

P018 Oxcarbazepine Form III: Observation of Twisted Habit in Crystals of an Elusive Pharmaceutical Polymorph

H. Polyzois^{1,2}, R. Guo³, M. Warzecha², S. L. Price³, A. J. Florence²

¹ National Physical Laboratory Scottish Hub, University of Strathclyde, Glasgow, G1 1RD, U.K.

² EPSRC CMAC Future Manufacturing Research Hub, University of Strathclyde, Glasgow, G1 1RD, U.K.

³ Department of Chemistry, University College London, London, WC1H 0AJ, U.K.

Crystals exhibiting twisted habit have been observed at the nanoscale, mesoscale, and macroscale and pose challenges with respect to structural characterisation because of their lack of long-range translational symmetry [1]. Crystal structure prediction (CSP) investigations of an active pharmaceutical ingredient's lattice energy landscape are a potent tool for assisting experimentalists in identifying and characterising novel polymorphic forms that are thermodynamically feasible, including ones that crystallise with twisted morphologies [2-4]. Oxcarbazepine (OXCZ) is a pharmaceutical used for the treatment of epileptic seizures and three polymorphic forms have been reported, two of which (form I and form II) crystallise in the monoclinic space groups P21/c and P21 respectively [5]. OXCZ form III was originally prepared by slow evaporation from methanol solutions containing polymer additives but structure determination was not possible because of the small size and poor quality of the crystals produced. Herein, we present robust protocols for the crystallisation of OXCZ III from both solution and the vapour phase. Our efforts combined CSP studies of OXCZ with physical vapour deposition and solution-based polymorph screening experiments. Needle-like and fibre-like crystals of form III exhibiting variable twisted habit were serendipitously obtained through vapour deposition of OXCZ onto metallic substrates. By performing scanning electron and atomic force microscopy investigations we have managed to gain insight into the mechanism of formation and growth of the twisted OXCZ III crystals over the course of the deposition process.

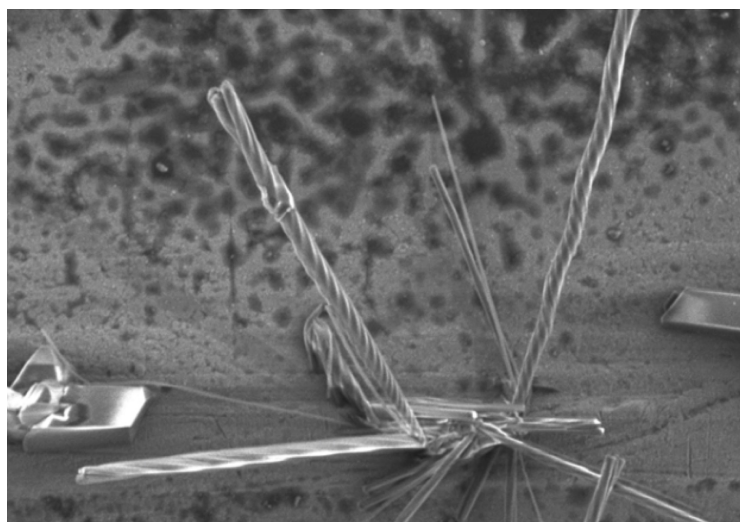


Figure 1: (SEM micrograph showing twisted crystals of OXCZ form III grown via physical vapour deposition.

References

- [1] A.G. Shtukenberg, Y.O. Punin, A. Gujral, B. Kahr, *Angew. Chem. Int. Ed.*, 2014, 53, 672 – 699
- [2] S.L. Price, *Phys. Chem. Chem. Phys.*, 2008, 10, 1996-2009
- [3] J.B. Arlin, L.S. Price, S.L. Price, A.J. Florence, *Chem. Commun.*, 2011, 47, 7074–7076
- [4] A.G. Shtukenberg, Q. Zhu, D.J. Carter, L. Vogt, J. Hoja, E. Schneider, H. Song, B. Pokroy, I. Polishchuk, A. Tkachenko, A.R. Oganov, A.L. Rohl, M.E. Tuckerman, B. Kahr, *Chem. Sci.*, 2017, 8, 4926-4940
- [5] K.M. Lutker, A.J. Matzger, *J. Pharm. Sci.*, 2010, 99, 794-803