

# Anti-irritant agents

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The tolerance of cosmetic preparations is an ongoing issue – among consumers as well as among manufacturers. Skin condition, subjective feeling and the objective properties of substances play a role in this context.

When it comes to skin irritations, the persons concerned usually try to substitute the triggering substances or lower the concentrations. Another alternative is to incorporate additives into the formulations that lower the sensitivity of the skin. The question arises now, what cosmetic ingredients can irritate the skin? This is difficult to answer. Substances cannot just be classified as 'irritant' or 'non-irritant'. The sensitivity threshold depends on the concentration of the substance as well as on the condition and sensitivity of the skin. Reactions are different from person to person. In the case of extremely barrier disordered skin even normally harmless substances may trigger redness, itching, burning sensation, swellings or irritations. Effects are more pronounced in the case of the often-quoted 'sensitive' skin that possibly already reacts to cold, heat, wind as well as to mechanical impact such as pressure and strain. When it comes to substances that are considered as comedogenic, it is observed that the threshold concentration not only depends on the skin condition but also on the concentration of the other components of the formulation. Preservatives, essential oils and perfumes, emulsifiers and tensides belong to the candidates that already can trigger reactions in 'normal' skin.

Cosmetic manufacturers are anxious to reduce the concentrations of irritative substances, substitute them by more tolerable products (substitution principle) or even completely avoid certain substance groups. If the preparations are intended for dry skin (= minor barrier disorder) easily penetrating fragrance substances or preservatives are omitted. In this way formulations are continuously adapted and optimized, but also because the knowledge on substance properties is constantly increasing and because cultural influences make the skin more and more sensitive.

In order to already minimize the onset of irritations, the consumer should improve an existing bad condition of the skin so that the individual sensitivity threshold is increased. In the case of barrier disturbed skin, this can be realized with skin care preparations that are oriented towards the components of the stratum corneum

and sebum. It is also beneficial to minimize tenside contact. Skin cleansing routines should be reduced as well to avoid wash out effects. When working with household cleansers, it is recommended wearing gloves.

## Acute irritations

Persons with acute skin irritations should refrain from using skin care products and maybe see a doctor. As a therapeutic emergency measure, pharmaceutical active agents are topically applied and, if needed, also orally administered. The repertory encompasses pharmaceuticals such as:

- antihistamines – for allergies
- local anaesthetics – for itching and pain
- corticoids – for inflammations
- antibiotics – for infection treatment
- antiseptics – for wound disinfection
- antimycotic agents – in the case of mycosis
- preparations for other dermal indications

After the skin has been soothed to the point that it is dry and receptive, the treatment can be continued with cosmetic preparations. Base creams that can be mixed with pharmaceutical but also with cosmetic active agents have proved beneficial because they allow a smooth transition from medical therapy to preventive measures.

With regard to their mode of action, cosmetic preparations offer an amazing variety of options to soothe skin irritations. Legislature however is critical of the wording in the context of cosmetic and medical preparations. Wrong wording in promotions and on labels for cosmetic preparations can imply legal consequences. The following active ingredients can be administered:

- Substances to stabilise the transepidermal water loss (TEWL): among these substances are phytosterols, ceramides and similarly structured compounds as well as long-chained

fatty acids. In combination with moisture-retaining substances they support and regenerate the skin barrier and its elasticity and impede the (re-)penetration of irritating external substances and germs.

- Substances to support and improve the skin hydration: amino acids, pyrrolidone carboxylic acid, glycerin, urea and salts retain water. Most suitable are the amino acids of the Natural Moisturizing Factor (NMF). They also eliminate the oxygen- and nitric oxide radicals that come from the environment.
- Astringent substances: tannins, gallic acid derivatives and tea extracts repair cracked skin by reacting with the proteins and forming natural polymers. Typical representatives are birch bark, oak bark and witch hazel extracts.
- Gel-forming substances: aloe-, alga extracts and polymer carbohydrates such as hyaluronic acid form a soothing film on the skin which partly is due to moisture retention.
- Essential fatty acids such as linoleic acid and alpha- as well as gamma-linolenic acid reduce the roughness of the skin. The natural 15-lipoxygenase of the skin enzymatically transforms them into anti-inflammatory metabolites. Phosphatidylcholine with its high linoleic acid content has similar effects; it also occurs in cell membranes.
- Antihistaminic and soothing substances: avenanthramides which, among others, are found in oat extracts have antihistaminic and soothing effects. A synthetic representative is dihydro-avenanthramide D alias hydroxyphenyl propamidobenzoic acid; it has anti-itching effects.
- Anti-inflammatory substances: A variety of natural extracts such as extracts of calendula, ribwort (alias buckhorn, ribgrass, ribwort plantain), mahonia, chamomile (main active agent (-)- $\alpha$ -bisabolol), aloe vera, willow bark, willowherb (alias fireweed), cone flower (alias echinacea, rudbeckia), ginger, leopard's bane (alias mountain arnica, mountain tobacco) contain anti-inflammatory substances. Their modes of action vary considerably. In-vitro tests (laboratory tests) could prove, among others, inhibition of interleukin IL-1 $\alpha$ , tumor necrosis factor TNF $\alpha$ , cyclooxygenase COX-2 and prostaglandin PGE<sub>2</sub>.

- Radical scavengers and antioxidants: UV filters transform the erythema triggering radicals, generated by the radiation energy of sunlight, into heat. An unspecific and excellent protection against radicals is the NMF. Polyphenols gained from extracts of green tea, red clover, soy and grape seeds also can neutralize exogenous and endogenous radicals. Classic representatives are vitamin C, vitamin E and their derivatives.
- Protease inhibitors such as boswellic acids (frankincense) are effective against hyperactive own proteases of the body and also against aggressive proteases of microorganisms. They impede the degradation of protein structures and thus inhibit resulting inflammations.
- Vitamins such as vitamin A, niacinamide (vitamin B<sub>3</sub>), D-panthenol (provitamin B<sub>5</sub>) and vitamin B-containing yeast extracts have excellent recovering effects in the case of irritations.
- Itching is reduced or inhibited by administering urea (carbamide), allantoin (cyclic amide) and other organic acid amides (see below) including D-panthenol.

The above mentioned irritation relieving substances can also be mixed into cosmetic preparations with irritation potential (additive principle). Hence, potential causes of erythema, itching and inflammations are minimized or eliminated in a variety of ways:

- Physical contact and penetration of irritating substances are impeded – for instance by films of aloe, polysaccharides and fatty oils.
- Chemical reactions with irritating substances or with the proteins of the skin are induced – for instance with the help of astringents.
- A potential histamine effect of natural cosmetics components is impeded – for instance with avenanthramides.
- The irritative effect of cosmetic ingredients is eliminated – for instance with anti-inflammatory essential fatty acids and extract components.

Manipulation and block of nerve impulses to the brain work in another way, though.

### Manipulating the conduction of stimuli

In case that not the local causes for irritation are manipulated but the nerve impulses that

send signals of itching and pain to the brain, the warning signals of the skin will no longer arrive in the brain. This type of additives in skin care products is not without controversy though.

- Polidocanol (INN) reduces the sensation of pain in the skin and is administered in dermatological therapy as a local anaesthetic to eliminate itching and discomfort in the case of neurodermatitis. The substance belongs to the polyethylene glycols (PEG); in cosmetic applications it is labelled as laureth-9 (INCI) and used as an emulsifier. The Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung - BfR, 2003) classifies skin care products containing the substance as critical for the human health.
- In the medical field, local anaesthetics are widely used. They are administered to numb local nerves. From a chemical viewpoint - with the exception of procaine, which is an aminobenzoic acid ester - they mainly are amides such as bupivacaine, lidocaine, mepivacaine, ropivacaine, articaine, epinephrine, prilocaine and takipril. All the compounds contain amino groups, in topical preparations however, they are added in the form of ammonium salts.
- In cosmetic applications, the synthetic compound 4-t-butylcyclohexanol is used to reduce the sensitivity of delicate ("sensitive") skin. It increases the tolerance threshold for physical and substance-based irritations of cosmetic products.
- N-palmitoylethanolamine (PEA) is present in the human body and has endocannabinoid-like effects. The amide is a component of the stratum granulosum and has anti-itching effects. The endogenous cannabinoids are found in the nervous system and influence ion channels and signaling pathways.
- Tetrahydro-6-pentyl-2H-pyran-2-one alias Meadowfoam delta-lactone (INCI) for instance can be applied together with oxidative hair dyes as it reduces their irritative effects.
- Capsaicin, the pungent component of chili peppers and hot peppers, binds to the vanilloid receptor 1 (VR1) of the nerve fibers and hence, after temporary heat sensation, suppresses the itching on the skin.

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