

# Microbiome and skin inflammation

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Inflammatory processes in the skin are caused by external impacts or endogenic predispositions. Common cause is a metabolism disorder characterized by modified enzyme concentrations or enzyme defects. Also the protective mechanisms in the epidermis can be impaired.

**W**hen the filaggrin proteins insufficiently crosslink the keratin structures that form during cornification, or when the proteases cause imbalances during the formation and degradation of the antimicrobial peptides (AMP) with the result of a pronounced degradation process, conflicts come up at the "demarcation line" between bodily structures and the natural microbiome of the skin plus transient exogenous germs. Facultative pathogenic populations then proliferate.

The immune system reacts with an enzyme-controlled and cascading formation of inflammation mediators. Visible symptoms are redness, swellings, possibly local temperature rise and pain as well as eczema, blazing neurodermatitis and rosacea etc.

## Hygiene & Co

Similar processes occur when the microbiome is disturbed by exogenous impacts, as for instance when the protective resident germs are impaired and depleted through misunderstood hygiene measures and working- and household chemicals. The consequences are that exogenous and virulent germs then have an easy job in forcing through the remaining resident flora and penetrating into the skin. In other words the following symptoms are indicative: fungal infections on feet, inflammations of the nasal mucosa and in the genital area as well as eye inflammations after swimming pool and hot tub baths with chlorinated water that usually has antiseptic effects. The infections are not caused in the water but shortly afterwards.

## Skin care

Another factor are skin care products and their ingredients that contribute to influencing the natural defense mechanism of the skin consisting of antimicrobial peptides (AMP) and the resident skin flora – frequently with adverse effects on the skin. In other words: even the well-intentioned skin care can be counterproductive and finally lead to skin problems. Some examples are compiled in the following:

- The preservatives listed in the German Cosmetic Directive (Kosmetikverordnung – KVO) reliably protect the cosmetic preparations during storage and, after opening, during usage. Just as antibiotics, the preserved cosmetic products have various selective effects on the germs of the resident microbiome of the skin and trigger imbalances in the system. Some kinds of germs are reduced while others and more resistant ones can proliferate.

At this point it should be mentioned that antiseptic substances, such as the already mentioned chlorine or hypochlorite used in swimming pools, as well as iodine solutions or hydrogen peroxide, but also aluminum chloride and acetate of alumina differ from most of the preservatives by chemically attacking and denaturing not only germs but all kinds of organic structures.

- The effects of the currently popular antioxidants on the microbiome still are completely unknown. Another point is that the disulphide bonds of cross-linked endogenous proteins (see above) can possibly react with strong antioxidants and cleave. The still observable competition in increasing the antioxidative potential and concentration of such substances in cosmetic products may not be helpful in this context – just to put it cautiously. As an example, the chemical treatment during the permanent-waving procedure should be cited which initially starts with an antioxidant process.

In this regard also strong physiologically non-degradable complexing agents such as EDTA should be mentioned that support the antioxidants by bonding heavy metals and preventing autoxidation. They inevitably interfere with the heavy metal metabolism of the skin flora but also with the endogenous oxidoreductases – including the AMPs among them.

- The effects of emulsifiers and tensides are of ambivalent character. They are inevitably required for skin cleansing purposes but also for a stable dispersion of fats and oils in aqueous creams unless lamellar emulsifier-free formulations are used which involve higher production costs, though. Among other features, emulsifiers affect the cellular and extracellular bilayer structures of the skin barrier and skin flora. Representatives with high critical micelle concentration (CMC – which is a substance constant) are aggressive enough to trigger skin irritations. Sodium Lauryl Sulfate (INCI) can be mentioned as an example in this context. In order to keep the quoted interactions at the smallest possible level, the used emulsifiers should be physiologically degradable, have a very low CMC, and the skin cleansing preparations should be used in small doses and at very low frequency.
- Microdermabrasion treatment involves that skin barrier and microbiome are damaged in the process. That is why emphasis should be laid on the skin recovery and both the above-mentioned cosmetic additives but also active agent concentrations should be used sparingly, in particular if the general and long-term effects during routine applications are unknown. Experiences with Celtic skin show that fruit acid peelings lead to similar results whereas the disposition to skin conditions such as rosacea and perioral dermatitis is increasing.

### Inflammation

Inflammatory reactions of the skin respectively infections can already be minimized with preventive measures and an essential aspect here is to use the synergy of skin and microbiome and refrain from (unintentionally) interfering with the skin flora but also avoid imbalances due to excessive skin care.

The high lipid content in creams is mostly felt as a pleasant product feature but it increases the ratio of anaerobic to aerobic germs. In the case of disorders of the connective tissue and superficial blood capillaries, this imbalance frequently and shortly leads to inflammatory processes which only can be controlled with the help of topical antibiotics. This progression is typical for rosacea. In this case it can be beneficial to inhibit specific enzymes of the anaerobic germs with additional active agents and thus also inhibit their proliferation.

At long last it can be said that every manipulation of the skin, be it with hygienic measures, skin care products, peelings or working substances in industry and household also triggers counter reactions of the microflora of the skin. To put it the other way round, it is also fair to say that minimizing the manipulations and keeping the skin condition as natural as possible will reduce the number of potential problems.

### Probiotics

Another alternative is to provide the skin from outside with “good” bacteria in the form of probiotic preparations so that the situation at the demarcation line between skin and microbiome remains peaceful and the cooperation of body and microbiome is supported. In the food sector, probiotics such as sauerkraut and kimchi have been known from time immemorial, but this also can be said for the skin care considering that yoghurt and curd cheese have been used as masks on skin and wounds. The first cosmetic finished products with lactic acid bacteria have also been on the market for decades but have not become very popular. There are various reasons:

- Bacteria-containing preparations require adequate storage temperatures and are not stable over a longer period of time.
- The effects on the microbiome are not validated. Basically it is a preferable objective to force back harmful microorganisms, however, the results are difficult to verify. Whether a dominance of lactic acid bacteria at the expense of other, possibly also “beneficial” bacteria is useful is hard to answer. In other words, we are dealing here with a strategy of “hit or miss” and “it cannot be harmful”.
- From today’s standpoint, the preparations, formally speaking, are considered as germ-loaded and mutations and small amounts of other species cannot be excluded. In other words, assuring a certain product quality is anything but simple. Whereas in the food sector the situation with yoghurt cultures with their short shelf-life is straightforward.

Picking up the exogenous germs of the mother already during birth is significant for the growing skin flora and its protective function – in contrast to Caesarean deliveries carried out in an aseptic environment. Later on the immune system also is better trained and becomes more resistant through exposure to unfiltered

external influences than in a clinically clean environment.

### Prebiotics

A simple and more practicable alternative to support the microbiome and its beneficial functions with cosmetic products is the use of prebiotics. They can serve as nutrition (substrates) for the growth of certain species. In the food sector, this strategy is pursued with dietary fibres, additives and food supplements that are preferably metabolized by specific bacteria in the colon. With regard to skin and mucous membranes, lactic acid substrates are popular. The pH value of the vaginal secretion is caused by lactic acid bacteria that degrade maltose and dextrose, both substances are naturally resulting from the glycogen cleavage. When it comes to restoring the natural vaginal milieu concomitant to therapy also probiotics are administered which release lactic acid and lactic acid bacteria and stabilize the pH value of approximately 4.

Similar metabolisation seems to occur after the application of polysaccharides. Also the effect of short-chained hyaluronic acid presumably is affiliated to a degradation phenomenon with formation of acetyl-glucosamine.

### Exclusion of counterproductive substances

Far more important is how the clearly proven counterproductive ingredients such as preservatives, complexing agents, emulsifiers and tensides in cosmetic products can be replaced by microbiome-compatible substances. And to mention an example: how can preservative-free cosmetic products remain microbially stable during storage and use. The most frequent alternatives today are hypertonic aqueous phases that become microbiome-compatible by superficial dissemination, low concentrated alcohol that in large part evaporates right away, or glycerin and glycols, that on the one hand are finely dispersed and on the other hand are degradable.

In the case of complexing agents, EDTA can be replaced by transient substances such as physiological citric acid. Emulsifiers in creams can often be substituted with phosphatidylcholine that forms lamellar, barrier-related and also physiological structures. The destination route for tensides already has been described above (off-line).

Immediately after the start of discussions on the microbiome functions, the first products with supposedly prebiotic or probiotic advantages for consumers have been presented on the market. The fact however is that currently we do not have any information on inter-

actions after the application of the cosmetic preparations.

With regard to oral and topical pharmaceutical drugs there only is little knowledge on whether their adverse effects in the form of inflammatory skin alterations are related to endogenous activities in the epidermis or rather are due to their interference with the microbiome, respectively the interaction of both. Experience has shown that the activity of facultative pathogenic fungi often is stimulated by oral antibiotics, just to mention an example.

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