The melting point phase diagram of a cocrystal between L-Proline and Naproxen

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Abstract

This experiment focuses on a selected cocrystal system model to understand cocrystal formation using Naproxen and L-Proline. Naproxen is known as a slow-absorbing pain reliever and nonsteroidal anti-inflammatory drug (NSAID) in the profen family, and L-proline is a very successful amino acid cocrystal stabilizing coformer. Researchers interested in zwitterionic cocrystals can use them to make cocrystals due to their conventional chemical properties in active pharmaceutical ingredients (API). We will be using a melting point phase diagram and Differential Scanning Calorimetry (DSC) to collect data and other measurements and analyze their temperatures. The melting point phase diagram of the solid cocrystals will be determined by mixing different ratios of L-Proline to Naproxen to note and analyze their changing melting points. To conclude this experiment, we will establish a melting point phase diagram of organic cocrystal formation using pharmaceutical drugs like L-proline and Naproxen.

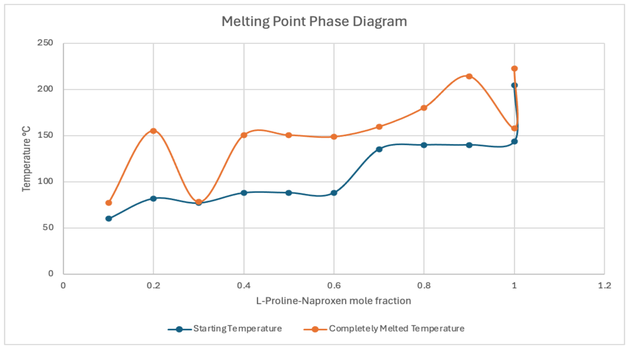
Introduction

The production of solid cocrystals using zwitterionic conformers like Naproxen and L-proline greatly influences pharmaceutical manufacturing. Cocrystals are made of many different elements, and they do not fully change the drug's chemical properties, making this approach better at dissolution, and a more eco-friendly, stable process compared to other techniques like salt formation or using more complicated solvents [1]. Crystallization does not change the therapeutic value of the drug but rather alters the API shape.

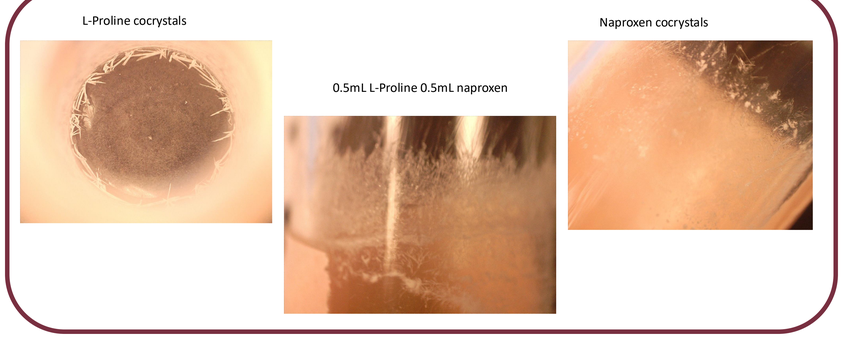
This experiment was done by gathering some cocrystal samples of L-proline and naproxen, using the liquid-assisted grinding techniques and then obtaining a melting point phase diagram to note their chemical or physical changes after boiling. The current state of the research field tells us that the most challenging part is to understand how zwitterionic conformers interact with other crystals and how that affects their boiling points. This work can result in limitations and delays with cocrystal bonding, which is why additional research needs to be done to understand these interactions in the world of chemistry research.

Methods

As observed in the above graph, the first sample measured 0.1mL of proline mixed with 0.9 mL of Naproxen, the second sample was 0.2 mL proline and 0.8 naproxen, and the third sample had 0.3ml proline and 0.7ml of naproxen etc. These 9 samples were collected and set aside, along with 2 more known samples of just 1mL Naproxen and 1mL proline. Finally, the cocrystal samples were prepped and ready to be set aside for evaporation at room temperature. This is done to give the crystals time to vaporize any unnecessary particles and dry up and solidify to a crystal shape. A bashing technique was used to gather the crystals that were stuck to the side of the tubes, and a clear capillary tube was used to get ready to melt them and note the chemical or physical changes and observe structural or thermal analysis.



Results



Discussion

Using liquid assisted grinding, we formed a cocrystal using liquid ethanol and observed its melting point. more Proline equated to a higher boiling point than naproxen cocrystals, as previously hypothesized. Based on this data and evidence, zwitterionic conformers play an essential role in determining the molecular interactions and melting points of organic cocrystals among pharmaceutical drugs like Naproxen and L-Proline. H-bonding was present more in the Proline structure but not in the Naproxen cocrystals. The intermolecular forces found in L-Proline and Naproxen have been chosen for this study because they can effectively play a part in understanding cocrystal interactions on a molecular level.

Conclusions

In conclusion, pure co-crystal formation techniques play an important role in altering and improving the characteristics of Active Pharmaceutical Ingredients (APIs), using proper experimental and lab mechanisms and formulas. This experiment focuses on a specific co-crystal formation process called Liquid-Assisted Grinding with ethanol as the solvent to gather a melting point phase diagram more effectively and efficiently, unlike Differential Scanning Calorimetry. Although DSC is a great and very useful technique in analyzing cocrystals, LAG provides a better approach to form cocrystals because it does not only focus on the thermal analysis of each solid sample but promotes faster pure cocrystal formation through grinding and a proper solvent system for the ratio in the experimental samples. Crystallization research is still growing, and with more advanced experimental techniques, LAG will be modified to a more hopeful outcome toward the future of pharmaceutical drugs.

References

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