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A study on the synthesis and characterization of 1:1 SMZ-ASA cocrystal with improved aqueous solubility and dissolution rate

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ABSTRACT

A 1:1 cocrystal comprising of sulfamethazine (SMZ), a potential sulfa drug with low aqueous solubility and antipyretic and anti-inflammatory drug acetylsalicylic acid (ASA) was synthesized through slow solvent evaporation from acetonitrile at room temperature. The needle shaped cocrystal of SMZ-ASA has been characterized by analytical methods like single crystal and powder X-ray diffraction, differential scanning calorimetry and Fourier transform infrared spectroscopy. Intermolecular hydrogen bonding between the nitrogen atom of the sulfonamide group in SMZ and the nitrogen atom of the pyrimidine ring with the carboxylic acid group of ASA, facilitated the cocrystal formation. The aqueous solubility of the SMZ-ASA cocrystals has been compared with the solubility of the individual components at different temperatures. It was found that the cocrystallization of SMZ with ASA can potentially increase the aqueous solubility of SMZ by 2 times at room temperature. Further dissolution studies showed that the SMZ-ASA cocrystal exhibited a faster dissolution rate compared to pure SMZ, achieving a concentration of 1 mM at 2 hours at room temperature. Cocrystal of SMZ-ASA was also produced using the isothermal slurry cocrystallization method through appropriate selection of co-former ratios at room temperature in acetonitrile system.

Keywords: cocrystal, solvent evaporation, solubility, dissolution, isothermal slurry

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