

Crystal Engineering of Pharmaceutical Cocrystals

Aleksandar Cvetkovski¹, Rubin Gulaboski²

^{1,2} Faculty of Medicine, University "Goce Delcev"-Stip, Krste Misirkov bb,
p.fah. 201, Stip, Macedonia; aleksandar.cvetkovski@ugd.edu.mk;
rubin.gulaboski@ugd.edu.mk

Cocrystals have recently gained attention as attractive alternate solid forms for drug development. A pharmaceutical cocrystal is a single crystalline homogenous phase consisting of a drug molecule and ligand i.e. cocrystal former that is excipient or another drug molecule [1,2]. The different components in the cocrystal are neutral in nature when compared to salts that have ionized components. [1,2,3]. The components in a cocrystal exist in a definite stoichiometric ratio, and assemble via non-covalent interactions such as hydrogen bonds, ionic bonds, π - π or van der Waals interactions. Cocrystals thus possess different composition and structure when compared to the crystals of parent components.

Examples in the preceding section show that cocrystallization alters the molecular interactions and composition of pharmaceutical materials. As such one can expect changes in physico-chemical properties such as chemical stability [4], hygroscopicity [5], dissolution rates and solubility [6] compressibility [6] due to cocrystallization of pharmaceutical materials.

To formulate Pharmaceutical Cocrystal(s) will be used two drugs which proton-acceptor and/ or proton-donor functional groups can form syntons toward H-bonding with appropriate to them functional group encompassed in their structure. The selection of drug models will be done according to their performance of dual or complementary pharmacological responds in therapy. The formulated cocrystal of two drug molecules will present New Chemical Entity (NCE) that offer opportunity to be cover with patent protection and further to be used as single Active Pharmaceutical ingredient in combo i.e. fixed pharmaceutical formulation that perform dual action in therapy.

Research methodology encompasses the drug cocrystal screening toward applying procedures for crystallization, and analytical techniques for characterization of formed cocrystal in solid state and in solution, respectively.

Keywords: drug cocrystals, crystallization, solid state characterization

Workshop – Skopje, March 2011

References:

1. Rodríguez-Hornedo, N.; Nehm, S. J.; Jayasankar, A. Cocrystals: Design, Properties and Formation Mechanisms. In *Encyclopedia of Pharmaceutical Technology*, 3rd ed.; Swarbrick, J., Eds.; Informa Health Care: 2006; pp 615-635.
2. Vishweshwar, P.; McMahon, J. A.; Bis, J. A.; Zaworotko, M. J. Pharmaceutical Co-Crystals. *J. Pharm. Sci.* 2006, 95, 499-516
3. Aakeroy, C. B.; Fasulo, M. E.; Desper, J. Cocrystal or Salt: Does It Really Matter? *Mol. Pharm.* 2007, 4, 317-322.
4. Nehm, S. J.; Rodríguez-Spong, B.; Rodríguez-Hornedo, N. Phase Solubility Diagrams of Cocrystals Are Explained by Solubility Product and Solution Complexation. *Cryst. Growth Des.* 2006, 6, 592-600.
5. Reddy, L. S.; Bethune, S. J.; Kampf, J. W.; Rodríguez-Hornedo, N. Cocrystals and Salts of Gabapentin: *Cryst. Growth Des.* 2008,
6. Sun, C. C.; Hou, H. Improving Mechanical Properties of Caffeine and Methyl Gallate Crystals by Cocrystallization. *Cryst. Growth Des.* 2008, 8, 1575-1579