's size, are all equally important. These characteristics interact to define the efficiency, size distribution, and shape of micronized particles. Thus, knowing and fine-tuning these parameters is crucial for achieving the appropriate micronization outcomes.

This study looks into the particle size distributions produced by conventional and supercritical manufacturing techniques. Its primary objective is to assess the efficacy and results of different methods for producing materials with certain features, using digital deposition photomicrographs. Advanced image digitization techniques are used to ensure a comprehensive investigation. High-resolution photographs of the deposits are collected and methodically processed using appropriate software to precisely determine particle size, shape, and distribution. This strategy produces precise information that can help improve manufacturing operations. Understanding how operational factors like as temperature, pressure, and solvent selection impact the finished product is critical. The project aims to provide a solid platform for generating high-quality materials with particular features. This knowledge not only improves our understanding of fundamental systems, but it also promotes innovation in a variety of industrial industries, from medicines to materials research.

Advancements in Particle Formation Techniques

Conventional processes

Conventional particle-forming procedures, while diverse, usually depend on mechanical, chemical, and thermal mechanisms to produce particles of the required size and shape. Precipitation is the creation of solid particles from a solution as a result of a chemical reaction, temperature change, or solvent evaporation, resulting in a variety of particle sizes and forms [6]. Mechanical milling, which encompasses procedures such as ball milling, jet milling, and hammer milling, uses mechanical force to reduce particle size, resulting in tiny powders with a broad size distribution and irregular form [7]. Spray drying involves atomizing a liquid solution or suspension in a hot drying media, resulting in

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fast solvent evaporation and the creation of dry particles [3]. Emulsification is the process of generating an emulsion of two immiscible liquids and then evaporating the solvent to leave solid particles, which is extensively employed in pharmaceuticals for drug encapsulation [8]. Spray-in-liquid freezing (SFL) involves spraying a solution into a cryogenic liquid, which causes fast freezing and the production of solid particles [3]. The residue produced by these operations is a common feature and, in most situations, causes environmental difficulties.

Supercritical fluid processes

Supercritical crystallization techniques, such as RESS (Rapid Expansion of Supercritical Solutions) and SAS (Supercritical Anti-Solvent), can produce a variety of particle types, including nanoparticles, microparticles, and composite particles [9]. This adaptability is useful in the creation of specialty materials for specific purposes such as drugs delivery systems, catalysts, and coatings. These techniques increase particle quality by removing contaminants via selective solubility. Furthermore, supercritical fluid technologies are scalable and carefully regulated, assuring constant particle size and shape across batches, which is vital for industrial applications that need great consistency [10]. Supercritical fluids, especially supercritical carbon dioxide ($ScCO_2$), are commonly utilized in particle-forming processes because to their adaptable qualities. The capacity to change temperature and pressure enables fine control of solute solubility and precipitation behavior, which is critical for modifying particle size and shape. In fact, the supercritical state permits precise control over nucleation and growth processes, resulting in particles of homogeneous size and shape [11; 12]. This is especially useful for applications that need constant particle qualities, such as medicines and materials research. In fact, by altering temperature and pressure, the solvent power of supercritical fluids may be carefully controlled [13; 14]. This enables selective dissolution and precipitation of chemicals, resulting in the creation of particles with specified properties.

Furthermore, supercritical procedures are adaptable, generating a wide range of particle types with excellent purity and consistency [4]. They are also scalable and energy-efficient, requiring lower temperatures than traditional processes and allowing for fluid recycling, making them excellent for industrial applications needing precise and consistent results [5].

RESS process techniques and availability

The RESS process uses the unique features of supercritical fluids to create small particles of regulated size and form. By quickly expanding a supercritical solution, the technique assures consistent particle production, excellent purity, and repeatability. The RESS method involves dissolving a solute in a supercritical fluid, commonly $ScCO_2$, which has customizable solvent characteristics. The solution is then rapidly depressurized through a nozzle into a low-pressure area. This fast expansion produces a significant drop in solubility, resulting in the nucleation and production of tiny particles when the solute precipitates from the supercritical phase [14]. The rapid depressurization in the RESS process allows for practically immediate nucleation, resulting in particles with a narrow size distribution. This homogeneity is critical for businesses requiring constant particle sizes, such as medicines and advanced materials.

The effective elimination of residual solvents is very useful in RESS. This approach produces particles with increased performance characteristics such as solubility, bioavailability, and reactivity. Their compact, consistent size allows for more effective interactions with other compounds. These features make RESS an appealing solution for industries that require precise particle properties, such as medicines, nanotechnology, and innovative materials.

SAS process technique and availability

The SAS Process is extensively used to produce fine particles with precise morphology, leveraging the properties of supercritical fluids, especially supercritical carbon dioxide ($ScCO_2$). In this method, a solute initially dissolves in a suitable organic solvent to form a solution. This solution is then introduced into a chamber containing $ScCO_2$, where the supercritical CO_2 acts as an anti-solvent [15]. Rapid mixing with the organic solvent reduces its solubility, causing the solute to precipitate out of solution and form fine particles. The high diffusivity of $ScCO_2$ ensures rapid and uniform precipitation [11]. By exploiting these unique properties, the SAS process yields high-purity particles with controlled size and shape. This scalable, reproducible, and environmentally friendly technology is suitable for industries that require high-quality particle manufacturing. However, applying this technique to medicinal molecules imposes several limits, notably in solvent selection [16]. The solvent must meet three criteria: excellent miscibility with the anti-solvent (CO_2), solubility of the material to be crystallized, and safety for human use. Common

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solvents that satisfy these requirements include ethanol, toluene, acetone, and ethyl acetate, which are totally miscible with $ScCO_2$ and classed as non-toxic (class 3) according to pharmaceutical recommendations. Regardless of the solvent employed, the residual solvent in the crystalline powder cannot exceed 5000 ppm.

Scalability and Reproducibility of recrystallization processes:

Scalability and repeatability are critical to the efficiency of the crystallization process, particularly in industrial applications that need constant quality and efficient output. However, factors impacting the scalability and reproducibility of both conventional and supercritical recrystallization processes need to be optimized.

Thus, conventional processes, also known as traditional crystallization, are frequently used in batch and continuous processing. Although the batch technique is simple, scaling up can be difficult. Several writers have highlighted that larger batches might cause variations in temperature and solvent distribution, compromising crystal growth and purity. Continuous processing can boost scalability by giving you more control over process parameters and making it easier to scale up by increasing throughput.

On the other side, supercritical fluid particle generation can increase scalability. The unique solvent characteristics, which can be fine-tuned by altering temperature and pressure, provide more control over crystal size and shape. The process may be scaled by increasing flow rates and reactor size, which affects particle size and shape.

Reproducibility, the ability to consistently produce crystals with the same characteristics in repeated runs, is another crucial factor. In conventional techniques, control over parameters depends heavily on precise control of temperature, concentration, and solvent purity. Minor variations can lead to significant differences in crystal quality. Additionally, these methods often rely on manual interventions, introducing variability. Conversely, supercritical techniques are more efficient due to faster mass transfer rates and the ability to dissolve a wider range of solutes while reducing environmental and health risks [17]. Supercritical recrystallization offers superior control over process parameters. Indeed, the use of supercritical fluids (SCFs) allows for fine-tuning of solvent power, leading to more uniform nucleation and crystal growth. This approach reduces reliance on hazardous organic solvents and aligns with green chemistry principles by minimizing waste and emissions. Using supercritical CO_2 in these processes enhances environmental friendliness, reduces reliance on toxic organic solvents, and aligns with green chemistry principles to reduce waste and emissions.

State of Art and Methods

In this context, we investigate how micronization using supercritical fluids alters particle shape, size, and dispersion. This study examines both mineral (copper oxide) and organic matrices (crystallized benzoic acid and *Retama Raetam* plants). This study is essential for improving the micronization process for various applications and ensuring the creation of high-quality, consistent products.

The major focus involves qualitative and quantitative assessments of recrystallized powders. Qualitative analysis entails thorough evaluation of the physical appearance, shape, and structural features of particles utilizing modern imaging methods such as Scanning Electron Microscopy. These approaches provide information on surface roughness and probable particle agglomeration.

The study also explores the effects of various factors on particle growth, including thermodynamic parameters, solvation, and hydrodynamics [18; 19]. Thermodynamic parameters such as temperature and pressure play a significant role in the supercritical fluid micronization process. By adjusting these parameters, we can control the solubility and supersaturation levels of the solute, which directly impact nucleation and crystal growth rates [20]. For example, higher temperatures might increase solute solubility but could also lead to larger, less uniform particles if not carefully managed [14]. This finding not only advances our knowledge of particle creation in supercritical fluids, but it also has practical implications for industrial applications that need precise control over particle features [10].

Studying the Morphology of Supercritical Process Deposits

Identifying the morphology of particles generated by supercritical fluid processes is essential for understanding and optimizing their characteristics for specific applications. Particle deposit size, shape, surface structure, and distribution can be investigated and characterized using a variety of analytical methods. Scanning Electron Microscopy (SEM) generates high-

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resolution pictures of particle surfaces, enabling for extensive analysis of particle form, texture, and size distribution. It is commonly used to examine the morphology of crystallized particles and identify any aggregation or irregularities, [21].

Dynamic Light Scattering (DLS) determines the size distribution of particles in a fluid by studying the scattering pattern of laser light. It gives information on particle size distribution, as well as the consistency and homogeneity of the particles generated. These technologies can detect concentration throughout a large dynamic range of concentrations and sizes, as well as perform particle size analysis, ensemble particle zeta potential measurement, particle mass measurement, and particle fluorescence.

X-ray diffraction (XRD) is used to determine the crystalline structure of particles, providing information on phase composition, crystallite size, and crystallinity. This is especially important for understanding how the RESS process, as well as the SAS process, affect the crystalline characteristics of the solute [12; 15].

Polarization microscope analysis can produce pictures that demonstrate the optical structure of particles and aggregates created from treated matrices, which are more consistent than raw material. This suggests a demand for consistent alignment and a well-defined structure, which is achieved by rapid particle germination followed by ultra-fast transport.

PSD methods

The results of particle size analysis are sometimes taken for granted, but measuring and reporting the particle size distribution necessitates competence in the analytical techniques employed and the data produced [22]. While using appropriate analytical methods is essential for quality control, defective results might lead to wrong conclusions. Consistent methodology is required to analyze batch-to-batch variability, but the precision of the data is determined by the measuring technique's dependability. Determining the "true" particle size distribution is difficult because of technique-dependent results [23-24].

However, there are verification methods available that improve confidence in data accuracy. Natural materials often have a lognormal or skewed Gaussian distribution [25]. The range of distributions can vary depending on particle form, size, and aggregation state, with secondary peaks appearing on occasion. Disconnected modes from the main distribution require further research to confirm the results. In contrast, unlike natural materials and minerals, the distributions of materials treated by supercritical processes are dramatically influenced by the parameters supplied, resulting in the acquisition of correct PSD and recrystallized particle shape.

Software for counting and morphologies reconnaissance

Particle shape is another important element of morphology that may be quantified via image-based counting. Researchers can characterize particles by evaluating their outlines or cross-sections in microscopic pictures, such as round, elongated, or irregular. To further depict particle shape fluctuations, quantitative characteristics such as aspect ratio and circularity may be determined. Particle counting software is a valuable instrument used in scientific research, medicine, pharmaceuticals, and materials science to quantify and analyze particle size distributions in samples. *ImageJ /Fiji*, an open-source program created by the National Institutes of Health (NIH), is widely used for image analysis because of its flexibility, which includes particle counting and size measuring. It combines superior imaging capabilities with powerful tools for extensive image analysis, such as accurate particle counts and morphological evaluations. When compared to manual investigation, counting software is distinguished by its precision in detecting particle size from digital pictures, as well as extra features for shape analysis and dispersion evaluation [26]. These software solutions expedite and standardize particle counting and analysis operations, assuring precision and repeatability, which is critical for improving scientific and industrial applications. This method entails evaluating pictures taken using microscopy techniques such as scanning electron microscopy (SEM) or optical microscopy to evaluate different aspects of particle properties such as size, shape, and distribution.

Discussions

The following discussion is based on analysis of photomicrographs from several precipitation papers. In order to achieve reliable imaging and particle analysis, adequate sample preparation methods must be used. Advanced image processing methods are used to efficiently evaluate big datasets and extract useful morphological information. Individual particle outlines can get hidden in conditions of excessive particle density or agglomeration, making precise counting and shape analysis difficult.

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Standardized procedures for image collecting, processing, and analysis are critical for ensuring reproducibility and comparability of results across investigations. Photographs taken under various conditions can be compared to analyze how particle shape is affected by various process factors (e.g., temperature, pressure, and solute concentration) in RESS and SAS processes.

We further demonstrate the particle size distribution and morphology obtained from classical benzoic acid crystallization and then obtained using supercritical fluid for the CuO mineral and organic molecules of benzoic acid and *Retama raetam* extracts.

Conventional crystallization of organic materials

The discussion is on SEM imaging and optical microscopy of materials treated with supercritical techniques. The study begins with an investigation of the size and shape of benzoic acid crystals produced via ordinary evaporation. The crystals are commonly prism-shaped, with a variety of sizes and morphologies. The size distribution is rather vast. After determining an acceptable threshold, picture digitization generates a binary data representation of the edges of the targeted particles. Plotting the Particle Size Distribution (PSD) versus the average size of each class reveals a lognormal trend toward generation of bigger particles, even if the most numerous class stays in the micrometer range.

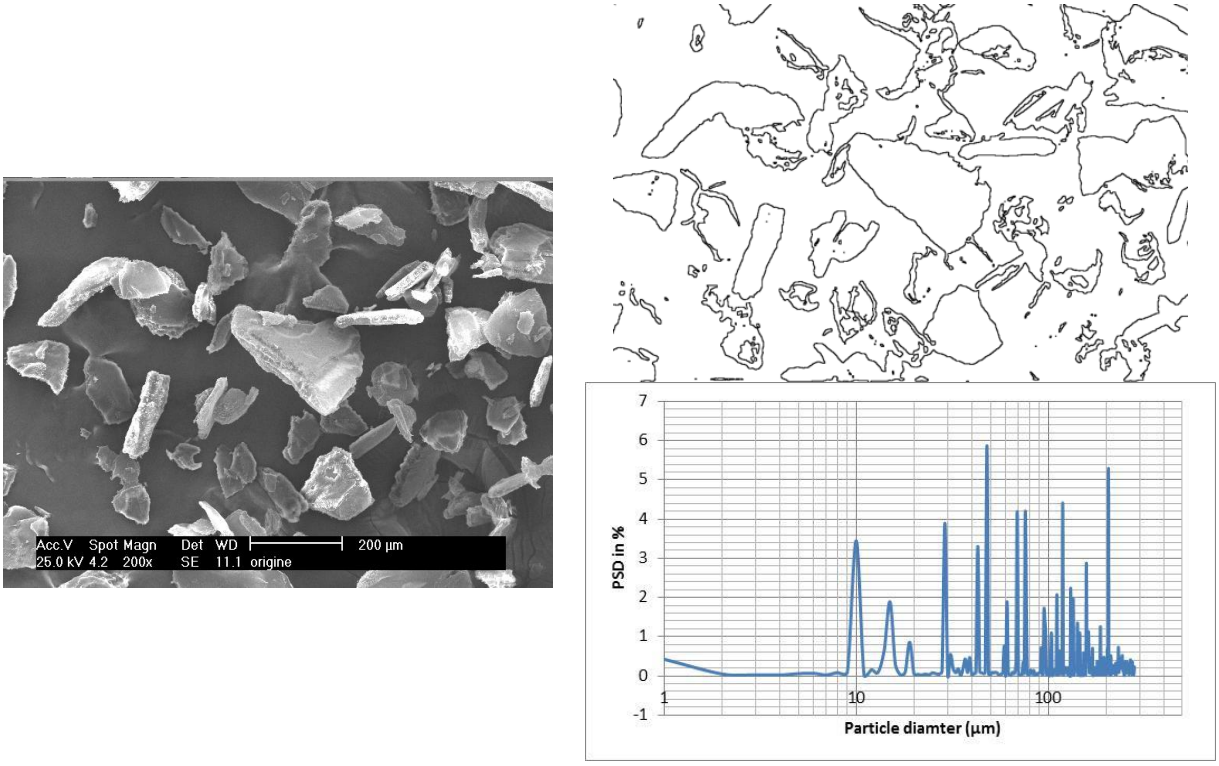
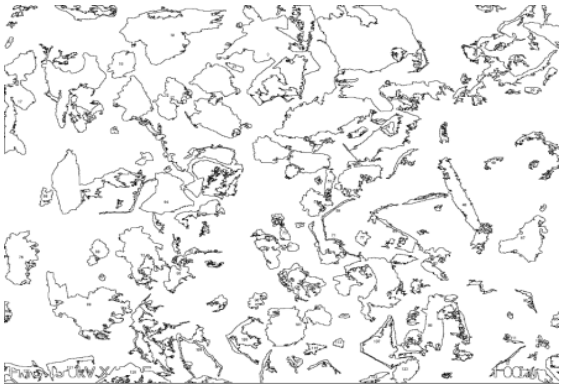


Fig. 1. Crystals of benzoic acid obtained by conventional precipitation: Recognition of particle edges and relative size distribution



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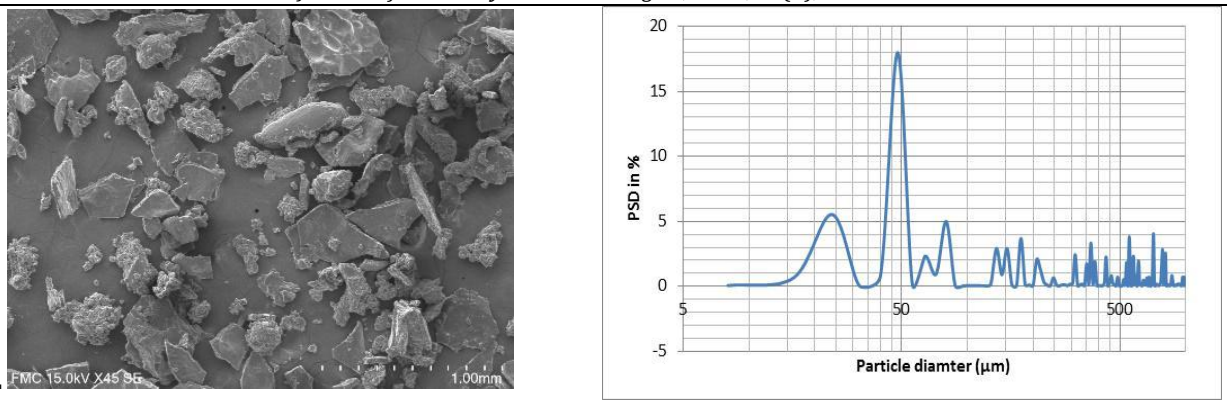

Fig. 2. particles of dried *retama raetam* extract obtained by grinding: Recognition of particle edges and relative size distribution

In the case of the *Retama raetam* extract, the preparation method involves drying the plant material first. Subsequently, the dried material undergoes grinding and sieving processes to achieve the desired particle size distribution. It's noteworthy that particles can exceed 0.5 mm in size, and the distribution tends to be irregular.

Hydrodynamics and Precipitator Design

Hydrodynamics of fluids during the micronization process has a substantial impact on particle formation [12]. The dimensions of the expansion chamber and separation unit, as well as the precipitation of solubilized products, have been shown to impact a wide range of particle sizes and morphology [14]. Research papers on supercritical crystallization have reported a wide range of results, from exceedingly small particles to strongly adherent coatings on substrates, notably in the case of organic molecules [9]. Effective mixing maintains uniform supersaturation and consistent particle production throughout the process. In reality, inadequate hydrodynamic conditions can result in irregular particle sizes and morphologies, lowering the overall quality of the recrystallized powder [27].

The form, support, and size of the expansion or precipitation chamber are important determinants in particle sizing, as evidenced by theoretical and experimental modeling studies. Indeed, a huge chamber in which the expanded fluid flows at high speeds (up to Mach numbers of 3 or 4) is vastly different from a compact enclosure, even when vented, where recirculation zones and shock waves produce an environment conducive to considerable particle coagulation and growth [14]. These findings emphasize the significant impact of operating settings on the final properties of micronized materials. Therefore sizing fine particle precipitators is a complex process that takes into account several aspects such as particle type, gas flow rate, gas temperature and pressure, and collection support needs.

Furthermore, optical approaches can assist to clarify and define these effects, offering critical insights for optimizing micronization procedures. The tendency to produce spheres, sticks, long filaments, and needle-like structures varies with product, culminating in particles with larger diameters approaching semi-industrial sizes [28]. This pattern is a deliberate reaction to changing market demands, with varied forms and sizes tailored to certain uses and processing capacity. Manufacturers may better fulfill industrial-scale production demands by offering such variety, while also boosting product flexibility and performance across several sectors.

Thermodynamic parameters effects

The effect of thermodynamic factors, particularly dissolution conditions, on particle size and shape has been widely studied and reported. Previous research has repeatedly shown that increasing temperature or pressure during the dissolving stage considerably improves solubilization, resulting in a larger yield of recrystallized particles [12]. This improvement happens because greater temperatures increase molecule kinetic energy, which improves solubility in the supercritical fluid. Similarly, higher pressure increases the density of the supercritical fluid, hence increasing its solvating capacity. However, thermodynamic conditions during the precipitation phase have an even greater impact on particle shape, especially for organic substances like caffeine, salicylic acid, and benzoic acid [12–24]. It is shown that lower temperatures during precipitation promote the development of tiny, needle-like particles due to decreased solute mobility and slower crystal growth rates. Higher temperatures, on the other hand, can encourage the formation of bigger,

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irregularly shaped particles by increasing molecular mobility and nucleation rates [14]. To summarize, while increasing temperature and pressure during dissolution improves solubility and gives more recrystallized particles, precise management of these parameters during precipitation is critical for getting the ideal particle shape. Finding a balance with these thermodynamic parameters is critical for improving the micronization process and producing particles with precise size and morphological properties.

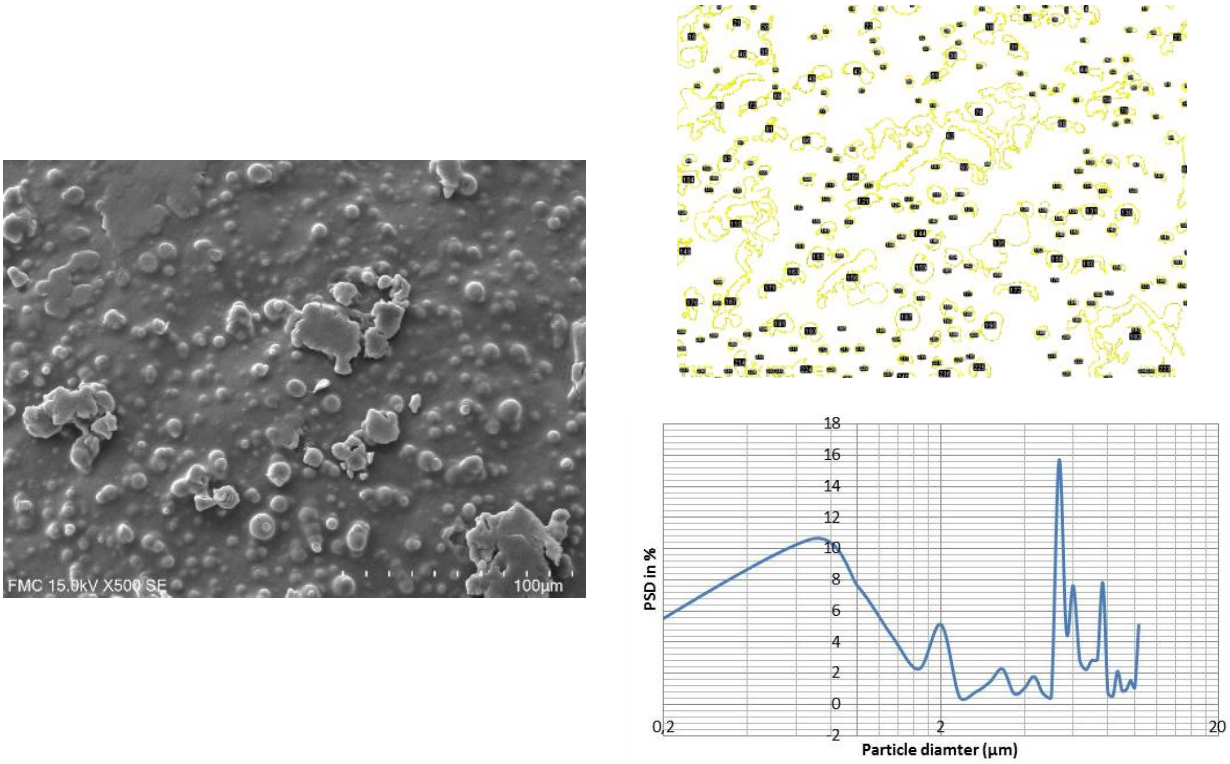

Fig. 3. Particles of *Retama raetam* obtained via SAS process: Recognition of particle edges and relative size distribution

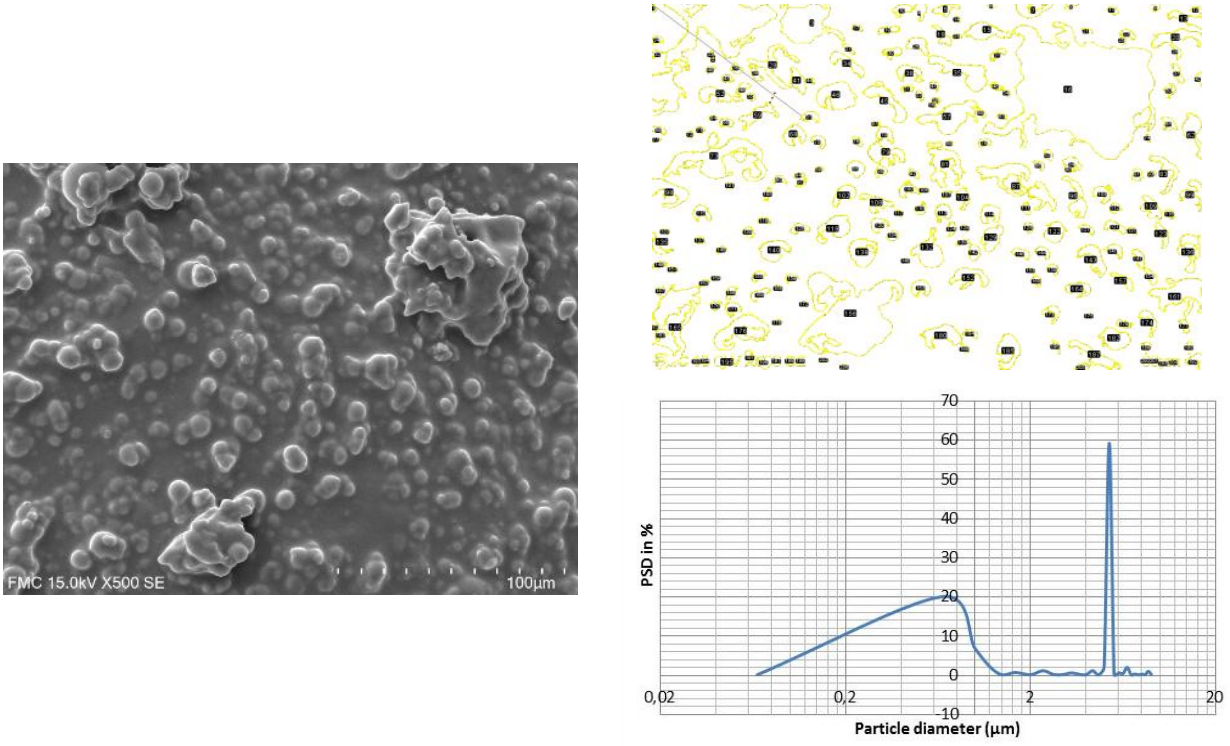

Fig. 4. Particles of *Retama raetam* obtained via SAS process: Recognition of particle edges and relative size distribution

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Effect of deposition time

The influence of deposition time on particle size distribution (PSD) was investigated by altering the length of recrystallized particle deposition on the deposition plate, which is also an important parameter in determining the size and shape of deposited aggregates. Indeed, under constant hydrodynamic circumstances in the dissolution and recrystallization units, the deposition time might range from a few to several minutes, especially in large expansion chambers. In the case benzoic acid experiments (45 and 60 minutes), figure5 shows a change in particle size distribution from 3 to 8 µm, with smaller sizes decreasing and bigger structures increasing. Furthermore, extended exposure of the deposition plate to the growing jet resulted in more severe coagulation.

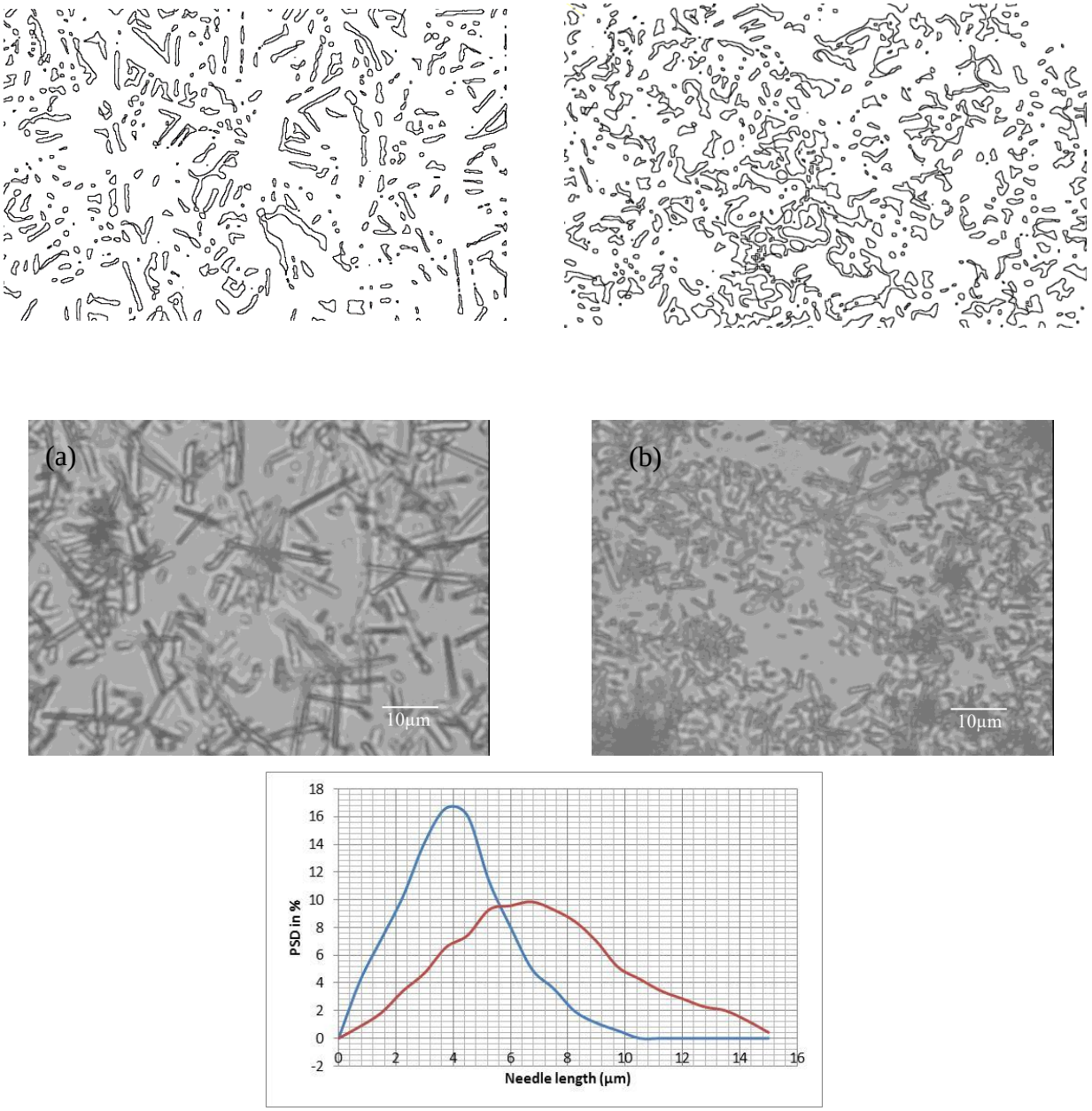

Fig. 5. Particles of *benzoic acid* obtained via RESS process: relative size distribution at both deposition times; 45 mm (bleu)and 60 mm (red)

Additionally, we make attention on observation of benzoic acid particles obtained via the RESS process reveals a spongy morphology (Figure 6), often appearing in a rod-like form. This structure arises from particle agglomeration orientation within a small chamber, collected at its edge, and probably facilitated by OH groups on the benzoic acid molecule. Such a structure provides a large specific surface area, enabling high product reactivity.

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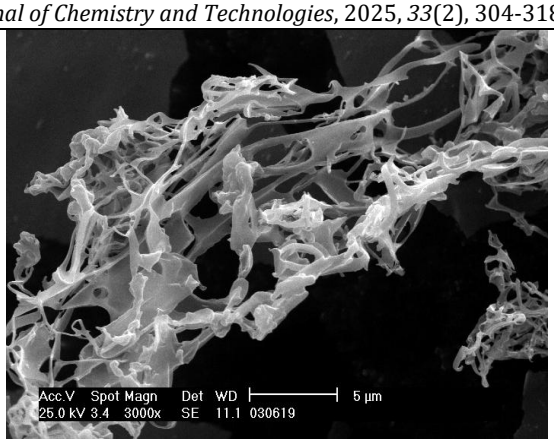

Fig. 6. Spongy Aggregate of Benzoic Acid Produced by the RESS Process: Influence of Precipitator Hydrodynamics with Small Dimensions

Case of minerals

Metal oxides are widely found as minerals and chemical compounds composed of metal and oxygen. Copper oxide, a significant example, plays a crucial role in various industries, including paint and ink production. In a recent study by Chen et al. a novel approach was introduced for synthesizing amorphous nano-metal catalysts [29]. This method involved oxidizing metallic copper using supercritical carbon dioxide, highlighting advancements in controlled synthesis techniques.

Earlier research by Kondoh and Kato explored the deposition of copper films utilizing supercritical carbon dioxide [30]. They achieved this through hydrogen reduction of Copper(II) hexafluoroacetylacetonate, $Cu(hfac)_2$, under specific conditions: temperatures ranging from 250 to 400 °C and pressures between 10 and 15 MPa. Figure (7) from their work illustrates the deposited copper particles, revealing a nearly spherical morphology with sizes approaching 2 µm. Despite a perturbed lognormal distribution, the particles exhibit uniformity in shape, which is noteworthy for various applications in materials science and catalysis.

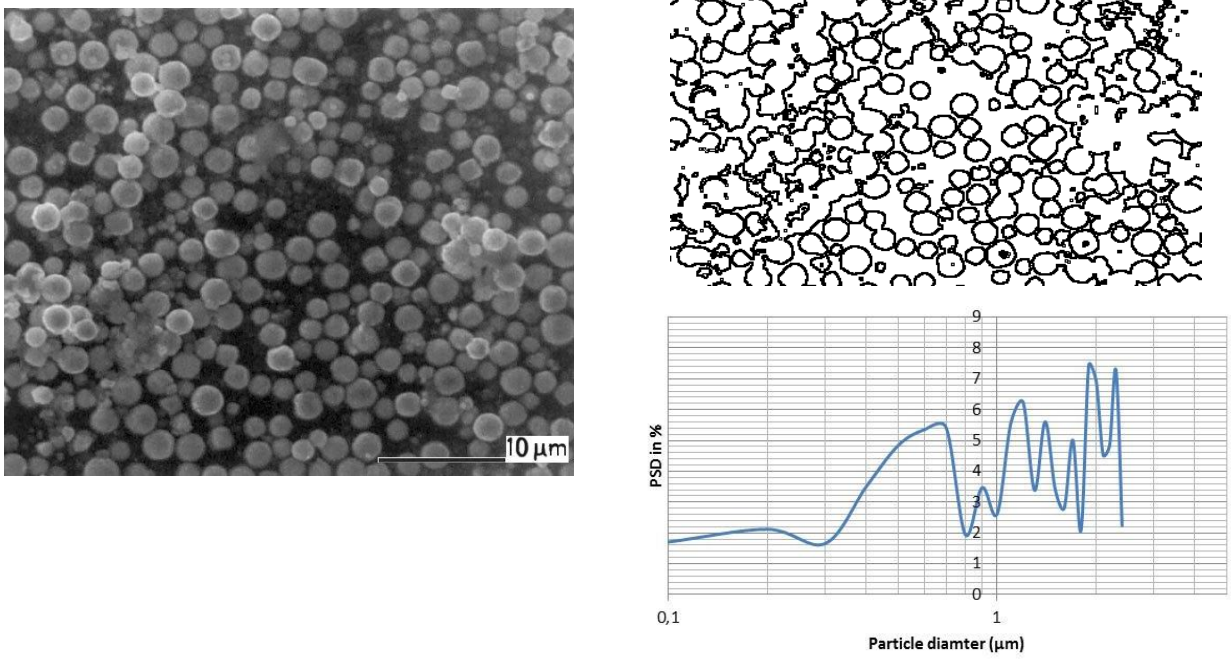

Fig. 7. Deposition of copper films utilizing supercritical carbon dioxide; Kondoh and Kato [30]: Recognition of particle edges and relative size distribution

Case of films and porous structure

Biomaterials, as plant derivatives, processed with SAS process are also submitted to atomization spray formation. In fact, tunable properties of $ScCO_2$ mean that material engineering can speed up the process. Ivanović et

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al. found that an increase of supercritical carbon dioxide flow rate led to a loss of relative activity and therefore, a narrow distribution of pore size with a quasi-uniform morphology [31]. It is important to call attention to the fact that no excipient was used during drying and the product (thin film) is free of solvent.

Depositing porous structures using supercritical processes is an important approach in materials science and engineering. With SAS process, a dried *Retama raetam* was dissolved or in the ethanol. The system is subsequently depressurized, causing the supercritical CO_2 to return to its gaseous state, accordingly. During this phase shift, the precursor material is left behind, which frequently results in a porous structure due to the quick creation of voids or pores as seen in figure 8. In this context, the difficulty is to generate holes and cavities with accurate dimensioning and shape, while assuring uniformity and consistency [32].

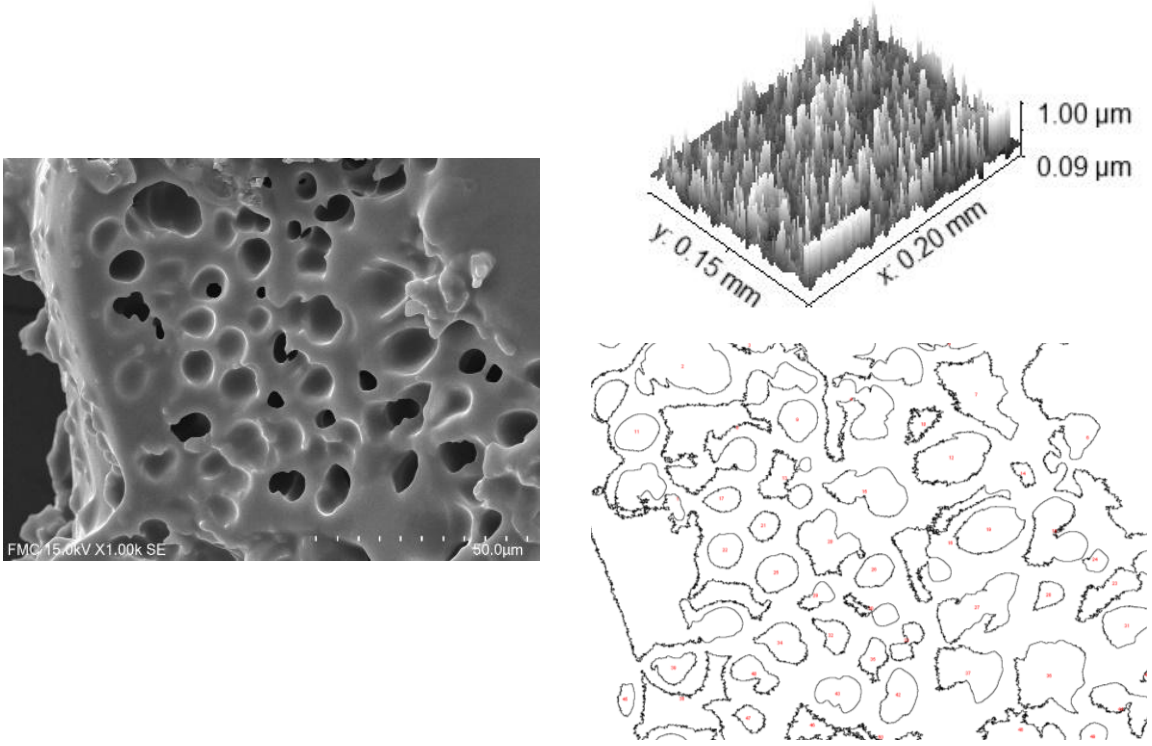

Fig. 8. Porous film of *Retama raetam* obtained via SAS process: Recognition of pores edges and relative depths.

Figures 9 and 10 present the outcomes from multiple experimental runs, revealing the consistent formation of spongy thin films in each case. The figures depicting *Retama raetam* deposits at a microscopic scale offer insights into the internal structure of the atomization slot and the resulting film. These variances in pore size can be attributed to working temperature, pressure conditions, and the volume to be dissolved, highlighting the intricate relationship between these factors in film deposition. The examination of regenerated *Retama raetam* film surfaces was carried out using a *Zeiss Auriga Compact* focused ion beam scanning electron microscope (FIB-SEM) with an accelerating voltage set at 10 kV. The scale was chosen at 50 µm to get a clear idea about pores morphology, area, distribution and depth. Thin films obtained by the SAS process have exhibited the highest organic porous film efficiency offering a best stability to incorporate active principles. With SAS process, it would be interesting to study optimal conditions *Retama raetam* extract deposition from spray-drying as thin film.

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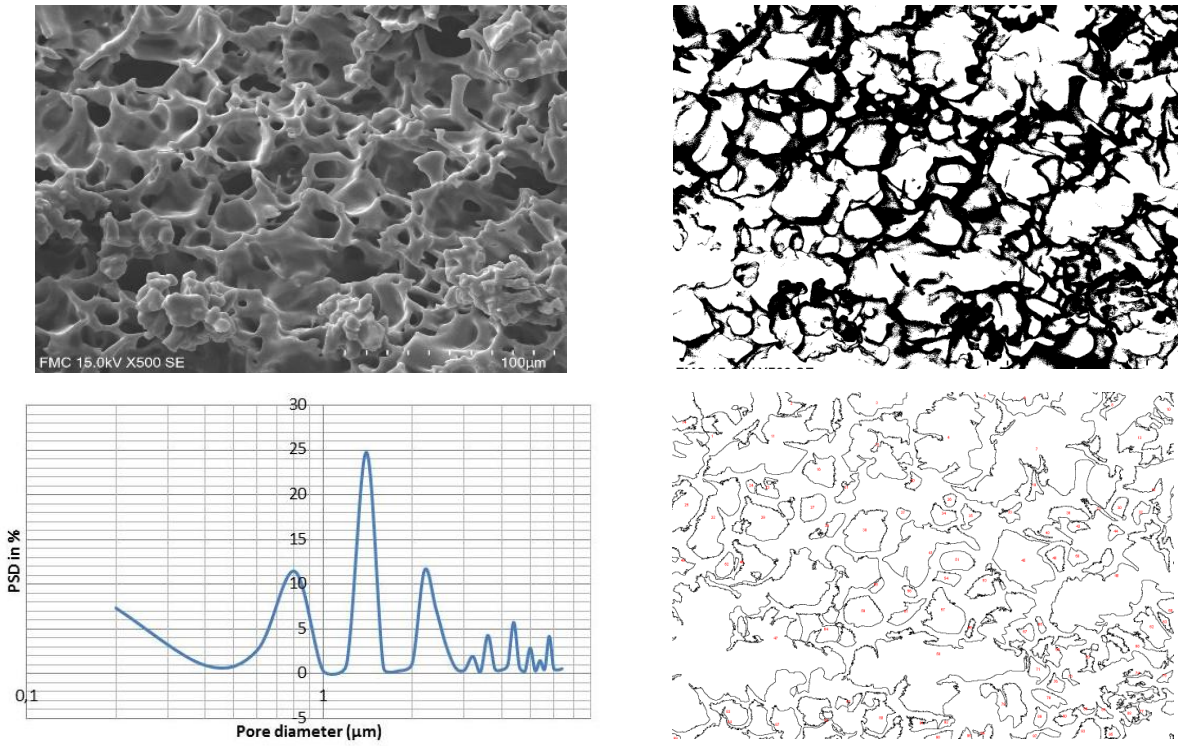

Fig. 9. Particles of *Retama raetam* obtained via SAS process: Recognition of particle edges and relative narrow size distribution

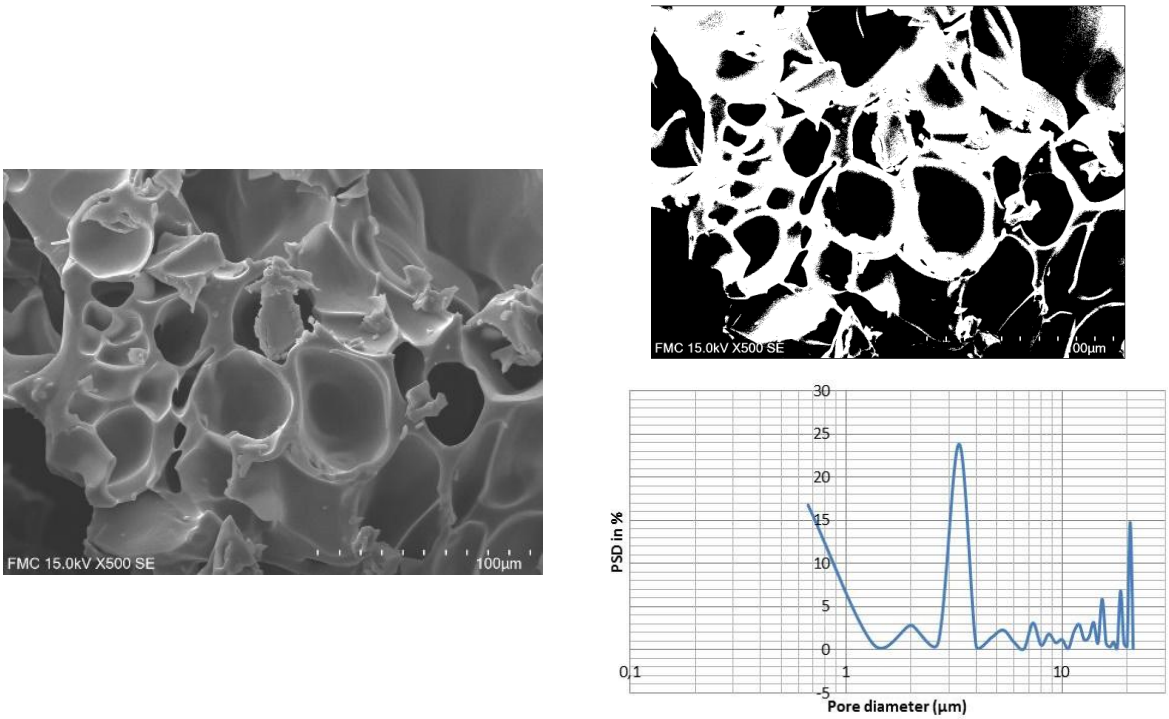

Fig. 10. Particles of *Retama raetam* obtained via SAS process: Recognition of particle edges and relative wide size distribution

The morphological properties of the produced particles determine the porosity of aggregate deposits, as demonstrated in this study. As a result, it was decided to create aggregates with dramatically different morphological properties and examine their influence on porosity. To determine these morphological traits, two approaches were used sequentially. SEM microscopy was used to determine aggregate size and primary pore diameter. Furthermore, particle analysis was carried out to assess their distribution in relation to the provided scale.

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These films can be used as biodegradable supports for integrating active substances. As a result, appropriately measuring holes relative to pharmaceutical product size is critical in the creation of novel drugs.

Table 1

Comparison of Micronisation Processes: Material, Size, Distribution, and Morphology

Micronisation Processes		Material	Size and Distribution		Morphology
Conventional methods	Cooling crystallization	Benzoic Acid	10–150 μm	polydisperse distribution	Prismatic forms
	Grinding followed by screening	Retama retam	20–500 μm	irregular particle size distribution	Prismatic forms
Supercritical techniques	RESS	Benzoic Acid	4–15 μm	narrow size distribution	Needles
	RESS	Benzoic Acid	Micrometric scale ≈ 5 μm	Chaotic structure	Highly porous spongy structure
	Sc Deposit	$Cu(hfac)_2$	Close to 1 μm	uniform particles	Spheres
	SAS	Retama raetam	2–10 μm	agglomerated particles with narrow size distribution	Roughly spherical shape
	SAS	Retama raetam	1–10 μm	uniform pores	Porous

Therefore, the following table1 highlights the main similarities and differences between the previously stated micronization techniques with relation to particle size, distribution, and morphology. It draws attention to the tendency of narrow-distribution micronization using supercritical methods. Supercritical techniques like RESS and SAS are clearly superior to traditional procedures like chilling crystallization and grinding and screening. These supercritical methods provide more accurate control over particle shape in addition to providing smaller size dispersion. Furthermore, when supercritical CO_2 and other ecologically friendly solvents are used, supercritical processes often produce purer products with less pollution and less energy use. Because of these benefits, supercritical micronization is becoming more and more appealing, particularly when high-performance materials with certain size, distribution, and structural characteristics that are challenging to obtain using conventional techniques are desired.

Advantages and Challenges

Supercritical fluid processes are recognized for their intrinsic simplicity, making them potentially applicable to a wide range of materials, mainly organic molecules for controlled-release systems. The RESS method takes use of conditions that provide significant supersaturation ratios as well as the solvent's return to a gaseous form at the end of each cycle. As a result, the particles are ultra-fine and monodisperse, the fluid is recyclable without any residual solvent, and it may handle heat- or shock-sensitive compounds. However, one notable disadvantage is that it is only applicable to extremely weakly soluble solutes, which has led to the development of alternative approaches such as supercritical fluid anti-solvent (SAS) technologies. Furthermore, challenges remain in scaling up the process, with limited investigation addressing it fully. However, it is found that industrial-scale manufacturing may match small-scale setups, supporting amounts of up to several tons per year, as demonstrated with some therapeutic proteins [33]. Another impediment to industrializing FSCs is the initial investment cost, which is frequently stated. Nonetheless, the value of the processed molecules can surpass these expenses, even in small amounts, and successful examples of large-volume extraction with lesser value-added chemicals demonstrate practicality in less favorable settings.

Conclusion

Supercritical processes operate at lower temperatures than conventional methods, resulting in reduced energy consumption. These procedures, which have been refined over decades, produce reliable and predictable results across a wide range of applications. Their scalability makes them excellent for large-scale industrial production, and they can produce a variety of particle forms, including powders, crystals, and composites. Crystallization technologies have improved standard precipitation procedures by providing smaller size and morphological regularity.

The implementation of precise control mechanisms and decision-making tools has considerably accelerated the transition to greener

processes, such as supercrystalline fluid applications. Supercritical process parameters enable precise particle size change via microscopic imaging and control of particle distributions and film pores. This degree of control is critical for industries that require homogeneous particle size, including medicines and materials research.

To produce desired particle shapes such as spherical or rod-shaped forms, parameters such as solute concentration, solvent type, and dynamics must be optimized during recrystallization using supercritical fluid. Particles created using supercritical techniques frequently have improved performance characteristics; for example, in pharmaceuticals, finely uniform particles can improve drug solubility and bioavailability, whereas increased surface area in catalysis can increase reaction rates.

Declaration of Competing Interest

I, Hatem Ksibi, declare that I have no financial, professional, or personal relationships with individuals or organizations that could inappropriately influence or bias the content and conclusions of this work. There are no competing interests that could potentially affect the integrity or objectivity of the research presented in this paper.

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