

# Vitamin E Encapsulation Within Pharmaceutical Drug-Carriers Prepared Using Membrane Contactors

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## Abstract:

Vitamin E, a physiological antioxidant, has been tested to prevent cigarette smoke toxicity since several pulmonary disorders are mainly caused by oxidative stress phenomena. Nevertheless, the use of conventional pharmaceutical forms (oral or intravenous administration) doesn't allow precise transport of vitamin E to its specific action site, the lung alveoli. Thus pulmonary drug delivery could present a promising alternative to the systemic drug administration. The present study investigated the preparation of pharmaceutical drug carriers encapsulating the vitamin E and intended for pulmonary administration after nebulisation.

The methods used for the drug carriers' preparation were based on the membrane emulsification principle. In these methods, the to-be-dispersed phase was injected in the continuous phase through the pores of a microporous membrane. The advantages of this method are: a better control over the diffusive mixing at the liquid / membrane interface and thus a fine control of droplets size distribution, a less energy consumption and an easy extrapolation of the obtained results for an industrial large scale-up. In order to study the preparation processes, the influence of the formulation factors and the process parameters on the particles characteristics was systematically investigated.

Different experimental set-ups were used: (i) tubular membranes with a cross flow circulation of the continuous phase, (ii) stirred cell device with a flat micro-engineered membrane, (iii) oscillating membrane module in a stationary continuous phase. For direct emulsification, various membranes were used such as: SPG membranes, micro-engineered membranes and ceramic membranes. For premix emulsification, a packed bed of glass beads, called dynamic membrane, was studied.

Four different drug carriers were developed during this study: liposomes, micelles, nano-emulsion and solid lipid particles. The different encapsulating systems were characterized in terms of size distribution, zeta potential, microscopic morphology, encapsulation efficiency and stability. Results showed that the obtained drug carriers presented convenient properties. After nebulisation, the vitamin E loaded particles aggregate leading to an increase in the aver-

age size. A balance between exhaled and lung deposited drug rates exists and it depends on the aerosols particle size. For small sizes, the nebulised suspension is mostly exhaled, larger sizes of the nebulised suspension led to its retention in the upper respiratory tract. In our study, the obtained aerosols presented satisfying aerodynamic characteristics which allowed the prediction (using a mathematical model: Multiple Path Particle Dosimetry "MMPD") of a high level of vitamin E deposit on its action site. Coming work includes an *in-vivo* administration of vitamin E loaded vectors to rats in order to confirm its safety and therapeutic efficiency.

## Keywords:

Encapsulation, Nanoparticles, Membrane contactor, Pharmaceutical vectors, Nano-medicine, Vitamin E, Industrial Scale-up, Cigarette toxicity

## References:

Laouini, A., Fessi, H., Charcosset, C. (2012) Membrane emulsification: a promising alternative for vitamin E encapsulation within nano-emulsion, *J. Membr. Sci.*, 423-424, 85-96.

Laouini, A., Charcosset, C., Fessi, H., Holdich, R. G., Vladisavljevic, G. T. (2013), Preparation of liposomes: A novel application of microengineered membranes – Investigation of process parameters and application to the encapsulation of vitamin E, *RSC. Adv.*, 3, 4985-4994.

Laouini, A., Charcosset, C., Fessi, H., Holdich, R. G., Vladisavljevic, G. T. (2013), Preparation of liposomes: A novel application of microengineered membranes – Scale-up from laboratory scale to large scale, *Colloid. Surface. B.*, 112, 272-278.

Laouini, A., Koutroumanis, K. P., Charcosset, C., Georgiadou, S., Fessi, H., Holdich, R. G., Vladisavljevic, G. T. (2013), pH-sensitive micelles prepared using a novel membrane contactor method, *ACS. Appl. Mater. Interfaces.*, 5, 8939-8947.

Laouini, A., Charcosset, C., Fessi, H., Shroen, K. (2014), Use of dynamic membranes for the preparation of vitamin E loaded lipid particles: An alternative to prevent fouled observed in classical cross-flow emulsification. *Chem. Eng. J.*, 236, 498-505.