Research Article

Development of non-covalent derivative of sulfasalazine with theobromine for its properties optimization

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ABSTRACT

To customize the biopharmaceutical parameters of a poorly soluble, disease modifying anti-rheumatic drug, sulfasalazine (SSZ) by preparing its novel non-covalent derivative (NCD). For this theobromine (TBR) was used as coformer. The novel solid form prepared by liquid assisted grinding of SSZ with TBR using catalytic amount of solvent and termed as SSZ-TBR. The ground product (SSZ-TBR) was characterized with various techniques such as differential scanning calorimetry, powder X-ray diffraction (PXRD), and spectrometric methods involving Fourier transform infrared and solid state nuclear magnetic resonance. The structure of the SSZ-TBR was determined from its PXRD pattern using Material Studio® by BIOVIA. The crystal structure also helped to understand the nature of complex and type of interactions involved in its formation and stabilization. The SSZ-TBR was further evaluated for *in vitro* solubility and intrinsic dissolution rate (IDR) profile. This NCD was characterized to be cocrystal of SSZ with TBR in 1:1 stoichiometry. Its crystal packing as well as nature of interactions was established by crystal structure determination. Further, the fulfillment of objective was witnessed byE increased solubility as well as IDR in comparison to the pure SSZ. The evaluation of this novel cocrystal of SSZ a poorly soluble drug with TBR exhibit potential to enhance the option of material phase in comparison to pure active pharmaceutical ingredient without disturbing its chemical structure.

Keywords: Characterization, cocrystal, intrinsic dissolution rate, solubility, sulfasalazine

Introduction

Recent decades have evidenced a tremendous growth of interest by various research groups in the design as well as synthesis of multicomponent crystals particularly pharmaceutical cocrystals.[1] Cocrystals are multicomponent single phase crystalline complexes in which two or more neutral molecular constituents (active pharmaceutical ingredient [API]-1 and coformer, and/or solvent of crystalliztion) in the crystal lattice bound together through non-covalent interactions, primarily hydrogen bonding.[2] To modulate physical as well as mechanochemical properties of drugs, namely, stability, hygroscopisity, solubility, dissolution rate, and compressibility while maintaining their pharmacological behavior, pharmaceutical cocrystallization is one of the most reliable and reproducible method.[1,3] During cocrystallization in the crystal lattice of cocrystal consists of API, coformer, and/or solvent of crystallization while maintaining the pharmacological activity of API.[4-6] The coformer can be either drug or inert excipient of generally recognized as safe status which comprises food additives, pharmaceutical excipients, and preservatives.[7,8] Pharmaceutical cocrystals offers an alternative materials to pure drug substance and has the advantage over established drug modifications such as polymorphic and amorphous form, salt, solvate, and conventional inclusion complexes, each of which have associated limitations in their application.[9,10] In addition, for neutral drugs, lacking ionisable group, cocrystals proved a viable method for optimizing the properties of such molecules. Moreover, the availability of cocrystal ligands is far than suitable counterions for developing salts.[11]

Sulfasalazine (SSZ) is a poorly water soluble drug with low aqueous solubility used to treat rheumatoid arthritis.[12] Pharmaceutical cocrystal of SSA was prepared with theobromine (TBR) with an objective to modulate its physicochemical properties, especially solubility and intrinsic dissolution rate (IDR). Both SSZ and TBR contain functional groups that are donor and acceptor of hydrogen bond, which is a pre-requisite for cocrystals formation. The prepared cocrystal was characterized thoroughly using various analytical techniques and further evaluated for solubility and IDR in simulated gastric and intestinal fluid.

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