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 $\Delta G°$ (kcal mole^{-1}) from $\Delta G° = -RT\ln K_S$.   The changes in enthalpy, $\Delta H°$ (kcal mole^{-1}), and entropy, $\Delta S°$ (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
$-\Delta G°$	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
$-\Delta H°$	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
$-\Delta S°$	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 $\Delta G°$ between 10°–50° were practically constant for each surfactant/steroid system.   Increasing the hydrophilic chain length increased $\Delta G°$.   This may be due to the increased degree of micellar hydration with increased hydrophilic chain length (El Eini

& others, 1973) thus hindering steroid incorporation. $\Delta G°$ also increased with increased steroid polarity. The steroids interacted exothermically with the surfactants.

ΔS was negative for hydrocortisone and dexamethasone and became positive for the less polar testosterone and progesterone. Two opposing factors account for this. (1) Crowding of the solubilized steroid in the micelle occurs with negative entropy change. (2) Configuration entropy of the solubilized molecules increases due to the breakup of the water structure surrounding nonpolar hydrocarbon molecules or groups. Effect 1 governs the solubilization of hydrocortisone and dexamethasone while effect 2 controls that of testosterone and progesterone.

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A method of testing the applicability of the diffusion layer dissolution model

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Fee, Grant & Newton (1973) reported an empirical equation connecting the Reynolds number, *Re*, of solvent flow and the intrinsic dissolution rate of a compressed disc of potassium chloride at 37° measured in a specially designed continuous flow apparatus. From this relationship the thickness *h* of the diffusion layer in the dissolution model of Nernst (1904) was calculated at various Reynolds numbers (Table 1). These *h* values were compared with those (Table 1) calculated from the physical constants of the system using equation (1) which Levich (1962) derived for flow past a flat disc.

$$h = 3x^{\frac{1}{2}}D^{1/3}(\eta/\rho)^{1/6}u^{-1/2} \quad .. \quad .. \quad .. \quad .. \quad .. \quad (1)$$

where *x* is the distance from the upstream edge of the disc measured along an axis parallel to the direction of flow (mean value 3.25×10^{-3} m), *D* is the diffusion coefficient of the solute (3.20×10^{-9} m² s⁻¹), η is the dynamic viscosity of the medium (6.915×10^{-4} kg m⁻¹ s⁻¹), ρ is the density of the medium (993.4 kg m⁻³) and *u* is the characteristic linear flow velocity of the system. Now *u* was calculated from *Re* using the equation

$$u = \eta Re/\rho d \quad .. \quad .. \quad .. \quad .. \quad .. \quad (2)$$

where *d* is the mean hydraulic diameter of the dissolution chamber (0.0312 m) and the other quantities are defined above.

Table 1. *Thickness* h *of the diffusion layer at various Reynolds numbers.*

Reynolds number	360	1335	3000	4500	6000
h/μm (experimental)	115	100	82	71	62
h/μm (equations 1 & 2)	265	137	92	75	65

The disagreement between corresponding values of *h* at low *Re* in Table 1 is attributed to the predominance of natural over forced convection. Considering the approximations made in deriving equation (1) the agreement between corresponding *h* values is good at high *Re* where forced convection predominates. Furthermore, the asymmetric pattern of erosion of the solid disc by the solvent is exactly as predicted by Levich (1962) for a diffusion controlled process. The validity of the diffusion layer model in the present system is supported by the effect of viscosity of the medium on the dissolution rate of potassium chloride in water (Zdanovskii, 1951).

Thus, by enabling dissolution rates to be expressed in terms of *Re* the apparatus of Fee & others (1973) provides a simple means of testing the applicability of the diffusion layer model for dissolving solids.