

Cocrystal polymorphs through experiment and theory

Pharmaceutical cocrystals are promising materials composed of two or more different molecules with at least one drug molecule in the structure. Cocrystals are of increasing interest as they enable to modify important pharmaceutical properties of the materials, i.e. stability, compressibility, taste or solubility which can in turn improve drug absorption in the human body. These modifications are attractive from both academic and industrial perspective in designing novel, improved drugs as they do not comprise the therapeutic benefit of the medicines.

Up to date several experimental methods have been developed to synthesise cocrystals with little consistency in the application of the proposed experimental protocols. The published research describes experimental pathways of finding new cocrystals with very little attention on understanding the different ways of arranging molecules (building blocks) in the solids (cocrystal polymorphs). These on the other hand significantly affect the targeted properties of the final material. Furthermore, the 'trial and error' approach is used in the majority of the studies as there is a substantial knowledge gap in our ability to predict if two selected molecules will form a cocrystal and specially to predict the properties of a final product.

The proposed project aims at developing predictable ways for cocrystal formation along with an understanding of different packing arrangements of molecules in the formulated solid and the relative stability of the obtained forms. In order to achieve this, a set of eight model drug molecules and eight cofomers of different structure and properties was selected to evaluate their propensity to form cocrystals with different arrangements of molecules in the solid. By applying a vast diversity of experimental and theoretical methods we will search for new cocrystals and their modifications in order to develop a guideline for predictable screening of cocrystals and cocrystals polymorphs. The obtained materials will be thoroughly characterised with advanced analytical techniques in order to understand the correlation between structural features and pharmaceutical applicability (dissolution, water sorption and compressibility).

The proposed project combines the expertise and research infrastructure of the "Preformulation and Polymorphism" group in Innsbruck (PI Braun) and the "Drug Forms Technology Department" in Wrocław (PI Nartowski), enabling a successful advancement for a broad range of single- and multicomponent solid forms. The unique position of both collaborators facilitates in a single project to investigate all aspects of cocrystal formation from theory through a variety of experimental synthetic methods to the determination of cocrystal properties. The outcome of this project will be beyond academic interest and will improve the general understanding of cocrystal formation and the prevalence and reason for cocrystal polymorphism. The developed concepts are transferrable to other materials (agrochemicals, fine chemicals, dyes, cosmetics, energy storage materials, *etc.*).