



CASE STUDY

Polymorphism in painkillers: a crystallographer's headache

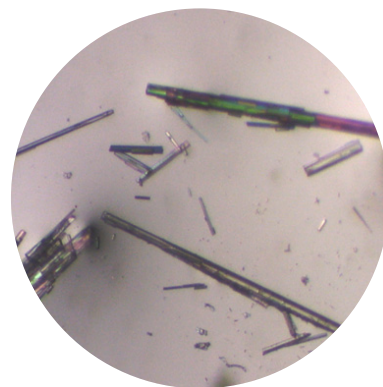
Along with many pharmaceutical materials, sodium diclofenac, a commonly used painkiller, can crystallise in many different forms depending on the manufacturing and formulation conditions. Each crystalline form may have very different biological and physical properties including bioavailability, drug delivery mechanism and shelf-life. Full characterisation and optimisation of solid forms of an API is therefore critical.



The Challenge

While some crystalline forms of sodium diclofenac are well characterised, others have eluded structure determination for many years. The particular form of interest in this case, the anhydrous form, only produced very small needle-like crystals of less than 10 microns in size which were not suitable for structure determination using laboratory sources.

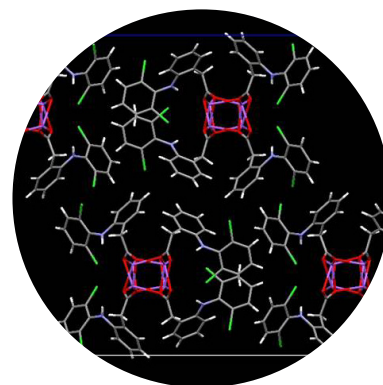
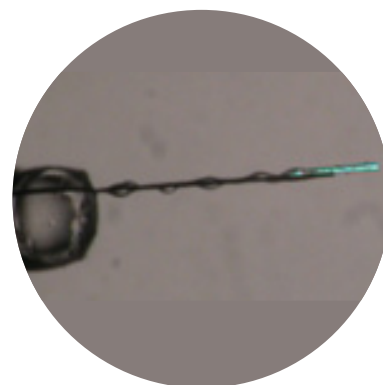
In order to determine the crystal structure, a more intense source of X-rays was required.



The Solution

SAFC Pharmorphix used Diamond to determine the single crystal structure of the anhydrous form of sodium diclofenac. The small-molecule single-crystal diffraction beamline I19 is ideally suited to collect data from such small samples and other weakly diffracting systems under a range of environmental conditions (e.g. variable temperature or high pressure).

Having gained a good understanding of the anhydrous form, Pharmorphix were able to perform controlled humidity experiments to compare the structures of all the different hydrate forms of sodium diclofenac including a previously unknown polymorph of the 3.5 hydrate.



“Pharmaceutical compounds, and in particular sodium salts, can form a wide range of possible solid state structures, sometimes yielding only very small crystals. Powder diffraction patterns are so complex that it can be difficult or impossible to be sure that you are looking at a pure phase or a mixture. Using Diamond, you get very high resolution reliable data where you simply can’t in the lab. We were able to use this information to characterise the structure of anhydrous sodium diclofenac which led us to discover a previously unknown polymorph. We can now be certain that our understanding of the crystallisation process is correct.”

Prof. Chris Frampton, SAFC Pharmorphix



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