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Title:	Cocrystals of Hesperetin: Structural, Pharmacokinetic, and Pharmacodynamic Evaluation
Authors:	Mandal, S. (/jspui/browse?type=author&value=Mandal%2C+S.)
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Abstract:	Cocrystallization by the solvent drop grinding technique has been employed successfully to generate highly water-soluble cocrystals of a poorly soluble nutraceutical hesperetin with different coformers, picolinic acid, nicotinamide, and caffeine. The miniscule amount of solvent (ethanol here), added during grinding, expectedly imparts high molecular mobility and efficiency to the method. On the basis of preliminary indication of the phase transformation by differential scanning calorimetry, these cocrystals were further characterized by Fourier transform-infrared and solid state NMR spectroscopy. However, the final structural confirmation of these distinct cocrystalline forms was provided by either single crystal X-ray diffraction (XRD) for HESP-PICO or powder XRD data in Material Studio software to generate the crystal structure of HESP-NICO and HESP-CAFF. The data revealed the existence of supramolecular synthons established by novel hydrogen bonds between hydroxyl groups of hesperetin with acid or amide carbonyl (C═O), and/or amidic NH2, and/or pyridine/aromatic nitrogen (Naromatic) of coformers. Dissolution studies of cocrystals in aqueous buffer showed maximum concentration of hesperetin to be nearly 4–5 times higher than the pure substance. This has led to optimized pharmacokinetics as exhibited by improved relative bioavailability (HESP-PICO:1.36, HESP-NICO:1.57, HESP-CAFF:1.60). Furthermore, the enhanced antioxidant and antihemolytic effect, coupled with the protective action against inflammation, signifies the development of a clinically useful and a pharmaceutically acceptable form of hesperetin.
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