Impact of Crystal Composition Anisotropy and Solid Solutions on Drug Dissolution and Solubility

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Purpose:
Poor aqueous solubility limits the bioavailability of many active pharmaceutical ingredients (APIs). Traditional crystallization approaches often overlook the influence of compositional anisotropic crystal growth and solid solutions on drug dissolution. This study aims to (i) establish fundamental links between composition anisotropy and dissolution kinetics, and (ii) quantify how molecular guests incorporated into host crystal lattices alter solubility and dissolution performance.

Methods:
Acetaminophen - Sulforhodamine B crystals were grown by batch cooling crystallization. Single crystal aging experiments suspended solid solution crystals and pure acetaminophen references on stainless-steel meshes in isothermal solutions, with concentrations between the solubility of the pure host and the solid solution. Facet evolution was tracked by time-lapse imaging and analyzed in ImageJ, while liquid composition was monitored by HPLC before and after suspending the crystals in the solutions.

Results:
Preliminary observations showed compositional anisotropic behavior, with Sulforhodamine B rich surfaces tending to dissolve while Acetaminophen rich regions exhibited growth under the same conditions. Uneven color distributions in the shape of hourglasses across the crystals confirmed that guest incorporation was not uniform. These observations suggest that lattice disorder from guest inclusion creates direction-dependent solubility. Ongoing analyses will assess how solution composition influences growth and dissolution and whether distinct solubility limits can be assigned to specific crystal orientations.

Conclusions:
Results indicate that guest incorporation introduces orientation-dependent stability in acetaminophen crystals, with SB-rich regions more prone to dissolution and purer regions remaining stable or growing under the same conditions. These findings highlight the combined influence of lattice purity and solution composition on apparent solubility. Future work will quantify orientation-specific solubilities, apply kinetic models, and probe lattice disorder using DSC, XRD, and HPLC. This work may guide the design of solid solutions that enhance dissolution performance and improve drug bioavailability.

Keywords:
Composition anisotropy, solid solutions, dissolution, bioavailability