

Pharmaceutical cocrystallization: polymorphs, salts and cocrystals

A. R. Choudhury¹, M. Karanam¹, M. Joshi¹, I. Verma¹, A. Gulati², C. Budhwar³, S. Rani⁴, A. Bhalla⁴, P. Garg⁵,
A. Mukhopadhyay², K. Raza⁶, Dev, Sagarika⁴

¹Department of Chemical Sciences, Indian Institute of Science Education and Research, Mohali, Sector 81, S. A. S. Nagar, Manauli PO, Mohali. Punjab, India. 140306,

²Department of Biological Sciences, Indian Institute of Science Education and Research, Mohali, Sector 81, S. A. S. Nagar, Manauli PO, Mohali. Punjab, India. 140306,

³Department of Chemistry, Indian Institute of Technology, Jodhpur, N.H. 65, Karwar, Rajasthan,

⁴MCM DAV College for Women, Sector 36, Chandigarh, Union Territory, India. 160036, India. 342037,

⁵Post Graduate Government College, Chandigarh, Union Territory, India. 160011, ⁶Department of Pharmacy, School of Chemical Sciences and Pharmacy, Central University of Rajasthan, Bandarsindri, Dist. Ajmer, Rajasthan, India. 305817.

angshurc@iisermohali.ac.in

Pharmaceutical cocrystallization has been an active field of research in the last couple of decades. A large number of research groups have been working in this area and have contributed significantly in the development of new materials derived from known active drug molecules. A number of reviews [1-3] have summarised the contributions of all the major research groups working in the area. In the last decade, our group has been involved in the development of salts and cocrystals of a library of drug molecules, which pose various challenges in formulations due to their poor aqueous solubility and low dissolution rates or high moisture sensitivity. Our experiments on fluconazole, voriconazole, valproic acid, enrofloxacin, lamivudine, amoxapine, levofloxacin, ofloxacin, etc has demonstrated a range of exciting results.

Our efforts in forming cocrystals of fluconazole (antifungal agent) with various monobasic and dibasic acids have resulted into a series of new polymorphs of the parent drug instead of formation of salts or cocrystals [4]. These results highlighted the importance of possible intermolecular interactions between the drug and the conformer in solution. In contrary, voriconazole (antifungal agent) resulted into a cocrystal with a dibasic acid. Valproic acid (mood stabilizing agent), which is liquid at room temperature, is available in the market as a sodium salt, which is highly moisture sensitive and dissolves in moisture soon. Our experiments with valproic acid resulted into stable crystalline salts with a few organic bases. Enrofloxacin, a well-known broad spectrum antibiotic, which also suffers from poor aqueous solubility, has resulted into a series of highly water soluble salts using solvent drop assisted grinding experiments [5].

Amoxapin, a tricyclic antidepressant, also suffers from poor solubility and dissolution rate. Our experiments have resulted into a few stable and highly water soluble salts of amoxapine [6]. Ofloxacin and Levofloxacin were also targeted for the formation of salts with pharmaceutically acceptable organic acids. Novel salts of these drugs were tested for their biological activity and based on enhancement in activity; salts of Levofloxacin were further tested for their activity in animal model as well. Our results indicated that the novel salts of Levofloxacin were more potent than the existing formulations.

Significant results achieved in last 10 years on these drugs from our laboratory will be highlighted in the presentation with special emphasis on their synthesis, characterization, physical and biological (both *in-vivo* and *in-vitro*) property studies of novel salts developed in our laboratory.

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