Localization of EPR probes and labeled drugs in nanocarriers and their penetration and release in skin

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Introduction

The successful inclusion of active substances into nanocarriers, their penetration into the skin and the release of the drugs at the target sites are essential and important for effective local therapy approaches. The exterior layer of the skin (horny layer, stratum corneum) has a distinctive barrier function that provides protection against environmental influences[1, 2].

Aim of the study:
- Improvement of the penetration of active ingredients into the skin.
- Research is focused on promoting solvents and nano-transport systems (NTS) [1].

Background information and experimental research:
- In the pharmaceutical industry, stearyl acid is used as an additive for, e.g., skin creams and ointments; their hydrophobic character (log P value 8.23) complicates the penetration into the skin extremely [3].
- Dendritic core-multi shell (CMS) nanocarriers belong to the multi-shell NTS. They allow the transport and storage of molecules with different chemical characters, consist of a polar core, a nonpolar inner shell and a hydrophilic outer shell.

In this study multi-frequency EPR spectroscopy (W, X band) was applied to investigate the localization of 5DSA within the carrier, the penetration properties of the carrier and the release of the drug.

Materials and Methods

Dendritic core-multi-shell (CMS) NTS

- Polar/ hydrophobic core of hyperbranched dendritic polyglycerol
- Intermediate shell is hydrophobic and consists of linear C18 dodecane building blocks which are covalently bound to the hyperbranched polar core and to the terminal hydrophilic outer shell
- Outer shell consists of monomethyl polyethylene glycol (mPEG)
- CMS particles are soluble in water and organic substances

5-oxyl-steric acid (SDSA)

- Stearic acid is a member of the saturated carboxylic acids
- For cosmetics: emulsifying, emulsion stabilizing effect, moisturizing
- Low penetration (log P value 8.23)
- Spin probe 5-oxyl-steric acid (SDSA)

Electron Paramagnetic Resonance (EPR) Spectroscopy

- Analysis of the localization, release and penetration profile of a hydrophobic drug, here SDSA
- Investigations in formulation and on porcine skin (ex vivo)
- Measurements were carried out with the use of an X: (9-10GHz; Miniscop, Magnetech, Berlin Germany), and W-band (94GHz; Bruker Biospin, Karlsruhe, Germany)

Fluorescence Microscopy (FM)

- Investigation of the penetration of CMS particle into porcine skin (ex vivo)
- Analysis of the localization of the CMS NTS within the skin
- Covalently bound fluorescent label indocarbocyanine (ICC) to the CMS-NTS

Results

Analysis of the localization of the EPR probe SDSA in solution (DMSO) respectively within CMS NTS (water) via X-band EPR spectra, before and after penetration into porcine skin (ex vivo)

- In DMSO SDSA shows a higher mobility than if loaded to CMS NTS
- Ex vivo studies demonstrate nearly the same properties for SDSA loaded to CMS NTS and in solution

Multi-frequency analysis

- Multi-frequency analysis for determination of magnetic parameters of the EPR label

Investigation of the penetration efficiency for SDSA-CMS NTS (ICC labeled)

- Average penetration depth into hair follicle: 340µm ± 82µm
- A penetration into the viable epidermis was not observed
- CMS NTS which had not penetrated into the hair follicles, remain localized on the stratum corneum (SC)

Summary

- SDSA is localized in the nonpolar shell
- Polarity within the nonpolar shell is similar to DMSO
- Penetration depth of the CMS into the hair follicles: 340µm ± 82µm

References