Dermatological reports on cosmetics : possibilities and pitfalls

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The importance of cosmetics in human affairs has long been appreciated by poets and artists. It is now time for scientists to use their powerful methologies for applying basic knowledge to everyday needs to improve the quality of life. Comsumers have the right to expect that the skin care benefits claimed for a cosmetic product are real.

The principles of cosmetics for the dermatologist have brought together an extraordinary collection of specialists whose common interest was the skin. This group encompasses chemists, physicians, engineers, sociologists, biologists, photobiologists, immunologists, indeed every subdivision of modern science. It is exceedingly important that the members of this fraternity have a forum for the exchange of ideas and a means of interacting with each other across national and professional boundaries.

But what about the relationship between dermatologists and cosmetologists? Too often physicians have given free rein to their prejudices about cosmetics. Cosmetics were denigrated as frivolous and insignificant in contrast to the serious world of disease and disability. This bias was evident in the one-sided view that cosmetics did more harm than good. Every medical student was warned about the hazards or irritation and contact sensibilization from harmless ingredients such as preservatives and fragrances. Some dermatologists fashioned for themselves the role of protectors of the public weal, stressing the frequency of adverse reactions to cosmetics and exulting when they could describe novel and rare cosmetic horrors. This policy prospered although it was based on two specious notions: an overestimation of risks and an underestimation of benefits.
Especially in Germany a lot of prejudices concerning cosmetics exist in the brains of dermatologists: for a long time it was not serious to be interested in cosmetics, nowadays the situation is changing, but very slowly, too slowly.

Finally, it is no longer excusable for dermatologists to know so little about the cosmetic products their patients use. Thousands of items are available for treating skin, hair, and nails. Patients seek guidance from dermatologists regarding the usefulness and safety of cosmetics. They want to know about the safest soaps, the best moisturizers, and the effectiveness of sunscreens in preventing ageing and skin cancer. Dermatologists can educate patients regarding these important health concerns only if they first educate themselves. To their surprise, dermatologists are being exposed to a substantial body of knowledge of which they know little.
According to an international study, published in the journal "Profi-Kosmetik" March, 1st, 1997, the co-operation between dermatologists and cosmetologists is enforced to investigate the healthy skin for the intention of better skin care and reducing skin ageing.

Which importance does dermatology have for cosmetics? Cosmetics contribute not only to appearance, they also contribute to health in the fullest sense of

cutaneous, psychological, and social wholesomeness. Cosmetical products in principal can be divided into two categories: first decorative products (e.g. lipsticks, mascara, nail vanishes), second products interfering with skin´s physiology, such as soaps, cleansers, shampoos and skin care products (e. g. facial moisturizers, hand and body lotions).
Many changes are being made. The distinction between cosmetics and drugs has become blurred. Cosmetics do, in fact, alter the structure and function of skin. These effects can be proven by scientific methods. Even agents as bland as "moisturizing" creams affect skin behaviour – to a far greater extent than ever suspected. The need to prove cosmetic claims has been a strong stimulus for appreciating induced changes. Sensitive instrumentation has given us the means to evaluate skin in new ways. Therefore the cosmetic industry has become increasingly bolder in calling attention to the beneficial efforts of cosmetics. Advertisements emphasise treatment aspects, and language that was formerly reserved for drugs is used today.

One objective of my report is to present detailed information concerning the scientific based methods for evaluating effects, and an update of "what is new" in this category.
Another objective is to review specific problems caused by cosmetics. The use of cosmetic products for people with particular needs because of skin disorders or special skin types is also stressed.
At least the value of dermatological reports directly depends on the respectability of the commissioned dermatologists. Pitfalls occur, whenever non qualified scientific results are generously used for advertising campaigns like "dermatologically tested", "allergy tested", "hypo-allergen" etc. Additionally a lot of reports are scientifically insufficient. Dermatological reports on cosmetics therefore must be valid in scientific method and practice.This results in a new ecomomical climate in dermatocosmetologic relations, that will be of great value in bringing improved and safer products to the market.

Dermatological reports on cosmetics are safety assessments. The following tests on humans are recommended.

TESTS ON HUMANS
Patch test
1.1. single patch test
1.2. repetitive patch test
1.3. photo patch test (= phototoxicity test)
1.4. repetitive photo patch test (= photoallergy test)
1.5. repetitive open epicutaneous test

2. **Wetting test after Burckhardt**
3. **Duhring-Chamber-Test**
4. **Dermatological controlled application test**
5. **Dermatological controlled use test**
6. **Dermatological controlled test on comedogenity**
7. **Tests on efficacy**

7.1. Sebumetry
7.2. Corneometry
7.3. Computer-aided laserprofilometry

The most important and mostly used test in dermatology and cosmetics is the patch-test. Variations are the single patch test, the repetitive patch test, and the photo patch test (= phototoxicity test). Since the introduction of patch testing eight decades ago, the use of this test has become widespread as a mean of investigating causes of exogenous dermatoses in human beings. When comparing patch testing with other diagnostic methods in modern medicine, patch testing is a low-risk procedure. When this method is performed properly, the potential benefit outweighs the potential risk to the patient.
By the occlusive application of 0.1ml of the substance, the acute irritation potential is assessed in the single patch test. Also positive reactions occur by also pre-existing sensitisation. The reading is taken 24, 48 and 72 hours after application. The assessment is made on the basis of redness, oedema, papulae, vesiculae and scaling.

The repetitive patch test is also an occlusive epicutaneous test which normally is repeated one and four weeks after the first application. Differentiations of cumulative irritation effects and the detection of a sensitisation effect of the proven preparation is possible. Distinction between allergic and primary irritant reactions demands special experience on the part of the dermatologist.

The phototoxicity test is a single patch test including subsequent exposure to light (UVA- and/or UVB-light) for the analysis of phototoxic properties of the tested product. The irradiated test reactions are compared with a control series not exposed to light.
Nonetheless, adverse reactions as a result of patch testing are not uncommon. I will summarise the possible complications that may arise.

PATCH TESTING - COMPLICATIONS -
1. **active sensitisation**
2. **irritant patch test reactions**
3. **adhesive tape reactions**

4. **“ectopic” flare of dermatitis**
5. **Koebner phenomenon**
6. **Persistence of a positive reaction**
7. **hyper- and hypopigmentation at the sites of positive patch test reactions**
8. **anaphylactoid reaction**
9. **the “angry back” syndrome**

For cosmetics the following items are of importance:

1. **active sensitisation: A response that occurs after 7 days or later with no preceding effect is a late reaction caused by interaction of residues of the allergen with the newly sensitised tissues. This type of reaction is sometimes called a “spontaneous flare”. The sign of such active sensitisation is either that the patch test becomes positive 10 to 14 days after application (flare-up) and is positive when repeated in 2 or 4 days or that reactions occur in patients who are systematically retested after an interval.**
2. **irritant patch test reactions: For most row materials and chemicals the correct concentration has to be determined for patch tests. An initial test concentration from 0.1 to 1.0 per cent is suitable for clinical use. Cosmetic creams and lotions are normally tested undiluted, rinse-off products in concentrations 0.5 to 5.0 per cent. The irritative substance affects the barrier of the horny layer, penetrates the stratum corneum and affects a cell disfunction of the live epidermis: histamine is released from mast cells and hence a vasodilatation including a visible redness (erythema) becomes visible. The inflammatory reaction starts with an activation of the arachidonic acid metabolism, release of prostaglandines, leucotriens and peroxide-precursors. Neutrophil granulocytes cause a clinically visible change of the skin, which is named “irritant contact dermatitis” in the acute state and “irritant contact eczema” in the chronic state. Irritant contact eczema may also be induced by the summation of subliminal noxae, then called a cumulative subtoxic eczema, e.g. house-wife eczema of the hands. The intensity of the irritation depends on the specific property of the substance, the concentration and reaction time, moreover on the point of application, possibly also on a predamaged skin as well as on endogenous factors in humans, e.g. atopic diathesis.**
3. **adhesive tape reactions: Mild adhesive tape reactions are not uncommon. Today there are a lot of industrial produced occlusive test tapes for patch testings. They are normally well tolerated and are not causes of positive skin reactions.**
4. **“ectopic” flare of dermatitis: on rare occasions, a positive patch test reaction may be accompanied by a flare-up of an existing or pre-existing dermatitis caused by the test allergen.**
5. **Koebner phenomenon: a positive patch test reaction in a patient with active psoriasis or lichen planus may reproduce the dermatoses at the patch test site.**

6. **persistence of a positive patch test reaction: a very seldom phenomenon.**
7. **postinflammatory pigmentary changes: strongly positive patch tests may result in hyperpigmentation or, occasionally, depigmentation. These reactions are more common in heavily pigmented individuals. Patch testing with brown depigmentating agents (e.g. monobenzyl ether of hydrochinone) may result in depigmentation.**
8. **the „angry back“ syndrome: is a regional phenomenon caused by the presence of a strongly positive reaction. The reaction produces a state of skin hyper-reactivity in which other patch test sites become reactive. I believe that these concomitant „positive“ reactions are unreliable and that false positive reactions were common when one strong positive reaction occured. To confirm or deny the significance of individual reactions found on the „angry back“ it is sequential testing later with each substance alone is recommended.**
9. **anaphylactoid reaction: very rarely, anaphylactoid reactions are seen within 30 minutes after topical testing with certain medicaments (e.g. antibiotics). This is therefore no problem in cosmetic tests.**

The term “contact dermatitis” is used in two ways: (1) to describe any rash resulting from substances touching the skin and (2) as a synonym for allergic contact dermatitis (ACD). This diverse usage indicates that materials coming in contact with the skin cause dermatitis by both allergic and nonallergic mechanisms. When an allergic mechanism is involved, the resulting rash should be called allergic contact dermatitis (ACD), although this term is often shortened to contact dermatitis. Materials that produce dermatitis on a nonimmunologic basis cause irritant dermatitis. Often a chemical acts as both an irritant and an allergen.

Irritant dermatitis, sometimes incorrectly called primary irritant dermatitis, results from contact with a substance that chemically damages skin. Irritant dermatitis is more common than acute contact dermatitis (ACD) and may occur after a single contact with a strong irritant such a battery acid or may require repeated contact with milder irritants, such as detergents and solvents.

Allergic contact dermatitis (ACD) results when a substance comes into contact with skin that has undergone an acquired specific alteration in its reactivity. This altered reactivity is the result of prior exposure of the skin to the material eliciting the dermatitis or to a chemically closely related substance.

In some cases, late-stage allergic and irritant contact dermatitis cannot be differentiated clinically or histologically. Allergic contact dermatitis is an immunologic phenomenon requiring antigen-presenting and antigen-processing cells without regard to the condition of the protective stratum corneum. Therefore, an intact stratum corneum cannot prevent developement of allergic contact dermatitis in sensitised individuals. The only course is avoidance of the allergen.

One additional remark: The declaration "hypo-allergenic" for a product tested only by a single patch test is nonsense !

Finally, patch testing, like many biologic diagnostic methods, is not without hazard. The risk is greatly decreased by expertise with the method. In any instance, the risk of not identifying the allergen is greater than that of performing such testing.

In the Wetting Test (Burckhardt) the undiluted or diluted substance is tested in an open epicutaneous test on the inside of lower arm over a period of 15 (30, 60) minutes by wetting the skin area every 30 seconds by means of a cotton pad or a glass rod. This test serves for the assessment of the acute irritation potential of raw materials or preparations.

In the Duhring-Chamber-Test 0.1ml of the test substance is applied in aluminium chambers (Duhring-chamber) on the inside of lower arms as a occlusive repetitive epicutaneous test, 24 hours on the first day and 6 hours each on the 2. – 5. day. With the help of a score system ranging from 0-4 by evaluating symptoms of redness, scaling and fissures in the test area the results are asssed. There are several variants of tests on human skin. This type of test is especially for the differentiation of irritant potentials of medium strong irritants.

The dermatologically controlled application test is a user-near examination of a finished formulation under the control of a dermatologist. By choosing special test conditions, the impact of the test can be increased, for example, by extended processing times, higher application amounts and a raised frequency of use of the test material on specially responsive panelists, e.g. persons with atopic dermatitis. This test can be made as a half-side test in order to attain a differentiation of products.
This test permits the assessment of irritative or allergic phenomena as well as the occurrence of subjective troubles, as for example itching, tingling, burning or stinging.

In a dermatologically controlled use test the finished product is tested under its conditions of use. If possible, 50 – 100 or more panelists should be tested. These panelists are selected by age, sex, skin type, sensitive skin or acne and are tailored to the intended target group for the product. The assessments of this test type are objective reactions of incompatibility, subjective discontent and cosmetic acceptance: the claim "clinically tested" can be supported by this test method. Special conditions, for example, are given for cosmetics used around the eyes. The co-operation between the dermatologist and the ophthalmologist is of great value to get validated results about the products.
This test may be well linked with analytical methods for the proof of effectiveness.

One additional remark:cutaneous stinging can not be evaluated by any of these tests! A lot of substances are known which induce stinging. But till now there is no exact test for this adverse effect of some cosmetics.

Proving the efficacy of cosmetic products are very important item within the co-operation between cosmetologists and dermatologists. To prove the physiological efficacy of a cosmetic product, possibly objective tests need to be employed. This can be done directly by quantifying already apparent, easily consumer noticeable effects, potentially under inclusion of the consumer as lay assessor of the benefit, in addition to the expert grader. Over the years validated test methods and approaches were developed by the cosmetic industry, by skin physiology institutes, and dermatological clinics. A very important purpose is to protect the consumer against fraud with regard to over-promising of real effects or raising expectations about non achievable effects. Certain quality requirements have to be met by all methods. They have to be safe and procedure-wise acceptable to the test persons, target at relevant endpoints, show good reproducibility, and follow detailed and biometrically valid test protocols. Ideally they are internationally accepted for relevance and validity by the professional community, in the case of skin by dermatologists.

PROVING EFFICACY
1. **effects on sebum (= Sebumetry)**
2. **moisturizing effects (= Corneometry)**
3. **skin roughness (= computer-aided laserprofilometry)**
4. **skin shininess**
5. **trans-epidermal water loss**
6. **skin elasticity**

Normally sebumetry and corneometry are well known. Laserprofilometry according to DIN-NORM is a new method and should replace the older optical methods for skin surface measurement.
For quantitative determination of skin shininess spectrophotometry e.g. with the Chromameter (Minolta Corporation) can be conducted.

High quality professional photography and side-by-side image comparison in a before and after setting may complete the typical laboratory instruments.

Principles for all efficacy tests are:
1. **clear objective**
2. **test design appropriate to claimed benefit**
3. **biometrically valid test design**
4. **tenable, scientifically acceptable extrapolations**

The tolerance of cosmetical products reflected in claimed mildness, suitability for sensitive skin and hypo-allergenicity is the last group of cosmetic benefits ranking high in consumers expectations. The lack of irritancy or the mildness to skin can be determined by the trans-epidermal water loss. Increasing trans-epidermal water loss is typical for a more or less pronounced impaired barrier function and thus a parameter for substantiating mildness claims.

For assessing product tolerance in sensitive and very sensitive skin, the same methods are applied. Just the test persons should be patients with atopic dermatitis within a eczema-free intervall. Here, well-trained dermatologists with high tactile sensitivity can approach this effect under use of valid, well-designed, and bio-statistically tenable protocols.

Methods to measure and quantify product efficacy, however, are not only protecting the consumer against misleading advertising, but they are also an important help for the cosmetic industry to develop better products.

The above mentioned test types permit a comprehensive safety assessment of a cosmetic product from the dermatological point of view. Depending on the innovation degree of a product and the claims of product effects and safety aspects, the chosen test may be of crucial importance.

The human single patch test, the human repeated patch test as well as the dermatologically controlled application and in use test are employed most frequently. After launching a product onto the market, a further observation has to be made of course in order to record reactions of incompatibility and find out the reasons for this. If a cosmetic formulation has been put on the market for a long time without any objections, this is a convincing argument for safety of the particular product.

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