Poster

Understanding the compression behaviour of artemisinin

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Artemisinin (ART) is widely known for treating malaria and it is well-tolerated within patients. However, it belongs to the BCS (Biopharmaceutics Classification System) class II drug meaning it has low solubility and bioavailability. Transitions between polymorphs which can be generated with pressure can affect bioavailability. Therefore, studying the mechanical properties using high pressure allows us to understand how materials react or may be altered in different conditions.

There are 2 forms of ART: orthorhombic (most thermodynamically stable) and triclinic. The aim was to investigate the effect of hydrostatic pressure on ART to elucidate the changes to the molecular packing and intermolecular interactions through the use of X- ray diffraction. In this study pressure was applied over two pressure regimes, the medium pressure (sapphire capillary cell; 0-0.12 GPa) and high pressure (Diamond anvil cell; 0-5 GPa). The first regime is close to tabletting pressures during compaction and the second regime pressures allows us to analyse the structural transformations of molecules and see what impact that has on our solid.

Results indicate that under pressure ART is compressed anisotropically and the volume was fitted to the 3rd order Birch Murnaghan Equation of State giving a bulk modulus (K0) of 2.9 (10) GPa, V0 = 1448.1 (10). This low value is reasonable for the artemisinin structure as ART does not contain any hydrogen bonds and so the crystal structure is composed of molecules interacting through van der Waals interactions. Using the PIXEL method, we have been able to rationalise the anisotropic behaviour where the molecules are stacked along the a-direction which is the strongest interaction in the solid. Neighbouring chains are related by the 21-screw axis along the b-direction which is the second strongest interaction in the structure therefore it is not very compressible. These two interactions fill half of the unit cell, and these are linked to the second half via Interaction 3 which has a larger void space that is compressible (Figure 1).

In conclusion, even in van der Waals solids the interaction energies between molecules have a significant impact on the anisotropic compression of the material.

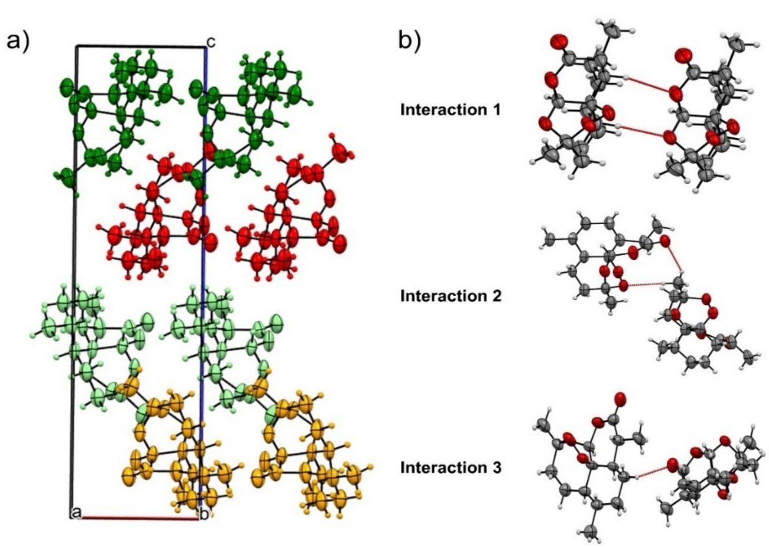

Figure 1: a) Strongest interactions in the Artemisinin structure. Interaction 1 (Similar colours); Interaction 2 (orange and light green), Interaction 3 (Light green to red); b) The interaction between the pairs of molecules.