INDUSTRIAL DEVLOPMENT PROJECTS

Physical state of drugs precipitated in confined space: A nano-focused X-ray diffraction study

THE INDUSTRIAL CHALLENGE

Disruptive Pharma develops drug formulations based on Formulite®, a mesoporous magnesium carbonate carrier into which active pharmaceutical ingredients (APIs) can be loaded. Loading poorly soluble drugs into the porous carrier can reduce or suppress crystallization, but crystalline drug domains may still form or persist depending on the formulation and processing conditions. It is therefore important to determine whether the loaded drug is amorphous or crystalline and, if crystalline, how the domains are distributed within and around individual Formulite® particles in order to clarify the precipitation mechanism.

WHY USING A LARGE-SCALE FACILITY

Conventional laboratory methods such as differential scanning calorimetry (DSC) and powder X-ray diffraction (PXRD) provide bulk-averaged information on drug crystallinity. But they cannot determine where crystalline domains occur within individual Formulite® particles, which are approximately 200 µm in size. Scanning nanofocused X-ray diffraction (nXRD) at synchrotron facilities can therefore be used to add spatially resolved structural information, allowing localized crystalline drug domains and their distribution across selected regions of individual particles to be investigated.

HOW THE WORK WAS DONE

Sorafenib was used as the model drug and loaded into Formulite® to produce formulations with different levels of crystallinity. Laboratory characterization by SEM, DSC and PXRD was used to establish their morphology and bulk solid-state characteristics and to select representative samples for synchrotron analysis. At the NanoMAX beamline of MAX IV, individual Formulite® particles were scanned in transmission using scanning nanofocused X-ray diffraction (nXRD). The ~63 nm beam was raster-scanned across selected particle regions in 100 nm steps, with a two-dimensional diffraction pattern recorded at every position. This allowed localized sorafenib diffraction signals to be converted into spatial maps showing where crystalline drug domains occurred across the investigated particle regions.

THE RESULTS AND EXPECTED IMPACT

The results increased the understanding of how formulation conditions influence whether sorafenib remains amorphous or forms crystalline domains in Formulite®. Nanofocused X-ray diffraction further revealed differences in spatial distribution of crystalline sorafenib that were not accessible from bulk measurements alone, including localized diffraction evidence at and outside projected particle boundaries. A new evaluation method converted sparse diffraction data into spatial phase-evidence maps.

This improved understanding of API crystallinity is relevant to the development of poorly soluble drugs, because their solid-state form strongly influences dissolution behaviour and, consequently, formulation performance.

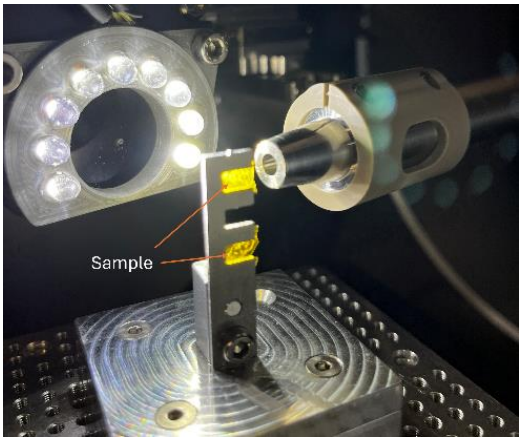


Image 1. An image of the sample (white powder) attached to the yellow Kapton film.

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