Enzymes – to inhibit or to stimulate?

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Enzymes control all the chemical reactions in living organisms. The following provides insight into their function and their effects and how they are used in the cosmetic field.

Enzymes cleave complex substances into absorbable components already during the intake of food. The natural enzymes of the body but also the enzymes of the mouth and intestinal microbiome participate in the process. There is more to it than that: also the enzymes of the skin flora are involved when it comes to absorb substances through the skin.
The process continues with the metabolic activities of the body during which enzymes act upon the food fragments by creating complex structures which they degrade again before the resulting waste products then are excreted via lungs, glands and kidney. Here too, the skin flora actively participates by degrading horny layer components and producing the acids required for the acid mantle of the skin.

Economically hand in hand

Compared with classical chemistry, enzymatic processes have the advantage of being catalytic processes or in other words, they work economically with minimal energy input. There's more to it than that: the activities are stepped up if needed, stocks can be built up and vice versa, activities can also be slowed down whenever necessary. Thus, enzymes also are biological control systems that adjust the activities of the body to changed conditions. In addition to it, they keep the body's temperature at a constant level and allow for motion and growth.
From a retrospective and earth historical point of view, catalytic working substances and later on the resulting enzymes are regarded as the first precursors of life. During the following evolutionary steps, individual enzymes have harmonized and increasingly worked hand in hand. Organisation and networking continued to improve and independent organisms formed which then even could enzymatically duplicate themselves. Our genes are the organisational key for all the enzymes built up later on and all their activities.

Disorders in the network

Disorders in the overall organism are implicated when individual enzymes within a chain or within the network are malfunctioning. This happens for instance with inherited enzyme defects or with changes in the intestinal microbiome. Various pharmaceutical drugs inhibit or stimulate the enzyme function in order to manipulate the course of a disease but in this context they also cause adverse effects as they involuntarily interfere with other enzymatic control systems. A typical example here is the group of non-steroidal inflammation inhibiting drugs (NSAID) which can cause damages of the gastric mucosa due to the changes in the prostaglandin metabolism.
It should also be mentioned that in the course of time various theories have become obsolete because the counterbalancing properties of the natural enzymes of the body had not been taken into consideration. Disproved theories, for example, are the influence of cholesterol-containing food on the cholesterol level, increased blood pressure through intake of salt or the control of free radicals with antioxidative food supplements.

Influence of skin care

An interesting aspect in this context is how the ingredients of skin care products are metabolized respectively degraded. To which extent are the enzymes of the skin microbiome involved and what is the share of epidermal enzymes? The answers will of course have consequences not only for the composition of cosmetic products but also for the "care" of the microbiome. That's all still up in the air, though, since the conditions are rather complex and reciprocal interactions are not easy to predict. However, several ingredients already are supposed to be counterproductive. The substances are:

- Preservatives: they alter the microflora since they can produce potentially resistant germs that spread at the expense of other populations.
- Disinfectant agents affect the development of the dermal immune system. In this context also the enzymatically formed antimicrobial peptides (AMP) play a part.

- Physiologically non-degradable complexing agents bind trace elements that are essential for many enzymes.
- Physiologically non-degradable emulsifiers cause disorders in the skin barrier. Besides their washout effect, they also can denature enzymes and even have irritative effects, as for instance sodium lauryl sulphate (INCI).
- Endocrine disruptors affect the enzymatically controlled hormonal metabolism by interacting with the hormone receptors and influencing the hormone degradation and the thus related formation of metabolites.

Degradation of proteins

Enzyme inhibition is beneficial in cases where facultative pathogenic germs of the microbiome with their proteases come upon an already damaged skin barrier and thus involve a degradation of endogenous proteins. The boswellic acids occurring in frankincense are beneficial in this context and successfully administered in the case of germ-induced, inflammatory skin conditions such as acne, neurodermatitis and rosacea. There even is a dual purpose in the case of rosacea, since also the AMP-degrading endogenous proteases are inhibited which work faster than the AMP-forming enzymes.
The NMF is mainly composed of amino acids and also results from the activity of epidermal proteases that degrade the proteins. The NMF is an important protective factor since it guarantees a physiologically-induced skin hydration and preserves the skin against atmospheric radicals. Enzyme peelings work in a similar way. Usually they are gained from pineapples or papaya and sold in the form of powders – blended with carriers such as kaolin, diatomaceous earth and aluminosilicates. They are mixed with water and applied in the form of masks and then removed from the skin after a fixed period of time (usually about 20 min.). In comparison with other keratolytic procedures they are rather regarded as mild peelings.

Antimicrobial peptides

The antimicrobial peptides (AMP) in the skin barrier virtually form a “line of defence” towards the skin flora where in general there is ceasefire but where every now and then also skirmishes may occur. In the case of forays of microbial proteases, the AMP level immediately is up-regulated by enzymes. Various AMPs also have enzyme properties, as for instance

- Lysozymes: They belong to an extensive family of enzymes occurring in flora and fauna and mainly have antibacterial effects.
- Ribonuclease-7 (RNase-7) is a highly effective AMP occurring in the genitourinary tract and attacks germs on the skin surface.
- Lactoferrin inhibits a variety of different bacterial proteases and occurs, among others, in milk and the vaginal secretion of mammals.

Imbalances

Enzymes play a major role in the case of inflammations and chronic skin diseases. Thus injuries, mechanical irritations, infections as well as barrier- and cornification disorders can trigger a cascade of enzyme-controlled reactions. A key enzyme in this context is 5-lipoxygenase that oxidises arachidonic acid into 5-hydroperoxyeicosatetraenoic acid (5-HPETE) which in turn forms the pro-inflammatory leukotriens LTA_4, LTB_4, LTC_4, LTD_4 and LTE_4.
In the case of vitiligo, increased hydrogen peroxide contents are found in the skin. The disease is supposedly triggered by insufficient activity of the dermal catalase which is an enzyme that converts hydrogen peroxide into water. Hydrogen peroxide inhibits the enzyme tyrosinase which is responsible for the melanin formation. Accordingly, melanin cannot be formed under such conditions.
Enzymes also control the formation and degradation of collagen in the connective tissue. With advancing age, more collagen is degraded than formed. The alternatives are either to inhibit the responsible matrixmetalloproteases or to stimulate the collagen-forming enzymes. The effects however are rather modest as studies in this field have shown.
There are many other skin problems that can be ascribed to hyper- or hypofunction of individual enzymes. Inhibition or stimulation but also the administration of enzyme-like substances can often be beneficial. As already mentioned in the context of pharmaceutical drugs, it should be considered that possibly also other functions within the network can be influenced which in turn can involve unwanted long-term effects.

Enzymes in the cosmetic field

Free enzymes are rather unusual in the cosmetic field. This mostly is due to the complicated structure of this substance class that only allows superficial effects. That is why only substance-degrading representatives can be found as already mentioned above in the con-

text of so-called enzyme peelings or probiotics with lactic acid bacteria. By means of their enzymes, they produce lactic acid from the polysaccharides of the body and thus reduce the pH level. The latter mentioned are primarily applied in the genital area. More often used are fragments of enzymes, the so-called co-factors. Just to mention a few: Coenzyme Q_{10} (ubiquinone), pantothenic acid (component of coenzyme A), D-panthenol (precursor of pantothenic acid), riboflavin (vitamin B_2), niacin, biotin and folic acid with a whole variety of different effects that usually bear no relation to enzymes.
Substrates of enzymes, by contrast, are relatively often used with focus on the interaction of available endogenous enzymes and those of the skin microbiome. Examples:

- Essential fatty acids (substrates of 15-lipoxygenase) – anti-inflammatory
- Triglycerides (substrates of lipases) – formation of acids to be integrated into the skin barrier

Apart from that, a variety of inhibiting substances are effectively applied, e.g. against hyperpigmentation (tyrosinase inhibitors) or dandruff (inhibitors of the ergosterol biosynthesis of fungi) and body odours (antimicrobial).

Conclusion

Various studies conclusively substantiate the correlation of enzyme defects and skin diseases. In practice, however, this knowledge almost never is used in dermatology and the cooperating service laboratories. Without having to administer medical drugs, many neurodermatitis patients could benefit from a laboratory-diagnosed defect of the delta-6-desaturase, an enzyme of the fatty acid metabolism, and consequently, the application of the missing gamma-linolenic acid in the form of an aqueous nanodispersion with evening primrose.

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