MS29-2-7 Crystal Engineering in the Design of Cocrystals / Salts of Quinoline Drugs
#MS29-2-7

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Abstract
Quinoline derivatives exhibit a very wide spectrum of biological activity, such as: antibacterial, antimalarial, antiviral. Compounds containing the quinoline system in their structure, such as Cinchona alkaloids, chlororoquine and mefloquine, have been used in the treatment of malaria for many years [1]. However, the growing resistance of malaria parasites to these drugs and the lack of a vaccine till 2021 mobilized chemists to applicate new solutions to the old drugs.
In modern drug chemistry, one of the approaches to achieving improved drugs is the formation of a co-crystal. It allows for a change in the physical properties of the parental drug, and hence the pharmacokinetic profile, without changing the main activity of the drug molecule itself. This is highly advantageous when the properties such as solubility, toxicity, and bioavailability can be improved. It also allows investigations into multiple drug therapies, in which two drug molecules could be co-crystallized, creating drug-drug co-crystal. This type of drugs combination can be very useful because it allows synergistic action, so it can highly improved pharmacological effect on the organism.
Recently, we have engineered series of quinoline drugs designing crystalline phases with modified important properties. We have selected coformers using in sillico statistical methods based on the CSD Materials module from the CSD database. We have used statistical methods for prediction of interactions between molecules using Full Interaction Maps, molecular complementarity tools, synthon analysis and estimating the possibility of formation of hydrogen bond. These methods give opportunity to predict occurrence of the most important factor in organic molecular crystals – intermolecular interactions – and how they affect on crystal structure formation. Combining of such tools gave us possibility to design new crystal phases with high probability of formation [3].
Based on initial engineering, co-crystallization or coupling of the above-mentioned drugs with selected coformers using modern crystal engineering methods were carried out under various pressure and temperature conditions. Obtained crystals were examined using X-ray diffraction studies to behold if new phases crystallized and to understand how intermolecular interactions affect on crystal packing. Thanks to this knowledge we better understand molecule behaviour in the crystalline state, so we can design and obtain more crystal phases with better and better properties until the satisfactory effect is achieved.
Our results will contribute to obtain new crystal phases with enhanced physical and/or pharmacological properties which will be used as drugs without undesirable side effects and another often presented common problems. It can clearly help todays medicine in treatment of many diseases and pharmacology in the production of improved drugs.

References
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