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Sonocrystallization Approach to Modify Crystal Habit for Improving Powder Processability

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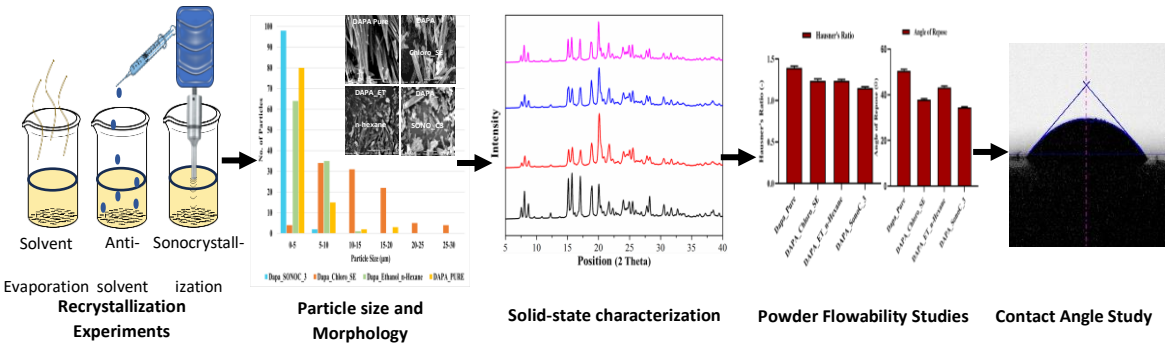
ABSTRACT

Most active pharmaceutical ingredients (APIs) present challenges during manufacturing into a tablet dosage form due to non-ideal crystal habits. Dapagliflozin (DAPA), a recently approved anti-hyperglycaemic agent is an example of drug that possesses poor powder flow properties due to its needle-shape crystals. In addition, DAPA is hygroscopic drug, thus necessitating stringent control measures during its manufacturing. Current research explores different crystallization methods (including sonocrystallization) using different solvents to modify the crystal habit of DAPA. Saturation solubility studies were conducted to select good solvent and anti-solvents for the drug. Recrystallization experiments were carried out by solvent evaporation (in chloroform), anti-solvent crystallization (ethanol as good solvent and n-hexane as anti-solvent), and sonocrystallization (in acetonitrile). The morphological evaluation revealed that recrystallization by solvent evaporation and sonocrystallization results in rod-shaped crystals, while anti-solvent recrystallization gave a mixture of rod and plate-shaped crystals of DAPA. The sonocrystallized powder had the lowest aspect ratio (3.56) compared to pure DAPA and other samples (5.94 – 6.98). Fourier transform infrared study revealed no changes in the structure of the recrystallized and pure DAPA. Solid-state analyses such as powder x-ray diffraction (PXRD), differential scanning calorimetry (DSC), etc. were carried out to rule out the possibility of polymorphic modification of recrystallized samples. Sonocrystallized powder outperformed all other samples regarding powder flowability as measured by angle of repose (34.42±0.33) and Hausner ratio (1.15±0.01). Further, the total surface free energy determination by contact angle studies of pure and modified DAPA crystals provided a hint of improvement in hygroscopic stability of recrystallized samples (~46.1 mJ/m^2 to ~49.8 mJ/m^2) when compared to pure DAPA crystals (~51.75 mJ/m^2).



Keywords: Crystal Engineering, Powder flow, Solvent evaporation, Sonocrystallization

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