Fundamental Experiments for Risk Assessment of Nanoparticulate Carrier Systems Using Validated In-vitro Test Procedures

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Nanoparticulate carrier systems are of increasing interest as drug delivery systems for topical application. Thereby, the assessment of the tolerability is of crucial importance. Solid lipid nanoparticles (SLN) and new-typed dendritic core-multishell nanotransporters (CMS NT) can increase the skin penetration of various substances significantly and have the potential to reduce side effects. Nevertheless, the local tolerability of the promising carrier candidates has to be assessed.

Thus, to test the dermal safety of SLN and CMS nanotransporters the EPISKIN® skin irritation test was performed. Prior to the main test, the MTT reduction potential of SLN and CMS nanotransporters was tested to avoid a misinterpretation of the data. The results predict no irritant potential according EU classification R38. Interestingly, the acute irritant potencial of the positive control sodium dodecylsulphate was reduced when loaded onto CMS nanotransporters.

As the nanocarrier systems can accidentally or intended come into contact with the eyes the eye irritation potential of both nanosystems was tested, too, using the HET-CAM test. The evaluation was carried out concerning the endpoints haemorrhage, coagulation and vessel lysis. SLN as well as CMS showed no eye irritating potential.

In conclusion SLN and dendritic core-multishell carriers are promising systems to increase effectiveness and tolerability of the local treatment of skin diseases. Furthermore, the *in-vitro* approaches Episkin® skin irritation test and the HET-CAM test are suitable test procedures for the risk assessment of nanoparticulate carrier systems according the principle of the 3Rs. With regard to the application as drug delivery system or cosmetic product the exposure time should be adapted and, thus, prolonged according the regular use in humans.