

Delivering nanomedicines to the airways

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Nasal and pulmonary administration of nanomedicines presents several challenges, not least the need of a suitable device to aerosolize and deposit them in the desired section of the airways.

Nebulization of nanomedicines can be extremely tricky due to the thermal and physical stress to which the nanosuspension is submitted during the aerosolization process using the commercially available nebulizers (air-jet, ultrasounds, vibrating mesh). Several nanomaterials, such as nanocrystals and polymeric nanoparticles have been proposed for applications in respiratory diseases using nebulizers. In our laboratories, coenzyme Q10 nanoemulsions were produced by high pressure homogenization with sufficient stability and particle size (below 100 nm) suitable for delivery with any type of nebulizer. In the case of dry powder inhalers, it is necessary to embed nanoparticles into larger structures with aerodynamic size suitable for pulmonary deposition. For example, calcium phosphate nanoparticles were successfully embedded in respirable microparticles of mannitol by spray drying in view of their administration by inhalation. Nanoparticles are efficiently re-dispersed upon contact with the lung fluids after administration and are then available for distribution in the body through the blood flow.

Concerning nasal delivery, the application of nanoparticles for vaccination and nose-to-brain delivery represent two of the most promising applications. We developed simvastatin-loaded lecithin/chitosan nanoparticles designed to be enzymatically biodegraded and able to deliver efficiently the lipophilic drug across *in vitro* and *ex vivo* models of the nasal epithelium. Furthermore, this nanomedicine showed neuroprotection against psychosine-induced astrocyte toxicity in a neurodegeneration model. Remarkable radioactivity accumulation in the rat brain was measured by gamma scintigraphy after nasal administration of nanoparticles labelled with technetium-99m.

Nanomedicines delivery to the respiratory tract represent an interesting opportunity to widen the pharmaceutical nanotechnologies applications and to enable new therapies for unmet clinical needs.