MS28-1-13 Rationalising the formation of co-crystals of nicotinamide and isonicotinamide
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Abstract
The creation of multicomponent crystals forms has provided an avenue that has become increasingly important in improving many physiochemical drug properties, such as aqueous solubility and bioavailability[1]. To further enhance the discovery of new multi-component forms, understanding intermolecular interactions, particularly hydrogen bonding is pivotal. We selected two common, GRAS (generally recognised as safe) cocrystal coformers from the Cambridge Structural Database (CSD)[2]; Nicotinamide (NA) and Isonicotinamide (INA) which have 178 and 233 cocrystals respectively. These coformers have the same chemical composition, except for the position of the nitrogen in the pyridine ring. Interestingly, they exhibit different hydrogen bonding, even with the same cocrystal coformer. This phenomenon is unexpected, as conventional cocrystal formation is synthon based[3], and with NA and INA having the same synthons, one would expect the same hydrogen bonding patterns. We analysed the hydrogen bonding of the cocrystals reported in CSD, and determined which synthons are preferred in NA and INA. To probe this further, we synthesized cocrystals of these coformers with 7 Active Pharmaceutical Ingredients (APIs) via liquid assisted grinding in different stoichiometric ratios, namely 1:1, 1:2, 2:1 and 1:3. The results of these crystallization experiments were analysed using DSC, PXRD, Solid-state NMR and SCXRD to ascertain the effect the varying of stoichiometry has on cocrystal formation.

References
1. Kavanagh, O. N.; Croker, D. M.; Walker, G. M.; Zaworotko, M. J., Pharmaceutical cocrystals: from serendipity to design to application. Drug Discovery Today 2019, 24 (3), 796-804.
2. Groom, C. R.; Bruno, I. J.; Lightfoot, M. P.; Ward, S. C., The Cambridge Structural Database. Acta Crystallogr. Sect. B-Struct. Sci.Cryst. Eng. Mat. 2016, 72, 171-179
3. Desiraju GR. Supramolecular Synthons in Crystal Engineering—A New Organic Synthesis. Angewandte Chemie International Edition in English. 1995;34(21):2311-27.

Structure of Nicotinamide and Isonicotinamide