Sterically stabilized liposomes for non-invasive peptide delivery to the lung

Ruth Prassl[1], Brigitte Stark[1], Fritz Andreae[2]

[1] Institute of Biophysics and Nanosystems Research, Austrian Academy of Sciences

[2] piCHEM Research & Development, Austria

Non-invasive routes of administration become more and more attractive to achieve organ-specific targeting (e.g. pulmonary delivery by inhalation). However, peptide drugs are often subject to degrading proteases in airway lumen and lung, which results in a poor bioavailability of the drug when applied as conventional formulation. To overcome these problems drug delivery systems are developed, which should act as efficient shelter-, storage-, transport- and release systems. Additionally, these formulations have to fulfil certain structural requirements to reach the deep lung combined with a high peptide loading, long half-life time, good stability and biocompatibility. All these criteria were achieved for a sterically stabilized liposomal formulation, which was developed to deliver vasoactive intestinal peptide to the lung by aerosolic application. VIP, a cationic neuropeptide and potent pulmonary vasodilator, is considered as therapeutic agent for the treatment of severe lung diseases such as pulmonary arterial hypertension (PAH). However, free VIP is prone to rapid enzymatic cleavage by neutral endopeptidases found in airway endothelium, thereby significantly reducing the efficiency and bioavailability of the peptide. In contrast, liposomal entrapped VIP is not degraded as determined in the presence of bronchoalveolar lavage fluid (BALF), a proteolytic lung surfactant solution, which was taken as representative for the lung environment. Moreover, the biological activity of liposomal VIP was preserved as shown in an *ex vivo* arterial model indicating a slow prolonged release kinetics for VIP.

Particle integrity during nebulization processes was assessed in terms of particle size distribution, membrane stability and drug retention.

In summary, we have established a negatively charged liposomal formulation passively loaded with pharmacologically relevant amounts of VIP, providing strong experimental evidence for the suitability of this system for non-invasive pulmonary application.