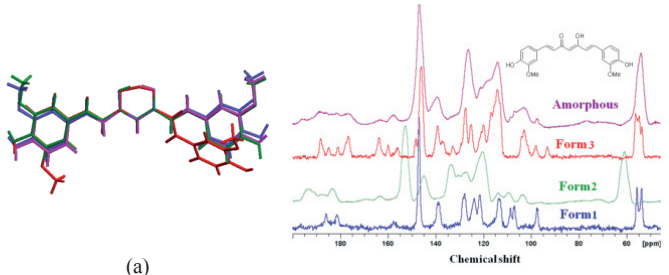
low bioavailability due to poor absorption. Curcumin decomposes upto 90% in pH 7.4 buffer solution within 30 minutes. Polymorphs and cocrystals were screened to improve stability and bioavailability of curcumin. The crystal structure of Stable form 1 (Z'=1) of Curcumin is reported in literature.[2] Single crystals of a new polymorph (form 2) were crystallized in the orthorhombic space group $Pca2_1$ (Z = 8, Z' = 2) upon attempted cocrystallization of curcumin with 4-hydroxypyridine in EtOH at room temperature. The same form 2 was obtained from DMSO at room temperature and also from a saturated solution of curcumin in EtOH. A third polymorph of Curcumin (form 3) was obtained with 4,6-dihydroxy-5-nitropyrimidine as the coformer, now in space group *Pbca* (Z = 8, Z'=1). Torsional flexibility[3] (Fig. 1a) along the seven carbon chain connecting two phenyl rings and also in phenolic –OH group orientation suggests conformational polymorphs of Curcumin. In the crystal structures, all the forms have similar O–H···O hydrogen bond between phenolic-OH and carbonyl group but differ in the C–H···O interaction. Curcumin amorphous form was also obtained by cooling of the melt phase. All the four forms are well characterized by IR, Raman and ss-NMR spectroscopy (Fig. 1b), DSC, HSM, XRPD and single crystal X-ray diffraction.[4] Metastable form 2 dissolves 3.1 times faster and is 1.8 times more soluble than commercial form 1 in 40% EtOH-water medium.



(a) (b)

Fig. 1 (a) Molecular overlay and (b) ss-NMR comparison of three polymorphs and one amorphous phase of Curcumin

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Keywords: polymorphism, solubility, x-ray diffraction

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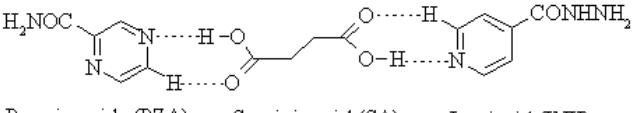
A Novel Ternary Complex Involving Two Antitubercular Drugs

Suryanarayan Cherukuvada, Ashwini Nangia, *School of Chemistry, University of Hyderabad, Hyderabad (India).* E-mail: chsuryan@gmail.com

Pyrazinamide (PZA) and Isoniazid (INH) are the first-line antibacterial drugs used in monotherapy and also in combination to treat tuberculosis.[1] A fall in the bioavailability of Isoniazid and Rifampicin due to drug interactions in the fixed dose combination (FDC) drug formulation was reported in the literature.[1] Recently, the cocrystallization approach is under active research as a means of modulating the physicochemical properties of drugs in addition to its conferment of Intellectual Property Rights.[2] We report the usage of cocrystallization strategy for bringing combination drugs together in a crystal lattice through a GRAS (Generally Regarded As Safe) coformer. The pyridyl coformers were reported to form 2:1 binary cocrystals with homologous alkanedicarboxylic acids wherein the carboxylic acid groups on either side of the diacid hydrogen bond to each of the pyridyl moieties of two coformer molecules.[3] 2:1 binary cocrystals of INH with succinic acid and few other diacids were reported in literature[4,5] and we prepared a 2:1 cocrystal of PZA and succinic acid. We reasoned that PZA and INH can bind to the diacid groups of succinic acid on either side through acid–pyridine synthon to form a 1:1:1 ternary complex (Figure). As such, a 1:1:1 ternary complex of PZA and succinic acid and INH (PZA·SA·INH) was synthesized and characterized by x-ray powder diffraction (XRPD), differential scanning calorimetry (DSC), nuclear magnetic resonance (NMR) and Fourier transform infrared (FT–IR) spectroscopy. Whether this new supramolecular material is a cocrystal, eutectic or solid solution, is not fully established. The multicomponent adduct is found to be stable at ambient temperature and humidity and has superior intrinsic dissolution rate (IDR) than PZA and INH and their respective 2:1 binary cocrystals with succinic acid.



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Cocrystallization of GABA Adducts

Nongnaphat Khosavithitkul,[a] and Kenneth J. Haller,[b] [a]*The Center for Scientific and Technological Equipment,* [b]*School of Chemistry, Institute of Science, Suranaree University of Technology, Nakhon Ratchasima 30000 (Thailand).* E-mail: nkhosavithitkul@yahoo.com

Pharmaceutical cocrystals are crystalline molecular complexes that contain therapeutically active molecules [1]. Polymorphs [2] and cocrystals, or other engineered multicomponent crystals [3] have been demonstrated to alter properties important to the bioavailability or processing of pharmaceutical solids. The structural elements (strong hydrogen bond donor, strong hydrogen bond acceptor, and nonpolar region) of γ-amino butyric acid, GABA, are typical of small drug molecules, and GABA is a major neurotransmitter inhibitor of the central nervous system. GABA and oxalic acid, OX, were cocrystallized as part of a study on formation of cocrystals of pharmaceutically interesting molecules via supramolecular bonding. 2:1 GABA/OX was prepared by both solution crystallization and solid-state grinding, and single crystal X-ray diffraction quality cocrystals were grown from ethanol solution by slow evaporation at room temperature. The single crystal X-ray structure of the resulting transparent colorless cocrystal shows it to be the oxalate salt of γ-amino butyric acid.

The supramolecular structure contains extensive O–H···O, N–H···O and C–H···O interactions leading to an elaborate three-dimensional hydrogen bonded network. The ammonium cation participates in three separate O···H–N–H···O motifs (half of the $R_4^2(8)$ synthon [3]), but the $R_4^2(8)$ synthon itself is not found. Notable features in the structure include an $S_3^3(10)$ string containing a serpentine carboxylic acid-