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Inhalation properties of water-soluble drug loaded liposomes atomized by nebulizer

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The pulmonary route presents several advantages in designing drug delivery systems in both systemic and topical administration. The use of particulate carriers is an attractive method for designing pulmonary drug delivery systems, because such carriers could control drug release and selective drug targeting when the carriers reach the target site in the lung. The prevention of local irritation, reduced drug toxicity, and improved drug stability are also preferable results of utilizing such carrier systems. Among a number of particulate carriers, liposomes have an advantage in safety, because they consist of phospholipids, which are bio-components. Moreover, liposomes are able to entrap both hydrophilic and hydrophobic drugs.

In the previous study, we have reported an application of liposomes in designing a dosage form of inhales [1,2]. In considering the actual dosage form design of liposomal suspension, the use of nebulizers or other inhalation systems is required. The inhalation properties of liposomal suspension are important to complete in final liposomal inhalation. The purpose of this study was to evaluate inhalation property and stability of liposomes after nebulization. Three nebulizer devices, namely air-jet, ultrasonic and passively vibrating mesh nebulizers were used in this study. Several types of water-soluble molecules having different molecular weights were selected as model drugs in the formulation. The water-soluble drug loaded liposomes were prepared by hydration method. Particle size of the liposomes was controlled by the extrusion method with an extruder equipped with a polycarbonate filter (100 nm). The liposomes were aerosolized by a variety of nebulizers to examine the optimal device for atomization of liposomal formulations. Furthermore, we studied the effects of physical properties of liposomes on inhalation properties. From the result of inhalation properties measured by Andersen cascade impactor (ACI), we found that the air-jet nebulizer is the most efficient device in delivering the liposomal formulations to the pulmonary parts (Fig. 1). The delivery efficiency to the lung decreased and the leakage of encapsulated drug increased with the increasing liposomal size. Furthermore, the small-molecular drug loaded liposomes tended to be leaked more from liposomes during atomization than macromolecular drug. However, the leakage amount of small-molecule drug depended on the particle size of liposomes and depressed by decreasing it up to 100 nm. From the above results, the air-jet nebulizer is concluded to be the most efficient devices for the nebulization of

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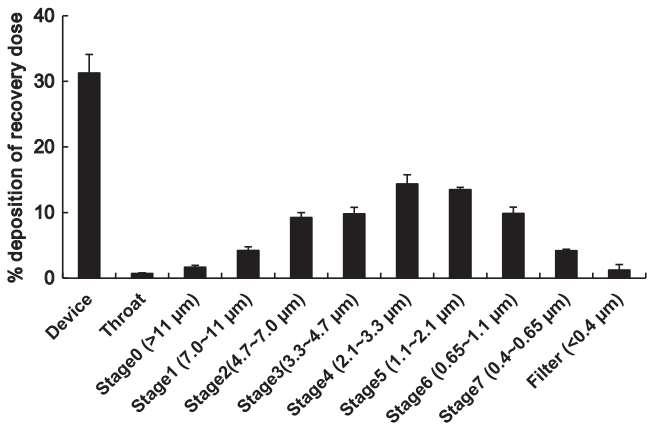

Fig. 1 – ACI dispersion data of liposomes nebulized by air-jet nebulizer (mean ± S.D., n = 3).

liposomes and the particle size of liposomes is also the key factor to design the liposomal inhales.

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