

Wissenschaftliche Posterausstellung: Poster 1

Quantification of nanoparticle uptake into hair follicles - in vitro in vivo correlation

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The hair follicle represents an interesting target site for drug delivery, as the stratum corneum (SC) is absent in the lower third of the hair follicle facilitating the absorption of topically delivered compounds. Nanoparticles (NPs) penetrate more efficiently into hair follicles than solutions (1), making them ideal carriers for drug delivery. Based on the differential stripping technique (2) we developed a fully quantitative, validated method to determine the exact dose of NPs delivered to hair follicles.

As model carriers NPs prepared from poly(D,L-lactide-co-glycolide) (PLGA) and chitosan coated PLGA NPs (Chit.-PLGA) (hydrodynamic diameter around 165 nm, PDI \leq 0.2 for both types of NPs) were used. The NPs were labeled covalently with a fluorescent dye for detection (3). Both polymers are widely used for drug carriers. Their opposite surface charge (PLGA-NPs -30 mV, Chit.-PLGA-NPs +26 mV) allows investigating the influence of charge on follicular uptake. The investigation was performed on pig ear skin in vitro and on the hairy outer forearm of 11 human volunteers in vivo (6 male, 5 female, skin type II-IV, ethical approval by Ärztekammer des Saarlandes and written informed consent by the volunteers). The NPs were applied, incubated and sampled by differential stripping with tape strips and cyanoacrylate biopsies according to a standardized protocol. Subsequent extraction of tape-strips and cyanoacrylate casts of particle filled follicles allowed quantification of the amount of NPs that had penetrated into the hair follicles.

For exact quantification of follicular uptake the efficacy of removing NPs from the skin surface is essential. This was proven by confocal microscopy detecting NP associated fluorescence on the removed tape strips, in follicle casts and on the skin surface, and by environmental scanning electron microscopy using metal core model nanoparticles (screen MAG chitosan coated nanoparticles, 100 nm, chemicell GmbH, Berlin, Germany). Thus we could demonstrate complete removal of NPs from the skin surface by tape stripping.

We found less than 5% of the applied NPs penetrated into the hair follicles, while the major fraction remained on the skin surface. This result was independent of the NPs used; indicating



that surface charge had no effect on follicular penetration of these particular NPs. Furthermore follicular uptake was very comparable in vivo in the human volunteers and in vitro on the pig ears. Plotting the mean amount recovered from skin surface, the hair follicles and total recovery in pig ears and human volunteers for both NPs, an excellent linear in vitro in vivo-correlation ($r^2=0.975$) was demonstrated.

In conclusion this study confirms pig ear skin as suitable skin model for quantifying follicular uptake of NPs. The uptake efficiency of NPs into hair follicles is relative low and seemed not to be influenced by the surface charge of the NPs.

REFERENCES

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