Title: A study of the polymorphic transformations of Sulphathiazole

Principal Focus: The objective of this project is to study the mechanisms of polymorphic transformations in the Sulphathiazole system.

Principal Outcomes to Date:

→The solution mediated polymorphic transformation of FV Sulphathiazole to FII and FIV has been fully characterized and a mechanism determined(Munroe et al. 2010).

The transformation initiates at the surface and the new polymorph grows into the mother crystal (Figure 1) as it dissolves. The mechanism suggested[1] for the transformation is as follows:

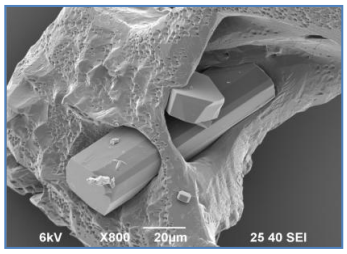

Figure 1 SEM image of FV crystal undergoing a solution mediated polymorphic transformation to FII and FIV Mother crystal FV is observed to be dissolving (pitted surface) as the new polymorphs FII and FIV grow into the mother crystal. Experiment was carried out at 10°C in Ethanol.

- *FV dissolution:* Pure FV dissolves when placed in solvent as initially the solution is undersaturated with respect to FV.
- *FII & FIV Nucleation:* The dissolution causes a localised supersaturation in the solvent with respect to the more stable polymorphs FII & FIV. Since FII and FIV are so close in stability they can both nucleate. The nucleation of these more stable polymorphs occurs on the surface of FV. All data collected supports the hypothesis of surface nucleation.
- *Continued dissolution of FV and FII & FIV growth into FV:* As FII and FIV grow inwards their growth consumes supersaturation and promotes further dissolution of FV. The localised supersaturation generated by the FV dissolution provides the path for the preferred growth of FII and FIV into the FV crystal.
- *FII and FIV growth:* Once FV has dissolved the solution is only supersaturated with respect to the more stable polymorphs. These polymorphs continue to grow until solution is saturated with respect to the more stable polymorphs.

→Another significant outcome to date has been the identification of the FIV polymorph of sulphathiazole in crystals of FII (Munroe et al. 2010).FII Sulphathiazole when isolated consistently exhibits an inclusion in the middle of the crystal(Figure 2). Analysis has shown this inclusion is in fact of FIV Sulphathiazole. FIV nucleates first as its solubility is slightly higher than FII. We have measured the solubility using gravimetric analysis and long equilibration times for FII as 0.0028 g/g ethanol and for FIV as 0.0031g/g ethanol at 10°C.

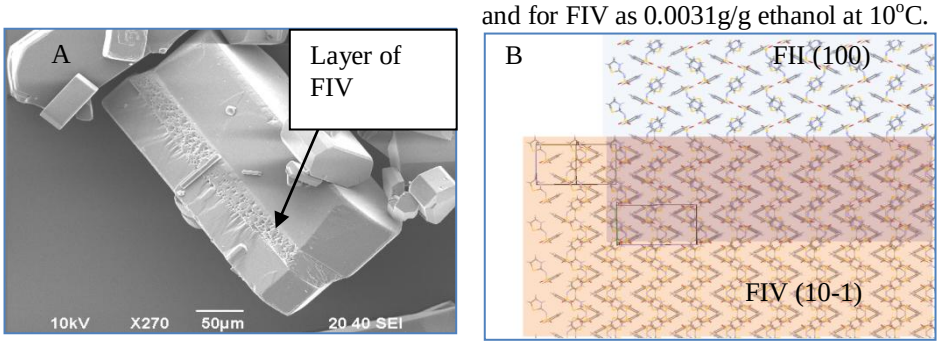

Figure 2 (A) Scanning Electron Micrographs of FII Sulphathiazole crystals exhibiting the characteristic inclusion the in centre of the crystal and (B) Mercury 2.2 representation of the molecular packing in FII and FIV Sulphathiazole viewed from the proposed faces in contact showing how the structures align. The (100) face in FII is highlighted in blue and (10-1) face in FIV is highlighted in red. The overlapping zone is highlighted in purple.

FIV facilitates the epitaxial growth of FII to the (10-1) and (-101) faces. The mechanism is summarized as follows:

- FII (100) attaches to the (10-1) face.
- FII polymorph continues to grow. FII must have a faster growth rate than FIV. As FII grows it consumes the supersaturation and this causes FIV to dissolve.
- The dissolving FIV middle layer becomes apparent because its surface roughens.
- As FIV dissolves it provides localised supersaturation for the growth of FII.
- FII therefore proceeds to grow into where the FIV layer was consuming the supersaturation and promoting further dissolution of FIV.
- FII grows from both sides and eventually meets in the middle.
- A very thin line is noted in the middle of crystals where both FII crystals have joined together after the dissolution of FIV.

Discussion: A recent review article (Croker and Hodnett 2010) on the role of surfaces in polymorphic transformations highlighted a number of recent studies which have shown the significance of the surface in the mechanism of a polymorphic transformation. This work has further evidence for the role of the surface in solution mediated polymorphic transformations.

Future Work: The triangular pitting observed on FIV during dissolution could also be studied further. Dissolution experiments could be carried out to monitor how the triangular dissolution proceeds on the surface of the FIV layer and how the surface features created through dissolution facilitate surface nucleations.

References

Croker, D. and B. K. Hodnett (2010). "Mechanistic Features of Polymorphic Transformations: The Role of Surfaces." Crystal Growth & Design **10**(6): 2806-2816.
Munroe, A., D. Croker, Å. C. Rasmuson and B. K. Hodnett. (2010). "Analysis of FII crystals of Suphatiazole : Epitaxial growth of FII on FIV." CrystEngComm **Submitted**.
Munroe, A., D. Croker, Å. C. Rasmuson and B. K. Hodnett. (2010). The Solution Mediated polymorphic Transformations of Sulphathiazole. CGOM. Poster Presentation CGOM Singapore.