

Flawless skin – active agents and active agent systems

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A radiant complexion is the beauty ideal per se. Light or dark spots are annoying and can be quite a nuisance if they are well-marked. The cosmetic sector offers a large variety of active agents to take remedial action.

Skin pigmentation is a complicated process. Correspondingly, various endogenous and exogenous influences may lead to temporary or permanent pigment disorders.

Hyperpigmentations...

Pigment formation occurs when tyrosine, assisted by the enzyme tyrosinase, reacts with oxygen into the blackish-brown eumelanin. The reddish-yellow pheomelanin also forms in several steps from dopaquinone and sulphurous cysteine. Varying ratios of eumelanin and pheomelanin produce the individual colour of the skin. UV radiation triggers melanin formation. Melanosomes and melanocytes multiply and the pigmentation process sets in.

...caused by photosensitization

Certain components of essential oils are photosensitizing and can intensify the pigmentation in some areas. Hypericin from the orally ingested St.-John's-wort for instance produces persistent macular hyperpigmentations. Grass dermatitis is caused by contact with the cartwheel flower (also called giant hogweed, among others), with cow parsnip (hogweed or eltrof, among others) but even celery. Also medical drugs such as diuretics, neuroleptics, cytostatic agents, antimalarial medication, antibiotics, angelique (archangel or masterwort, among others), 8-methoxypsoralene, vitamin A acid, hormones and NSAID can provoke photosensitization in the form of eye-catching marks on undressed parts of the body. Sun protection takes absolute priority here. Sun protection preparations however will not guarantee a 100% protection since the photoreactions sometimes are triggered by the wavelengths in the visible spectrum.

...caused by inflammations

If sensitizations are accompanied by inflammatory reactions, 5-lipoxygenase inhibitors such as boswellia acids (frankincense extract)

can be beneficial. Frequently the hyperpigmentations appear after the inflammatory processes have improved (post-inflammatory). In these cases, liposomal vitamin C phosphate can be applied which then is followed by a light peeling in order to facilitate the removal of pigmented skin layers. Vitamin A derivatives support the cell formation. During these particular treatments sun exposure either has to be avoided or alternatively adequate sun protection preparations have to be applied. A change in the hormone balance can also trigger temporary hyperpigmentations during pregnancy.

Actinic keratoses form after high UV exposure of the scalp. In this context redness will appear followed by whitish to yellowish-brown cornification. Symptoms preferably show up on head, neck, forearm and the back of the hand. These conditions can also be treated with boswellia acids, vitamin C phosphate and sun protection creams.

Post-inflammatory hyperpigmentations can be observed during or after the healing process of inflammatory skin alterations (dermatoses, allergic skin reactions). They result from the stimulated melanin formation through inflammatory mediators such as prostaglandins, cytokines etc. In general, the thus triggered melasmas will fade after some time however can also be rather intense and persistent. They are treated with cosmetic or medical bleaching agents. Since the hyperpigmentation often is clearly visible because of a temporarily intensified circulation, tranexamic acid together with vitamin B₃ (INCI: niacinamide) can be an interesting alternative treatment (see below). Scars developing after deep lesions however often show hypopigmentations, hence fair spots.

Pigmentations are not only formed from melanin but, as in the case of age marks, can also contain stored endogenous metabolic products (lipofuscin) formed through oxidation of proteins and lipids. AGE (Advanced Glycation Endproducts) that form from proteins and sug-

ars can also participate in the process. Bleaching active agents and supportive peelings with abrasive bodies are the means of choice in this case.

Whitening active agents

A number of people actually prefer a lighter complexion. Besides instrument-based techniques such as microdermabrasion there is a whole variety of cosmetic active agents on the market.

- Tyrosinase inhibitors impede melanin formation; therefore they are used on a preventive basis. Various antioxidants such as ascorbyl phosphate (vitamin C phosphate) that also partially reduces already formed chinoid structures of eumelanin, and polyphenols such as catechins, resorcinols, flavones, isoflavones and gallates occurring in plant extracts belong to this group. A synthetic substance used in topical pharmaceutical but also cosmetic preparations is rucinol (4-butyl-benzol-1,3-diol), a tyrosinase inhibitor of the resorcin family. In the case that antioxidants are not used in liposomal or nano dispersions that both boost their penetration, their effects are rather limited because they are sensitive to oxygen. The linoleic acid of the phosphatidylcholine based liposomes has synergetic effects.
- Herbal arbutin is a combination of hydroquinone and glucose and inhibits tyrosinase and the maturation of melanosomes. High dosages of arbutin are counterproductive since they even can trigger the adverse effect, i.e. hyperpigmentation. The effective component hydroquinone is only licensed in hair dyes (max. 0.3%) however with the health warning "contains hydroquinone"; it is no longer allowed in cosmetic bleaching preparations. Similar to hydroquinone, koji acid is a powerful reducing agent with effective bleaching features. A further natural substance with bleaching effect is liquorice root extract with the active agents glycyrrhizin, glabridin and liquiritin.
- Azelaic acid is a synthetically produced natural substance and competitively inhibits tyrosinase. Thus, in topical pharmaceutical creams it only is effective in high dosage (15-20%). Tranexamic acid originates from pharmacy as well and suppresses melanin formation but also reduces the reddish

colour which comes from blood vessels shining through the skin. A treatment with tranexamic acid results in an even complexion particularly in the case of post-inflammatory hyperpigmentation. Liposomal tranexamic acid dispersions are more effective when combined with niacinamide (vitamin B₃). Niacinamide does not inhibit the tyrosinase. Instead it affects the transport of melanosomes. It is still being discussed whether it inhibits AGE. Combined with N-acetyl-glucosamine, a structural component of hyaluronic acid, niacinamide also inhibits the melanin formation.

- In skin whitening pharmaceuticals, regenerative retinoids such as vitamin A acid are combined with hydroquinone and hydrocortisone. Vitamin A acid triggers an intensified cell formation and the pigmented skin components are faster removed. Hydrocortisone in medical bleaching preparations reduces the pigment formation by melanocytes. Biodegradable cosmetic nanodispersions with vitamin A which then is transformed into vitamin A acid in the epidermis work in a similar way.

An absolute necessity: sun protection products

Sun protection products reduce melanin formation by reflecting the UV radiation or by transferring it into heat. Parallel to the use of skin whitening products, the application of sun protection products is most important. Since the melanin-assisted protection of the skin is missing, the sensitivity of the skin to radiation is increased. CM-glucan can be administered as a supplementary cell protecting measure.

Keratolytic active agents support the removal of pigment marks with whitening active agents. Salicylic acid, free vitamin C (ascorbic acid) or fruit acids such as glycolic acid can remove superficial melanin-containing material. Cell formation is stimulated. The same applies for mechanical peelings with abrasive bodies, enzyme peelings and microdermabrasion. The immediate bleaching of melanin is a side effect of topically applied dibenzoylperoxide which is a component of pharmaceutical acne preparations. Hydrogen peroxide which is used for tooth bleaching and hair lightening purposes has the same effect.

Hypopigmentations

- In the case of vitiligo, it is assumed that the hydrogen peroxide balance in the body is disturbed either by stimulated peroxide formation, peroxide storage or delayed degradation. In this case the catalase concentrations in the skin are reduced. Further indications point to a peroxynitrite participation that similar to hydrogen peroxide, leads to oxidative respectively nitrosative stress in the case of pathological dosage. In combination with a narrow band UVB therapy (311 nm) manganese salts (Mn^{2+}) may induce a re-pigmentation in the case of vitiligo. In a way the effect corresponds to the catalase since intermediary formed Mn^{3+} -ions react with cellular hydrogen peroxide into Mn^{2+} and free oxygen.
- Characteristic signs for pityriasis alba are fair, diffusely outlined skin areas on the cheeks. They contain less melanin than the surrounding skin. The whitening process often is preceded by minor inflammations. Hence we speak of a post-inflammatory hypopigmentation that gradually decreases. The cosmetic treatment consists of anti-irritant base creams or balancing non-occlusive foundations.
- Pityriasis versicolor is a superficial infection appearing on sebum-rich skin areas. It is triggered by malassezia yeast fungi which belong to the human skin flora. Due to the fact that the melanin production is reduced in the infected skin areas, they appear fair after the skin has been exposed to sun radiation. Vice versa, the areas appear darker on fair-skinned people. The somewhat scaly and lightly bulging areas are treated with adequate antifungal preparations and selenium disulfide containing cleansing products.
- Injuries reaching into the dermal layer will cause scars. The scar surface often appears reddish and contrasts with the other skin since hair coat and sebum and sweat glands are missing. The blood vessels gradually decrease and the reddish colour fades out. The scar may even appear fair since the melanocytes are missing. The scarred skin has to be protected with UV filters in the form of sun preparations as the risk of sun burns is increased. Besides massages cosmetic peelings are beneficial for the removal of superficial indurations. An instrument-based al-

ternative is to scrape the scar edges via microdermabrasion. The abrasion of the scar edges stimulates recovery and reduces the contrast. Chemical peelings with fruit acids or trichloroacetic acid (medical) are successful although it should be mentioned that they are not a long-term remedy since the skin becomes intensely stressed. Nanoparticulate vitamin A also promotes the skin recovery.

Contrast reduction

The cosmetic-based contrast reduction has priority in the case of eye-catching pigment disorders. It can be achieved either by whitening the surrounding skin in the case of white or fair spots or by covering the hypopigmentation with the help of make-up, camouflage or self-tanning products. The same applies for hyperpigmented skin areas. Dihydroxyacetone (DHA) is a common self-tanning substance for this purpose.

DHA reacts with the amino groups of the superficial keratin. Since DHA is a component of the human metabolism, whole body spray products do not represent a risk. Problems rather are caused by the additives used in the preparations. The fact that DHA for instance may form small amounts of formaldehyde when exposed to sun radiation during storage is of less importance with regard to toxicological or allergenic effects. Besides DHA, erythrulose also is used, frequently in combination with DHA.

And to conclude with a tip: carrots influence the skin complexion. Similar effects can be observed with the consumption of large amounts of tomato paste which contains the red pigment lycopene that besides carotene also belongs to the carotenoid family. Carotene is stored in the skin and generates a yellowish to olive coloured skin undertone that is easy to detect by pressing a slide on the front. In this process the red fraction of haemoglobin is temporarily eliminated. Right beside it, the melanin (degree of tanning) becomes visible.

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