

The dissolution profiles were obtained using the method of Searl & Pernarowski (1967); particle size data was obtained by wet sieving and Coulter analysis methods similar to those of Shotton & Leonard (1972).

Considerable differences were observed between batches of tablets from different manufacturers. Examination of batches with differing dissolution profiles showed no relationship between disintegration time, tablet hardness and  $t_{50}$  (time for solution of 50 mg drug).

The median particle diameter obtained after the disintegration test was inversely related to the dissolution rate expressed as  $t_{50}$ . It was also possible to relate dissolution rate to surface area of particles in the subsieve range. The size rather than total amount of particles in the subsieve range was shown to be important since there was no correlation between dissolution rate and percent total tablet weight passing through the sieves.

Comparison of tablets from the same manufacturing batch indicated that coating delayed initial disintegration but had only a small effect on subsequent disaggregation, indicating that in this instance shellacing has minimal effect on tablet breakup.

Dissolution rate of phenylbutazone tablets therefore appears to be dependent on the degree of disaggregation, rather than disintegration time.

The results are summarised in Table 1.

Table 1.

Tablet batch	disintegration time (min)	$t_{50}$ (min)	Mean particle diameter after disintegration test ( $\mu\text{m}$ )	Subsieve range		Mean tablet hardness
				Surface area ( $\text{cm}^2 \text{cm}^{-3}$ )	% Total tab wt	
A	3.2	34	280	2962	7.05	3.4
B	11.5	51	330	3112	1.97	6.3
C	> 15	231	900	1725	1.54	4.3
D	> 15	393	1350	1764	1.74	4.8
E	6.4	158	520	2664	5.54	3.2
F*	25	197	620	2850	—	—

\* F comprises sugar coated tablets from the same manufacturing batch as uncoated tablets E. All other batches are uncoated.

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#### Size analysis of sub-micron particles by centrifugal photosedimentometer

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A new centrifugal photosedimentometer is described which uses light carried from a helium-neon laser to silicon photodiodes with optical fibres. The photo-detectors are set beneath a transparent centrifuge tank containing a dilute homogeneous suspension of the material under examination and in this manner a continuous series of measurements of the optical density of the sedimenting systems can be obtained as a function of time without the need for the electro-mechanical servo-systems which have been a feature of previous designs (Groves & Freshwater, 1968). The intense monochromatic character of the laser light has improved the sensitivity of the method and particles corresponding to a Stokes' diameter of  $0.018 \mu\text{m}$  have been detected in a sample of a commercial intravenous emulsion.

The relation between the cross-sectional area of the particles obscuring the light beam and the observed optical density at a given time is complex owing to diffraction effects as the diameter of the particles approach the wavelength of the incident light. However, in

a sedimenting system under the conditions used here the particles themselves are separated out in size according to the centrifugal analogue of Stokes' Law. The relation between the time of sedimentation and the optical density is therefore a characteristic of the sedimenting system and can be used for quality-control purposes.

Some systems under investigation failed to reach their base-line values which suggested that the centrifugal force in the apparatus was insufficient to overcome the viscous drag of the suspending medium, water, for the smaller particles present. The addition of electrolyte produced a progressive decrease in the size of the particles apparently stabilized in suspension. Since this limiting size can be determined with precision, use of the Stokes-Einstein equation enables the unsolvated molecular mass of the particles to be calculated.

Table 1. *Apparent limiting Stokes' diameter of particles detected in a 1:900 dilution of 'Intralpid 10%' at a radius of 11.0 cm rotating at 3000 rev min<sup>-1</sup>.*

Diluent	Stokes' dia. ( $\mu\text{m}$ )	Diffusion coefficient ( $\times 10^{-7}$ )	Relative molecular mass ( $\times 10^7$ )
Water	0.029	6.98	7.76
NaCl 0.083M	0.029	7.04	7.56
0.15M	0.022	9.29	3.30
0.20M	0.029	7.06	7.46
0.25M	0.026	7.75	5.69
0.35M	0.019	10.73	2.16
0.43M	0.018	11.43	1.81

These results suggest that the use of 'swamping' electrolyte to overcome electrostatic viscous drag on the charged emulsion particles reduces the molecular mass of the particles. This may be due to suppression of the hydrated layer around the particles which would itself not only increase the drag around the particles but also decrease the apparent density of the oil phase. Both factors are assumed to be constant when applying the Stokes' equation.

The same effect has been observed in some polyethylene latex systems and in some self-emulsifying oils, and clearly indicates a practical lower limitation in the method of size analysis. Nevertheless, the method may well have application in the size analysis of material at and immediately below 1  $\mu\text{m}$  diameter.

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#### The use of an image analyser to determine the particle size distribution of salbutamol for use in metered dose inhalation aerosols

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To ensure that metered dose inhalation aerosols for treating lung disease deliver the required dose of drug to the fine bronchioles in the lung, it is essential that the particles of the delivered aerosol cloud are sufficiently small, preferably within the range 1.0-3.0  $\mu\text{m}$  diameter (Task Group Report, 1966; Stuart, 1973). The size of aerosol particles emitted by a product containing drug in suspension is affected by various controllable factors such as spray nozzle dimensions, propellant pressure and type, drug concentration and the wetting agent.

A further important factor is the particle size of the input drug. However, it should be noted that due to particle aggregation, the sprayed-out aerosol is generally more coarsely dispersed than the input drug powder. The drug is normally ground in a micronizer and is then checked for conformity to the particle size specification before use. For size analysis,