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 'Intralipid 10%' at a radius of 11·0 cm rotating at 3000 rev min⁻¹.*

Diluent	Stokes' dia. (μm)	Diffusion coefficient ($\times 10^{-7}$)	Relative molecular 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 μm 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 μm 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,

microscopy or the Coulter Counter are often used, the microscope being more suitable for drugs such as salbutamol which have high solubility in polar solvents.

The microscope method (based on B.S. 3406 Part 4, 1963) is slow and errors tend to occur due to operator fatigue and the small number of particles measured.

The speed and accuracy of measurement are increased considerably by using the microscope in conjunction with an image analysing computer—we have used a Quantimet 720 (Metals Research Ltd; Fisher & Cole, 1968). Salbutamol is dispersed ultrasonically in a suitable oily dispersant containing surfactant and is then examined on microscope slides. The Quantimet measures the maximum horizontal chord (i.e. scanning in one direction) of each particle and the particles are automatically classified into eight pre-set size classes.

The retained samples from eighteen production batches of micronized salbutamol were measured in duplicate with the Quantimet. The size distributions on every batch are log normal and give similar slopes on a log probability graph. The mean slope (i.e. standard deviation) is 1·59 and the mean particle size by weight (d_{gw}) is 2·00 μm diameter (range 1·52–2·44 μm). On average about 70% of the particles by weight are between 1 and 3 μm.

The excellent uniformity between the batches is illustrated by the low standard deviation (0·20 μm) and the small range (1·52–2·44 μm) in d_{gw}.

The results illustrate the excellent reproducibility of the micronizing process and the suitability of particle size of the micronized drug for use in inhalation aerosols. Clearly the Quantimet 720 is suitable for accurate sizing of fine isodiametric drug particles.

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Disposition of disodium cromoglycate administered in three particle sizes

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A recent investigation showed that small particles of disodium cromoglycate (DSCG) exert, in asthmatic patients, a protective effect which is dramatically greater than that of large particles (Godfrey, Zeidifard & others, 1974). Another recent investigation showed that the response to, and urinary excretion of, DSCG are related (Benson, Curry & others, 1973). DSCG is assayed in urine by purification on Amberlite resin and coupling with p-nitroaniline to give a coloured solution which is assessed spectrophotometrically (Moss, Jones & others, 1971; Curry & Mills, 1973). We now report the results of an investigation of the disposition of DSCG inhaled in particles of three sizes by 5 volunteers.

Doses were inhaled in random order during three attendances at weekly intervals. DSCG was drawn from a spinning disc generator (described earlier) (Godfrey, Zeidifard & others, 1974). Each subject provided a set of urine samples at each attendance, consisting of a pretreatment sample and samples at 0·5 or 1-hourly intervals up to 5 h after the dose. Additionally, each subject provided a set of mouthwash samples, collected at a fixed time after completion of dosing, and any DSCG exhaled during dosing was collected in a filter. Particle sizes were (as median diameter): small, 2·0 μm; intermediate 6·0 μm; large 11·7 μm. The standard deviation on these readings was 1·1 to 1·4 in several experiments. Mean doses were: small, 940 $\pm$ 23·4 (s.e.m.) μg; intermediate, 1244 $\pm$ 105·7; large, 1016 $\pm$ 29·7. Mean urinary retrieval was: small, 34·9 $\pm$ 10·0 (s.e.m.) % of dose; intermediate 13·6 $\pm$ 6·0; large 13·9 $\pm$ 4·5. Mean retrieval in mouthwashes was: small, 5·2 $\pm$ 2·1; intermediate 7·8 $\pm$ 3·3; large 46·0 $\pm$ 20·0. Mean exhaled material was: small, 2·2 $\pm$ 0·7 (s.e.m.) % of dose; intermediate 2·1 $\pm$ 1·0; large 2·3 $\pm$ 1·3.