Piggyback – an overview on transport systems

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Speaking of transport systems for cosmetic active agents, we automatically think of tiny filled spherical bodies that wriggle their way through the gaps between the corneocytes and then empty their load in the deeper layer of the epidermis. That is a good story though, but unfortunately not a true one. The following article will deal with the actual facts.

Vesicular structures belong to the more recent cosmetic structures. The term vesicle originates from biology and denotes capsular membranes that contain liquids whose composition is different from the surrounding environment of the shells. In cosmetics for instance the shells may be liposomes in whose interior aqueous active agents are "encapsulated". We then deal with "loaded" liposomes. In that case, the respective liposome is called a "carrier".

Membranes with in-built effects

Main functions of carriers are:

- to protect the content against oxidation or against the impact of other substances
- to provide a convenient application of active agents
- to condition the skin and improve the bioavailability of active agents

The conditioning of the skin implies the reaction of the capsule material with the skin. As a matter of fact, the membranes of the vesicles merge with the membranes of the skin barrier and make them more permeable (more fluid). The encapsulated active agents can so pass the skin barrier. The original membrane completely dissolves and the different ingredients slowly permeate into the skin in the form of molecules. As a general rule, the membrane material consists of phosphatidylcholine (PC) which itself is an effective agent. That is why the cosmetic also uses "empty liposomes", as for instance in the context of acne prevention, just to mention a typical application. In simplified terms, we summarize the above mentioned applications as "transport" however it should be mentioned that in physical respect, the means of transport act like regular cosmetic ingredients after contact with the skin barrier.

Effects – entirely different though

The increased dermal bioavailability of vesicular preparations allows reducing the concentration of active agents. This not only is a very interesting economic aspect, it can also improve the tolerance and as far as pharmaceutical active agents are concerned, it can reduce the side effects too. The effects may also adopt a totally different functional quality. Just to mention an example: free vitamin C (ascorbic acid) in high concentrations has the same keratolytic effect as a fruit acid and hence can scale off the cells of the horny layer. Even so, it has little impact on the collagen synthesis due to the fact that the acid remains on the skin surface. However, if low concentrations of ascorbic acid esters of the phosphoric, stearic or palmitic acid are encapsulated into liposomes (water-soluble esters) or in biodegradable nanoparticles (fat-soluble esters), the ascorbic acid can be transported to the areas where it is actually needed. The esters are far more resistant to oxidation than free ascorbic acid. The carrier bodies have the size of about 50 to 200 nm (nanometre). After the "transport" into the skin, the esters are enzymatically hydrolyzed into substances that are identical to the natural substances of the body and in the present case, into free ascorbic acid and phosphoric acid, stearic acid or palmitic acid. At this point, the ascorbic acid can take full effect.

Two-way traffic

The above mentioned fluidizing of liposomes with the skin barrier can easily be observed from the outside. A temporarily increased transepidermal water loss (TEWL) can be measured, since the improved permeability of the skin barrier is not a one-way street. Reciprocally, also aqueous vapour can escape out of the skin. Nanodispersions compensate for the TEWL increase with their escape preventing lipid content. In the longer term, the phosphatidylcholine-bound linoleic acid is to be found again in ceramide I, the most significant

barrier component. In the case of dry skin, the temporary effect of liposomes can be compensated by subsequently applying an adequate cream.

More membranes...

On and off it is discussed that multi-lamellar liposomes (multiple-shell, onion-shaped vesicles) can transport higher amounts of active agents than unilamellar ones (one-shell vesicles). This, however, rather seems to be a pseudo-discussion since cosmetic liposomes on the whole represent a potpourri of one-shell and multiple-shell vesicles which is due to the manufacturing process. The manufacturing of unilamellar liposomes would be far too expensive. On top of that, the number of shells (membranes) has no impact on the above-described "transport mechanism". Solely the low or high dosage of the fluidizing membrane component (PC) influences the efficacy of liposomes.

Nanodispersions

Meanwhile, four different systems of nanodispersions can be found:

- Liquid, biodegradable nanoparticles based on PC: Apart from the above-mentioned encapsulation of ascorbic acid esters, they also can be used as a medium for vitamin A, E and their esters (e.g. Tocopheryl Acetate and Retinyl Acetate). A wide range of applications are vegetable oils with their triglycerides whose acid components are long-chained and polyunsaturated (omega-3 and omega-6 acids). These emulsifier-free dispersions can be applied like water, they are non-greasing, penetrate instantly and show a high anti-inflammatory potential due to the metabolites of essential fatty acids formed in the skin. A typical field of application is the care of sun-damaged and atopic skin.
- Solid, non-biodegradable nanoparticles (solid lipid nanoparticles, abbreviated SLN) based on wax, mineral wax or polymers. They do not contain membrane-active components such as PC and hence cannot fluidize the skin barrier. The emulsifier-free lipid-in-water dispersions cover the skin like a fine film and release the encapsulated active agents from the tight film into the interior of the skin. Similar to paraffins, the carrier material itself has no active agent characteristics and cannot be exploited by the skin.
- Solid biodegradable nanoparticles. Among other ingredients, they can contain barrier components such as ceramides, sterols and long-chained carboxylic acids; frequently they are also equipped with active agents. They are emulsifier-free and in contrast to the PC-based nanoparticles which require natural antioxidants (urea, vitamin C, E etc.) they are more resistant to oxidation since they do not contain the unsaturated essential fatty acids of PC. This involves however that also the temperatures for phase transition are far higher than for the PC-containing nanoparticles (native PC < 0 ºC). Hence, these particles are not able to fluidize the skin barrier; their penetration-improving effect on incorporated active agents is insignificant. Nevertheless, appropriately compounded, they can fill gaps in the skin barrier (dry skin).
- Solid inorganic, non-biodegradable nanoparticles consisting of metal oxides (titanium oxide, iron oxide) or nanosilver. These particles cannot be used for the transport of active agents. They serve as UV filters or preservatives (nanosilver).

Masks

The improved permeability of the skin barrier based on the use of PC-containing liposomes and nanoparticles is particularly advantageous for the application of masks. If the permeability is to be reversed after the mask, a membrane-active cream should be applied. Its membrane structure is formed by saturated phosphatidylcholines with increased phase transition temperature as well as ceramides and phytosterols. Just to mention an example. The transition point from a crystalline to the liquid-crystalline phase of the physiological dipalmitoylphosphatidylcholine (DPPC) is 42°C. A similar reaction shows saturated PC (PC-H), which is gained from native PC in a hydrogenation process; it contains both chemically bound palmitic as well as stearic acid. Just as DPPC, it is a physiological substance.

Limits of the systems

Liposomes and nanoparticles based on PC are incompatible with a series of substances commonly used in cosmetic preparations. They are sensitive to emulsifiers, tensides and solvents above all – just like the skin after dissolving the lamellar structures. SLN are far less sensitive in this respect. According to their manufacturing technology however they are only applicable for a certain variety of cosmetic active agents.

As far as encapsulating is concerned, the molecular weight of the active agents is of significance. Macromolecules like hyaluronic acid, polysaccharides and proteins only form physical mixtures with PC-containing carriers. These physical mixtures however also are beneficial due to the above-described reactions of the carriers. With regard to skin hydration and skin smoothing for instance they can complement each other very well.
In addition, it has been observed that added, non-encapsulated low molecular substances also benefit from the fluidization of the skin barrier and that their dermal bioavailability increases. Even highly polar substances such as amino acids, azelaic acid, fumaric acid, caffeine as well as hydrophilic vegetable extracts such as green tea, eyebright or butcher's broom can pass through the skin barrier. These effects are not observed with SLN. Since most of the preservatives and perfume components also are low molecular substances, the PC-containing carriers can intensify a potential disposition to irritations or allergies in their presence. Hence they definitely should not be used in lamellar formulations. This aspect can be neglected in the case of SLN.
In the context of the revision of the European Cosmetic Regulation, the particle size of carriers is being discussed. However in terms of the risk assessment of biodegradable liposomes and nanoparticles, no higher standards have been set since small intact particles will not merge into the human body even in the case of skin barrier disorders. As far as SLN are concerned, the sensorial behaviour and the formation of an external film depend on the particle size and the phase transformation temperatures of the particles.

Reference:

H. Lautenschläger, Nanoparticles in cosmetic products - good or bad? Beauty Forum 2009 (5), 44-47

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