Poster Presentation

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Crystal engineering of multicomponents and the impact of high pressure

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Solid state modification such as cocrystallisation can improve the physicochemical properties of the end multicomponent construct without altering the chemical composition of the individual components. High pressure is known to alter the thermodynamic stabilities of materials with the potential for isolating materials that have not been observed before.

The challenging cocrystalline structure of the non-steroidal, anti-inflammatory indomethacin with the sweetener component saccharin was investigated up to 6.33GPa using a Diamond Anvil Cell. Previous literature has revealed indomethacin as a singular component undergoes polymorphic transformation between its α- and γ-forms below 0.4GPa, the present study investigates how the cocrystallisation of indomethacin and saccharin introduces a new stability against pressure induced phase changes.[1] Single crystal X-Ray diffraction measurements show that the co-crystal remains in the same phase throughout the compression with a triclinic, P-1 unit cell containing a busy 116 atoms with plenty of void space to allow for compression in the originally 1143.9Å3 volume unit cell. The increase in pressure up to 6.33GPa led to an overall compression of the unit cell axes with a large decrease in the b axis. The c axis lies in the same direction as the bulk of both the indomethacin and saccharin molecules making this axis fairly stable against compression. Diagonal arrangements of the molecules within the unit cell allow for sheets of void space to dissipate, contributing to the large decrease in the b axis.

Pixel calculations reveal strongly coulombic forces supporting the stability of the cocrystal between indomethacin molecules and saccharin molecules with energetic interactions bridging the two components in the cocrystalline structure. Surprisingly strong molecule to molecule dispersive interactions were found to largely be attributed to CH / π interactions between indomethacin molecules. Discussion of in situ high pressure crystallisation with the chosen components and the potential for isolating new forms concludes the compression-stability study of indomethacin and saccharin.

[1] Okumura, T. & Ishida, M. & Takayama, K. & Otsuka, M (2006). Journal of Pharmaceutical Science, 95, 689–700

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