

Improved dissolution rates of naproxen and its cocrystals via eutectic formation

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Inadequate solubility of active pharmaceutical ingredients (APIs) is a lingering problem in many synthetic drugs, which translates into poor API bioavailability. Various strategies have been explored to alleviate the solubility problem of so-called class II APIs of the biopharmaceutical classification system. Selecting appropriate polymorphs, salts, and cocrystals of the APIs is a method to employ the thermodynamic aspect of solubility increase. Reducing the size of API particles or domains is another way to utilize the kinetic side by increasing the surface area available for dissolution. Eutectic formation with additives is one way to form finely divided micro-domains through the phase separation of the miscible liquid components upon solidification.

The present study aims to find eutectic-forming additives for naproxen (NPX), a class II API. Screening based on the proximity of the solubility parameter values identified dicarboxylic acids (succinic acid, glutaric acid, and suberic acid) as desirable additives for NPX. Binary melting diagrams were constructed to confirm the eutectic compositions, and the eutectic mixture with suberic acid was further investigated [1]. In addition, eutectic compositions of some NPX cocrystals with three pyridinecarboxamide isomers were evaluated to maximize the utility of the cocrystals [2]. The dissolution (at pH 5.0) of the melt crystallized eutectics was enhanced compared to the simple physical mixtures, which was attributed to the microscopically observed lamellar structures. The current study should support the systematic investigations of API eutectic mixtures by selecting appropriate eutectic-forming additives.

References

- [1] Kim D et al. Eutectic formation of naproxen with some dicarboxylic acids. *Pharmaceutics*. 2021;13(12):2081.
- [2] Kim H et al. Enhanced dissolution of naproxen by combining cocrystallization and eutectic formation. *Pharmaceutics*. 2021;13(5):618.