

Systematic workflow for crystallization process design for a polymorphic system: An experimental case study of Imatinib mesylate

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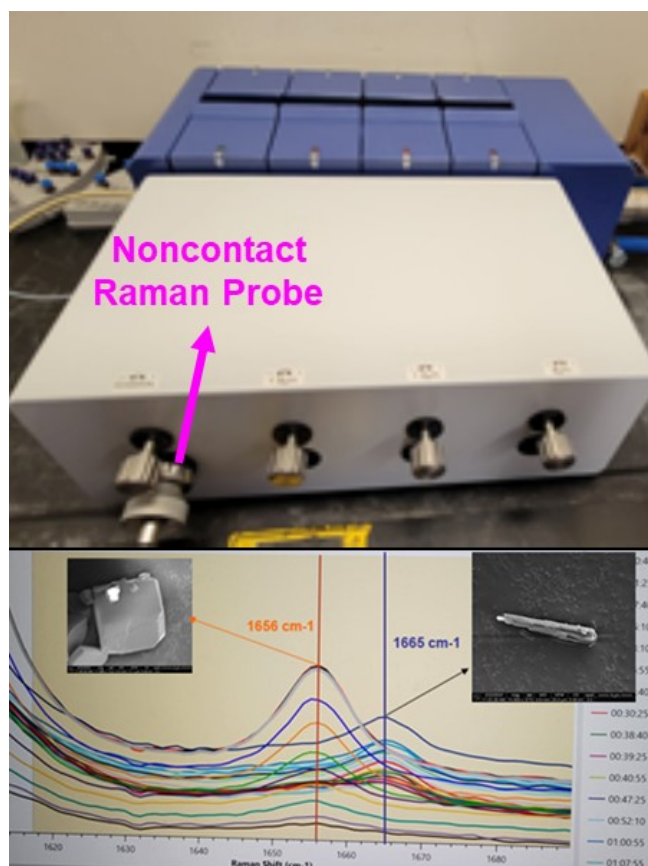
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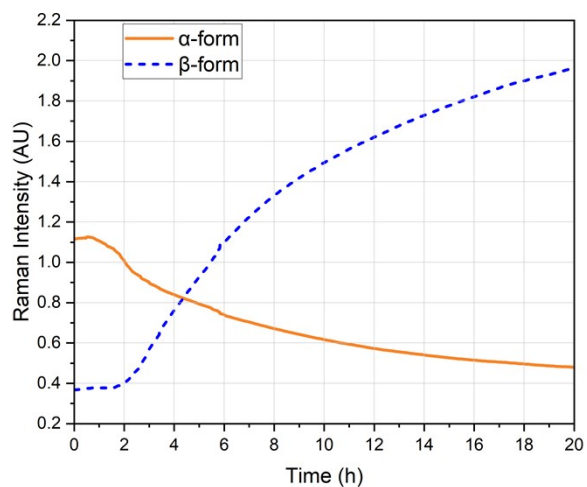
Supplementary Material

The transformation of imatinib mesylate from the metastable α -form to the thermodynamically stable β -form in methanol was monitored using in-situ Raman spectroscopy. Figure S1a shows the Raman intensity trends for the characteristic peaks of both polymorphs. As the transformation progresses, the α -form signal gradually decreases, while the β -form intensity increases, indicating a complete conversion over the course of 20 hours. A non-contact Raman probe was employed for real-time monitoring, as shown in Figure 1b, where the probe is integrated with a Crystalline PV setup. The lower panel in Figure S1b illustrates representative spectra capturing the transition between polymorphs. In addition to intensity changes, spectral evolution was also evident through peak shifts in the Raman signal, as displayed in Figure S1c. This spectral shift corresponds to changes in molecular environment and packing during the transformation and provides further confirmation of the solid-state transition from α - to β -form.

(a)



(b)



(c)

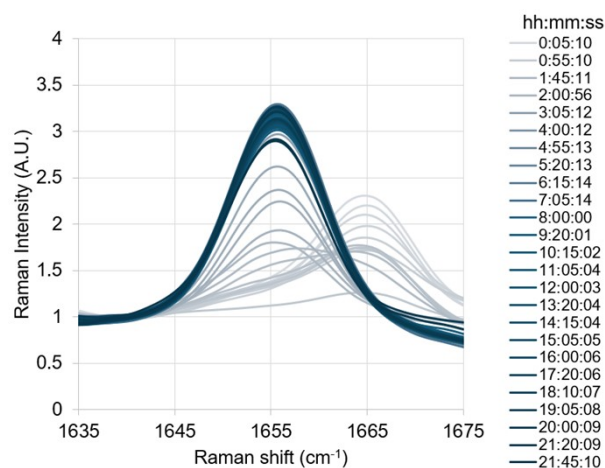


Figure S1. Transformation experiment for α -form imatinib mesylate in methanol transformed to β -form (a) Non-contact Raman probe attached to Crystalline PV (b) In-situ Raman intensity peaks for α -form and β -form (c) In-situ Raman intensity peak shift during transformation

The comparison studies of the starting materials confirm that the obtained form from the supplier is α -form. β -form is obtained through transformation of the α -form in our experiments in the laboratory. Furthermore, it is conformed that the α -form is the metastable form that transforms into more stable β -form which does not undergo further transformation during any of our experimentation. The spectra collected with an insitu Raman probe: pure solvent, pure α -form solid suspension, α -form fully dissolved in methanol, and pure β -form and methanol suspension spectra is given in Figure S2a. Figure S2b focuses on the Raman shift values between 1500 and 1700 cm^{-1} for better comparison.

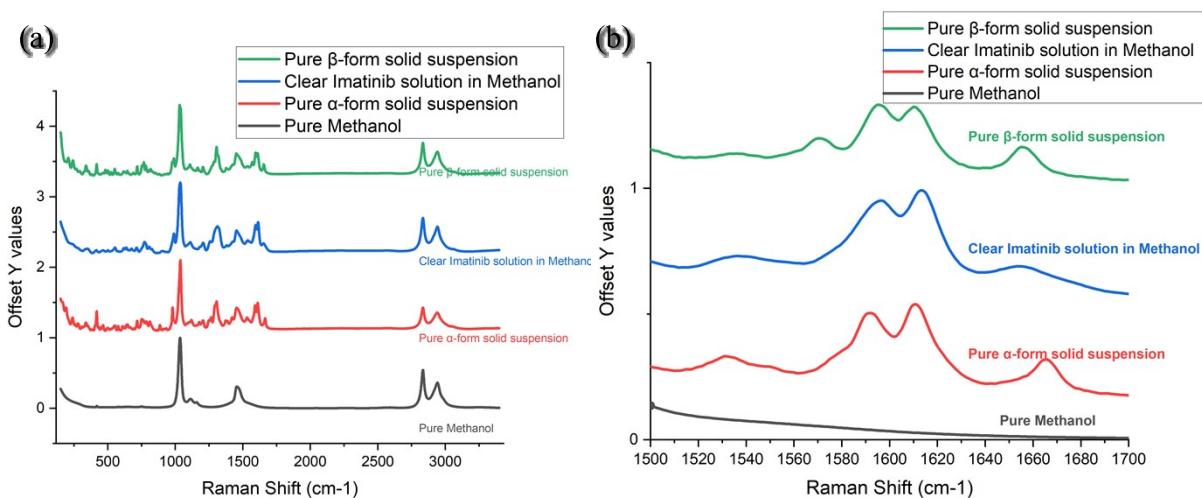


Figure S2. Online monitoring of Imatinib mesylate polymorphic forms using Raman probe in solution and solid suspension (a) range 50-3800 cm^{-1} (b) range 1500-1700 cm^{-1}