MS32-O3 Pharma: improving and controlling properties. Cocrystals, bio-inspired MOFs and Ionic Liquids. Gabapentine a case study.

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Up to now pharmaceutical industry has relied predominantly on crystalline solids, for the delivery of active pharmaceutical ingredients (APIs), however major drawbacks exist in particular their propensity to exhibit polymorphism, their thermal and shelf stability and their solubility. These issues can have a strong impact on the physic-chemical properties of the different solid forms, causing severe bioavailability and drug efficacy problems as well as commercial losses and patent issues. Gabapentin, an amino acid-based drug used to treat neurodegenerative diseases, presenting three polymorphic forms that easily interconvert, has been extensively studied in our laboratory [1-4]. Here we present the work done in its polymorphic control and reactivity, recently recurring to ionic liquids as crystallization solvents and final pharma products. Studies on their multicomponent forms crystal forms presenting enhanced properties at different pH and new gabapentin coordination networks will be extensively presented and discussed. Our results are very exciting and their applications in the pharmaceutical field particularly promising.

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MS32-O4 Traversing the solid form jungle using the power of the Cambridge Structural Database

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The solid form jungle can be a place of high risk or untold opportunity. Uncontrolled crystal form polymorphism can have a critical impact on formulated product robustness, particularly exemplified by the pharmaceutical cases of Norvir™ [1] and Neupro™ [2], which were withdrawn from the market after the unexpected appearance of a more stable polymorph. However a detailed understanding of that same solid form landscapes can provide us with an opportunity to generate materials with desired properties by choice through crystal engineering[3].

At the CCDC we are developing structural informatics approaches that can mitigate solid form risk and move us towards the notion of solid form by design. Here the vast knowledge base of over 800,000 crystal structures of the CSD and the millions of discrete data points on the geometry of intermolecular interactions contained therein are mined to explore likely crystal packing landscapes. Such an approach complements ab-initio energy calculations yet offers the advantage of being applicable across all solid form types and accessible to solid state scientists rather than just computational specialists. For example, we have developed a CSD based Hydrogen-Bond Propensity tool which would have clearly predicted the likely existence of a more stable polymorph of ritonavir (Norvir™) [4].

Our structural informatics approach to solid form understanding is being developed under the guidance of the Crystal Form Consortium (CFC); a partnership between the CCDC and global pharmaceutical/agrochemical companies. Here we will describe the tools and methodologies developed under the CFC currently available within the CSD-Materials and CSD-Enterprise packages.

In this presentation we will review and demonstrate the impact that structural knowledge derived from the CSD can have on formulated product development as well as broad applications to crystal engineering.

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