

Table 1. *Effect of dye on dissolution of sulphathiazole Form I.*

	25°	30°	37°	40°	45°
Sulphathiazole	R	R	D	D	D
„ + dye 0.04%	R	R	R	R	D
„ + dye 0.08-0.16%	R	R	R	R	R

Table 2. *Effect of grinding time on dissolution.*

	R	R	D	D	D
0-144 h	R	R	D	D	D
144-288 h	R	D	D	D	D

(R = interfacial reaction control: D = diffusion control).

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The thermodynamic properties of sulphathiazole

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Some explanations have been suggested (Grove & Keenan, 1941; Shenouda, 1970) regarding the presence of a "melting species" in recrystallized sulphathiazole polymorph Form I. In this study, the "melting species" was observed to melt at 174° on a hot stage microscope, i.e. 8° higher than the transition temperature of Form I → Form II (mp. 201°). The proportion of "melting species" in a given batch was determined by separation of non-melted crystals after heating to 180°, followed by chemical assay of the melt remaining as a glass.

In our studies of crystal growth we are investigating the effect of dyestuffs as growth inhibitors and also the effect of prolonged grinding on growth behaviour. It was of interest therefore to see whether these two factors would affect the occurrence of "melting species".

Sulphathiazole was recrystallized from 95% ethanol containing varying amounts of malachite green. The effect of this on the proportion of "melting species" is shown in Table 1. The effect of prolonged vibration ball milling (Fritsch Pulverisette O) is shown in Table 2.

Table 1. *The effect of concentration of malachite green dye on the percentage of "melting species".*

% dye in recrystallization solvent	Melting species
0	3.52
0.04	5.13
0.16	7.25

Table 2. *The effect of milling time on the percentage of "melting species" present.*

Hours milled	Transition temp.	Melting species (% w/w)
0	166°	3.52
96	149°	—
144	148°	2.32
192	147.8°	1.00
288	147°	0.71

Dye adsorption gave an increase, and milling gave a decrease, in the percentage of "melting species" suggesting that changes in overall crystal activity had been produced. Since the usual transition temperature is only some 8° below that of the melting-point, it is more likely that low activity crystals will reach the melting-point before sufficient heat energy has been acquired for transition. The decrease in proportion "melting species" in milled samples can also be explained this way as can the reduction of transition temperature on milling, as already reported in the literature (Moustafa & Carless, 1969).

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Thermodynamic parameters for the solubilization of some steroids by non-ionic surfactants

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In a study investigating the effect of surfactants on the bioavailability of steroidal drugs the interaction of four steroids with non-ionic surfactants of general structure $C_{16}H_{33}[OCH_2-CH_2]_nOH$, ($n = 17, 32, 44$ and 63) (El Eini, Barry & Rhodes, 1973), was studied by solubility and equilibrium dialysis. Steroids solubilities in surfactant solutions (0.5-3.0% w/w) were determined between 10° and 50°. Equilibrium dialysis across a cellulose acetate membrane was investigated at 25°.

A linear relation between surfactant concentration and amount of steroid solubilized indicated that solubilization was governed by a form of the Distribution Law. This was confirmed in dialysis, where non-micellar steroid concentrations were directly proportional to micellar concentrations.

Partition coefficients of the steroids between micellar and non-micellar phases were determined by dialysis, (K_D), and by solubility, (K_S), and compared. K_S was used to calculate the free energy change for micellar solubilization ΔG° (kcal mole⁻¹) from $\Delta G^\circ = -RT \ln K_S$. The changes in enthalpy, ΔH° (kcal mole⁻¹), and entropy, ΔS° (cal mole⁻¹ deg⁻¹), for the process were derived.

n	Hydrocortisone				Dexamethasone				Testosterone				Progesterone			
	17	32	44	63	17	32	44	63	17	32	44	63	17	32	44	53
K_S	110	101	86	68	314	273	244	199	786	661	570	452	2160	1790	1550	1250
K_D	110	103	87	66	295	269	240	208	807	654	588	442	2230	1730	1400	1000
$-\Delta G^\circ$	2.8	2.7	2.6	2.5	3.4	3.3	3.3	3.1	3.9	3.8	3.8	3.6	4.5	4.4	4.3	4.2
$-\Delta H^\circ$	4.9	5.0	5.0	5.5	4.2	3.9	3.7	3.8	4.4	3.7	3.5	3.3	2.7	2.2	2.4	2.0
$-\Delta S^\circ$	7.2	7.5	7.8	10.0	2.6	1.9	1.5	2.2	1.5	-0.4	-0.7	-1.1	-6.1	-7.6	-6.4	-7.3

Mean values of ΔG° between 10°-50° were practically constant for each surfactant/steroid system. Increasing the hydrophilic chain length increased ΔG° . This may be due to the increased degree of micellar hydration with increased hydrophilic chain length (El Eini