Enhancement of Bioavailability of Poorly Soluble Naringenin by Co-crystal Technology

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Abstract:

Naringenin, a biologically active flavonoid found in citrus fruits, has demonstrated diverse therapeutic properties including antioxidant, anti-inflammatory, anticancer, and metabolic effects. However, its poor aqueous solubility and limited oral bioavailability significantly hinder clinical translation. Pharmaceutical co-crystallization, a solid-state modification technique involving the combination of active pharmaceutical ingredients with suitable coformers, has emerged as a promising strategy to enhance the solubility, dissolution rate, and bioavailability of poorly soluble molecules. This study investigates the application of co-crystal technology to improve the physicochemical performance of naringenin. A series of naringenin co-crystals with Generally Recognized as Safe (GRAS) coformers such as sorbitol, ascorbic acid, and oxalic acid were synthesized using solvent evaporation technique. Co-crystals were characterized by differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD), Fourier-transform infrared spectroscopy (FTIR), and dissolution studies. Among the co-crystals studied with various co-formers, naringenin plus ascorbic acid (1:2) demonstrated the lowest particle size (i.e., highest surface area), signifying the most efficient reduction in particle dimensions. In vitro studies further confirmed significant enhancement in solubility (99.5% drug release, significantly higher than the 47% observed in the crude naringenin). The findings support the potential utility of co-crystallization in developing improved oral delivery systems for naringenin and similar biopharmaceutical class II compounds.

Keywords:

Co-crystal, flavonoid, naringenin, poor solubility, solid-state modification.