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Perspective

Effects of Sonocrystallisation on Salbutamol Sulphate Particles

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DESCRIPTION

The application of an anti-solvent sonocrystallisation technique was examined for the production of salbutamol sulphate fine particles intended for Dry Powder Inhaler (DPI) formulations. The effects of process variables, including sonication power and the volume ratio of anti-solvent to solute solution, on the particle characteristics of salbutamol sulphate were systematically investigated. By adjusting these variables, fine particles with a size distribution ranging from 2 μm to 5 μm were successfully produced. Following sonocrystallisation, spray drying of the anti-solvent suspension yielded micron-sized crystalline salbutamol sulphate particles. The emitted dose of this powder was 42%, significantly higher than that of the amorphous form produced by traditional spray drying methods. This value was assessed using the Fine Particle Fraction (FPF) emitted for a blend of coarse lactose and spray-dried sonocrystallised salbutamol sulphate. The results from this study highlight the potential of the designed process for producing particles with a micron size distribution and a highly crystalline form, making it a highly effective approach for DPI formulations.

Fine particles of pharmaceutical compounds are critical for the development of inhalation aerosols, injectable suspensions, transdermal formulations and controlled-release dosage forms. Micronisation, commonly employed in the industry, typically involves crystallisation processes followed by milling, grinding, or spray drying. However, these traditional methods often lead to challenges such as the production of amorphous fractions, contamination from mechanical attrition, broad particle size distributions and incompatibility with thermally sensitive compounds. These issues can adversely affect the therapeutic properties of the resulting drug particles. Although various techniques have been proposed to achieve more controlled particle size distributions during crystallisation, large-scale production can face difficulties such as poor mixing, which results in heterogeneous growth of crystals, further affecting particle morphology and size uniformity.

To address these challenges, alternative techniques for micronisation have been developed. Super Critical Fluid (SCF) techniques have been proposed for micronising particles, but their large-scale application remains limited. Advanced Liquid–Liquid Anti-solvent (LLA) processes have been studied to improve phase mixing and produce homogeneous micron-sized particles. Technologies such as Spinning Disc Reactors (SDR) and ultrasound-assisted crystallisation have been integrated with LLA to achieve more controlled micronisation.

Sonocrystallisation is an efficient technique that combines High-Intensity Ultrasound (HIU) power with crystallisation. The application of ultrasound creates a phenomenon called cavitation, where localized temperature and pressure fluctuations lead to the formation of micron-sized bubbles. These bubbles grow until they can no longer absorb further energy from the sound field, causing them to collapse. This collapse releases energy that accelerates the crystallisation process. As the number of primary nuclei increases, the solute is distributed across a larger number of crystals, resulting in smaller final particle sizes. Sonocrystallisation offers advantages over conventional methods, such as faster primary nucleation and easier initiation of nucleation for materials that are otherwise difficult to crystallize. Additionally, it allows for the production of smaller, purer crystals with more uniform sizes. The particle size is influenced by both the induction time and micro-mixing time, with sonocrystallisation typically ensuring uniform nucleation and narrow particle size distributions.

In this study, the sonocrystallisation technique was successfully used to enhance the homogeneous nucleation of salbutamol sulphate, reducing crystal size significantly. The anti-solvent sonocrystallisation method was specifically employed to produce crystalline particles of salbutamol sulphate. The dried powder produced was suitable for inhalation drug delivery, with an average particle size between 3 μm and 7 μm. A high volume ratio of organic solvent to solute solution and significant sonication power were required to achieve these desired particle characteristics.

CONCLUSION

In conclusion, the anti-solvent sonocrystallisation technique successfully produced micron-sized, highly crystalline salbutamol sulphate particles suitable for dry powder inhaler formulations.

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By optimizing process variables such as sonication power and the anti-solvent to solute ratio, particles with a narrow size distribution and enhanced aerosol performance were achieved. Compared to traditional spray drying methods, the sonocrystallised powder showed a significant improvement in emitted dose. This study demonstrates the potential of sonocrystallisation as an effective technique for producing fine, crystalline particles with consistent size distributions, offering an advanced approach for inhalation drug delivery.