Specific active agents and bases in corneotherapy

published in Kosmetische Medizin 2004 (2), 72-74

The term corneotherapy was coined in the late nineties[1)] by Professor Albert M. Kligman. The basic idea of corneotherapy is that topically applied substances as e.g. moisturizers and lipids influence the biochemistry and physics in the horny layer as well as subsequent processes in deeper skin layers which again have effects on the constitution of the horny layer.

Kligman hence speaks of an "outside-in therapy" in contrast to an "inside-out therapy" with pharmaceutically active agents as for example corticosteroids or typical inflammation inhibitors which first of all have to penetrate the horny layer to become effective. As an appropriate corneotherapy may have effects similar to a medical drug, skin caring active substances more and more become the focus of attention for the treatment of barrier and cornification disorders. Among others also natural substances like ceramides, proteins and their synthetically produced analogous substances, the peptides, are part of this physiological concept. The following article describes the connections between these different substance classes and gives advice on the effects to be expected in practical use.

Ceramides – an extended and rather complicated family

Ceramides (CER) and sphingomyelins (SM) belong to the much diversified group of barrier active substances with specific functions. They have a major influence on the condition of the human skin; however, they are different in terms of structure and proportion depending on the particular skin layer and their specific function. Among other substances also transmitters like sphingosin 1-phosphate (SPP) are part of this group. Phospholipids and particularly phosphatidylcholine (PC) are involved in their biochemical and transport processes.

Homeostasis in skin

Live and healthy skin cells show a perfect balance (homeostasis) of ceramides (CER), phosphatidylcholine (PC), diglycerides (DG), sphingomyelins (SM), sphingosin (SP), sphingosin 1-phosphates (SPP) and fatty acids (FA). This can be illustrated by a simplified example: an increase of CER in cells initiates their differentiation and subsequently their controlled cellular death (apoptosis). Therefore the highest CER concentrations can be found in the stratum corneum where they have a major protective function against external influences. A decrease of PC concentration also leads to cellular death as there is not enough CER to be transmitted to SM by using the phosphocholine group of PC. A high content of SM in cells provides protection against the CER-controlled cellular death.

Ceramides for topical application

CER is one of the major key substances against skin aging, neurodermatitis, psoriasis, ichthyosis as well as further CER-related cornification disorders. Short-chain CER and SP may diffuse from the stratum corneum back to the stratum granulosum where, with the help of cytokines they can induce the cellular death of keratinocytes. Long-chain, topically applied ceramides theoretically might fill the gaps in the barrier layers whereas a further penetration into deeper skin layers is not appreciated due to the above mentioned reason. It would however be appreciated to have specific ceramides at disposal which could be transported to wherever they are needed with the help of appropriate transport systems. In cream bases however most of the ceramides are more or less insoluble. An alternative here is the application of PC rich in linoleic acid which easily penetrates into the skin when applied in form of liposomes or nanoparticles. The linoleic acid already will be released in the stratum corneum by ester hydrolyzing enzymes like phospholipase A_2 and then is used as a substrate for the natural synthesis of the linoleic acid-containing ceramide I of the human organism. A further advantage of PC is that the phosphocholine group integrates into the CER/SM balance and thus may have a lasting effect on the cell aging process. Its efficacy for the neurodermitic skin has been proved in practice especially for products which, besides linoleic acid-containing PC, also contain saturated PC (PC-H) as the last named is able to compensate the PC-related

fluidization of the barrier layers. Thus PC is an indirect key factor for influencing the CER balance. For some time now, appropriate products in form of liposomes, nanoparticles and derma membrane structure (PC-H-containing base creams)[2] have gained acceptance in the field of dermatological cosmetics.

Ceramide I

Ceramide I (about 8% of all ceramides) reduces roughness and brittleness of skin. A diet without essential fatty acids, among others also linoleic acid, causes a ceramide I deficiency with the result that instead of linoleic acid the natural oleic acid of the body will be integrated into ceramide I[3] which consequently leads to major barrier disorders. For therapeutic purposes topically applied linoleic acid is easier available than orally supplied one as the liver primarily transforms the last named into polyunsaturated fatty acids like arachidonic acid and its metabolites. Low ceramide I contents in the skin correlate with an increased susceptibility for neurodermitic conditions. Ceramide I hence is an important protective factor for the skin.

Topically applied amides

On the skin surface, topically applied ceramides like ceramide III for instance which is easily available in yeast, have excellent skin caring effects, although these may rather be attributed to their specific chemical structure than to their natural function. As the name already indicates, ceramides contain an amide group (-CO-NH-). Amides show the specific feature of building up hydrogen bonds to similar or also different amides. These hydrogen bonds cause the molecules to adhere to each other. By definition, these adhesive properties are also effective on protein surfaces like the keratin of the horny layer whose amino acid components are likewise linked by amide groups. Depending on the composition ceramides and amides generally may cause a noticeable firming and smoothing of the skin and in cases where saccharide-containing hyaluronic acid is involved this may also lead to increased retaining of water without the rather unpleasant filming on the skin surface. The protein-related and synthetically produced peptides as well as their fatty acid condensates also belong to the group of amides, like e.g. palmitoyl-pentapeptide [containing amino acids in the following order (palmitoyl), lysine, thyreonine (2x), lysine, serine] or acetyl hexapeptide [containing amino acids in the following order: (acetyl) glutamic acid (2x), methionine, glutamine, arginine (2x)]; all of them represent a further development of the protein hydrolysate condensates which have already been known for some time. Topically applied collagen has similar effects due to its protein structure but is less frequently used due to the complex BSE problem and the discussion of animal raw materials. Peptide condensates are applied in relatively high doses of up to 5 percent of solids; however, whether additional effects which were measured in vitro are of any practical importance still has to be clarified. The structure of single fatty acid monoethanolamides resembles the ceramides, as for example the palmitic acid monoethanolamide (INCI: Palmitamide MEA) and the stearic acid monoethanolamide (INCI: stearamide MEA). These substances which are also called skin protective substances[4] may have anti-inflammatory and antipruritic effects just like urea and allantoin (amides with very low relative molecular weight). Palmitamide MEA as the metabolite of N-palmitoyl kephaline (N-Palmitoyl-phosphatidylethanolamin), which belongs to the phospholipids, is a natural component of the epidermis.

Natural regeneration

As already known, in the healthy horny layer the barrier lipids CER, cholesterol and FS show a molecular ratio of 1:1:1. Any changes in the molecular proportion lead to barrier disorders and pathological conditions which is a clue that there is a layered structure of special geometrical conditions which is stabilized by molecular forces like e.g. hydrogen bonds. Any artificially caused barrier disorders (stripping) results in a relatively fast regeneration of the barrier lipids – which can be recognized by the fast decrease of the initially augmented transepidermal water loss (TEWL).

Topical substances free of emulsifiers

If corneotherapeutic active substances are used in cosmetics or dermatics the application of emulsifiers is out of question as it may cause disorders within the barrier layers. Furthermore, if the penetration or permeation of product components into the stratum granulosum and even deeper skin layers is part of the therapeutic strategy also preservatives listed in the appendix of the German Cosmetic Decree (KVO) as well as

perfumes should be avoided. Liposomes, nanoparticles as well as creams based on derma membrane structure can be produced free of any emulsifiers[5]. For about two years now also specially composed oleogels have been used for this purpose. Their composition even permits the integration of polar amides like urea.

Individual adaptation

Concluding, it should be noted that besides adding liposomes and nanoparticles the derma membrane structure bases may also be adapted to the individual skin with specific prescriptions which contain hydrophilic and lipophilic active agents[6] and are prepared at room temperature. Depending on their composition the modular systems resulting here as well as appropriate finished products are used in dermatology for the treatment and in skin care for the prevention of barrier and cornification disorders as well as for skin protection[7,8,9]. Skin analyses based on corneometry (skin hydration), sebumetry (skin lipids) and tewametry (TEWL) help to select the appropriate prescriptions and to test their efficacy[10].

1) Lübbe J.
Evidence-Based Corneotherapy
Dermatology 2000; 200: 285-286
2) Lautenschläger H.
Universelle Basiscremes mit Membran-Struktur für Hautpflege, Hautschutz und Dermatika
Österr. Apothekerzeitung 2002; 56 (14): 679
3) Proksch E.
Linolsäurehaltige Externa
Internist. Prax. 1998; 38: 877-883
4) Lexikon der Hilfsstoffe für Pharmazie, Kosmetik und angrenzende Gebiete
Hrsg. H. P. Fiedler
Verlag Editio Cantor, Aulendorf 1996, S. 1457-1458
5) Lautenschläger H.
Liposomes
Handbook of Cosmetic Science and Technology. Hrsg. A. O. Barel; M. Paye; H. I. Maibach
Marcel Dekker, Inc. New York Basel 2001, S. 201-209
6) Lautenschläger H.
Kosmetik International 1999; 1: 104-106
dermaviduals – Dienstleistung der Zukunft
7) Lautenschläger H.; Albrecht M.; Bohn. M.; Weisser M.
Hautschutzpräparate zur Prävention von Hautschäden
DE 198 57 490 (Anm. 14.12.1998)
8) Lautenschläger H.; Albrecht M.; Bohn. M.; Weisser M.
Wasserhaltige Hautschutzpräparate zur Prävention von Hautschäden
DE 198 57 492 (Anm. 14.12.1998)
9) Lautenschläger H.
Base creams for the prevention and treatment of atopic dermatitis
Acta Dermatovenerol Croat 2004; 2 (12): 132
10) Lautenschläger H.
Hautanalyse - moderne Geräte helfen
Kosmetik International 2003; 3: 102-104

Dr. Hans Lautenschläger