

## **Pulmonary delivery of drug nanoparticles-containing microspheres**

Tetsuya Ozeki, Hiroaki Okada  
(School of Pharmacy, Tokyo Univ. Pharmacy and Life Sci.)

The lung is an attractive route for drug delivery because it has a large surface area, because the thickness of the air-blood barrier in the alveolar epithelium is less than 1  $\mu\text{m}$  and because the blood capillaries are packed around the alveoli. Nano-particles are expected to apply in the new drug delivery systems. However, the surface energy of the particles is extremely high for nanoscale particles. Therefore, it is difficult for them to exist in a solid state because of extremely high adhesion and cohesion forces, and when the particles adhere, it is difficult to disperse them again, resulting in their loss of function as nanoparticles. In the inhalation therapy, the particles are efficiently delivered to the bronchi and alveoli when their aerodynamic diameter is from approximately 0.4 to 5.8  $\mu\text{m}$ . 4-fluid nozzle spray drier has a unique nozzle with two liquid and two gas passages, which allows drug and carrier to be dissolved in separate solvents, thereby avoiding the need for a common solvent. We have developed new technology to prepare mannitol microspheres containing nano-sized drug in one-step using the 4-fluid nozzle and succeeded in improving the absorption of water-insoluble drug by pulmonary administration of the particles. We also developed the particles for inhalation therapy of tuberculosis and studied the delivery to the lung, retention in the lung and uptake to the alveolar macrophages. The devices and carriers for dry powder inhalation are discussed.