## MS31-P05

### Discovering new cocrystals via coformer-network analysis

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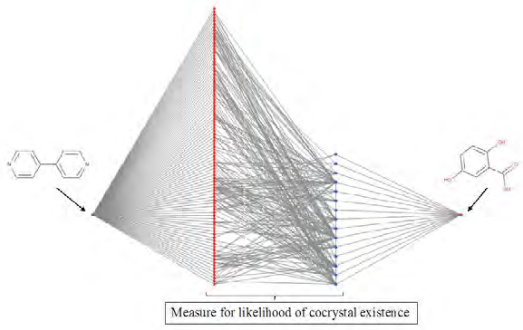
The use of multi-component crystals, such as salts, solvates and cocrystals, is an effective way of optimizing the physicochemical and biopharmaceutical properties of active pharmaceutical ingredients (APIs) without modifying the chemical nature of the APIs [1]. Since most APIs are produced in the form of racemic mixtures, the formation of multi-component crystals may also lead to purification of the enantiomers [2]. Therefore, knowledge of the solid-state landscape of an API, in terms of polymorphism and multi-component formation, is of paramount importance during the design and optimization of the final drug product.

The experimental screening of new multi-component systems, and specifically cocrystals, is a labor and time intensive job and computational tools to understand and predict new cocrystals can significantly speed up the discovery of new solid forms. In this contribution, we present a data-mining approach that exploits the vast amount of information contained in the Cambridge Structural Database [3] in order to predict new multi-component systems. First, all information on salts, solvates and cocrystals is converted into component networks. Next, the networks are analysed to discover their organizational principles and to find the best algorithm for cocrystal prediction. These algorithms are then used to discover unknown cocrystals on the basis of the coformer network (Figure). The prediction results from this new network approach were validated for both a common coformer and an API, resulting in the discovery of several new cocrystals.

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**Keywords: cocrystals, Cambridge Structural Database, networks**

## MS31-P06

### Solid form landscapes and access to polymorphs and solvates of several chlorontrobenzoic acid isomers

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Five different isomers of chlorontrobenzoic acid – 2-chloro-4-nitrobenzoic acid (2C4NBA), 4-chloro-2-nitrobenzoic acid (4C2NBA), 2-chloro-5-nitrobenzoic acid (2C5NBA), 5-chloro-2-nitrobenzoic acid (5C2NBA), and 4-chloro-3-nitrobenzoic acid (4C3NBA) were crystallized from numerous different solvents. The obtained results showed that only 2C4NBA forms more than one polymorph (polymorphs I and II) and a hydrate (these forms have already been reported in previous studies of 2C4NBA [1,2]). Meanwhile, several solvates with organic solvents were obtained for each of the isomer (6 for 4C2NBA and 2C5NBA, 4 for 4C3NBA and 3 for 5C2NBA), although again 2C4NBA formed the most - 8 (with some already reported [2]). Interestingly, all isomers formed solvate wit N,N-dimethylacetamide and N-methyl-2-pyrrolidone, while all except for 5C2NBA also formed solvates with DMF and DMSO. This observation indicates on tendency of these molecules to crystallize together with amides and sulfoxydes.

Crystal structure analysis of non-solvated forms was used to try to obtain insight into the differences observed for the solid form landscape of chlorontrobenzoic acid isomers. As crystal structures of non-solvated 2C5NBA, 5C2NBA and 4C3NBA were not available, they were determined from the PXRD measurements in capillary.

More detailed study was performed for 2C4NBA. Crystallization experiments of unsolvated 2C4NBA in several different conditions were performed from numerous solvents selected to represent different physicochemical properties. The obtained results clearly showed that the solvent as well as crystallization conditions affect the outcome of the crystallization experiment, although conclusions about the conditions for selective crystallization of polymorph II (less stable form at ambient and elevated temperature) were ambiguous.

Characterization of 2C4NBA monohydrate MH showed that it is not particularly stable. Additionally, crystallization experiments from solvent mixtures with different water activity suggested that the crystallization of MH is kinetically hindered even in conditions where MH is thermodynamically stable. Crystallization 2C4NBA from mixtures of water and solvents forming 2C4NBA solvates (e.g., DMSO, 1,4-dioxane) clearly pointed out that in slow crystallization only the solvate with the respective organic solvent could be obtained even at very high water activity, while MH could only be obtained by fast solvent exchange crystallization using excess amount of water.