Title:	Co-crystallization, structural and physicochemical analysis of active pharmaceutical ingredients for enhanced properties
Authors:	Joshi, Mayank
Keywords:	Co-crystallization physicochemical
Issue Date:	Nov-2021
Publisher:	IISER Mohali
Abstract:	Cocrystallization is utilized to combine and optimize the properties of different compounds for specific applications such as improving energetic materials, pharmaceuticals and other compounds. One of the most widely studied applications of cocrystallization is the formation of novel materials using active pharmaceutical ingredients (API's) for modifying the structure and physical properties of the API's. Cocrystallization influences the physical properties viz; solubility, melting point, stability and bioavailability. The objective of pharmaceutical cocrystallization is to produce novel cocrystal analogs that have enhanced properties compared to the pure API's without making and/or breaking any covalent bonds. In the last couple of decades several different drug molecules were targeted for cocrystallization to improve their physical properties. Herein, in this work we have used drugs of two categories: (1) psychiatric drugs like Amoxapine (AMX), Doxepin (DOX) and Zaleplon (ZLP); (2) antibiotic drugs like Ofloxacin (OFX) and Levofloxacin (LFX). The basis of selection of these drugs was their poor solubility and dissolution rate in water. We have developed cocrystals/ salts of these drug molecules in combination with generally regarded as safe organic acid molecules by the rational use of ΔpKa rule of three and crystal engineering. These newly developed solid phases are characterized by PXRD and DSC analysis. Crystal structure analysis of the cocrystal is done by the SCXRD and hirshfeld surface analysis. Hydrogen bonding plays an important role in the formation of cocrystal/salt and contribute the most in the crystal packing of the all compounds. We have seen the hydrophilic behaviour of the cocrystals by partition coefficient. We have determined the solubility and intrinsic dissolution rate in the phosphate buffer solution at pH 7 and these physical properties are found enhanced by many folds then pure API. We have studied the biological aspect of the salts in the part 2 of the work (antibiotic drugs). MIC is found improved in E. coli and S. typhymurium bacteria for OFX and LFX. Salts of LFX are more effective in Caco-2 cell line infected with S. typhymurium and IC50 value is found up to 4 times potent then pure drug. Pharmacokinetics of the LFX salts in Balb/c mice shows hydrophilic nature and found comparable with the pure drug with improved physical properties. Biodistribution study shows LFX salts are more likely to reach in the brain and kidney then heart and liver of the Balb/c mice. These new solid phases of the API are better alternative then pure drug with enhanced physical and biological properties.
URI:	http://hdl.handle.net/123456789/4118
Appears in Collections:	PhD-2016

Files in This Item:

File	Description	Size	Format	
Mayank joshi PH16019 Thesis.pdf		9.17 MB	Adobe PDF	View/Open

Show full item record

Admin Tools

Edit...
Export Item
Export (migrate) Item
Export metadata