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CMS nanotransporters for topical delivery of dexamethasone

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In order to overcome the main skin barrier, the stratum corneum, and to increase the dermal penetration of drugs, various nanoparticulate carrier systems were developed during the last decades. Of particular interest are hyperbranched polyglycerol-based nanoparticles such as dendritic core-multishell (CMS) nanotransporters. CMS nanotransporters consist of a polyglycerol core which is surrounded by a lipophilic inner shell and a hydrophilic outer shell. The special architecture enables the encapsulation of a wide variety of guest molecules [1] and can transport them to polar and nonpolar environments. Their efficacy in terms of topical drug delivery of hydrophilic [2] and lipophilic [3] guest molecules was demonstrated previously.

The glucocorticoid dexamethasone (DXM) is the gold standard for the topical therapy of inflammatory skin diseases. However, long term use is often accompanied by severe side effects such as skin atrophy. Loading of DXM onto CMS nanotransporter may reduce side effects as shown with liposomes [4].

Hence, in this study we established a method to determine the loading properties and loading capacity of the CMS nanotransporter for DXM using high performance liquid chromatography (HPLC). A RP-18 column, the eluent acetonitrile/water (40:60) with a 0.5 ml/min flow rate, an external standard and a detection wave length of 254 nm was chosen. Based on x-ray microscopy measurements, a DXM concentration of 5 % loaded onto CMS nanotransporters was calculated. Analyzing the HPLC data, we recovered about 3 % DXM. However, we only detect unloaded DXM. Considering the maximal solubility of DXM in water (80-100 µg/ml), we detected about 2-fold higher DXM concentration in the presence of CMS nanotransporters. This solubilization effect can be explained by the ability of the CMS to form spontaneous aggregates simultaneously encapsulating DXM [1]. However, these aggregates are not stable under strong shear stress as occurring in an HPLC (40 bar). Hence, the CMS nanotransporters disaggregate and release the DXM. Nevertheless, investigations using fluorescent life time imaging microscopy (FLIM) showed an encapsulation of hydrophobic cargos also in the unimolecular state clearly indicating that the loading properties for the CMS nanotransporters are highly drug dependent [5].

By combining different analytical methods such as FLIM and HPLC the loading properties of CMS nanotransporters can be unraveled most effectively demonstrating the diversity of the

CMS nanotransporters. More detailed studies on drug release and the dermal delivery capacity of DXM loaded CMS nanotransporters are currently under investigation.

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