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Ternary systems of terbinafine hydrochloride inclusion complexes: preparation, solid-state characterization, dissolution studies

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Cyclodextrins (CDs) are cyclic oligosaccharides with the ability to modify the physicochemical characteristics of low-soluble drugs via the formation of inclusion complexes. Applying a third component (e.g., polymers, organic acids) may increase the solubility of the complexes. These are usually produced using an organic solvent-requiring method, but there are environmentally friendly, solvent-free methods, such as co-grinding.

In this study, our aim was to prepare terbinafine hydrochloride (TER) containing ternary cyclodextrin systems via co-grinding technology and evaluate physicochemical properties by several analytical tools. As excipient CD derivative, sulfobutylether-β-cyclodextrin (SBEBCD) and two polymers (polyvinylpyrrolidone, PVP; hydroxypropyl methylcellulose, HPMC) were used. Physical mixture (PM) contained TER, SBEBCD, and either PVP or HPMC. Co-ground products were prepared from the same composition by grinding PM until complete amorphization. The solvent evaporated and kneaded products were also prepared from the same composition. Products were compared to the pure drug and a marketed product. Following analytical instruments were used to evaluate solid-state properties: X-ray Powder Diffractometry (XRPD), Differential Scanning Calorimetry (DSC), Scanning Electron Microscopy (SEM). In vitro dissolution studies were performed in simulated intestinal and gastric mediums. XRPD and DSC measurements showed amorphous properties for almost every product, only kneaded products contained a small amount of crystalline TER. According to SEM images particle size of products and TER was comparable. Dissolution properties of the marketed product and TER were similar, while all the products exhibited a better dissolution rate in simulated mediums with higher solubility in the simulated gastric medium.