

"I cannot tolerate this product" - the influence of medical drugs on skin and skin care

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Again and again beauty institutes and practices are confronted with spontaneous or chronic skin reactions. As a rule, the skin care used is then suspected to be the culprit. Frequently it is wrongly accused, as there are various other factors that play a significant role - as for instance medical drugs.

Quite a commotion in the beauty institute: a good customer comes in with red spots on neck and back and explains „I cannot tolerate your products any longer!" Did the manufacturer change the formula? No, certainly not! But to ease tensions at her cervical spine the customer had applied an anti-rheumatic ointment containing the active agent 2-Butoxyethyl nicotinate. Even if the customer stopped applying the ointment some time ago, spontaneous redness may still develop especially if she has taken a warm shower or used cosmetics which intensify the penetration. Stress - associated with breaking sweat in the true sense of the word - shows the same effects when the bloodstream gets into top gear and the blood flow in the skin is increased. Evidently the customer had already forgotten that she applied the above mentioned ointment. Some pointedly asked questions however quickly uncovered the cause of the problem and the mentioned effect turned out to be quite harmless, by the way. There are still other and more complicated cases. Besides pharmaceutical agents and their degradation products or in other words, their metabolites, also additives like preservatives, essential oil components and photosensitizing effects play a significant role. An interesting example in this context is **dithranol** (anthralin) that heals psoriasis however may cause irritations on healthy skin which then can take weeks to recover (anthralin dermatitis).

It is estimated that about 5 per cent of the skin diseases can be attributed to the influence of pharmaceutical drugs. Accordingly, elder people are more frequently affected as they often take several drugs at the same time. A difference is made between immune system-dependent and immune system-independent reactions; the latter mentioned are more frequently observed. There are also individuals with a genetic disposition for certain skin diseases which then are activated by medical drugs. This specifically applies for beta blockers, antibiotics, psychotropic drugs and antidepressant agents containing lithium, aurates,

antimalaria drugs, as well as non-steroidal anti-inflammatory drugs (NSAID) which can cause psoriasis. There are other cases where the skin condition is changed due to the effects of medical drugs with the effect that aggressive foreign substances may then penetrate the skin barrier from the outside. A long term use of glucocorticoids leads to atrophic skin, facilitates teleangiectases, steroid acne, perioral dermatitis, increased hair growth (hypertrichosis) and stretch marks. Urticaria may develop after the non allergic histamine release of x-ray contrast media and NSAIDs. It is recommended to check the Red List (Publishers: Rote Liste Service GmbH, Frankfurt am Main) for details. It informs on the side effects of any given pharmaceutical agent. The Red List is updated annually.

Some groups of medical drugs are already well-known for their potential of causing skin reactions which partly depends on their frequent use which in its turn again leads to the fact that extremely rare reactions can be more often observed. The following agents belong to these groups:

Acne therapeutics

Retinoids like tretinoin (vitamin A acid) may cause erythema (inflammatory skin reddening), cheilitis (inflammation of the lips), hair loss and pruritus (itching).

Benzoyl peroxide: Most frequent side effects here are skin irritations and dry skin.

Analgetic agents, antirheumatics

Inflammation inhibitors, NSAID, NSAR (non-steroidal antirheumatics): Representatives here are pyrazolones (as for instance phenyl butazone) and arylacetic acid derivatives (as e.g. diclofenac). They may cause hypersensitive reactions like exanthema (skin rash) and quite rarely also the Stevens Johnson syndrome (see below). Acetylsalicylic acid („Aspirin") which is widely used against headaches also belongs to this group. Side effects are

erythema, urticaria and in isolated cases also erythema exsudativum multiforme (see below).

Rheumatism ointments: Nicotinic acid esters (flush, erythema).

Aurates: Exanthema, hair loss, chrysiasis (deposition of gold particles in the skin). Aurates are applied quite rarely.

Antibiotics

Sulphonamides: Erythema, exanthema, Stevens Johnson syndrome. Well-known representative of this group is cotrimoxazol which is a combination of sulfmethoxazole (sulphonamide) and trimethoprim (pyrimidine compound).

Gyrase inhibitors (as e.g. ciprofloxacin): Itching, petechia (tiny capillary bleedings), erythema, Stevens Johnson syndrome.

Nitroimidazoles (e.g. metronidazole): Exanthema, itching.

Penicillins (e.g. ampicillin): "Ampicillin rash".

Aminoglycosides (e.g. neomycin B, or also called framycetin): Contact dermatitis, urticaria.

Macrolides (e.g. azithromycin): Erythema, urticaria, Stevens Johnson syndrome.

Tetracyclines: Hypersensitive reactions.

Griseofulvine (antimycotic): Stevens Johnson syndrome.

A long term use of antibiotics may cause antibiotic resistance and makes the skin susceptible to fungal infections.

Anticoagulants

Overdoses of **heparin** or **coumarins** may cause angio-oedema and petechia in skin and mucous membranes. This effect can specifically be observed with wet shavings after heparin injections to prevent thrombosis during long travels e.g.

Antiepileptics

Carbamacetin shows allergic skin reactions like erythema, pruritus, urticaria, dermatitis, Stevens Johnson syndrome.

Phenytoine (Diphenylhydantoin): Rarely Stevens Johnson syndrome as well as toxic epidermal necrolysis (TEN; see below)
Guaifenesin: Skin rash, pruritus.

Antihistamines

In case of hypersensitivity exanthema and urticaria. Rarely Stevens Johnson syndrome (e.g. ketotifen)

Antihypertensives (drugs to lower the blood pressure), coronary therapeutics

ACE inhibitors: Angio-oedema (vascular oedema: skin swellings), exanthema, psoriasis.

Beta blockers: Triggering psoriasis, deterioration of psoriasis.

Calcium antagonists (diltiazem, verapamil): Flush.

Nifedipin: Flush, erythema, frequently erythromelalgia (painful hyperaemic redness and swelling of the skin).

Antilipemics

Allergic skin reactions (e.g. bezafibrate).

Antimalaria drugs

Chinine: Exanthema; **Chinidine:** Hypersensitivity reactions, urticaria, skin redness;

Chloroquine: Pigment disorders, yellow skin discoloration.

Cytostatics

Mitosis inhibiting substances (inhibiting cell nucleus division): Vinca alkaloids (e.g. vincristine) have toxic effects and cause hair loss.

Alkylating cytostatics (e.g. cyclophosphamide): Toxic effects: hair loss, erythema.

Cytostatic antibiotics: Hair loss, dermatitis (e.g. doxorubicine). Cytostatics may trigger hyper pigmentations.

Folic acid antagonists (e.g. methotrexate): May cause exanthema, erythema, and frequently also pruritus and reactions around injection spots.

Pyrimidine antagonists (e.g. fluorouracil): Photosensitizing effects, hyper pigmentation.

Diuretics

Thiazide derivatives (e.g. hydrochlorothiazide): Skin reddening, urticaria, photosensitivity.

Loop diuretics (e.g. furosemide): Exanthema.

Essential oils

They are used as active agents and additives. The oils of anise, fennel, eucalypt, spruce needle, pine needle, juniper berry, thyme, turpentine, lemon, peppermint, lavender, clove as well as cedar wood oil and menthol may contain individually irritating, sensitizing or photosensitizing components. Corresponding substances like geraniol and limonene for instance are sometimes not mentioned in the INCI despite the fact that the INCI directives require their declaration.

Expectorants (mucolytics)

Acetylcysteine may trigger angio-oedemas, pruritus and urticaria. Essential oils (see above) are also used as expectorants.

Glucocorticoids

After a long term use of glucocorticoids the skin becomes sensitive and tends to atrophic conditions. Teleangiectases are encouraged and steroid acne, perioral dermatitis, increased hair growth (hypertrichosis) and stretch marks are observed. Glucocorticoids increase the permeability of the skin which facilitates allergic responses to foreign substances as well as a penetration of micro organisms.

Hormone preparations, contraceptives

These medical drugs may trigger acne and chloasma (yellowish brown spots); Estrogens: Porphyria cutanea tarda (see below).

Immunostimulants

Interferons may cause herpes labialis, exanthema, dry skin and hair loss.

Local anaesthetics

As e.g. lidocaine or procaine can trigger hypersensitive reactions, urticaria, contact dermatitis with erythema or pruritus.

Narcotics

Barbiturates and thiobarbiturates cause allergic skin reactions, porphyria cutanea tarda and hypersensitive reactions.

Psychotropic drugs

Neuroleptics: Phenothiazines may trigger exanthema, photosensitivity and hyper pigmentation as well as allergic skin reactions.

Antidepressants: Psoriasis (lithium salts), photosensitivity of the skin (St. John's wort).

Thyreostatic drugs

Drugs against thyroid hyper function: Exanthema in connection with thiouracil use.

Uricostatics

Drugs against gout: Exanthema (allopurinol)

Vegetable extracts

Comparable to the extracts used in cosmetic products there is an individual risk of intolerances. In case of mountain arnica blossoms there have been observed contact allergic reactions with oedematous blistering.

X-ray contrast medium

Angio-oedemas, urticaria.

This list is not intended to be exhaustive. A large number of active agents listed are used for various indications. Statements regarding side effects can only be taken as references.

Medical drug additives

The following additives may trigger skin allergies or irritations and should therefore be mentioned:

Antioxidants: Butylhydroxyanisole (E 320), Butylhydroxytoluene (E 321).

Benzalkoniumchloride: Active agent in antiseptics and widely used additive in ophthalmologicals (eye preparations).

Benzyl alcohol: Widely used preservative in watery or watery-alcoholic oral and topical preparations.

Dibutylphthalate: Still contained in various medical formulations however no longer licensed for cosmetic products (see Cosmetic Decree).

Dichlorobenzylalcohol: antiseptics.

Dyes: Many of the azo colors should be mentioned in this context: Tartrazine (E102), orange yellow S (E 110), azorubine (E 122), amaranth (E123), cochennille red A (E 124), allura red AC (E 129), brilliant black (E 151), lithol rubin BK (E 180). Further relevant synthetic dyes are: Erythrosin (E127, containing iodine), chinoline yellow (E 104; not licensed for food in the USA), patent blue V (E 131), indigo carmine (E 132) und brilliant blue (E 133).

Flavouring agents, aromatic substances are mentioned as such in package leaflets. Specific details on components as for instance vanilla or bergamot oil are only sometimes listed.

Formaldehyde and formaldehyde donors: Among this group are methenamine (E 239, synonym for urotropine), bis(hydroxymethyl) urea, tetrahydrotetrakis(hydroxymethyl) imidazoimidazoldione. They are components of disinfectants.

Parabens: Are applied as preservatives in oral and topical watery or watery alcoholic pharmaceutical drugs. Butyl-, ethyl-, isobutyl-, methyl-,

propyl-4-hydroxybenzoate are frequently contained in antiseptics.

Phenols: 2-Phenylphenol ("orthophenylphenol", E 231): Is used for surface and laundry disinfection. Phenol, meta-cresol, triclosan (5-chlor-2-(2,4-dichlorphenoxy)-phenol) are contained in disinfectants for hands and surfaces.

Phenoxyethanol: Is used as an additive in mouthwashes, antiseptics, in urea ointments and for the surface disinfection. It is a component of ophthalmologicals.

Thiourea: Is rarely used as an additive in disinfectants (surface disinfection) today. It is considered to be cancerogenic and teratogenic.

Side effects

In the following you will find a glossary of some of the most important technical terms related to side effects of pharmaceutical drugs on the skin:

- **Alopecia:** Hair loss
- **Angio-oedema:** Skin swelling due to the formation of oedema in the skin vessels
- **Cheilitis:** Inflammation of the lips
- **Chloasma:** Yellowish brown spots
- **Erythema:** Inflammatory skin reddening comparable to a sun burn
- **Erythromelalgia:** Painful, hyperaemic redness and swelling of the skin
- **Flush:** Temporary skin reddening due to increased blood circulation, frequently in combination with hot flashes
- **Hypertrichosis:** Excessive hair growth
- **Petechia:** Tiny punctate capillary bleeding
- **Porphyria cutanea tarda:** Porphyrin metabolism disorder, may show symptoms like pigment disorders or blistering
- **Pruritus:** Itching
- **Rash:** Efflorescences on extensive areas of skin („flowering")
- **Urticaria:** Hives

Serious skin reactions to pharmaceutical drugs are:

Steven Johnson syndrome (SJS): Painful blisters, erosions and efflorescences of the body surface including mucous membranes (less than 10 percent of the skin surface).

Erythema exsudativum multiforme majus (EEMM): Blisters and erosions, rosette-like erythema (cockades) on body surface predominantly in the hand and foot area (less than 10 per cent of the skin surface).

Toxic epidermal necrolysis (TEN): Blisters and erosions with simultaneous erythema symptoms and patches that can merge. More than 30 percent of the skin surface is affected.

Beyond that, there is a whole variety of **intermediate forms**. Triggers for these very rare skin reactions may be antibiotics (as e.g. cotrimoxazol), antiepileptics (e.g. phenytoine) and pyrazolones (see NSAID).

Statements regarding side effects differ depending on the specific sources (Red List, dermatological and pharmaceutical standard references, original publications) and their year of publication. In retrospect, also the definitions and descriptions of side effects have changed over and over. This applies above all for severe skin reactions.

If a group of active agents has been cited in general it is still possible that single representatives of this substance group have different or even no side effects at all. Not mentioned are side effects which are linked to additional conditions. As an example may be stated that smoking influences the degradation of pharmaceutical drugs in the liver which can also have effects on the skin appearance. Beyond that, reciprocal action between several medical drugs may lead to unwanted side effects. Not considered are also vaccines and their additives. Furthermore it has to be kept in mind that small amounts of additives will accumulate as they are also used in the food industry like for instance azo colors. It is therefore highly recommended that beauty institutes and dermatological practices with affiliated skin care institutes ask their customers for details in order to receive comprehensive information regarding pharmaceutical drugs and nutrition.

As already mentioned above, the basic disposition of single individuals and specific external conditions as e.g. environment and pre-existing defects due to illness, or even slimming cures play a significant role whether pharmaceuticals will lead to side effects. Hypersensitivity with varying severity due to cotrimoxazol use for instance is more often observed in connection with HIV infections.

Most individuals can tolerate pharmaceutical drugs without any reactions. In this context it should be mentioned that the present survey is not intended to fan fears but to offer practical assistance in case a customer shows up in the institute with the words „I cannot tolerate this cosmetic product".

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