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A similar cocrystal design strategy for two different antipsychotic drugs

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Identification of robust intermolecular interactions which drive the crystallization process is the central theme of crystal engineering [1] and has a direct relevance to the pharmaceutical solid dosage forms. Herein we discuss about the strategies we followed to design novel cocrystals of two antipsychotic drugs, aripiprazole and olanzapine, based on the ability of the drugs to form favorable hydrogen bonding interactions with the coformers. Both drugs have the donor-acceptor disparity in their polymorphic crystal structures and as a result a strong hydrogen bonding acceptor (piperazine/diazepine nitrogen) is left unutilized. This disparity is overcome by co-crystallization of the drug with a strong donor hydroquinone and other aromatic hydroxyl molecules to facilitate the robust phenol-piperazine and phenol-diazepine synthons which could easily compete over the self complementary synthons of the parent drug molecules. As per the strategy, we were able to obtain several novel cocrystals with the expected hydrogen bond motifs. A combined crystallographic, spectroscopic and thermal investigation was carried out to establish the structure-thermal property correlation in both the systems. The crystal structure analysis allowed us to identify underlying structural features for the melting point alteration in aripiprazole cocrystals [2] and the desolvation behavior of olanzapine ternary cocrystals. [3] The higher melting cocrystals of aripiprazole were noticed in structures sustained by strong helical networks of O–H···N and O–H···O hydrogen bonds along the three-dimensional space and lower melting cocrystals were noticed when strong hydrogen bonds are restricted to two-dimensional layers. Likewise, the different thermal behavior of ternary cocrystal polymorphs of olanzapine drug were linked to the intermolecular contacts and location of toluene in the open channels of cocrystal polymorph II vs. closed cavities of polymorph I.

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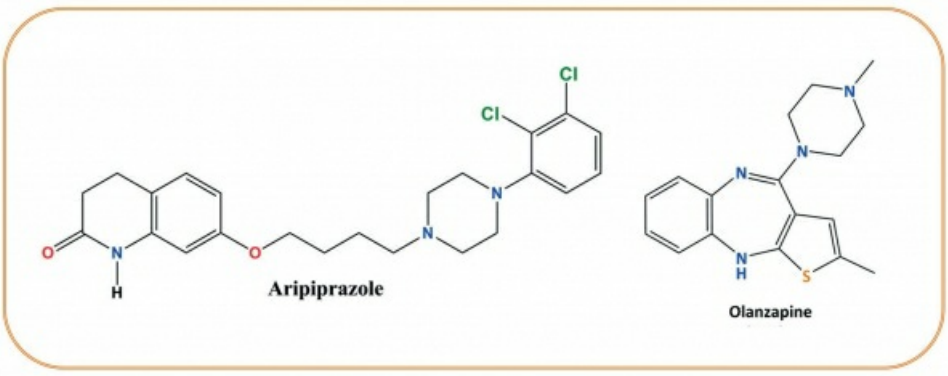
[3] Nanubolu, J. B. & Ravikumar, K. (2016), CrystEngComm, 19, 355-366.



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