Using synergies – How active agents and cream bases interlink cosmetics and pharmacy

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No doubt – the grey area between pharmaceutical and cosmetic skin care products is expanding. Dermaceuticals and dermocosmetics are keywords which demonstrate that the cosmetic product market is gaining grounds in the pharmaceutical field, not least because of legal claims for a proof of efficiency.

Pharmaceutical agents, on the other hand, are contained in numerous cosmetic products by now. It seems, however, that the development of pharmaceutical base creams came to a standstill whereas otherwise, innovative cosmetic cream bases have made their way into medical prescriptions in the pharmacy.

Target organ: the skin

Dermatology and cosmetics have identical objectives: the healthy and physiologically intact skin. The respective approach to achieve this goal, however, is subject to different legal regulations. Pharmaceutical creams are licensed for medical therapy, cosmetic products are allowed for the supportive prevention of skin problems, which means for the care of the skin. In Germany, with a few exceptions only, pharmaceuticals are subject to strict regulations and hence only available on prescription and in pharmacies. There is also a risk of side effects involved. A detailed overview covering the undesired effects of such active agents on the skin was published in Kosmetische Praxis 2009 (2), 11-14.
Also the substances used in cosmetics may have immediate or long term side effects. Among those, irritations and allergies are the easiest to diagnose, though (see Beauty Forum 2008 (9), 114-116). In this context, some also hold the opinion that cosmetic ingredients, in contrast to pharmaceuticals, should not penetrate into the deeper layers of the skin. Use and mechanism of action of vitamins or essential oils already show that this idea is quite unrealistic, though. With the exception of high molecular or polymer substances that remain on the skin, practically every substance will more or less penetrate the skin. Even highly polar substances are made available for the dermis with the help of modern transport systems like liposomes and nanodispersions. In addition to that, techniques like peelings microdermabrasion, microneedling and ultrasound facilitate the permeation of cosmetic products. There is only a gradual difference to transdermal pharmaceutical applications like e.g. the nicotine patch or creams against rheumatism.
That is why high standards in terms of purity, physiological tolerance and degradability of the cosmetic ingredients are required. Furthermore, it has to be ensured that they will not cause systemic effects. Many of the formulations are not in compliance with today's requirements if used in combination with the above mentioned equipment-based techniques. Hence, the cosmetic industry it requested to completely eliminate problem substances or provide warning labels as for instance "Do no use during ultrasound treatments.

The role of base creams

The connecting link between dermatological therapy and preventive skin care are base creams which are suitable for both applications. Typical pharmacological agents for the dermatological therapy are for instance antibiotics, antiseptics, anti-inflammatories, therapeutic agents for the immune system, local anaesthetics and vitamins. Typical cosmetic agents are extracts, essential fatty acids, lipids (emollients), moisturizers (NMF, gelling agents), vitamins, UV-filters.
How important the formulation of base creams is in this concept is shown by the fact that the use of inappropriate cream bases will immediately lead to relapses after the application has been stopped. The mineral oil containing DAC base cream which is frequently prescribed may be stated as an example in this context.

Composition of a DAC base cream:
- 4.0 g glycerol monostearate
- 6.0 g cetyl alcohol
- 7.5 g medium-chain triglycerides
- 25.5 g white vaseline
- 7.0 g poly(oxyethylene)-20-glycerol monostearate
- 10.0 g propylene glycol
- 40.0 g water

This cream is rather inappropriate for the treatment of the neurodermitic or acne-prone skin when mixed with corticoids or antibiotics for medical prescriptions.
Mineral oil containing products like vaseline and paraffin oil, polyethylene glycols (PEG), emulsifiers, preservatives like parabens and benzyl alcohol as well as perfumes and silicones also are frequent ingredients of pharmaceutical base creams. Empirical data recorded by professional cosmeticians who have experienced the problems with these ingredients for quite some time now, could be helpful in this context. As a matter of fact, there has been a change of thinking, not least because of the more frequent cooperation with professionals and experts from the cosmetic field. This also explains the fact that innovative base creams developed by the cosmetic industry, without emulsifiers, mineral oils, preservatives and perfumes are more and more frequently used in the pharmaceutical practice. Studies show that they significantly accelerate the recovery of the skin barrier and frequently lead to a long-term improvement in cases of chronic skin problems.

Corneotherapy

Based on clinically significant results, the doyen of the US-American dermatology, Professor Albert M. Kligman, Ph.D., could show that the use of appropriate cosmetic compounds for the care of the problem skin could even replace the pharmaceutical active agents. He founded the corneotherapy which, just like the base creams described above, aims primarily at the recovery of the barrier function and hence actively avoids persistent irritations and infections due to external influences. This therapy is recommended for the following indications:

- dermatoses
- barrier disorders
- cornification disorders
- actinic keratoses
- inflammatory processes
- pruritus

Adequate formulations may also have immediate effects. A mixture of urea, nanodispersed evening primrose oil (contains gamma linolenic acid) in an emulsifier free cream base is a quick and effective way to cure pruritus, inflammations and swellings after mosquito bites. Pharmaceutical antihistamines, local anaesthetics and inflammation inhibitors are not required in this case.
The direct combination of pharmaceutical-based therapy and corneotherapy is called “adjuvant” corneotherapy. “Enhanced” corneotherapy means that the skin barrier is purposefully opened with specific penetration- enhancing substances to improve the passage of active agents and then closed again.

Multi-faceted active agents

On the other hand there is a whole variety of cosmetic active agents which originate from the pharmaceutical field. Some of them, as e.g. preservatives, may cause side effects as shown in the following table.

Active agent	Pharmaceutical function	Cosmetic function
allantoin	wound healing	used against skin irritations and dry skin (like urea)
azelaic acid	acne and rosacea agent (concentrations of about 20%)	consistency agent (licensed up to 1 %) in acne and rosacea skin care products
benzalkonium chloride	antibacterial and preservative effects in eye products and throat drops)	preservative, licensed up to 0.1 %
benzyl alcohol	preservative	preservative, fragrance component
calendula extract	inflammation inhibitor, wound healing	inflammation inhibitor
carbomers (polyacrylates)	covering of wounds	sodium carbomer: thickening agent (consistency agent), ingredient of ultrasound gels
chamomile	inflammation inhibitor, soothing of irritations, wound healing	inflammation inhibitor
clotrimazol	antimycotic agent	active agent against dandruff
D-panthenol	wound healing	skin moistening, skin smoothing, stimulating cell proliferation, anti-itching, antibacterial effect
echinacea extract	wound healing, immune stimulation	used in skin care products for the treatment of couperosis, rosacea and perioral dermatitis

Active agent	Pharmaceutical function	Cosmetic function
essential fatty acids: linolenic acid, α- and γ-linolenic acid	anti-inflammatory effect, neurodermatitis	dry skin, barrier disorders, anti-inflammatory effects
fumaric acid	psoriasis therapy with fumaric acid esters	prevention of bad and hyperactive skin in combination with carriers
green tea	condyloma treatment	stimulation of microcirculation; astringent
hamamelis extract	wound healing, inflammation inhibitor	mild astringent: ingredient of tonics, lotions and aftershaves
hyaluronic acid	in eye formulations against redness and inflammations ("dry eye symptom")	wrinkle smoothing, forms elastic moisture film
laureth-9	local anaesthetic (polidocanol) in cases of neurodermatitis, dermatoses and eczema; antipruritic and analgesic	emulsifier for creams and cleansing products (cf. annotation of the Federal Institute for Risk Assessment – BfR- dated 15-10-2003: Polidocanol in cosmetic products"
salicylic acid	acne (comedolytic and keratolytic; starting at 5 %), wart removal (ca. 10% solution)	antimicrobial and keratolytic activity, peeling (ß-hydroxy acid). Up to max. 2 % are allowed in skin care creams and 3 % in shampoos.
tranexamic acid	inhibition and soothing of bleeding (antifibrinolytic)	skin whitening
triclosan	antiseptic agent for disinfection purposes	preservative (allowed up to 0.3 %) in toothpastes, deodorants and cleansing products
urea	keratolysis in case of onychomycoses, soothing of pruritus, skin moistening	moisturizer, soothing of irritations, powder additive
vitamin-A-acid	tretinoin, isotretinoin: skin recovery, chemical peeling, acne treatment	banned from cosmetic products. Vitamin-A-palmitate is allowed (will transform into vitamin-A-acid in the skin). Used for collagen formation and recovery of the atrophic skin, treatment of acne, cornification disorders.

Of course, identical substances have identical effects, no matter whether they are used in cosmetics or pharmaceutical creams. The only difference is, that the cosmetic market is not allowed to use the terms healing or soothing of diseases. The prevailing public understanding may decide in specific cases whether the application falls under the pharmaceutical guidelines or the cosmetic decree. Sometimes the dosage in cosmetic products is higher than in pharmaceutical formulations (e.g. D-panthenol). On the other hand, the cosmetic industry also successfully uses fractions of the required active agent concentrations only and combines it with a potent carrier system like liposomes or nanodispersions. Both the biologically degradable carrier systems are only rarely used in the pharmaceutical sector because of their complicated and costly standardization procedures. In isolated cases also precursor substances of banned active agents are used in cosmetic formulations. An example in this context is vitamin-A-palmitate which is metabolized in the skin into vitamin-A-acid (see table).

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