EQUILIBRIUM DIAMETERS OF INHALATION AEROSOL DROPLETS

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Particles of inhalation aerosols attempt to attain thermodynamic equilibrium by exchange of water and heat with the environment in the respiratory tract. Neglecting surface effects, the drug concentration in the equilibrated droplet will be isoosmotic with isotonic saline at 37°C.

The isoosmotic drug concentrations were found by vapour pressure osmometry (H. Knauer Osmometer). Densities of dry powders of the drugs were found by air comparison pycnometry (Beckman, model 930). The ratio of geometric diameters of the equilibrated droplet, D^e, and the original dry particle, D, and the corresponding ratio for aerodynamic diameters D^e_{ae}/D_{ae} were calculated by previously published methods (Groom and others 1980). The results are shown in the table below:

Drug	Isoosmotic[1] concentration (mol kg^{-1})	Density of powder (g cm^{-3})	Molar mass (g mol^{-1})	$\frac{D^e}{D}$	$\frac{D^e_{ae}}{D_{ae}}$[3]
Sodium cromoglycate	0.177	1.62	517	2.7	2.1
Isoprenaline hydrochloride	0.157	1.32	248	3.3	2.9
Isoprenaline sulphate	0.124	1.36	557	2.8	2.4
Salbutamol sulphate	0.107	1.5[2]	576	3.0	2.4

1) at 37°C 2) sample too small for greater accuracy 3) valid for D & $D^e > 0.3\mu m$

Since the aerodynamic diameter is a primary determinant of the site and extent of aerosol deposition, the last column in the table suggests that condensation growth may have a large effect on the behaviour of inhalation aerosols containing the tested drugs. The values for D^e/D and D^e_{ae}/D_{ae} are substantially different from those calculated assuming ideal solution behaviour (Ferron 1977).

Vapour pressure osmometry also revealed that water activities of aqueous solutions of sodium cromoglycate reach a plateau at 0.13 mol kg^{-1} (25°C) and 0.23 mol kg^{-1} (37°C), in agreement with the phase diagram published by Cox and others (1971). Furthermore, at 25°C the water activity at the plateau is higher than the value for isotonic saline, whereas the converse is true at 37°C. It is therefore recommended that similar measurements for other drugs should be made at physiological temperatures.

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