Elastase - the target of a novel anti-aging strategy to defy skin aging, loss of skin elasticity and wrinkle formation

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In the skin, the epidermal stem cells are responsible for the formation and regeneration of all the different cells in the epidermis. Since the skin progressively differentiates and regenerates, the epidermal stem cells are the most important skin cells in charge of the epidermal homeostasis, of the regeneration of the elastin and collagen fibres as well as the regeneration of the skin barrier. With aging, the number of epidermal stem cells decreases and accordingly also the capacity of the skin to regenerate with the consequence that barrier disorders develop, hydration and elasticity of the skin are reduced and wrinkles will form. The skin elasticity is influenced by the quality and quantity of elastin and collagen fibrils.

The ongoing attacks of free radicals damage the elastin and collagen fibres. The skin protects itself against these impairments with the aid of radical scavengers. Since many of the radical scavengers belong to the NMF (Natural Moisturizing Factor) and contribute to the osmotic balance in the skin, the ingredients of skin care products should be adjusted to the natural moisturizing factor. Moisturizers play a decisive role in the skin. They increase its elasticity and smooth the skin. Until today, the majority of the cosmetic anti-aging preparations consisted of antioxidants.

Just recently, the scientific interest in dermatology and cosmetology has been focused on the collagen degrading enzymes elastase and matrix-metalloproteinases.

Increased elastase activity triggers various diseases as for instance rheumatoid arthritis, cystic fibrosis, chronic obstructive airway disease, psoriasis, delayed wound healing and premature skin aging with wrinkle formation [3-5]. Elastase cleaves proteins, preferentially at the amino acid valine. Valine residues occur in a multitude of protein compounds, particularly in collagen and elastin fibrils. In addition, elastase plays a decisive role in the control of inflammatory processes.

Under physiological conditions, the elastase activity is controlled by inhibitors (serpines). This balance can however be susceptibly impaired by reactive oxygen radicals (ROS), the consequence being a destruction of healthy tissue and a continued inflammatory process. Furthermore, it could be proved that elastase also is involved in the UV radiation induced skin aging process and the associated formation of wrinkles.

In searching for elastase inhibitors, different plants of the tropic rain forest turn out to be an interesting source for research. However, also European medicinal plants show an increased elastase inhibiting activity.

Immediate elastase inhibition could be proved through numerous polyphenols such as agrimonilin and pedunculagin occurring in lady's mantle, and epigallocatechin gallate found in green tea. It could also be established that already low concentrations of resveratrol, genistein, parthenolid gained from tanacetum parthenium and 11,13 dihydrohelenalin acetate found in arnica blossoms, inhibit the release of elastase from neutrophil granulocytes and impair the NF-kappa-B activity. Hasan Safayhi [1] has proved that boswellia acids gained from frankincense not only block the biosynthesis of the pro-inflammatory leukotriens but also decrease the activity of the human leukocyte elastase. Acetyl-11-keto-ß-boswellia acid is a non-competitive 5-lipoxygenase inhibitor and reduces the human leukocyte elastase (HLE) activity in vitro with an inhibitory concentration of IC50 in 15 µM. Boswellia acids provide an exceptional dual suppression of inflammatory processes by inhibiting the 5-lipoxygenase as well as the human leukocyte elastase. The inhibition of both the pro-inflammatory enzymes in the skin through boswellia acids seems to be the rationale behind their antiphlogistic effects in the case of skin diseases such as atopic dermatitis (neurodermatitis), acne, rosacea, psoriasis and actinic keratosis.

In natural medicine, extracts of the above-mentioned plants are externally applied in the case of skin diseases.

It could be established that frankincense extract encapsulated in nanoparticular carrier systems is highly effective against inflammatory skin diseases and also has a distinct wrinkle-smoothing effect [2, 6-11]. In order to impair the skin damages induced by increased elastase activity, the active agents need to permeate the protective barrier of the skin and arrive in the deeper skin layers in an adequate concentration.

As far as the transport of encapsulated active agents is concerned, a difference has to be made between penetration and permeation of substances. Penetration means that the agents infiltrate into the horny layer, permeation signifies that they pervade the entire skin. The skin barrier consists of a lipid layer which is almost insuperable for hydrophilic substances. Hence, in order to transport the substances through the lipid layer, the active agents need to be encapsulated into adequate transport vehicles such as liposomes or nanoparticles.

The liposome shell consists of phosphatidylcholine bi-membranes (bilayers) which are needed for the natural formation of cell membranes too. Nanoparticles also have a phosphatidylcholine shell. Yet, this particular membrane consists of a monolayer. Liposomes are used to encapsulate hydrophilic substances, nanoparticles serve for lipophilic substances. The vehicle shell serves not only as a wrapping for transporting purposes but also contains essential skin recovering agents as for instance unsaturated fatty acids and choline, a substance with cell protective functions.

Vegetable polyphenols and sequiterpene lactones are promising substances: in adequate cosmetic formulations, they can inhibit the collagen and elastin degradation and thus stop the loss of skin elasticity and smooth out wrinkles [12]. Along with the traditional radical scavengers such as the vitamins A, C, E, CoQ10 and OPC gained from grape seed extracts, and the elastase inhibiting polyphenols, sesquiterpene lactones and triterpenes, cosmetics now disposes of a variety of preparations equipped with a dual mechanism that inhibits the degradation of both elastin and collagen.

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