

# Unwanted adverse effects

published in *Ästhetische Dermatologie (mdm)* 2016 (7), 50-55  
Lecture at the Dermatology Forum (Beauty Forum Munich), 23 October 2016

When cosmetic products trigger allergies and intolerances often the ingredients are the troublemakers. Frequently overlooked are essential (co-)factors such as the individual skin constitution, random exogenous impacts, inappropriate preparations, too much or too many skin care products and, last but not least, the psychological make-up.

**U**nwanted effects – in particular intolerances – of cosmetic products are multifaceted and sometimes rather complex. All too fast the problems are narrowed down to the composition of the products. However, it is worthwhile considering the root cause of the problem even if it sometimes requires investigative skills.

## What is an adverse effect?

The definition of unwanted adverse effects after the application of cosmetics is rather complex due to the fact that **objective or subjective effects** may be present. As a first approach the comprehensive definition of dermatoses could be helpful since all conditions other than normal skin are considered to be dermatoses:

- redness,
- inflammations,
- blisters,
- barrier and cornification disorders (keratoses),
- swellings,
- itching,
- pain,
- changed local sensitivity
- or other discomforts such as sensation of tenseness and dry skin.

There can even be major differences between objectively normal skin and the subjectively perceived individual skin as experience repeatedly has shown. Just to mention a few examples:

- (1) At the same grade of hydration, an open-pored skin is perceived in another way than a sealed skin. A change from a certain type of preparations to a different product type normally takes time getting used to. The term “moist” usually is associated with smooth and supple skin.
- (2) Low spreading or/and higher consistency of a new preparation may cause temporary

redness in sensitive skin as more mechanical energy needs to be applied to spread the product which stimulates the microcirculation.

- (3) A shiny skin is associated with unwanted fattening. However, this condition frequently is caused by filming agents that stabilize the transepidermal water loss (TEWL).

Unwanted side effects of cosmetic ingredients:

- **Allergic contact dermatosis** – alias allergic contact dermatitis or allergic contact eczema: Allergic reactions imply the passage of substances with low molecular mass via skin barrier and the subsequent triggering of excessive immune reactions. There are immediate reactions or late onset allergies (up to 72 hours after contact) to observe. The biological mechanisms may vary substantially.
- **Irritative contact dermatosis** – alias toxic contact eczema or irritative contact eczema: The term irritation means that exogenous substances directly attack the skin structures and trigger acute inflammations in the process. Synthetic but also natural substances can be such triggers.
- **Cumulative sub-toxic contact eczema** – alias sub-toxic degenerative eczema, irritative eczema or abrasive eczema: This kind of irritation is an insidious process and frequently occurs in combination with the medium water either at the workplace or during housekeeping activities.

## Objective troublemakers – frequent triggers of irritations and allergies

- **Preservatives** listed in the annex of the German Cosmetic Regulation (KVO): sensitizations may accidentally happen when changing from one cosmetic product to another. Contact allergens are all around us and lurk in places where we even don't

assume. A tour through building supplies stores can be instructive. Today (documented in summer 2016) practically all the solvent-free coatings and dispersion paints based on aqueous acrylate for interior and exterior use are preserved with methylchloroisothiazolinone and methylisothiazolinone (alias Kathon CG). Among them also are wood lacquers for indoor use which are marketed as saliva-proof. Only recently both the chemicals have been banned by the German Cosmetic Regulation (KVO) for a leave-on use because of their allergic features. Similar applies for aqueous solutions for waterproofing purposes (primers), gypsum based fillers and wood glues. The division for household cleaners, detergents and liquid laundry detergents in supermarkets also is a rich seam of information. In this context it should be kept in mind that express wash cycles with comparatively few spin cycles can, depending on the fabric, lead to detergent residues which then are transmitted to the skin via sweat as for instance in the case of sportswear.

Cosmetics containing the preservatives listed in the German Cosmetic Regulation (KVO) can trigger similar allergies. **All the licensed preservatives have allergenic potential.** There would be no need for such kind of a list if the substances were harmless.

The preservatives of natural origin used in natural cosmetics have the same effect since immune reactions do not differentiate between natural, synthetic or biotechnologically produced substances of the same chemical type.

Perishable food such as fruit and particularly citrus fruit are treated with preservatives. Most frequently used are diphenyl (E230), imazilil (INN: Enilconazol), ortho-phenylphenol (E231), thiabendazol (INS 233). The substances find their way to the mouth area via hands and can trigger perioral dermatitis in the case of susceptibility to the substances. In the event of coincidence, usually the cosmetics are suspected to be the triggers.

- **Essential oils and scents:** For some time past, legislature has started to define particular components of essential oils as declarable substances. In the INCI they are listed separately at the end of the enumeration, a regulation which is not really convenient for the inexpert consumer as he cannot ascribe the allergens to a particular essential oil if several are contained. The declaration does not inform on all the problematic substances involved as some of them only form during storage under the

influence of atmospheric oxygen and/or radiation. Typical examples are the allergenic ascaridol in tea tree oil and the oxides of abietic acid in colophony resin.

- **The polyethylene glycols (PEG)** used in cosmetic products as emulsifiers, filming agents and consistency stabilizers form peroxides under sun exposure; hence they are jointly responsible for Majorca acne.
- Apart from allergies, the **halogenated aromatic compounds** of disinfectants also can trigger chlorine acne. Triclosan, alias 5-chloro-2-(2,4-dichlorophenoxy)-phenol, which also is a component of toilet seats, forms halogenated dibenzodioxins and dibenzofurans on the skin when exposed to sun radiation. The German Cosmetic Regulation has recently banned the use of triclosan in leave-on products.
- **Antioxidants** are popular ingredients to stabilize PEGs (see above), essential oils (see above) and other components which tend to oxidise – particularly the synthetic butylhydroxytoluol (BHT). Allergic reactions are known. Moreover, high doses of antioxidants can trigger radical chain reactions.
- **Complexing agents** such as EDTA disable the radical-supporting heavy metal traces but they also bind heavy metals such as iron, copper, zinc contained in antimicrobial peptides and particularly in oxidoreductases.
- **Emulsifiers and detergent substances (tensides):** the higher the critical micell concentration (CMC) of a tenside, the higher is the irritative potential. Sodium lauryl sulphate (CMC =  $7.2 \times 10^{-3}$  mol/l at 25 °C) is used as a standard irritant in comparative skin tolerance measurements. Exsiccation and housewife's eczema develop very slowly. They are a consequence of the current bathing and washing routines when shampoo and body washing lotions degrease the skin on a daily base. The skin becomes dehydrated, reddish and starts to crack. Tensides such as lauryl(ether)sulfate intensify the process during housekeeping and professional activities. Often literally the "single" droplets then show their effects when working with water for a longer period. Diaper rash develops if urine comes in contact with the baby skin after deep pore cleansing.
- **Water:** Hard water with calcium and magnesium salts damages the already disordered skin barrier of dry skin as it forms lime-based soaps respectively magnesium soaps with the fatty acids of the skin (e.g. palmitic acid).

- **Hair dye products and thioglycolic acid preparations** for perms and depilation purposes are typical allergy sources in barbering.
- **Dye stuffs** – particularly azo dyes
- **Plant extracts** are multi-component systems. The higher the number of plant extracts in a skin care preparation, the higher the probability that allergenic proteins, biogenic amines and other individually intolerable substances are contained. Exceptions are homeopathic doses.  
There also are carry-over effects caused by the use of preserved extracts which contain preservatives that have not been declared in the final products.

#### Quantity – too much of a good thing

- Even high-end skin care products are not suitable for every skin type. **Wrong product recommendations** frequently lead to counterproductive effects.
- Examples for **overdone skin care** are a blazing rosacea or perioral dermatitis in the case of a fat-rich skin care. The situation is similar in the case of acne prevalence. A relatively frequent mistake in antibiotic magistral preparations is that they contain a fatty base cream (paraffins).
- Skin care which tends to produce **occlusive conditions** on the skin (mineral oil components) leads to skin swellings which sometimes are intended in order to remove wrinkles.
- A high dosage of **vitamin A** irritates the skin due to the formation of vitamin A acid.
- Day creams with UV filters lead to **vitamin D deficits**.
- **Acids** such as concentrated fruit acids (AHA), medical acid peelings and herbal peelings cause irritations of the skin (intentional) or chemical burns (unwanted) due to their low pH values. Long-term effects of repeated acid peelings are rosacea and perioral dermatitis.

#### Random co-factors

- **Fashion jewelry**, buttons, zippers, belt-buckles, wrist watches etc. which come into close contact with the skin shall only emit 0.5 µg nickel per cm<sup>2</sup> (piercings 0.2 µg per cm<sup>2</sup>) and week at maximum according to a EU Regulation dated 2001. A memorandum of the German Federal Office of Consumer Protection and Food Safety (BVL) states that 17.4% of the tested (new) fashion jewelry in 2014 was above the threshold values – with tendency to rise. The release of this or other

metals even is intensified by skin care preparations containing polyethylene glycols (PEG) and complexing agents such as EDTA, and the presence of atmospheric oxygen. Analogous to crown ethers, PEGs are considered to be phase transition catalysts.

- **Furocoumarins (psoralens)** are transmitted after contact with the cartwheel flower (alias giant hogweed, giant cow parsley or giant cow-parsnip), cow parsnip (alias el-trot, hogweed, common hogweed or meadow-parsnip) or celery; they have phototoxic effects (grass dermatitis). They also occur in lemon and orange peels and can cause perioral dermatitis after contact.
- **Bulking material of cardboard packaging** such as calcium carbonate damage the acid mantle of the skin in the case of long-term exposure. Recycled paper and cardboard contain the above mentioned abietic acid oxides and can trigger hand eczema.
- **Tightly fitting clothes** can cause sores (chafing) due to the constant mechanical friction – comparable to a permanent peeling. The waterproofing substance of new clothes will be transmitted.
- Skin care preparations are not designed for extreme stress situations for the skin as for instance **strong UV radiation** (high position of the sun, high altitude). There is a risk of adverse reactions as e.g. due to a formation of peroxides if PEGs and herbal unsaturated oils are contained in the preparations.
- **Seasonal problems:** Pollen, chlorine (indoor pools) and both together (outdoor pools) may cause itching and irritations which, in the absence of better knowledge, often are blamed on skin care products.
- The individual **tolerance of cosmetic preparations** can change after peelings and microdermabrasions. Typical symptom is the short sting after the application of hypertonic O/W emulsions.
- **Mite infestation** (demodex infestation) in the case of rosacea

#### Personal factors

- **Age-related skin changes** (rosacea, dry skin etc.) can involve the problem that well tolerated preparations which have been used for quite some time now all of a sudden are causing trouble.
- **Diseases** influencing the metabolism (exacerbations) and **medical drugs** (adverse effects) change the skin properties. Beta blockers are a well-known cause of psoriasis, antibiotics can trigger eczema.

Also non-prescription drugs can involve problems as for instance the apparent age marks (hyperpigmentation) after the intake of amber (alias hypericum, St. John's wort etc.) preparations.

- Hereditary **prevalence** can be provoked by external factors.
- **Temporary hormonal fluctuations:** puberty, menstruation, pregnancy, menopause
- In cases where the skin cannot adjust imbalances in the **hypertonic osmotic pressure**, O/W emulsions usually are poorly tolerated. The skin tends to sting and itch.
- Reactions after the **change** from strongly preserved to non-preserved liposomal preparations. Liposomes transport the preservatives into the deeper layers of the skin. A similar problem occurs with a simultaneous use of the above-mentioned types of preparations.
- Changes of **nutrition and diets** influence the skin condition. Simplest case: disorders of the water balance.
- **Anaerobic microflora** in the case of rosacea
- **Multiple chemical sensitivity** (MCS)

### Psychological make-up

- **Myth "alcohol":** Alcohol in a concentration of 10% and more has bacteriostatic effects. Hence it often is used in preservative free preparations. The fear that it might dehydrate the skin is unfounded for the above mentioned concentrations. Problematic are shaving and face lotions with an ethanol content of more than 30%. In this case the interaction with emulsifiers is a factor than can support barrier disorders in the form of dry skin. The intolerance already starts with reading "alcohol" on the INCI and the idea "I cannot tolerate alcohol" (negative placebo effect).
- **Myth "comedogenic substances":** Cetyl alcohol (hexadecanol) and stearyl alcohol (octadecanol) are popular co-emulsifiers in O/W emulsions. They also are used as a mixture (cetyl stearyl alcohol). Their comedogenicity is physically induced and depends on the concentration. Similar conditions occur with stearic acid. The same applies for a multitude of other substances that are not appropriately dosed (manufacturers).
- **Myth "pH value":** After the application of cosmetic products with pH values between 5.5 and 8.0, the skin rebalances its specific, individual pH value already within a few minutes. Problematic are strongly

buffered alkaline preparations with pH values of more than 7 since the buffer is stabilizing the high pH value for some time. This type of products however is less common and can be recognized from the fact that salts are among the first mentioned substances on the INCI list.

- **"I'm allergic to everything":** The statement rather is a paraphrase for sensitive skin; usually it is a matter of temporary irritations.
- **Myth "natural cosmetics":** The origin of the ingredients (synthetic, natural, biotechnological) is not a criterion for an excellent tolerance of the product. What matters is whether the substances correspond with the physiology of the skin. A larger number of extracts statistically implies more adverse effects, from a subjective point of view there are less adverse effects due to the positive placebo effect.
- **Myth "antioxidants":** Antioxidants only are effective in cases where deficits have been diagnosed. They are counterproductive in higher dosage.
- **Nanoparticles:** Biodegradable nanoparticles react in the same way as conventional ingredients. They only are better available. Solid non-degradable nanoparticles smaller than 100 nm have to be declared as such.
- **Review sites:** The INCI information of commercial sites reviewing cosmetic products of specialist retailers on the basis of their ingredients can be incorrect since the entries usually are written by external users. Commercial sites of course have a commercial self-interest. The site notice informs on the maintainers of a site.
- **The Yuck! effect** falls into the category of psycholinguistics and expresses the disgust for certain haptic properties (slimy, sticky etc.), colour and smell.

### Manipulated sensitivity and adverse effects

Today the trend is towards minimizing both the sensitivity of the skin and potential adverse effects of skin care preparations by adding substances which prevent redness, sting and itching.

- Laureth-9 is a cosmetic emulsifier. In topical pharmaceutical preparations the substance with the INN term polidocanol is used to soothe and anesthetise irritations in the case of neurodermatitis.
- 4-tert-butylcyclohexanol has a similar spectrum of activity by influencing the conduction of nervous stimuli.

The Federal Institute for Risk Assessment (BfR – Bundesinstitut für Risikobewertung) assumes a critical attitude towards these substances as they suppress the sensitivity but also the natural warning signals of the skin.

Dr. Hans Lautenschläger