SELECTION AND REGULATION OF PARTICLE SIZE OF AEROSOLS IN INHALATION TOXICITY STUDIES

Shuji TSUDA (Division of Pharmacology and Metabolism, Imamichi Institute for Animal Reproduction, 1103 Fukaya, Dejima-mura, Niihari-gun, Ibaraki 300-01)

Particle size of an aerosol is generally considered very important in assessing its inhalation toxicity. In order to select and regulate particle size, effects of particle size on inhalation toxicities of aerosols should be examined.

Thus, a practical inhalation chamber with a size discriminator for mists was developed to provide high concentration liquid aerosols of defined particle sizes¹⁾. Liquid aerosols generated with an atomizer were separated by an impinging separator which was composed of an aerosol jet directed upward against a flat plate. The principle of the separator eliminates particles larger than a calculated cutoff size in micrometer and submicrometer ranges by changing the orifice diameter of the jet nozzle under constant air flow. The mists thus separated are introduced into the space between two concentric cylinders just above the impaction plate. Ten rats can be positioned around the periphery of the chamber all equidistant from the impaction plate, with their snouts thrust into the inhalation space. Mists of respirable particles larger than a selected size were also exposed to rats using an atomizer which produces coarse aerosols and without applying any aerosol jet nozzle.

Male rats were acutely exposed to either the mists of liquid organophosphorus insecticides, chlorfenvinphos (CVP) and fenthion (MPP) using the size-selective inhalation chamber. CVP which is a P=O type organophosphate causes toxicity by directly inhibiting the cholinesterase activity, whereas MPP which is a P=S type inhibits cholinesterase activity after being metabolized in the animal body. For each insecticide, mists with two different particle size distributions were used: small mist of which MMAD was 1 μm or less,

and large mist having the MMAD of 6-8 μm . It is considered that particles smaller than 1 μm are mainly deposited in the lung, while those of 6-8 μm are deposited in the nasopharyngeal regions. The inhalation toxicity based on LC50 of the large mist was three or five times greater than that of the small mist for each of the two insecticides. The toxicity was related to the acetylcholinesterase inhibition. Concentration of CVP and MPP in the blood from the rats exposed to these mists were measured, and analyzed pharmacokinetically in conjunction with the results from iv injections. The higher toxicity of the CVP larger mist was attributed to the greater deposition of the mist in the respiratory tract and similar rate of systemic availability from the deposition site, the coupled effect of which resulted in a higher blood CVP concentration and a stronger inhibition of cholinesterase activity²⁾. The deposition of the larger MPP mist was also considered greater than that of the small mist. However, the blood MPP concentration after the larger mist exposure was lower, because of much lower systemic availability of the larger mist. Thus, the greater toxicity of the larger mist of MPP was ascribed to the preferential metabolism of the larger mist to the active metabolite(s) after deposition in the respiratory tract³⁾.

The larger mists of BPMC and propaphos also showed greater inhalation toxicity compared with the corresponding smaller mist. According to the analysis of these factors it was suggested, however, that if absorption of a chemical from the nasopharyngeal region is smaller than from the lung and its active form is the parent compound, then the toxicity of its larger mist would be lower than that of the small mist. From these results the inhalation toxicity of a chemical mist with a given particle size distribution may be related to i) total and regional depositions of particles in the respiratory system, ii) fraction absorbed of the chemical from the deposition site, and iii) whether the active form of the chemical is parent compound or its metabolite(s).

If we do not have enough information about

these factors, the selection of particle size of 3-5 μm seems to be reasonable for the inhalation exposure because of the relationship between particle size and deposition of particles in the respiratory tract.

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