MODEL OF AERODYNAMIC BEHAVIOUR OF AGGREGATES FORMED ON NEBULISATION OF SUSPENSIONS

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Formation of aggregates of particles when drug suspensions are aerosolised, was documented (Morén, 1982). Thus, changes in the drug mass median aerodynamic diameter (MMAD) occur, and this is important for airway deposition of aerosols.

Consider a suspension of monodisperse spherical particles, diameter d, aerodynamic diameter $d_{ae}(1)$, concentration c (% v/v) in a volatile liquid. On nebulisation, the probability that a droplet of diameter D contains k drug particles is given by the Poisson probability (Raabe, 1968):

$$P(k,D) = \frac{e^{-n} n^{k}}{k!} \; ; \; n = \left(\frac{D}{d}\right)^{3} \frac{c}{100}$$

The probability that k particles are found in droplets of any size is

$$P(k) = \int_{D_{min}}^{\infty} P(k,D)\,p(D)\,dD$$

p(D) is a log-normal size distribution with droplet mass median diameter MMD_D and geometric standard deviation σ_D. D_{min} is the diameter of the smallest droplet which can accommodate the aggregate of k particles (Callingham, 1980; Gonda, 1985). It is assumed that, on evaporation of the liquid, the aggregates are spherical and consist of hexagonal close-packed primary particles. The cumulative mass fraction M(i) of aggregates containing up to k=i particles/aggregate is computed as a function of the relative aerodynamic diameter $d^{r}_{ae}(i)$ (Gonda,1985):

$$M(i) = \frac{1}{n}\sum_{k=1}^{i} kP(k) \; ; \; d^{r}_{ae}(i)/d_{ae}(1) = \sqrt[3]{\frac{i}{f(i)}} \sqrt{\frac{K(1)f(i)}{K(i)}}$$

f is the occupied volume fraction and K is the dynamic shape factor (Davies, 1979; Gonda, 1985). The plots of M(i) on probability scale vs. log $d^{r}_{ae}(i)$ are nearly linear. From the graphs, the increase in the drug mass median aerodynamic diameter, $R_1 = MMAD/d_{ae}(1)$, and the apparent geometric standard deviation of MMAD, σ_d, are obtained. The increase of MMAD is calculated also on the assumption of uniform drug distribution throughout the droplets (R_2). It may be concluded (see Table 1) that the statistically-based R_1 is similar to R_2, and that the apparent σ_d of the aggregates is governed by the geometric standard deviation of the droplets σ_D.

Table 1. Dependence of aerodynamic properties of aggregates (R_1, R_2, σ_d) on the concentration of suspension (c) and the droplet size distribution (MMD_D, σ_D).

c	MMD_D/d	σ_D	R_1	R_2	σ_d
0.5	10	1.5	1.61	1.55	1.5
	10	2.0	1.61	1.55	1.9
1.0	10	2.0	2.02	1.95	1.9
	15	2.0	2.95	2.93	1.9
2.0	10	1.5	2.47	2.46	1.5
	10	2.0	2.47	2.46	2.0

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