When drug–drug eutectic solids are formed instead drug–drug cocrystals: what to do?

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Abstract

In this work is described the formation by mechanochemical procedures of drug–drug solid forms containing metformin hydrochloride (MET·HCl) in the presence of thiazide diuretics: hydrochlorothiazide (HTZ) or chlorothiazide (CTZ). The thorough characterization indicates the formation of binary eutectic conglomerates, that we have denominated as drug–drug eutectic solids (DDESs). The DDESs were characterized by diverse techniques: thermal analysis (DSC and TGA), solid state NMR spectroscopy (ssNMR), Powder X-Ray Diffraction (PXRD) and Scanning Electron Microscopy/Energy Dispersive X-Ray Spectroscopy analysis (SEM/EDS). Intrinsic dissolution rate experiments demonstrated a slight enhancement in the % release of HTZ in the solid forms MET·HCl-HTZ 1:1 and 2:1 compared with pure drug. However, solid forms MET·HCl-CTZ 1:1, 1:2 or 2:1 showed a decrement in the % release of CTZ in the dissolution profiles.