Poster Presentation

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Celecoxib cocrystal polymorphs†

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Celecoxib (CEL) is a well-known nonsteroidal anti-inflammatory drug (NSAID) and selectively used from the cocxib family. It is a specific COX-2 inhibitor for pain and inflammation without inhibiting COX-1. A major downside of this popular NSAID is its poor aqueous solubility (9 mg L−1), which limits bioavailability (40%). Several methods were attempted in recent past to overcome solubility issues of the drug. A metastable form-IV showed four times greater solubility and improved bioavailability compared to commercial CEL form-III. Cocrystal of CEL with nicotinamide (CEL–NIC) is reported, but it rapidly dissociates to form-III.[1] Cocrystals of the CEL were screened in this study to improve the poor aqueous solubility and bioavailability through crystal engineering approach of supramolecular synthons.[2] Cyclic syn-carboxamides (with five to eight member ring lactams) produced cocrystals of CEL with different supramolecular synthons were reported.[3] Among them valerolactam (VLM) gave trimorphic cocrystals which showed synthons of sulfonamide/syn carboxamide functional groups (dimer and catemer) others gave only single form exclusively. The alteration of the coformer ring size offers crystal engineering approach to form sulfonamide-syn carboxamide supramolecular synthons sustained by SO2N–H···H–N–C=O hydrogen bonds. Binary systems including trimorphic cocrystals were characterized by FT-IR, PXRD, DSC and Hirshfeld surface analysis and finally confirmed by single crystal X-ray diffraction. Solubility and dissolution study of all the cocrystals and API carried out in 50% EtOH-water medium. Interestingly, we found there is a correlation between Hirshfeld surface analysis of F···H, O···H with the cocrystals stability following the order CEL–VLM-I>CEL–CPR>CEL–VLM-II (39.8>38.1>34.5%). The 2D finger print Hirshfeld % follows the stability order of the trimorphic cocrystals examined.

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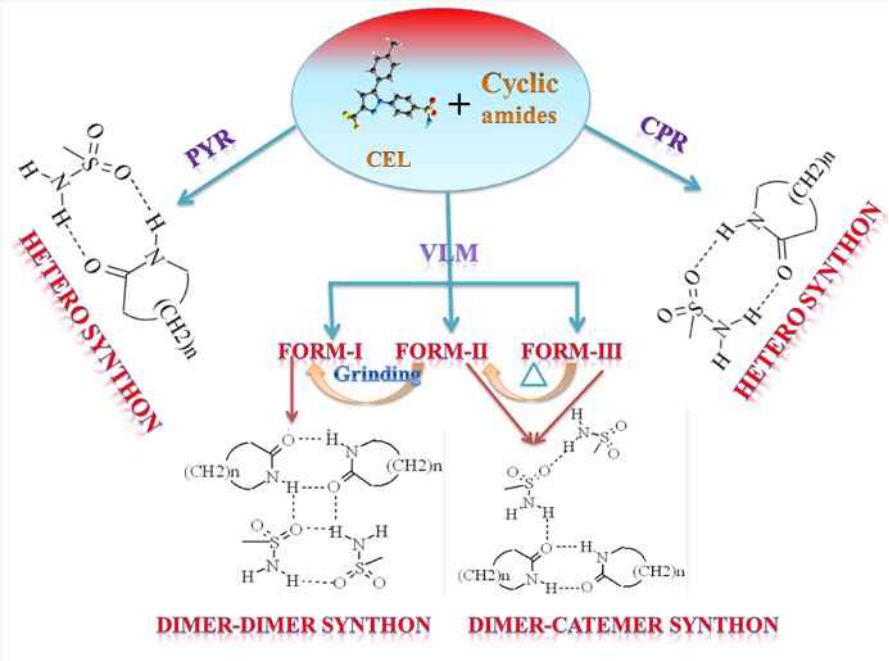

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