

MS36-P03 | MOLECULAR BASIS OF WATER SORPTION BEHAVIOR OF RIVAROXABAN-MALONIC ACID COCRYSTAL

Kale, Dnyaneshwar P. (National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar, Mohali, IND); Ugale, Bharat (Indian Institute of Technology (IIT), Ropar, Rupnagar, IND); Nagaraja, C. M. (Indian Institute of Technology (IIT), Ropar, Rupnagar, IND); Dubey, Gurudutt (National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar, Mohali, IND); Bharatam, Prasad V. (National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar, Mohali, IND); Bansal, Arvind Kumar (National Institute of Pharmaceutical Education and Research (NIPER), S.A.S. Nagar, Mohali, IND)

We aim to investigate the molecular basis of water sorption behavior of rivaroxaban-malonic acid cocrystal (RIV-MAL). It was hypothesized that the amount of water sorbed by a crystalline solid is governed by surface molecular environment of different crystal facets, and their relative contributions to crystal surface. Water sorption behavior was measured using Dynamic Vapor Sorption Analyzer. Surface molecular environment of crystal facets and their relative contribution were determined using SC-XRD and face indexation, respectively. The surface area normalized water sorption for rivaroxaban (RIV), malonic acid (MAL), and RIV-MAL at 90% RH/25 °C was 0.28%, 92.6%, and 11.1% w/w, respectively. The crystal surface of MAL had larger contributions (58.7%) of hydrophilic (*Hphi*) chemical groups, showed the 'highest' water sorption (92.6% w/w). On the contrary, RIV had larger contribution (65.2%) of hydrophobic (*Hpho*) groups and smaller surface contributions (34.8%) of '*Hphi+Hpho*' groups, exhibited the 'lowest' water sorption (0.28% w/w). The 'intermediate' water sorption (11.1% w/w) by RIV-MAL as compared to RIV, was ascribed to the increased '*Hphi+Hpho*' contributions (from 34.8% to 42.1%) and reduced hydrophobic contributions (from 65.2% to 57.9%). However, the significantly higher water gained (~39 fold) by the cocrystal as compared to RIV, despite nominal change in the surface contributions, was further attributed to the relatively stronger hydrogen bonding interaction between the surface exposed carboxyl groups and water molecules. This study highlights that water sorption behavior of the cocrystal is governed by surface molecular environment, and additionally by the strength of hydrogen bonding interactions.