

## CRYSTAL ENGINEERING STUDIES WITH AN EXCIPIENT MATERIAL (ADIPIC ACID)

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The reproducible modification of crystal habit by the deliberate addition of trace amounts of non-toxic (GRAS status) impurities during crystallisation, can facilitate the production of powders with desirable physical properties.

In a previous paper (Fairbrother and Grant, 1978) the effect of traces of n-alkanoic acid additives on the habit of growing adipic acid crystals was described. At the threshold concentration (ranging from 500  $\mu\text{g/ml}$  for valeric acid to 2  $\mu\text{g/ml}$  for undecanoic acid) the additives promote the development of a number of additional crystal faces on the regular hexagonal plates. The most important of these truncate the corners formed by the (100) and (110) faces. At higher additive concentrations the adipic acid crystallises in the form of cigar-shaped spars with smoothly rounded edges. Further increase in additive concentration leads to the formation of fused pairs of spherules. An attempt has been made to study the mechanism by which the n-alkanoic acids modify the crystal habit.

Examination of the retarding effect of trace amounts of n-octanoic acid on the rates of growth of the (110) and the (100) faces of single crystals of adipic acid suggests that modification of shape results from the selective adsorption of the additive on the various faces altering their relative growth rates. The adsorption of the additives onto the faces of growing crystals in a batch crystallisation (34.0°C; 20.8% supersaturation; stirred at 200 rpm) and their incorporation into the crystals has been investigated using  $^{14}\text{C}$ -labelled n-alkanoic acids. Illustrative of this work are the results obtained with n-hexanoic acid (caproic acid). Incremental concentrations of hexanoic acid (50 to 400  $\mu\text{g/ml}$ ) in the crystallisation medium proportionately slow the rate of nucleation and retard subsequent growth of the crystals. Thus, a plot of the maximum growth rate slope of the desupersaturation curves against additive concentration is linear up to the concentration at which spherules are formed.

The rate of loss of  $^{14}\text{C}$ -hexanoic acid from the crystallisation medium parallels the adipic acid desupersaturation curve except at low levels of supersaturation where additive incorporation is greatly reduced. Thus, the adipic acid crystals contain a uniform concentration of hexanoic acid except near to the surface. Progressive dissolution experiments confirm this finding.

The effect of variables such as stirrer speed and the initial supersaturation level have been studied both in the presence and absence of hexanoic acid. Stirrer speed (200 to 365 rpm) and initial supersaturation (15 to 25.5%) are both linearly related to the maximum slope of the desupersaturation curve. Microscopic examinations have been made of all the crystals produced in the above experiments and shape factors calculated. Attempts have been made to correlate the shape factor data with crystal growth rate and additive concentration as described above.