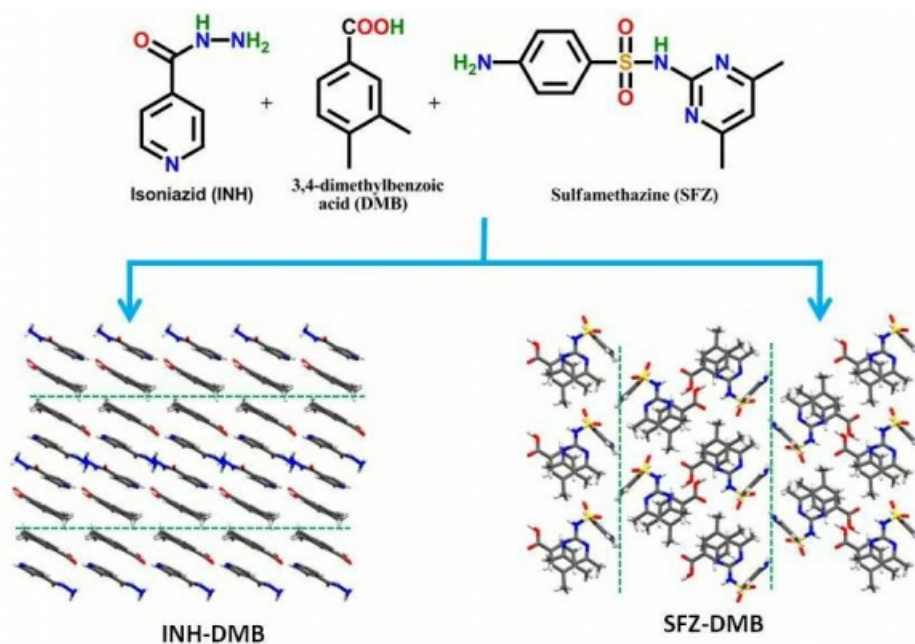


Improving tabletability of active pharmaceutical ingredients through cocrystallization

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Poor tabletability is a long term problem in the pharmaceutical industry. Successful development and commercialization of pharmaceuticals, material properties of these solid active pharmaceutical ingredients (API), particularly mechanical properties, often play an important role in bulk powder compaction behaviors. Such mechanical properties are essentially determined by the crystal packing, thus understanding the molecular crystal structure from a mechanistic point of view is important.¹ The creation of alternative polymorphic forms, salts, or cocrystals or hydrates of a drug substance through crystal engineering approach can result in structural variations in the molecular packing of the crystals and thereby, can alter the deformation behavior of the materials.² Cocrystallization is a viable tool for improving or optimizing these physicochemical properties of a drug substance. Therefore, in this study, we illustrate "Supramolecular Shape Synthron" strategy in cocrystals of highly brittle APIs by introducing weakly interacting functional groups capable of generating slip planes for enhancing plasticity as well as tabletability.³ We have synthesized two new cocrystals of isoniazid (INH) and sulfamethazine (SFZ) with 3,4-dimethylbenzoic acid (DMB) through the liquid assisted grinding method and characterized by single-crystal X-ray diffraction and other physicochemical methods. Both the INH and SFZ crystals have a three-dimensional hydrogen bonded network, which engender to very low plasticity as well as poor tabletability. The presence of a number of slip planes and a smaller number of interactions due to the systematic arrangement of methyl groups in cocrystals, makes cocrystals much softer than INH and SFZ crystals. Mechanical properties and bulk powder compaction studies of INH, SFZ and both the cocrystals are now being investigated.

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