MS28 Navigating crystal forms in molecular and pharmaceutical materials

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Complex Structures for a Simple Organic Salt: The Extraordinary Self-Assembly of Fampridine Hydrochloride
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Abstract
Crystals are the result of a highly symmetric and periodic arrangement of molecules, assembled together via a set of intermolecular interactions and weak forces. Depending on the nature of the interacting entities, (their molecular shape and the type and the strength of the intermolecular interactions involved), atoms, molecules and ions can self-assemble generating different types of crystal packing. In general, small organic molecules tend to form simple supramolecular arrangements. Excluding rare cases, this usually produces crystal structures with simple and relatively small unit cells. Although molecular self-assembly in solid state has been extensively investigated and remains the focus of continuous and growing interest, sometime, a simple serendipitous discovery can remind us that we are still far to understand the rules governing the crystallization process.
In this contribution one of these fortuitous discoveries is described. A simple hydrochloride salt of fampridine crystallized as four different crystalline phases, two of which adopted an incredibly complex self-assembly. [1] The two structures represent the first observation of Frank-Kasper phases in small organic systems, a special class of crystalline phases previously observed only in metal alloys and different classes of supramolecular soft matter. The two FK structures crystallized from a precursor dense liquid obtained after a liquid-liquid phase separation. Investigation of the liquid phase by cryogenic electron microscopy reveals the presence of spherical aggregates, suggesting that a complex pre-organization is in place prior the nucleation. These structures, together with the experimental procedure used for their preparation, invite interesting speculation about their formation and open different perspectives for the design of organic crystalline materials.

References
[1] Montis, R., Fusaro, L., Falqui, A. et al. Nature, 2021, 590, 275–278. https://doi.org/10.1038