

MS37-P01 | EXPANDING SOLID-STATE LANDSCAPE OF FLUCONAZOLE: COMBINED APPLICATION OF SOLID-STATE NMR, X-RAY DIFFRACTION AND COMPUTATIONAL METHODS TO UNCOVER POLYMORPHISM IN FLUCONAZOLE SOLVATES

Nowak, Maciej (Wroclaw Medical University, Wroclaw, POL); Nartowski, Karol (Wroclaw Medical University, Wroclaw, POL); Janczak, Jan (Institute of Low Temperature and Structure Research Polish Academy of Sciences, Wroclaw, POL); Morrill, Alexander (School of Pharmacy, Univeristy of East Anglia, Norwich, GBR); Fábián, László (School of Pharmacy, Univeristy of East Anglia, Norwich, AUT); Karolewicz, Bozena (Wroclaw Medical University, Department of Drug Form Technology, Wroclaw, POL); Khimyak, Yaroslav (School of Pharmacy, Univeristy of East Anglia, Norwich, AUT)

Fluconazole (FLU) is a drug widely used in treatment of fungal infections. Due to its activity against broad spectrum of fungi and its prescribing frequency, it was placed on the WHO Model List of Essential Medicines. The extensive polymorphism of fluconazole, which can be explained by conformational flexibility of the molecule and the presence of many hydrogen bond donor/acceptor groups, makes it an excellent model to investigate the effect of solvent properties and crystallization methods on the formation of new crystalline phases and solvates of the drug.

New solvates of fluconazole were prepared by slurring or cooling crystallization from the n-propanol, n-butanol, acetonitrile, toluene, DMSO and dichloromethane saturated solutions and analyzed using solid-state NMR and FTIR spectroscopy, single crystal and powder X-ray diffraction and thermal methods. The NMR parameters of solved structures were obtained using DFT calculations with CASTEP.

FLU forms isostructural solvates with known ethyl acetate solvate in acetonitrile, toluene, DMSO and n-butanol with a 4:1 FLU:solvent stoichiometry in cooling crystallisation experiments. This was confirmed using powder and single-crystal X-ray diffraction, solid-state NMR and FTIR spectroscopy and TGA analysis.

Second group of solvates with a 4:1 FLU:solvent stoichiometry was prepared by slurring crystallization from n-propanol, n-butanol, dichloromethane and acetonitrile. The structural similarity of the obtained solvates was confirmed by PXRD analysis. The PXRD patterns were indexed into tetragonal $P-4_2c$ space group using Expo2014 software.