Poster Presentation

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Amide-pseudoamide motif in the co-crystal of theophylline and bis(amide) conformers

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Crystal engineering plays an important role in the preparation of multicomponent co-crystals with an objective to obtain compounds with enhanced physicochemical properties.[1] For synthesizing a co-crystal, a typical first step is to consider the functional groups that are present in the compound of interest and to select coformers that have complementary groups, which might be expected to form strong hydrogen bonding and/or π-π interactions. On the other hand, identifying and understanding the important motif(s) involved in such systems are of great interests. Cocrystallization of an active pharmaceutical ingredient (API) with a relevant coformer has been challenging to develop new pharmaceutical products.[2] Theophylline (THP) pharmaceuticals are utilized as bronchodilators that unwind the muscles in the breathing tubes like asthma and chronic obstructive pulmonary disease (COPD).[3] For this work, the cocrystal between THP and a new (bis)amide-polypyridyl coformer, namely 2,2'-((1,4-phenylenebis(methylene))bis((pyridin-2-ylmethyl) azanediyl)) diacetamide (2-BPXG), was selected as a model system to (a) demonstrate the presence of a rare amide-pseudoamide hydrogen bonding motif in it, (b) identify structural features by SCXRD, and (c) establish the relevant physicochemical properties by FTIR, TGA, DSC and PXRD. Through a comparison of their morphology and thermal behaviour monitored by FESEM and Hot Stage Microscopy, respectively, further bulk properties were established. Hydrogen bond propensities, Hirshfeld surface analysis and quantitative crystal structure analysis allowed us to understand the rare amide-pseudo amide interactions in detail.

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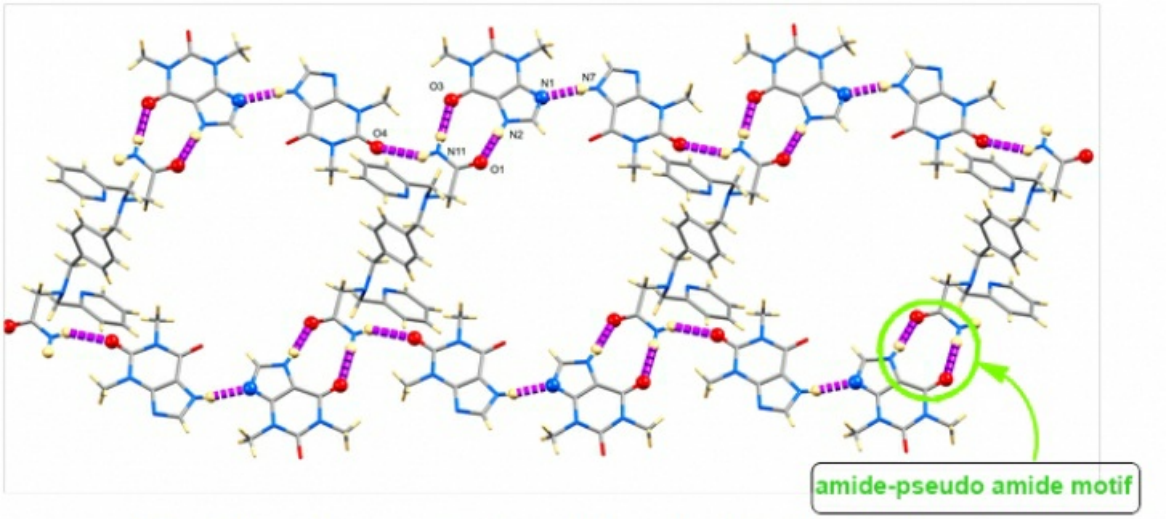

Figure. Schematic representation of strong hydrogen bonding (color: violet) interactions in the cocrystal **(2-BPXG·4THP)$_n$** forming a 1D chain.

Keywords: Amide-pseudo amide hydrogen bonding motif, Theophylline