DISRUPTANT EFFECTS OF SURFACTANT MOLECULES INCORPORATED INTO PHENYLBUTAZONE CRYSTALS

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Crystal lattice defects develop during crystallization and also occur due to the presence of low concentrations of additives or impurities (Mullin, 1972). These imperfections, which exert major effects in formulation, processing and product performance (Huttenrauch, 1978) are difficult to examine and quantify and 'state of the art' techniques are limited.

Further understanding and quantification of crystal defects are required and York & Grant (1985) have proposed a 'disruption index' (d.i.) which, based on entropy terms, quantifies the disorder induced by low level additives in a host crystal lattice.

We report the application of d.i. to phenylbutazone samples containing Pluronic F68 (E. Kohlmann, Manchester).

Ethanolic solutions of phenylbutazone B.P. at 50°C were added to aqueous solutions of Pluronic F68 to achieve final surfactant concentrations of 0.01, 0.1, 1, 2 and 5% w/v. After cooling and filtration, the resulting crystals were dried and stored under vacuum over desiccant until assayed for phenylbutazone content and tested by differential scanning calorimetry (DSC) (DuPont 1090/91.0), at 10°C/min in pierced pans under a nitrogen atmosphere, to obtain latent heats of fusion (ΔH_f) from integrated areas under the endotherm at the melting point (Tm). The d.i. is obtained from the negative slope of the linear plot of entropy of fusion (ΔS^f) (Fig. 1), where $\Delta S^f = \Delta H_f/Tm$, versus the ideal entropy of mixing (ΔS_m^{ideal}) associated with incorporating the surfactant molecules into the host crystal lattice assuming the formation of ideal solid solution.

$$\Delta S^f = \Delta S_o^f - (d.i.) \cdot \Delta S_{ideal}^m$$

where ΔS_o^f represents the entropy of fusion of the pure sample of the host substance, and $\Delta S_m^{ideal} = -R \Sigma x_j \ln x_j$, where R is the universal gas constant and x_j is the mole fraction of the solid solution components. The numerical value of d.i. reflects the degree of disorder induced into the host crystal lattice by the guest molecules.

For the phenylbutazone-Pluronic F68 data, d.i. = 213, which compared with 7.9 for phenacetin-benzamide systems (York & Grant 1985) and 75.2 for adipic acid - octanoic acid - water systems (Grant & York 1985). The linearity of the graph supports the validity of the hypothesis, and the high d.i. figure suggests that the surfactant molecules exert a major disruptive effect on the host crystal lattice which may account for the greater than threefold increase in intrinsic dissolution rate observed at low concentrations (1% w/w:mole fraction 0.04%) of surfactant in phenylbutazone crystals.
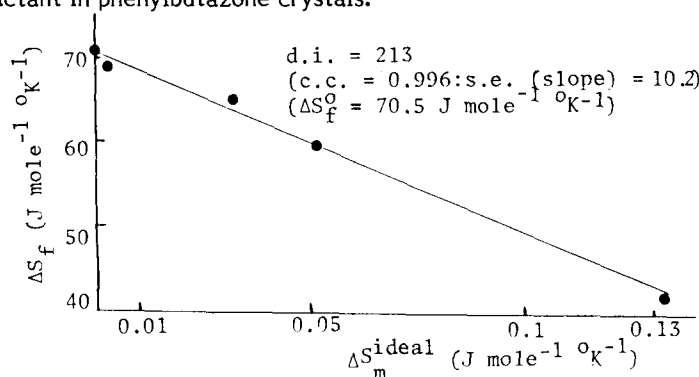

Fig. 1. Correlation between ΔS^f at melting point and ΔS_m^{ideal} for phenylbutazone-Pluronic F68 systems.

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