Hygroscopic Particle Deposition Model for Rat Lungs

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During inhalation, particles are transported into the lungs and partitionally deposited. By computer models, the cumulated number, surface area or mass of the deposited particles can be calculated and related to body mass, lung surface area or cell number as a deposited dose parameter. Model calculations are a repeatedly used to estimate the deposited dose.

Usually, particle properties like sedimentation**,** diffusion and impaction are taken als the basic mechanisms for model calculations. A computer model was developed for the human airways (Ferron *et al.,* 1988) which additionally considers the hygroscopicity of the inhaled particles. This model was tested and adjusted using measured human deposition data for both non-hygroacopic and hygroscopic particles. It could be shown that there were notable differences compared to non-hygroscopic particle model calculations.

For inhalation studies, rodents are frequently used as test subjects. Here we present a model of the deposition of hygroscopic aerosol particles in the rat airways.

Table 1. The maximum and minimum ratio of the total lung deposition of a salt (drug) and a non-hygroscopic material (with a density of 1 g cm^{-3}) with the same initial dry particle size.

Substance	Max. ratio	Min. ratio
NaCl	3.28	0.57
CoCl2.6H2O	2.44	0.63
ZnSO4.7H2O	2.13	0.70
Histamine-dihydrochloride	1.86	0.65
carbenicillin-disodium	1.53	0.70
atropine sulfate	1.5	0.76

In a first step, a model for the deposition of non-hygroscopic particles in the rat lungs was derived from the human model (Schmid *et al*., 2008). As no data have been available for hygroscopic rat lung deposition, the hygroscopic model was scaled from human to rat lung conditions by physical assumptions. The lung structure of Weibel (1963) was used for the human, while the rodent airways are taken from the model of Yeh et al. (1979).

The changes by hygroscopicity are expressed as the ratio of the diameter achieved by hygroscopic growth and the initially dry particle diameter. Ratios from 0.57 to 3.28 were calculated for materials listed in Table 1 for particle diameters between 0.02 and 5 µm. The corresponding changes for human airways were higher (0.62 and 3.43), what can be explained by the smaller residence time of aerosol particles in the rat airways.

The shift of deposition curves compared to the ones for non-hygroscopic particles is nearly proportional to the growth factor (defined as the ratio of the particle size at humid and totally dry conditions). The growth factor can be calculated from a salt's physical properties for a known humidiy. It therefore can be used to estimate the deposition of an arbitrary hygroscopic material using the growth factors and deposition curves presented from the model.

As a conclusion, the hygroscopic properties of salts and drugs substancially influence the lung deposition in rodents and should therefore be considered in lung deposition modeling. The growth factor of a salt or drug can be used to estimate irs deposition.

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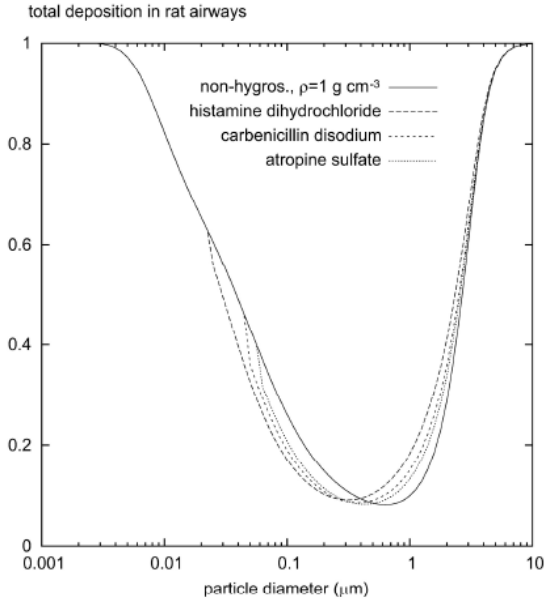

Figure 1. Total deposition in the rat lungs for non-hygroscopic particles and different drugs (Table 1).

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