Precious load - transport of active agents

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Within the field of skin care and dermatology active agents play the most important role. Appropriate transport systems ensure that active agents are transported to the areas where they are really needed.

The most important item of skin care are active agents and frequently high dosages are the decisive promotion argument. Reality however shows that excellent active agents and high dosages are not enough to achieve the optimum effect. In cases where a safe transport cannot be ensured to the areas where the agent is required, the desired effect already falls flat at the skin surface. There are a lot of examples where an external application of skin-identical or similar substances is supposed to correct imbalances in the skin, and where this penetration is emphasized as the appropriate deep layer effect. Today it is a fact, however that many of the active agents just remain on the skin surface.

The desired transport of active agents from the skin surface into deeper skin layers is a very complex process and the most important factors will be explained in the following.

Minuscule particles

Regarding the transport of substances the discussion on the respective particle size has played a major role for quite some time. It has already started with a droplet size in emulsions ranging between 20 to 1µm which means 0.020 to 0.001 mm. By increasing the emulsifier concentrations the droplet size may be reduced until microemulsions have developed with a minuscule particle size that can hardly be measured. In extreme cases these are transparent formulations ensuring an excellent transport of active substances but at the same time frequently damaging the skin barrier structure. That is the reason why said substances were not successful apart from cleansing products which remain on the skin surface only for a short time.

A further strategy has been the use of nanotechnology with a particle size of several nanometers (1 nanometer = 1 nm = 0.000001 mm). And to state an example in this connection: solid iron oxide nanoparticles may be selectively transported into tumor tissue in order to be heated up from the outside with the help of alternating magnetic fields, a process which only affects tumor tissue. However, there have been side effects reported in connection with injections of iron oxide nanoparticles which prompted the newspaper magazine Focus to launch a report speculating on potential health risks in connection with ultrafine (micronized) mineral based UV filters like titanium dioxide (in sun screens) in 2004. Whereas the assumption may be well-founded related to powder substances reaching the lung tissue it is quite made up regarding liquid and partly solid skin caring products. Insoluble lipid substances no matter how small they are may not penetrate an intact skin barrier. This, by the way, also applies for solid cosmetic nanoparticles which remain on the skin surface. They may be loaded with active agents which then are gradually released. The small particle size in this case also suggests that particles may be transported between the dead corneocytes of the horny layers and through the skin barrier substances. This however is not the case. Solid nanoparticles develop a filmy layer on the skin surface connected with a certain occlusive condition in which gradually and with depot-like effect active agents in molecular form are released. This occlusive condition is also responsible for the increase of the skin hydration. As the matrix of solid nanoparticles contains non physiological substances like mineral waxes and/or polymers, the carrier substances are not integrated into the skin and that is why they cannot be seen as substantial skin care components.

While discussing particle sizes it is quite important to state that the smallest relevant particles are molecules which means that in dissolved form as e.g. in aqueous solutions the active agent has the smallest possible particle size i.e. the molecule. Compared with cosmetic nanoparticles of about 100 nm it is about 100 to 1000 times smaller. Though, why not further using aqueous or even oily solutions?

Impermeable skin barrier

Experience shows that also components of solutions only insufficiently penetrate the stratum corneum and the reason for it may be explained with the structure of the stratum corneum. Besides the dead horny layers it consists of two-dimensional barrier layers with a typical bilayer structure. They are hydrophilic on the outside and lipophilic on the inside. Such structures which are typical for cell membranes are called bilayers. In the horny layer they mostly consist of ceramides, cholesterol and palmitic acid in a 1:1:1 molecular ratio. Provided that the layers are intact they form a hurdle which even for substances in molecular size is difficult to clear.

There are different ways to penetrate the barrier layers with active agents and one of them has already been mentioned above in connection with microemulsions: through their surface activity emulsifiers transform the barrier structure. The barrier becomes fluid but as a rule the surface structure will also be impaired. This process however is not a physiologically recommended solution as the barrier should close again after the penetration of active agents in order to take up its original function.

Occlusive filmy layers also cause a fluidity of the barrier layers and as far as the occlusive condition will be achieved with masks which remain only a short time on the skin there are no objections to make. In cases where high concentrations of petrolatum or mineral oils seal up the skin surface for a certain period of time the persistent swelling of the stratum corneum connected with it leads to barrier disorders and a delayed regeneration of the skin (dry skin). Alcoholic products in high concentrations also result in barrier disorders as they severely affect the osmotic balance of the skin.

Similar substances are best compatible

An interesting alternative are substances which form structures similar to the barrier layers and which combine with them due to their comparable physical structure. One of these substances is native phosphatidylcholine which is a component of the cell membranes. In form of liposomes which have the same structure like cell membranes it spontaneously fuses with the barrier layers without affecting their physical structure. The barrier layers become fluid which enables the active agent molecules to slip through. Dissolved in the barrier layers liposomes release the encapsulated active agents into the deeper skin layers. This is the reason why liposomal products should be free of preservatives, perfumes and further potential allergens.

It goes without saying that the fluidity of the skin can be increased by microdermabrasion or peeling as these procedures reduce the number of barrier layers. However the procedures also involve the disadvantage that they impair the regulative function of the horny layer depot which means that active agents flood in spontaneously in high concentrations. By contrast, active agents released from barrier layers conditioned or fluidized with liposomes have a long term and well-proportioned effect. Besides liposomes the cosmetic sector uses liquid nanoparticles which additionally contain oil or lipid components apart from the native phosphatidylcholine. They are used for lipid soluble active agents and above all applied in cases of dry skin. In contrast to solid nanoparticles they only contain physiologically usable components. Liquid nanoparticles also are completely integrated into the barrier layers.

Still increasing their efficacy...

Concluding, a remark about active agents: it is not only a matter of concentration. If the active agents are precisely transported to their appropriate sphere of activity already small dosages will show the desired effects. The efficacy may still be increased by the local release of active agents from "prodrugs" by reaction of enzymes or by influencing natural enzymes in order to trigger booster effects.

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