Investigating the Dissolution of the Metastable Triclinic Polymorph of Carbamazepine using *in situ* Microscopy

Marcus O’Mahony,*a, b Colin C. Seaton, a Denise M. Croker, a Stephane Veesler, c Åke C. Rasmuson a and Benjamin K. Hodnett a

a Synthesis and Solid State Pharmaceutical Centre, Materials and Surface Science Institute, Department of Chemical and Environmental Sciences, University of Limerick, Limerick, Ireland. Fax: +353 61 213529; Tel: +353 61 233754; E-mail: colin.seaton@ul.ie, ake.rasmuson@ul.ie, kieran.hodnett@ul.ie.
b MIT-Novartis Center for Continuous Manufacture, Department of Chemical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Ave, Cambridge, MA 02138. Tel: +1 617 324 4525; E-mail: *omahonym@mit.edu.
c CINaM-CNRS, Campus de Luminy, Case 913, 13288 Marseille Cedex, France. Tel: +33(0)4 91 17 28 00; E-mail: veesler@cinam.univ-mrs.fr

Electronic Supplementary Information

Shown below in Fig. S1 to S3 is the sublimation of FI at 165 °C. The sublimation rate is in addition to examples showing the dissolution of FI in acetonitrile and methanol (20 °C, $\sigma_u=0.18$), also with dissolution rates measured.

![Sublimation images](image)

**Fig. S1** *in situ* microscopy for the sublimation of FI. (a)-(c) Time lapsed images under the hot stage microscope showing the FI crystal subliming at 165 °C. Inset: time of image and scale bar of 500 μm. (d) Sublimation measurements of the width ▲ and length ● of the subliming FI crystal from over time at 165 °C.
**Fig. S2.** *In situ* microscopy for the dissolution of FI in acetonitrile. (a)-(c) Time lapsed images showing the dissolution of FI in acetonitrile at 20 °C with $\sigma_u = 0.18$ (solution concentration 0.0512 g CBZ / g MeCN). Inset: time of image and scale bar of 500 μm. (d) dissolution measurement of the width ▲ and length ● of the dissolving FI crystal in acetonitrile over time. A reduced number of data points were collected due to the rate at which the dissolution proceeds.

**Fig. S2.** *In situ* microscopy for the dissolution of FI in methanol. (a)-(c) Time lapsed images showing the dissolution of FI in methanol at 20 °C with $\sigma_u = 0.18$ (solution concentration 0.0964 g CBZ / g MeOH). Inset in each image: time of image and scale bar of 500 μm. (d) dissolution measurement of the width ▲ and length ● of the dissolving FI crystal in methanol over time.
The following videos files are also available as part of the ESI:

- Sublimation of FI at 165 °C – Fig. S1
- Sublimation of FI at 145 °C – Fig. 3e-h
- Dissolution of FI in ethanol at 20°C with $\sigma_u = 0.18$ – Fig. 3a-d
- Dissolution of FI in acetonitrile at 20°C with $\sigma_u = 0.18$ – Fig. S2
- Dissolution of FI in methanol at 20°C with $\sigma_u = 0.18$ – Fig. S3
- Dissolution of FI in ethanol at 20°C with $\sigma_u = 0.045$ – Fig.5a-c
- Dissolution of FI in ethanol at 20°C with $\sigma_u = 0.045$ – Fig.5d-f
- Dissolution of FI in ethanol at 30°C with $\sigma_u = 0.023$ – Fig.5g-i