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Physicochemical characterization and dissolution studies of terbinafine hydrochloride–cyclodextrin complexes prepared by solvent-free co-grinding

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The purpose of this study was to prepare terbinafine hydrochloride (TER) solid binary systems with amorphous cyclodextrin derivatives (hydroxypropyl-β-cyclodextrin (HPBCD), heptakis(2,6-di-O-methyl)-β-cyclodextrin (DIMEB)) by co-grinding and perform analytical studies. Cyclodextrin–TER complexes were prepared in the 1:1 molar ratio. The products were investigated for both solid phase characterization (differential scanning calorimetry (DSC), X-ray powder diffractometry (XRPD), hot-humidity stage X-ray powder diffractometry (HOT-XRPD), Raman spectroscopy, Fourier transform infrared spectroscopy (FT-IR)) and dissolution properties (dissolution studies). DSC and XRPD studies indicated that with the increasing grinding time the crystallinity of products gradually decreased, and the products were completely amorphous after 75 minutes of grinding. HOT-XRPD studies were carried out in a wide temperature range and revealed that product containing HPBCD remained amorphous with the increasing temperature, while in the case of DIMEB the complex recrystallized in a different crystalline phase. Raman and FT-IR spectroscopy were used to investigate the molecular interactions between the components. Both products presented a notable improvement in its dissolution rate, and the solubility of TER increased both in simulated gastric and intestinal fluid, depending on the dissolution medium. Co-grinding is a solvent-free method to prepare stable amorphous cyclodextrin complexes and improve solubility and dissolution ratio. This could cause enhanced biopharmaceutical properties of the active ingredients in solid pharmaceutical products.

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