Cocrystal Formation and Melting Point Analysis Using a Phase Diagram

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Abstract

Cocrystal formation plays a crucial role in pharmaceutical science by enhancing bioavailability and solubility of active pharmaceutical ingredients. This study investigates the melting points of cocrystals formed from L-proline and quercetin using ethanol and methanol as solvents. Cocrystals were synthesized by preparing solutions with varying molar ratios of L-proline and quercetin in alcohol. The resulting samples were analyzed using a melting point apparatus to determine thermal properties, while qualitative observations were recorded to assess structural changes. Melting point data served as an indicator of cocrystal formation; however, limited results were obtained due to the absence of distinct melting points in some cases. These findings highlight challenges in cocrystal formation and suggest further investigation into alternative methods for characterization.

Introduction

By modifying the crystalline structure of a drug, cocrystals can improve dissolution rates and properties that increase therapeutic treatment. This study focuses on the formation of cocrystals using l-proline and quercetin and employs melting point phase diagrams as a method of analysis. The melting point data serves as an indicator of cocrystal formation; however, significant limitations were encountered due to the constraints of the melting point apparatus, which was unable to measure high-temperature samples. Consequently, cocrystals with high quercetin concentrations could not be accurately assessed. These findings highlight the challenges associated with high-temperature cocrystal characterization and suggest the need for alternative analytical techniques.

Methods

- Cocrystals were formed based on solubility principles
  - Ethanol used for Quercetin
  - Methanol used for L- Proline
- Molar calculated ensured equal concentrations of each compound
- Samples were prepared with varying L-Proline: Quercetin molar fractions, decreasing by 0.10 per sample.
- Melting point phase diagram was created from observations of melting points using melting point apparatus and magnified lens
  - Melt was determined based on sample being fully liquid
- Melting phase diagram created using Microsoft Excel

Figures

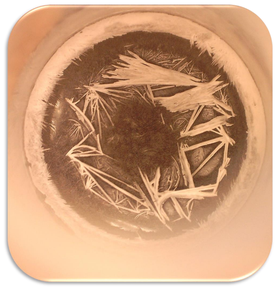

Figure 1: 1:0 Proline to Quercetin

Figure 2: 3:7 Proline to Quercetin

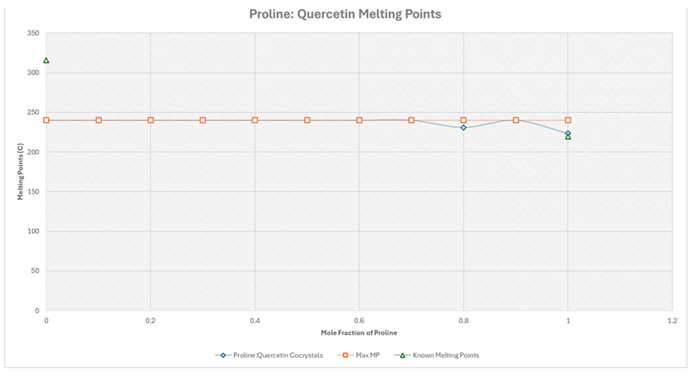

Table 1: Melting Point Phase Diagram

Discussion

A melting point phase diagram was created; however, several limitations arose due to equipment constraints. While images in Figure 1 and 2 suggest successful cocrystal formation, Table 1 highlights significant data gaps in the melting point phase diagram. Since melting points were not observed below the equipment limit of 240°C, it is likely that the actual melting points fall between those of pure proline and pure quercetin. Further research using higher-temperature equipment is needed to accurately determine these values. Despite these limitations, the successful formation of cocrystals underscores the importance of continued research, as cocrystals exhibit unique properties such as improved solubility and modified melting points

References

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- He, H., Huang, Y., Zhang, Q., Wang, J.-R., & Mei, X. (2016). Zwitterionic cocrystals of flavonoids and proline: Solid-state characterization, pharmaceutical properties, and pharmacokinetic performance. Crystal Growth & Design, 16(4), 2348–2356. https://doi.org/10.1021/acs.cgd.6b00142