MS29-1-4 Crystal engineering of pharmaceutical ICCs involving $NH^{+}\cdots N$ heterosynthons: antifungal agents as case studies
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Abstract
During recent decades, crystal engineering, which is the understanding and exploitation of intermolecular interactions to design molecular solids [1], has shown to be a very successful strategy for the formation of new materials with desired properties. In this context, the discovery of multi-component molecular solid forms of active pharmaceutical ingredients (APIs) [2], particularly ionic cocrystals (ICCs) [3], expands the possibilities for improving API physicochemical properties without requiring chemical modification. Herein we report the design and synthesis of a new family of ionic cocrystals (ICCs) containing miconazole (MC) and econazole (EC) (the imidazole-based antifungal drugs with poor aqueous solubility). Fourteen new ICCs of MC and EC, formed by combining a series of imidazole/ 1, 2, 4-triazole-based coformers with hydrobromic acid or hydrochloric acid, were identified, as well as five new salt forms of these APIs. A charge-assisted $NH^{+\cdots}N$ supramolecular heterosynthon is detected in all but one of them. Detailed investigations of the crystal structures and packing of these ICCs demonstrated that the nature of the model compounds used in ICCs could play a significant influence in modifying physicochemical properties. This novel design strategy can pave a facile route for designing and synthesizing novel multi-component crystals of several clinical medicines containing azole rings that suffer from poor physicochemical properties.

References
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