Active agents: liposomes, nanoparticles & co

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Life can only exist in an atmosphere which provides protection against outside influences. Thus, monocellular living organisms are protected by cell membranes whereas multicellular organisms are provided with an exterior skin whose outermost layer, the epidermis also has a membrane-like structure which together with its specific composition serves as a model for cosmetic and dermatic products.

Nature provides an abundance of different membranes which offer protection and simultaneously serve as a regulative for the exchange of substances between the inside and the outside. Compared with today's fabrics they can be seen as Mother Nature's Goretex. The major component of natural cell membranes is phosphatidylcholine, a substance which contains fatty acids, glycerin, phosphoric acid and choline in chemically combined form. The fatty acids may differ according to the specific cell type. Plants predominantly contain unsaturated and essential acids like linoleic acid, alpha-linolenic acid as well as palmitic acid.

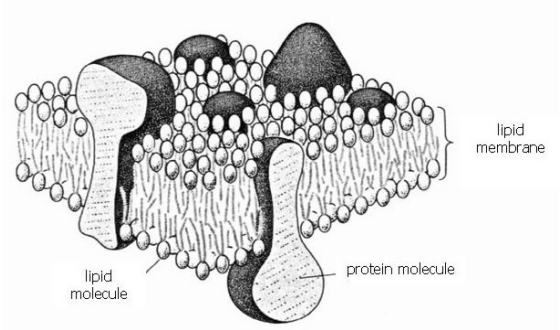

Figure 1:
Sectional view of a cell membrane (according B. Alberts et al.: Molekularbiologie der Zelle, VCH-Verlagsgesellschaft)

For a long time phosphatidylcholine has been used as a food supplement in form of lecithin which contains about 20 per cent of it. Also the choline contained is essential for human beings. It provides multiple protective functions among others for instance also in the liver against cell toxins like alcohol. It is a vital support for brain functions. With the help of high-resolution electron microscopes and freezing technology it could be demonstrated that phosphatidylcholine acts in the same way whether inside or outside of living organisms. In contact with water it spontaneously forms cellular structures which became known as "liposomes".

Liposomes: the condensed power

Liposomes have a variety of interesting features for cosmetic and dermatological applications:

- They are provided with a membrane structure just like the barrier layers of the skin.
- Their membranes can easily be integrated into the barrier layers of the skin without changing their physical structure.
- They supply the skin with essential fatty acids and choline in combined form. The different substances are released by reaction of enzymes. Linoleic acid supports the formation of ceramide I and choline the skin protection.
- As they are able to transfer their phosphocholine group to ceramides, they interfere with the homeostasis (biochemical balance) of the skin and thus can influence cornification disorders. Minor forms of acne can successfully be treated and in this connection also the content of linoleic acid has positive effects.
- Liposomes are tiny spherical bodies (vesicles) with a shell of one or several bilayers of phosphatidylcholine and lipids. Various cosmetic active agents which are generally water-soluble can thus be encapsulated into the liposomal cellular bodies in order to protect the agents and to provide the transport into the skin.

Depending on the manufacturing process, the liposomal membranes may be smaller or larger-sized (mostly with a diameter of 100 to 300 nanometers, 1 nanometer = 0,0000001 cm) with a single or multi-layered (onion-like) shell, whereas the number of layers will have only little influence on the shelf life and transportability at least as far as we know today. On that score only the absolute content

of phosphatidylcholine in the liposome product is important.

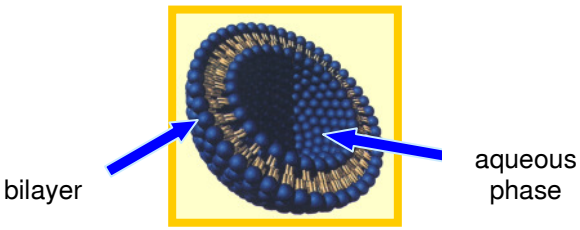

Figure 2:
Liposome (model)

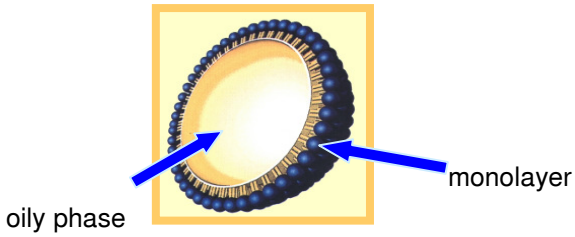

Figure 3:
Nanoparticle (model)

In connection with surface-active substances, where tensides (in detergents) and emulsifiers (in skin care creams) belong to, liposomal membranes react like the membrane-like skin barrier layers which means that depending on the substance concentration they will be destroyed. Hence, combinations of conventional creams containing emulsifiers with liposomes should be avoided. It is recommended to use liposomes in form of sera only locally or in combination with other membrane-containing formulations (see below).

Liposomes: the way they work

Liposomes **merge** with the skin barrier layers where they release the encapsulated active agents. This leads to an increased local permeability of the barrier layer membranes and the active agents are able to pass through. On the other hand, the trans-epidermal water loss (TEWL) temporarily increases with the result that the skin hydration will be reduced. In the **long term** however the linoleic acid which is contained in the liposome base substance supports the ceramide I formation and consequently causes increased skin hydration. When Liposomes are included in a cream matrix for instance also the specific properties of the respective cream have to be considered.

Nanoparticles: the ”oily” nucleus

By adding oils and using high pressure homogenizers it is possible to actuate the formation of so-called nanoparticles (nanoparts) from liposomes. These are particles of about the same size as liposomes they however contain an oily instead of a watery phase inside.

Unlike liposomes, within these particles which are provided with single membranes (monolayer) fat-soluble active agents can be encapsulated. Vitamin A, vitamin E, fat-soluble derivates of vitamin C and primrose oil should be mentioned as examples here.
Nanoparticle dispersions with their watery consistency are not only the appropriate solution for a local treatment but also adequate lotions free of spreading substances (creeping oils) thus providing an excellent greasing effect. The greasing components are not deposited on the surface but permeate into the barrier layers of the skin. The major advantage of nanoparticles is the absence of any emulsifiers which guarantees that the greasing substances of the skin will not again be washed out when the skin get in contact with water.
Lotions based on nanoparticles only need a minimum amount of additives, a fact that especially is convenient for sensitive skin.

Derma membrane structure

DMS creams (derma membrane structure) are also free of emulsifiers and they likewise contain membranes. Instead of the well-known drop-like structures which creams containing emulsifiers show under the electron microscope they are characterized by layered bi-membranes (bilayer). Besides the membrane-forming phosphatidylcholine, in this case containing combined palmitic and stearic acid, DMS creams consist of natural oils like shea butter, neutral oils (from palm oil) and olive oil, squalane, ceramides and moisturizing substances.

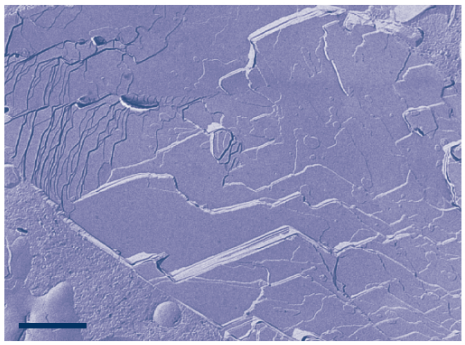

Figure 4:
DMS cream free of emulsifier (electron microscope)

Increased hydration

Characteristic features of DMS creams for instance are an increased skin hydration and a visibly smooth skin which both are still measurable several days after the application. With creams containing emulsifiers however already shortly after suspending the treatment there are no longer any positive but sometimes even negative effects to observe. Just like with nanoparticles the long-lasting efficiency of DMS creams can be attributed to the fact that they will not cause any wash-out of essential substances (see above).

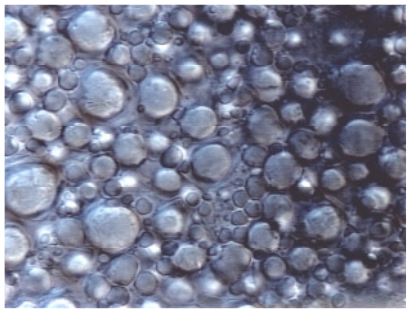

Figure 5:
Conventional cream with emulsifiers (emulsion)
[microscope]

While liposomes and nanoparticles predominantly serve for the transport of active agents, DMS creams have distinct skin protection properties which are of benefit for individuals suffering from skin barrier disorders i.e. they are an excellent care for dry and sensitive as well as atopic skin.
For the cosmetic treatment it is important to know that liposomes and nanoparticles prepare the skin for the permeation of active agents while DMS re-closes it. Thus, it is possible to treat the problem areas independently with liposomal active agent concentrates and subsequently protect them with DMS.

Effective membrane family

By combining the members of the membrane family various different types of skin can be treated. In the meantime extensive collections of different preparations have been compiled which are not only used in the cosmetic sector but also in the field of dermatology. The modular system as the result of the above-mentioned development enables beauty institutes to work with a basic product set and to bring in their own experience in order to adapt the treatment to the individual needs of their customers.
If the membrane products are simultaneously used with other products some basic rules have to be observed:

- The effects of active agent concentrates and extracts will be increased in combination with liposomes and green tea extract can be mentioned here as an example.
- In combination with liposomes, preservatives and other cosmetic substances with allergenic potential will penetrate deeper into the skin layers. Hence these combinations should be avoided.
- Neither should perfumes be used together with liposomes and nanoparticles as they also include a higher risk of sensitization for skins with a certain disposition.
- Besides, additives should anyhow be limited to a minimum as they unnecessarily strain the skin.

A very interesting fact is the specific influence of the different members of the membrane family on the relative skin hydration. The strong increase of skin hydration directly after the application is due to the water content in the products. Along with the evaporation of water also the skin hydration will naturally be reduced. An application of pure liposomes will temporarily lead to relatively low values due to the increased permeability of the skin barrier. When applying nanoparticles, this effect will however be levelled out because of the additional oil content.
The skin protection properties of DMS lead to a significantly higher skin hydration. Oleogels which are oil-containing gels with a composition similar to DMS without containing water however show a continuous increase of skin hydration. They penetrate excellently due to their phosphatidylcholine content and just like the water-containing DMS creams they are an

appropriate care for the neurodermitic skin. There is a multitude of different applications of the membrane family and because of their physiological concept they provide a long-term support for the care of sensitive and problem skin.

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