MS29-2-6 Supramolecular Synthon Promiscuity in Phosphoric Acid–Dihydrogen Phosphate Ionic Cocrystals #MS29-2-6

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Abstract
The majority of active pharmaceutical ingredients (APIs) studied as lead candidates in drug development exhibit with poor aqueous solubility, which typically results in such APIs being poorly absorbed and exhibiting low bioavailability. Salts and pharmaceutical cocrystals can address low solubility and other relevant physicochemical properties of APIs. Pharmaceutical cocrystals are amenable to design through crystal engineering because supramolecular synthons, especially those sustained by hydrogen bonds, can be anticipated through computational modelling or Cambridge Structural Database (CSD) mining.
In this contribution, we report a combined experimental and CSD study on a class of ionic cocrystals (ICC) containing dihydrogen phosphate (DHP) salts and phosphoric acid (PA). This type of ICC is present in marketed drug product, but remains understudied from a crystal engineering perspective. Ten novel DHP:PA ICCs were prepared comprising nine organic bases and one anticonvulsant API, lamotrigine. From the resulting crystal structures and a CSD search of previously reported DHP:PA ICCs, 46 distinct hydrogen bond motifs (HBMs) have been identified between DHP anions, PA molecules, and, in some cases, water molecules. Our results indicate that although DHP:PA ICCs are a challenge from a crystal engineering perspective, they are formed reliably and, given that phosphoric acid is a pharmaceutically acceptable coformer, this makes them relevant to pharmaceutical science.

References
Haskins M. M., Lusi M. and Zaworotko M. Crystal Growth & Design 2022, 22, 5, 3333-3342