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A Combinational Approach of DSC-HSM with Image Analysis in the Study of Sulfathiazole Polymorphism

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Abstract

Polymorphism of an active pharmaceutical ingredient (API) is known to have an impact on downstream process operations, such as isolation, filtering and drying, and can affect the therapeutic properties of the final product. Therefore, it is important for pharmaceutical manufacturers to characterise extensively all known polymorphs of an API. Since all the available characterisation techniques may deliver ambiguous results, a combination of techniques is used to provide a comprehensive characterisation of the sample. A reliable technique that can quickly differentiate between different polymorphs and determine if a solid contains a pure polymorph or a mixture of polymorphs would be preferable.

Here a combination of differential scanning calorimetry (DSC) and hot-stage microscopy (HSM) coupled with image analysis has been used to investigate the polymorphism of sulfathiazole, an antimicrobial agent, which has at least four polymorphs that are well characterised and clearly described in the literature [1, 2]. The approach provides a unique insight into the polymorphic transformations and thermal behaviour exhibited by this compound. The use of light intensity profile obtained from the HSM images was calculated as the sum of the grey levels in all pixels (pixel value ranges from black = 0 to white = 255). The method provides an alternative and quantitative way to present results of HSM analysis and it was found to correspond very well with the DSC thermogram, as shown in Figure 1(a). The results of the experiments, as exemplified by Figure 1, show that sulfathiazole tends to crystallize as mixtures of polymorphs although the literature methods of producing pure polymorph were followed.

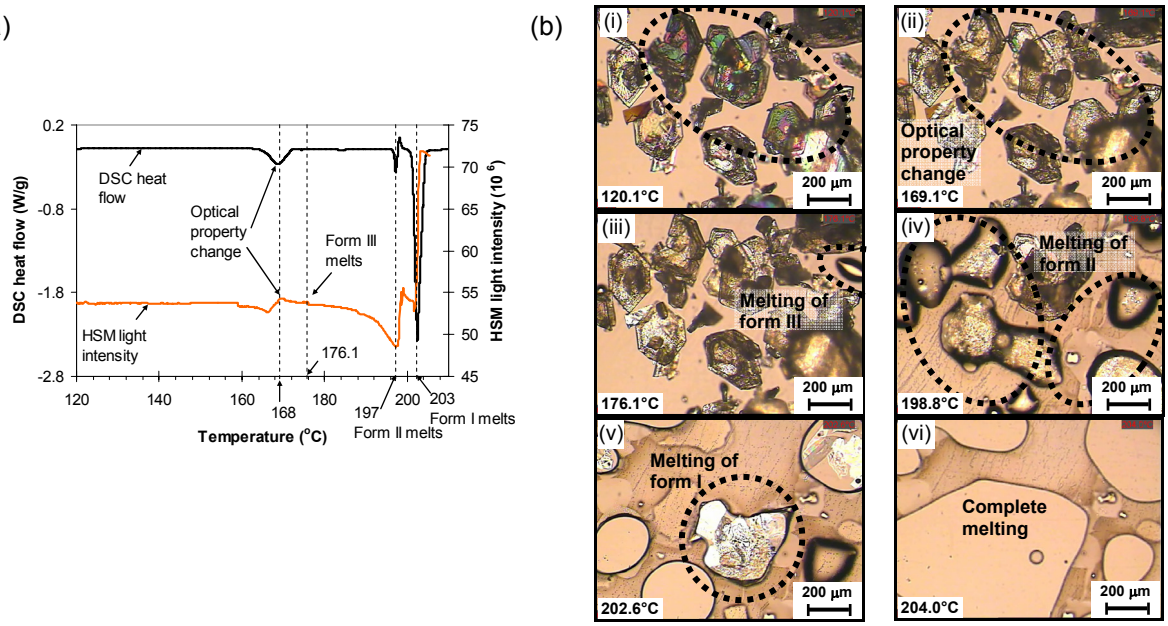

Figure 1. Analysis results of sulfathiazole crystals prepared by rapid cooling, which is supposed to produce form II: (a) DSC thermogram and HSM light intensity, and (b) the corresponding images of the crystals during HSM analysis taken at (i) 120.1°C; (ii) 169.1°C; (iii) 176.1°C; (iv) 198.8°C; (v) 202.6°C and (vi) 204.0°C.

References

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[2] Blagden, N., Davey, R. J., Lieberman, H. F., Williams, L., Payne, R., Roberts, R., Rowe, R., Docherty, R., Crystal chemistry and solvent effects in polymorphic systems: sulfathiazole, *J. Chem. Soc., Faraday Trans.*, 1998, 94(8), 1035-1044.