Assuming that drug and polymer exist as a complex in solution then it is possible that drug dissolution rate will be affected. For example, if a diffusion layer is operating, dissolution rate would be governed by the solubility of the complex and the diffusion coefficients of all species. Dissolution rates of the following non-disintegrating discs were measured

(a) allopurinol into 0·1 M HCl and into P.V.P. solutions up to 20% w/v.

(b) allopurinol/P.V.P. physical mixtures into 0·1 M HCl and into P.V.P. solutions.

Dissolution rates of allopurinol into P.V.P. solution decreased with increasing P.V.P. concentration. The presence of P.V.P. in the disc did not influence dissolution rate even when present up to 40% w/w of the disc. These findings indicate that the controlling factor in dissolution is viscosity of the dissolution medium rather than a change in diffusion coefficient of the drug due to complexation in the diffusion layer. Estimates of diffusion coefficients are required before these findings can be regarded as conclusive.

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The dissolution kinetics of sulphathiazole form I

J. E. CARLESS AND D. JORDAN

Department of Pharmacy, Chelsea College (University of London), Manresa Road, London SW3 3LX, U.K.

Work on the growth of sulphathiazole Form I under temperature cycling conditions has already been reported (Carless & Foster, 1966) and this present study was designed to investigate, in detail, the dissolution kinetics involved. Sulphathiazole Form I was prepared by recrystallization from 95% ethanol in water and characterized by differential scanning calorimetry, infrared and melting point behaviour.

Sulphathiazole discs were made at a compressional pressure of 238 kNm^{-2} and the dissolution profile determined in distilled water at 25° to 45° using a rotating disc apparatus. The theoretical rate constant K_t for the diffusion process was calculated from the Levich equation

$$K_t = 0{\cdot}620\, D^{\frac{2}{3}} \nu^{-\frac{1}{6}} \omega^{\frac{1}{2}}.$$

where ν is the kinematic viscosity and ω the angular rotation of the disc. This was compared with the experimental rate constant calculated from the Noyes-Whitney equation which assumes that diffusion control operates. Agreement between the two rate constant values at temperatures above 30° indicated that diffusion control was operating but at lower temperatures, the dissolution was controlled by the interfacial reaction. Energies of activation derived from Arrhenius plots were consistent with diffusion control and interfacial control operating at the higher and lower temperatures respectively.

Dyestuffs reduce the rate of dissolution of sulphathiazole (Piccolo & Tawashi, 1970). In this study, the presence of malachite green reduced the rate of dissolution, this being explained by the interfacial reaction control operating over the temperature range 25–45°. This was consistent with adsorbed dye interfering with the detachment of sulphathiazole molecules from the crystal surface.

Extensive grinding of the original sulphathiazole crystals resulted in the dissolution being changed from interfacial controlled to diffusion controlled. This is not unexpected since grinding will increase crystal defects and dislocations and so would be expected to enhance interfacial reaction.

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

	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.*

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

J. E. CARLESS AND D. JORDAN

Department of Pharmacy, Chelsea College (University of London), Manresa Road, London SW3 3LX, U.K.

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 1→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