THE ASSOCIATION AND PARTICLE SIZE DISTRIBUTION OF DRUG AND SURFACTANT DISCHARGED FROM A METERED-DOSE INHALATION AEROSOL

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Hygroscopic drug particles may increase in size when inhaled (Gonda 1981), although there is recent evidence that surfactants present in inhalation aerosols may inhibit such growth (Martonen 1980). Since particle size is a major factor governing drug deposition in the lung, the association between drug and surfactant is crucial to the role of the latter in the discharged aerosol. Ventolin Inhaler is a suspension aerosol containing salbutamol with oleic acid (10% w/w of drug) as surfactant. Forty metered doses of Ventolin Inhaler were discharged into an eight-stage Andersen sampler (Andersen 1966), which measures the aerodynamic size distribution of aerosols by cascade impaction. Samples from each impactor stage were analysed for salbutamol and oleic acid by colorimetry and gas chromatography respectively. The results are presented as log-probability graphs of particle size (AD = aerodynamic diameter in μm) vs. cumulative weight % undersize. (Fig. 1).

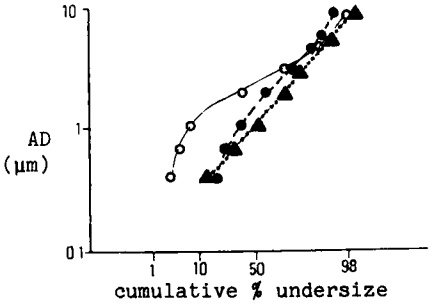

Fig. 1

o—o Salbutamol (Ventolin Inhaler) MMAD 2.4μm σg 1.5

●- - -● Oleic acid (Ventolin Inhaler) MMAD 1.5μm σg 2.1

▲····▲ Oleic acid (placebo inhaler) MMAD 1.1μm σg 2.5

σg -geometric standard deviation

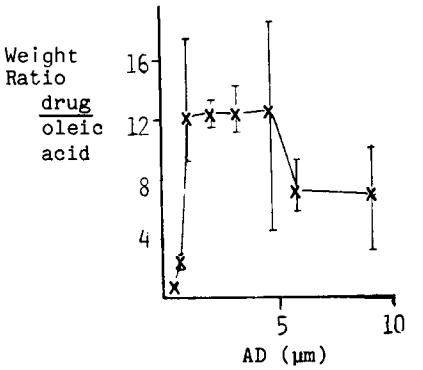

Fig. 2

Figure 1 shows that the particle size distribution of oleic acid in a placebo inhaler is log-normal and this distribution is changed by the presence of salbutamol particles in Ventolin Inhaler. The largest differences between the salbutamol and oleic acid distributions occur below 1μm; see also Figure 2. Assuming distribution of propellant droplets in the discharged spray to be log-normal, and a uniform suspension entering the atomizing nozzle of the inhaler, the size separation of the two components in the discharged aerosol may be explained by two factors:

(i) The oleic acid is in solution in the propellant mixture.

(ii) Calculations from the oleic acid distribution of the initially discharged spray droplet size distribution show that there are far more discharged droplets than drug particles; this ratio increases steeply below 1μm. It follows that the decreasing tendency for droplets to contain drug particles is enhanced as the droplet size decreases.

Above 1μm the weight ratio of drug to oleic acid approximates to the theoretical composition of the inhaler contents.

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Gonda,I.(1981) Particle Size Analysis Conference Proceedings, Loughborough

Martonen,T.B.(1980). Proceedings 5th Int. Symp. on Inhaled Particles, Cardiff

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