PO A 1

Microcrystallisation
A Study of the Influence of Solvents and Substrates on Crystallisation and on the Formation of Polymorphic Forms

O.M.R. Wenger[1], A.G. Heig [2], C. Marcolli[2], M. Szelagiewicz[2]

[1] Pharmacenter of the University of Basel, CH; [2] Solvias AG, Basel, CH

A standard study of polymorphism is based on a number of crystallisation methods and normally requires one to several grams of active substance. Only a very small amount of substance is necessary for Raman microscopy. Investigations by hot-stage Raman microscopy [1] allow screening for new solid forms of thermally stable compounds by crystallisation from the melt and solid-state transformation by varying the temperature. However, investigations including solvents are not possible with this method.

The goal of our study was to miniaturise the evaporation/crystallisation method and to find out if the solvent and the substrate influence the crystallisation. We evaporated small amounts (0.5 microliter) of dilute solutions (1%) on different substrates (Ag, Au, Cu, Fe, Sn, Zn, graphite, mica, glass) and investigated the resulting solid form by Raman microscopy.

Crystals of carbamazepine and sulfathiazole were obtained by drop evaporation from minute amounts (about 5 micrograms) of substance. It was possible to assign crystal forms on the basis of Raman spectra. We observed an influence of the solvent on the form obtained, but no clear indication of an induction by the substrates was found. Other compounds and substrates need to be investigated in this way; however, this technique shows promise for the screening for new solid forms at microgram scale, including evaluation of the influence of the solvent.

[1] *In situ* characterization of polymorphic forms, the potential of Raman techniques; Journal of Thermal Analysis and Calorimetry, Vol. 57 (1999) 23-43. M. Szelagiewicz, C. Marcolli, S. Cianferani, A.P. Hard, A. Vit, A. Burkhard, M. von Raumer, U. CD. Hofmeier, A. Zilian, E. Francotte and R. Schenker