## Phospholipid Bicelles as Topical Delivery Systems for Porphyrinic Photosensitizers

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Topical photodynamic therapy (PDT) serves as a minimally invasive and safe treatment approach for various superficial skin diseases such as actinic keratosis [1]. PDT treatment of skin employs the delivery of a precursor (5-ALA) that is converted into the active form, the photosensitizer (PS) protoporphyrin IX, followed by targeted irradiation. This causes the PS to undergo a photochemical reaction, producing reactive oxygen species, which induce oxidative damage to surrounding cells [2]. Directly applied porphyrinic PSs are interesting candidates for topical PDT due to their absorbance range in the therapeutic window [3]. However, these lipophilic compounds require solubilization to remain active for PDT, thus a carrier is necessary [4]. Bicelles are biocompatible disc-shaped phospholipid nanocarriers. Their lipid bilayer offers an environment for lipophilic drug molecules [5]. Smaller than liposomes, bicelles might facilitate penetration into the skin surface. The aim of this current project is to investigate bicelles as a topical drug delivery system for porphyrinic PSs.

Bicelles with differently combined phospholipids are loaded with PSs (Chlorin e4, m-THPP, or m-THPC). During the bicelle production the PSs are encapsulated. The resulting system is characterized using NMR spectroscopy and dynamic light scattering (DLS). With NMR spectroscopy the bicelle formation, drug encapsulation efficiency and the size of the system can be determined. DLS is used to measure the size and stability of the empty bicelles. With the successful formulations in vitro skin penetration tests are performed to investigate the penetration of PS into the skin. Furthermore, cell uptake studies are conducted to quantify PS uptake in keratinocytes.

Results so far show that with the right phospholipid combination PS can efficiently be encapsulated into small bicelle systems and the PS remains solubilized in the formulation. Depending on the delivery system and the PS an average skin penetration ranged from 100 ng/cm<sup>2</sup> – 860 ng/cm<sup>2</sup> has been achieved employing porcine ear skin as model, comparable to other vesicular delivery systems [6].

To increase the penetration efficiency the addition of various chemical penetration enhancers to the bicelle system is planned. Due to the biological variations of the skin samples, the results of the penetration experiments show a high variability. In coming efforts, we aim to address this concern with experiments using an artificial human skin model. Furthermore, microscopic localization of the PS in the skin or skin model are planned

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