A Journey into the Complex World of Fampridine Salts

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Crystal engineers aim to apply the principles of supramolecular chemistry to design crystalline materials with tailored properties. Complete control over crystallization processes and the ability to predict self-assemblies in solution and solid state are critical to achieving this goal. However, Mother Nature often challenges this ambition, and although extensively investigated, self-assembly in the solid state remains a complex process that sometimes produces surprising results.

Recently, we reported on the complex behaviour of a simple hydrochloride salt of fampridine1,2, an aminopyridine derivative used for the symptomatic treatment of multiple sclerosis. This salt produced unexpectedly complex structures, including Frank-Kasper (FK) phases, previously observed only in metal alloys and soft-matter. These phases crystallised from a precursor dense liquid phase produced by liquid–liquid phase separation. Cryo-electron microscopy revealed spherical aggregates, indicating a complex molecular pre-organization in place before crystallization. In this contribution, we explore the potential reasons for this behaviour and share some of our attempts to isolate similar complex structures for other systems.

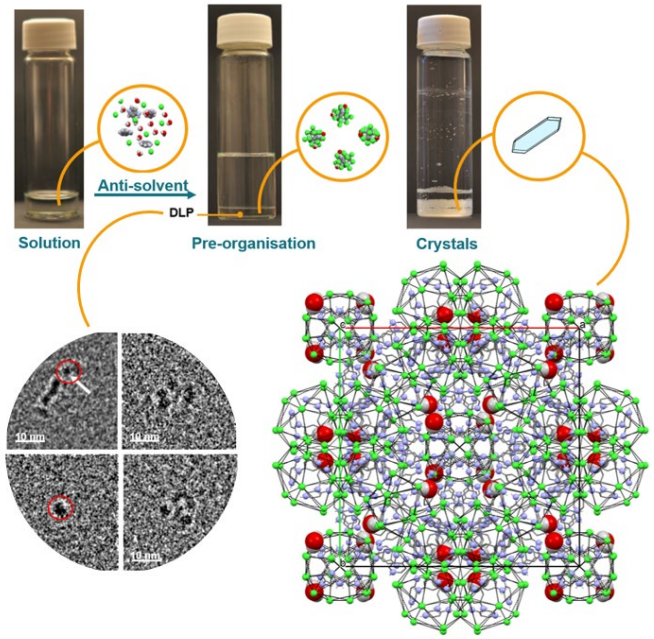

Figure 1. Example of Frank -Kasper phase for fampridine hydrochloride

[1] Montis, R., Fusaro, L., et al. (2021). *Nature.* **590**, 275.

[2] Fusaro, L., Tumanov, N. Saielli, G. Montis, R. (2023). *Pure and Applied Chemistry.*, **95**, 1043.