Poster Presentation

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Melting point- solubility relations of cocrystals

N. Bathori[1]

[1]*Cape Peninsula University of Technology, Department of Chemistry, Cape Town, South Africa*

Active pharmaceutical ingredients (APIs) with poor physicochemical properties, such as solubility and stability, lead to the failure of many drug candidates. The design of a new solid form of these molecules, such as cocrystals may improve the required physical chemical property. The successful prediction of a new crystal structure has improved recently with the aid of high performance computing. However, the prediction of certain properties, such as solubility of the new solid form, is still a desired achievement. The melting point and solubility are crucial pharmaceutical properties related to the processability. The measurement of the melting point is a simple, fast and reliable analytical method. However, the measurement of the solubility is a more time consuming step. It is commonly accepted that a crystal with weak secondary interactions has a lower melting point and heat of fusion and is more soluble compared to those with stronger intermolecular interactions. The ultimate goal of the project is to find a link between the effortlessly detectable melting point and the more challenging solubility values by analysing and quantifying the intermolecular interactions in the cocrystal and turn the 'guessing game' into a state where we are able to 'dress' the API with the requested property via cocrystallisation. As a first attempt, we designed and synthesized a series of model cocrystals where the API is replaced by a simple chemical unit with restricted secondary interaction possibilities and conformational motions (bipyridine and its derivatives), while the cocrystallising compound was varied systematically (series of dicarboxylic acids). It is required that the type of possible intermolecular interactions are limited to make achievable the identification of the relevant differences in their strength, or their contribution to the overall changes observed during the subtle modification of the cocrystal. In the second phase, we have investigated more advanced pharmaceutical cocrystals with a variety of different additional intermolecular interactions to map the influence of these newly introduced functionalities. The solubility and melting point data were correlated to the qualitative and quantitative changes observed in the different type of secondary interactions in the crystal structures.

Keywords: cocrystals, solubility, melting point