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Ultra-small nanoparticles promote thepenetrationof CoQ10inthe skin – a counteract against oxidative stress

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The exterior layer of the skin protects against negative environmental influences and (UV-) radiation. UV radiation leads to the formation of free radicals, in particular the formation of reactive oxygen species (ROS). ROS are produced in the whole organism and are thus in equilibrium with the antioxidant systems of the body which consists of enzymatic and non-enzymatic antioxidants. If the antioxidant system is disturbed, cell damage, premature skin aging and the development of skin cancer can occur. To counteract these processes antioxidants are contained in many cosmetic products and sunscreens, such as the coenzyme Q10 (CoQ10, alternative name: Ubiquinon). CoQ10 is a lipophilic non-enzymatic antioxidant, produced by the body itself and is localized in the mitochondrial membrane. In its reduced form (ubiquinol) CoQ10 has a high antioxidant potential, scavenges free radicals and thus protects against oxidative stress and leads to minimization of cell damage. Free CoQ10 is sparingly soluble in water and cannot penetrate into cells. In recent years, lipid nanoparticles have been developed to facilitate the penetration of lipophilic molecules into the skin. NLC (nano structured lipid carriers) represents a good basis for transporting molecules into the cell. In order to further improve and optimize the penetration efficiency, ultra-small nanoparticles (usNLC) of < 100nm in size were developed. They consist of a solid lipid core and a sheath of liquid lipid in which the active ingredient (CoQ10) is mainly localized. Their small size (85nm) should facilitate the uptake of agents into the cell, thereby increasing the bioavailability of the drug. This was investigated using fluorescence microscopy on nile red loaded usNLC. To test the antioxidant effect, CoQ10-loaded usNLC were analyzed via electron paramagnetic resonance spectroscopy (EPR) in HaCaT keratinocyte cells which were exposed to UVA/B radiation (1J/cm^2/ 18mJ/cm^2), triggering the formation of free radicals. The non-toxic CoQ10 concentration was evaluated via a cell viability test (XTT cell proliferation assay), determining the viability of the cells which is proportional to the number of living cells.

The XTT assays revealed that CoQ10 concentrations of 10, 25 and 50 µg/ml show no significant effect on the cell viability; in contrast to 100 µg/ml which results in a strong limitation of the cell viability. Therefore, the antioxidative effect of usNLC was examined on HaCaT cells using the concentrations 10 to 50µg/ml of CoQ10. For UVA a higher radical formation could be detected, UVB radiation is indeed more energetic but will damage more cell

compartments and structures. The EPRinvestigations with usNLC-CoQ10 demonstrated a clear reduction of the radical formation of up to 9% in UVA irradiated cells compared to control but no dependence on usNLC-CoQ10 concentration. Using fluorescence microscopy, the penetration of the loaded usNLCs into the cells could be shown.

In this study, it could be demonstrated that CoQ10 loaded usNLC penetrated into HaCaT cells and showed an antioxidant potential. These particles are a further development of the previously analyzed nanoparticle systems and represent a new era of nanocarrier systems.