

Poster Presentation

MS67.P28

Furosemide solvates: can they serve as precursors to different polymorphs?

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The importance of polymorphism of molecular crystals is hard to overestimate, especially when dealing with compounds used as materials or drugs. Different polymorphs of a drug substance may have different properties related to their manufacturing, therapeutic usage, or storage (density, hygroscopicity, melting points, thermal stability, solubility, rate of dissolution, surface free energy, toxicity, bioavailability, tableting, etc.). Different polymorphs, solvates, and co-crystals can be patented, and this opens the way for a competition with brand drugs. Since the energies of different polymorphs are sometimes very close, producing desirable crystalline forms is quite a challenge and can also be complicated by the phenomena of concomitant polymorphism (when several polymorphs crystallize simultaneously from the same batch), or erratic and poorly reproducible (when crystallization gives different polymorphs even at seemingly identical experimental conditions). The aim of the present study was to crystallize various solvates of furosemide, to check whether these solvates can be used as precursors for producing different polymorphs of pure furosemide on their subsequent decomposition upon heating, and to search any correlation between the crystal structures of the solvates and on the furosemide polymorphs produced by desolvation. Four solvates of furosemide with tetrahydrofuran, dioxane, dimethylformamide, and dimethylsulfoxide were crystallized. The detailed structural analysis of furosemide-containing crystal structures showed that the molecule of furosemide has a high conformational lability because of the rotations of the sulfamoyl and furanymethylamino fragments. Some of the furosemide conformations were shown to be stabilized by the intramolecular N–H•••Cl H-bond. Desolvation of the four solvates was studied by TG and X-ray diffraction and was shown to give different products depending on the precursor and particle size.

[1] V.S. Minkov, A.A. Beloborodova, V.A. Drebuschak, E.V. Boldyreva, *Crystal Growth & Design*, 2014, DOI: 10.1021/cg401257w.

Keywords: drug solvates, desolvation, polymorphism