MS35-04 | Direct Proportionality between Structural Features and Property in Multicomponent Crystals of Salicylic Acid

Nyamayaro, Kudzanai (Cape Peninsula University of technology, Cape Town, ZAF); Hearshaw, Meredith (Cape Peninsula University of technology, Cape Town, ZAF); Bathori, Nikoletta (Cape Peninsula University of Technology, Cape Town, ZAF)

Crystal engineering involves the manipulation of intermolecular interactions to design functionalised crystalline materials and has proved to be an effective tool for the modification of physicochemical properties of active pharmaceutical ingredients (APIs).

Our aim was to systematically influence the rate of dissolution of a highly soluble API using crystal engineering principles. Salicylic acid (SA) was employed to form multicomponent crystals with a series of selected cinchona alkaloids: quinine (QUIN), quinidine (QUID), cinchonine (CINC), cinchonidine (CIND), N-benzylquininium chloride (NBQUIN), N-benzylcinchonidinium chloride (NBCIND) and N-benzylcinchoninium chloride (NBCINC). These compounds were selected because of their ability to form strong intermolecular interactions with the API, i.e. salts; and because of their size and flexibility that allow them to shield the API's polar groups and thus limit the access of the solvent molecules during dissolution.

The resulting novel crystalline forms were found to be salts, and were characterised using single crystal X-ray diffraction, powder X-ray diffraction, differential scanning calorimetry and thermogravimetric analysis. The dissolution profiles of the salicylate salts, measured from an aqueous medium using high performance liquid chromatography-mass spectroscopy, show a significant decrease in the rate of dissolution of SA. Subsequently, Hirshfeld surface analysis was used as a tool for quantitative and qualitative comparison of the crystal structures. Crystal morphology studies showed that the clear disparity in the rate of dissolution between the unsubstituted cinchona alkaloid salicylates and the N-benzyl substituted cinchona alkaloid salicylates can be attributed to the presence of more faces that are covered by hydrophobic groups in the latter.