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TITLE

PHARMACEUTICAL COCRYSTALS TO MODIFY PHYSICO-CHEMICAL AND DISSOLUTION PROFILE OF APIS

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Pharmaceutical cocrystals, or hydrogen-bonded crystalline complexes between API and benign co-formers (preferably from the GRAS list), offer rational approaches to make new supramolecular entities for drug deliver and formulation. Crystal engineering principles for cocrystal synthesis through robust heterosynthons have been developed for drugs containing carboxylic acid, carboxamide, sulfonamide, alcohol, amine functional groups with complementary co-formers such as pyridine, pyridine-N-oxide, acid, amide, etc. A major advantage of cocrystals over traditional salts is that APIs containing non-ionizable functional groups are amenable to solid-state control and modification of properties, such as hydration, ambient stability, dissolution, color, tableting, etc. Moreover, cocrystals offer a way to control polymorphism or phase transition discovered at late stages of an active lead compound or a marketed drug. Examples of bioavailability improvement for anti-fungal & anti-bacterial drugs and an SNRI inhibitor, and stability improvement for an anti-cancer drug in cocrystal adducts will be shown. From a preparative viewpoint, solution crystallization, solvent-less and solvent-drop grinding, ultrasonication, slurry crystallization, etc. can be used, preferably in high-throughput automated crystallization screens. Pharmaceutical cocrystals are the new paradigm in the repurposing and patenting of new medicines.