

Understanding rationale behind carbamazepine cocrystallization with acids, amides and hydrazides

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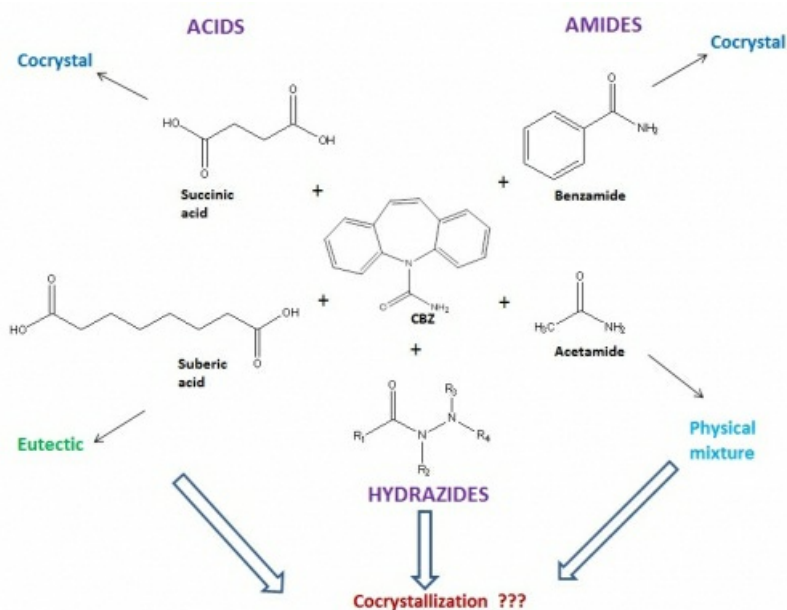
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Carbamazepine is an active pharmaceutical ingredient with anticonvulsive properties. Cocrystallization is of an API helps in fine tuning its solid-state properties such as shelf life, melting point, solubility, dissolution and bioavailability. Cocrystallization of carbamazepine with several structurally-related cocrformers belonging to class of amides and acids has been widely studied till date. However, an indepth understanding of rationale behind carbamazepine cocrystallization with acids or amides has not been exposed yet. Also, the potential of hydrazides to form cocrystals with carbamazepine has not been investigated yet. In this work, we propose to understand the rationale behind carbamazepine cocrystallization with different structurally related cocrformers. Dicarboxylic acids (Pimelic acid, suberic acid, azelaic acid, sebacic acid), tricarboxylic acids (Trimellitic acid), carboxamides (acetamide, salicylamide and p-hydroxybenzamide) and hydrazides (niazid, isoniazid and maleic acid hydrazide) has been used as cocrformers for our study. The role of number of C atoms in dicarboxylic and tricarboxylic acids, the influence of aromatic rings present in amides and the influence of -R functional group in hydrazides in cocrystallization process has been investigated in detail. Our experimental observations illustrated that some systems result in cocrystals whereas some others result into eutectics or physical mixtures. Succinic acid tends to form cocrystals whereas suberic acid resulted in eutectic as a consequence. Similarly, benzamide resulted in cocrystal whereas acetamide resulted in a physical mixture based on the DSC thermograms. An indepth understanding is being developed to identify the rationale responsible for cocrystallization with further characterization techniques. Hence, we suggest that conducting a thorough study to understand the rationale behind cocrystallization can be implemented to different drug systems which can further simplify the cocrystal screening process for structurally-related drugs in a pharmaceutical industry.

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