MS34-P2 Formation of chiral and racemic multi-component crystals *via* solvent assisted ball milling

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Solvent assisted ball milling has been shown to enable the formation of multi-component crystals in cases where conventional solvent based crystallisation fails. In this study chiral starting materials, both enantiopure and racemic, are employed in co-crystal formation via ball milling. Previously we could show, that competitive ball milling of racemic mandelic acid and racemic proline amide resulted exclusively in the formation of the thermodynamically more stable diastereomeric co-crystal. This approach has now been extended to other carboxylic acids and carboxylic amides which did not form co-crystals, if only the pure enantiomers were involved.

Keywords: co-crystals, chirality, powder diffraction

MS34-P3 Growing cocrystals by stoichiometric cosublimation

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We have designed a cosublimation device, which allows for separate heating of multiple compounds sharing one water-cooled condenser as a crystallization target under vacuum. This apparatus allows scientist to optimize vapour stoichiometry of the sublimed compounds. Obviously, it is capable to cocrystallize compounds with high difference between temperatures of sublimation, which is impossible when heating a mixture or sensitive compounds. Interchangeable condensers of various shapes can be used. The temperature of each component can be optimized to reach desired stoichiometry of sublimation, which we believe is the key to reach proper crystal growth conditions. Our "home-made" apparatus is easily built and effortlessly maintained.

Multi-component crystals offer a variety of properties, which allow pharmaceutical industry to tune up many parameters like crystal morphology, stability or solubility rate. While the world of solvated structures is limited to a couple of FDA acceptable solvents, the reign of cocrystals covers dozens of acceptable compounds. Aside from routine methods for preparation of cocrystals, sublimation is the least used technique. Only few fruitful experiments were published, in which a mixture of active pharmaceutical ingredient (API) with relevant coformer was heated. In such arrangement only the compounds with similar temperature and rate of sublimation, or those having high affinity to each other, would form multi-component crystals. The effectivity of the process should improve with optimization of the vapour stoichiometry, which is usually "maintained" by empiric adjustments of the solid mixture stoichiometry. Hence, the ratio of compounds in the mixture and in the vapour is time dependent. The stoichiometry gets out of control, when the difference between temperatures of sublimation is too high. Heating the components separately allows to work under different and optimized sublimation temperatures, protects sensitive compounds and stabilizes vapour stoichiometry.

Our cosublimator and the results of cocrystalization experiments of APIs with suitable coformers will be presented.

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Keywords: multi-component crystals, cocrystals, crystal growth, sublimation