Crystal structure landscape of Ethenzamide: their physicochemical property study

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Pharmaceutical cocrystallisation is one of the modern methods of solid-state modification of active pharmaceutical ingredients (APIs) based on crystal engineering principles.[1-2] Ethenzamide is a common analgesic and anti-inflammatory drug that is used for the relief of fever, headaches, and other minor aches and pains. Pharmaceutical cocrystals/ cocrystal hydrate of ethenzamide (ETZ) with various hydroxy-acid coformers namely 2,4-dihydroxybenzoic acid (24DHBA), 3,5-dihydroxybenzoic acid (35DHBA), ferulic acid (FRA, nutraceutical molecule) and 35DHBA dihydrate (1:3:2) were synthesized using solution crystallisation as well as mechanical grinding. All the multi-component systems were characterized using various solid-state characterization techniques such as single crystal X-ray diffraction (SCXRD), powder X-ray diffraction (PXRD), differential scanning calorimetry (DSC) and FT-IR spectroscopy. Structural analysis reveals that position of hydroxyl group governs hydrogen bond synthon present in the cocrystals/ cocrystal hydrate system. ETZ•24DHBA is having unusual amide-amide catemer synthon and is 3D isostructural to the reported ETZ•4HBA cocrystal. Solubility study shows that ETZ•35DHBA cocrystal is 13 times more soluble in water compared to pure ETZ. Solubility order of ETZ cocrystals along with pure ETZ can be represented as ETZ•35DHBA >ETZ•24DHBA >ETZ>ETZ•FRA, and follows the trend of coformer solubility.[3]


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