Unraveling the mystery of Pharmaceutical cocrystals by analyzing intermolecular interactions via charge density studies

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The ability to alter physicochemical properties without compromising the structural integrity of an Active Pharmaceutical Ingredient (API) is an attractive prospect in pharmaceutical industry.[1] Efforts have been directed towards making molecular complexes involving the drug molecule with a component which ensures cocrystal formation. Such efforts result in getting compounds without significant alterations in the bioactivity (melting point, stability, conductivity, dissolution rate, bioavailability etc), but with a new crystal structure which is patentable. However, there are several unanswered questions like for example (1) what is the driving force which allows the formation of a cocrystal ?(2) How is this different from a salt? (3) Is there a cocrystal to salt continuum which could be traced? The industry is keen on the development and understanding of cocrystals since it opens up avenues for multiple drugs combinations blended into a single dosage. So far there are only studies which provide details of the crystallographic studies, but the real working definition for a cocrystal is missing. We have been interested in mapping the topological features of the charge density distributions in the intermolecular space between the two coformers and have come up with several clues which help in solving the mystery of formation of cocrystals. The methodology developed from both experiments using high resolution X-ray diffraction data and theoretical calculations [2] to derive features of salt- cocrystal continuum will be outlined.

References:
1. N. Schultheiss; A. Newman, *Crystal Growth & Design* . 2009, 9, 2950
2. V.R. Hathwar, Rumpa Pal and T.N. Guru Row, *Crystal Growth & Design*, 2010, *10* 3306