

Studies in cosmetics – What is true?

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If the question "Are there any studies on an active agent or a preparation" can be answered with "yes", you can be sure that science is involved and that there is an objective certificate for the truth content of an issue. However, can we really rely on it?

Efficacy is an essential criterion for the selection of pharmaceutical drugs and cosmetic products. Efficacy means that somebody observed or measured a modified condition after applying an active agent or a cream. Since individuals react in very different ways, an isolated observation usually is not sufficient. Similar to a survey, a representative group of individuals has to report on their perceptions or alternatively, appropriate series of tests are required. Results then are combined and evaluated. If only a small number of cases are available, we speak of a practice-based study. Sound studies however imply a high number of cases and statistical evaluation according to approved standards and defined parameters. In this context, statistical significance is calculated to identify objective efficacy in contrast to unavoidable random effects.

To remain with the example active agent and in order to exclude placebo effects, it is advisable to compare conditions "with" and "without" active agent but also "before" and "after" the application. In these test runs, neither patients nor treating persons should know who received the active agent and who did not receive it. This procedure is called double blind study.

Studies frequently unreliable

So far to the theoretical background of scientific studies: In practice it turns out, however, that the majority of studies are unreliable or in other words, that significant facts have not been considered. They are perhaps disproved by other studies.¹ The non-expert outsider wonders: What is correct now? Within our media-dominated culture, this situation causes confusion since the arguments that are brought forward pro or contra certain results depend on particular interests or alternatively, studies are preferred that fit best into the mould. A more recent example for such kind of a deadlock in studies is the discussion on the harmfulness of

aluminum salts used in deodorant- and anti-perspirant products.²

In order to evaluate studies and tests, they have to be accessible for public use. It is a fact though, that the statement "dermatologically tested" is completely useless. Admittedly, it insinuates that a dermatologist was present during the test or that the product was examined according to dermatological criteria however, neither the type of test nor the result has been disclosed in detail. A similar example is the term "hypoallergenic" which also is useless without a closer explanation of the conducted tests. Another example in this context are "before" and "after"-pictures that were taken in non-standard conditions such as lighting, contrasts, background etc. No need to be an expert to recognise manipulations and realise that these are not reliable studies.

In-vitro- and in-vivo studies

The situation is more complex when in-vitro results are extrapolated to humans. A measurable inhibition of inflammatory mediators of a particular substance gained through cell culture experiments (in vitro) can be an interesting academic result on the one hand but on the other hand it is also fact that it cannot be automatically carried over to humans (in vivo). Product marketing willingly uses such kind of results and communicates them in unfiltered form without mentioning the artificial parameters.

This all the more applies for the communication media when negative reports are concerned. Thus a series of cosmetic ingredients has fallen into disrepute because they have been identified as endocrine disruptors in some laboratory studies (in vitro) or in animal tests. Subsequent studies have proven that some of the mentioned substances have hormonal effects in humans however others do not.

An interesting example to mention in this context is the group of frankincense (olibanum)

¹ Ionannidis J, Why most published research findings are false, PLoS Medicine 2005(2);8:e124

² Die Akte Aluminium, TV movie from Bert Ehgartner

extracts with anti-inflammatory effects which have been well-known for quite some time already. The inhibition of 5-lipoxygenase through the 3-acetyl-11-keto- β -boswellic acid contained in the extract which was observed in vitro indeed fits the mould. Measurements on humans could not prove this effect but it turned out instead that α - and β -boswellic acids which also are contained in the extracts inactivate protein-decomposing proteases of endogenic and exogenous origin and that this is the mechanism which inhibits inflammations.³

Oral & topical application

Nor is it possible to bring the effects of orally applied substances in line with topically applied substances.

Orally taken evening primrose oil only is effective in a certain percentage of atopic patients with delta-6-desaturase deficit or with a low level of essential fatty acids in general. The dominating topical effect is due to the fact that the contained gamma-linolenic acid is metabolized through the natural 15-lipoxygenase of the skin into anti-inflammatory metabolites.⁴ That is the reason why the results of oral and topical studies are diverging and show a broad range of efficacy from non-effective to highly effective substance. It is important to know these underlying conditions in order to understand the effects, to predict them in isolated cases and use them accordingly.

In this context, also the features of oral collagen preparations have to be mentioned. While topical collagens lead to a light tension on the skin surface through hydrogen bridge linkage and together with a slight bolster effect show a measurable wrinkle reduction, the amino acids of orally taken preparations are partly integrated into the dermal collagen. Studies account on a significant wrinkle reduction in the case of regular oral intake ("wrinkle smoothing from inside").⁵ Pleasant effect though, that

³ Lautenschläger H, Weihrauch – Harz mit Heilkraft, medical Beauty Forum 2015 (4), 12-16

⁴ Lautenschläger H, Kettenreaktion – Hautenzyme und Enzymdefekte, Beauty Forum 2017;1: 52-55

⁵ Proksch E, Segger D, Degwert J, Schunck M, Zague V, Oesser S. Oral supplementation of specific collagen peptides has beneficial effects on human skin physiology: a double-blind, placebo-controlled study. *Skin Pharmacol Physiol* 2014;27(1):47-55

Proksch E, Schunck M, Zague V, Segger D, Degwert J, Oesser S. Oral intake of specific bioactive collagen peptides reduces skin wrinkles and increases dermal matrix synthesis. *Skin Pharmacol Physiol* 2014;27(3):113-119

does not need to be doubted in particular. Nevertheless, a pointer should be allowed that the studies only confirm known wisdom: Food influences the complexion. It would be interesting to know the respective share of test persons in this study, who more or less avoid meat in their diet.

Chain length in HA

Completely different aspects arise in the discussions around topical hyaluronic acid preparations. Just remember that there always is talk of chain length in the context of hyaluronic acid. Studies give reasons to believe that low molecular hyaluronic acid with a molar mass of 20,000-50,000 Dalton can penetrate through the skin and hence stimulates the natural hyaluronic acid of the body.⁶

From a physical point of view this still is impossible – apart from the fact that the mentioned scales always are average values based on a more or less broad Gaussian distribution. It has not been examined whether, besides the average molar mass, production-related fragments of the used hyaluronic acid such as glucosamine (179 Dalton) and N-acetyl-glucosamine (221 Dalton) are contained in the raw material or whether the molecules are formed by the skin flora. Both compounds can easily pass through the skin barrier and stimulate the production of hyaluronic acid, as described in technical literature.^{7,8} In other words, the study results probably are correct with regard to the used material and the test persons, however the causality as purported is incorrect. The term hyaluronic acid certainly is easier to use for marketing purposes than N-acetyl-glucosamine which is almost unknown to consumers.⁹

⁶ Kaya G, Tran C, Sorg O et al: Hyaluronate fragments reverse skin atrophy by a CD44-dependent mechanism. *PLoS Med* 3 (2006) e493

⁷ Uitterlinden EJ, Koevoet JLM, Verkoelen CF, Bierma-Zeinstra SMA, Jahr H, Weinans H, Verhaar JAN, and van Osch GJVM, Glucosamine increases hyaluronic acid production in human osteoarthritic synovium explants, *BMC Musculoskelet Disord*. 2008;9:120

⁸ Sayo T, Sakai S, Inoue S, Synergistic effect of N-acetylglucosamine and retinoids on hyaluronan production in human keratinocytes, *Skin Pharmacol Physiol*. 2004 Mar-Apr;17(2):77-83

⁹ Chen JK, Shen CR, Liu CL, N-Acetylglucosamine: Production and Applications, *Mar Drugs*. 2010;8(9):2493–2516.

Tolerance of oils

Precise specifications also are needed when reports cover the reactions to plant oils. Cold-pressed oils can contain residues of unwanted concomitant substances and metabolites while refined oils contain glycidol and glycidyl esters with epoxy structure, among others.¹⁰ In tolerance studies on oils not only the mentioning of the type of oil and its origin are significant but, besides the fatty acid pattern, also a quantitative information on the concomitant components. It is assumed that in the case of oral intake, the acidic pH of the stomach already converts the glycidyl esters of refined oils into harmless glycerides and that partly also glycerin is formed. Conditions are different on the skin. Epoxides can react with the amino acids and peptides and form sensitizing compounds in this process. This already can occur with physiological epoxides as for instance with the epoxide-containing vitamin K₁ that has been banned for topical applications some years ago¹¹. At that time the commercial vitamin K₁ contained a certain percentage ($\leq 4\%$) of the natural vitamin K₁-epoxide (trans-epoxyphytomenadione) of the body and caused a number of serious cases of allergy in France after topical application.¹²

Allergenic effects of substances

Another issue to deal with is that reports on the allergenic effects of cosmetic ingredients continue to be communicated although the quality of components and particularly their purity has been changed over the years. This is the case with the frequently used propylene glycol which in the past obviously was fraught with impurities such as the allergenic base component or other impurities forming in side reactions, both due to its synthesis from propylene via propylene oxide (also an epoxide).

Today we can be assured that the substance neither has irritating effects¹³ nor is its allergenicity worth mentioning.¹⁴ With regard to

¹⁰ FAQ of Bundesinstitut für Risikobewertung (BfR) from 07. July 2016: Fragen und Antworten zur Kontamination von Lebensmitteln mit 3-MCPD-, 2-MCPD- und Glycidyl-Fettsäureestern

¹¹ Directive 2009/6/EG of 4.2.2009

¹² Information RT 8/2005 (January 2005) and RT 65/2006 (June 2006) des IKW

¹³ Propylene glycol, OECD Screening Information DataSet (SIDS) High Production Volume Chemicals www.inchem.org/pages/sids.html

¹⁴ M. Gloor, K. Thoma und J. Fluhr, Dermatologische Externtherapie, Springer-Verlag, Berlin 2000, S. 146-147

health and toxicity, the 100% pure propylene glycol has not a single (!) GHS marking. This is indeed an exceptional case for such kind of ingredient as a pure substance. Just compare, for instance, the situation with emulsifiers, preservatives and essential oils.

Apropos plant oils: Numerous comparisons have been compiled on the high contents of vitamins, essential and other nurturing fatty acids, the anti-oxidative features and the wholesome effects of oils in which the exceptional position of argan oil is particularly emphasized. A detailed comparison of parameters however shows that the characteristic values of the oil rather are in the medium range and that studies covering the properties of argan oil should better be filed in the category product marketing.

Dosage

When it comes to tolerance, there are also cases in which the particular dosage plays a role. In the public opinion, glycerin still is suspected to have dehydrating effects. This opinion however has been disproved a long time ago in long-term practice-based studies¹⁴. The concentrations in cosmetic products are far from reaching this threshold.

Studies frequently only examine a partial aspect of the issue. This particularly applies for antioxidants and radical scavengers. Considering unwanted effects and adverse effects, the studies often exercise restraint. Various physiological processes and almost all healing processes take place with the collaboration of endogenic radicals. This also applies for external treatments with red light, blue light and infrared radiation for instance. Hence there is a multitude of sound studies that point to the counterproductive features of highly dosed antioxidants within this kind of treatments.¹⁵

Short- and long-term effects

A holistic approach also is recommended when examining the studies with respect to short- and long-term effects. By the very nature of things, short-time studies are predominant which, for instance, after fruit acid treatments reveal excellent results regarding the skin regeneration. Long-term observations in the daily practice however lead to the assumption that regularly applied fruit acid peelings over a long period will cause an increased prevalence of rosacea and perioral dermatitis. Particularly

¹⁵ References see: Lautenschläger H, Antioxidantien und Radikalfänger – zu viel ist zu viel, ästhetische Dermatologie (mdm) 2015 (8), 12-16

susceptible is the Celtic skin of the inhabitants of Anglo-Saxon countries.

Tolerance studies

Another word to tolerance studies: these studies usually are carried out on adults with healthy skin. The tested products, however, also are applied on problem- and children skin later on, whereas both types of skin are different from the normal skin of adults. In individual cases it is advisable to consider the INCI declaration of the products and refrain from relying on results of studies and the related product marketing.

Market launch

Studies often are used as a basis to prepare the market for new products. This is currently done with reference to the successful antioxidant story with detox products that are supposed to help against harmful environmental impacts as for instance particles from combustion engines. A closer analysis of the studies however shows that a well-combined conventional skin protection, and skin care and skin cleansing preparations which are well-adapted to the individual skin already are sufficient for this purpose.¹⁶

Studies show that the medium pH value of the skin ranging from 4.5-5.5 increases up to 6.0 in old age. This is the reason why pH-adapted preparations are applied to balance this increase.¹⁷ In this connection it will be interesting to learn whether the pH-stabilizing buffer capacities are included in the considerations. As long as the preparations do not contain buffers or only few buffers, the pH value of preparations in the range between 4 and 8 does not play a role since the buffer capacity of the skin immediately balances the physiological pH value.

Study requirements

Important requirement for a relevant result of a study is the selection of test persons. There are also negative examples such as testing anti-aging creams on the skin of 20 year old test persons or testing moisturizers on a sufficiently hydrated skin. Product comparisons, among others, then show a low efficiency of preparations.

¹⁶ Lautenschläger H, Anti-Pollution-Kosmetik, medical Beauty Forum 2017 (3), 12-15

¹⁷ Blaak J, Kaup O, Hoppe W et al: A long-term study to evaluate acidic skin care treatment in nursing home residents – Impact on epidermal barrier function and microflora in aged skin, Skin Pharmacol Physiol 28 (2015) 269-279

Summary

It is no use going that far to comment every study with the well-known academic annotation: "Don't believe in studies that you didn't falsify yourself." Nevertheless, the examples mentioned above show that the available studies and reports should not induce people to shut off their sound reasoning.

Furthermore, it can be interesting to know whoever ordered the study. Meanwhile, many publications either conclude with annotations of the authors excluding such kind of cross-linkage or alternatively with disclosures.

And vice versa, there are also niches in the fields of cosmetic and medicine that cope without studies, just to mention gemstone cosmetics, Bach flowers, Schüßler salts and homeopathy.¹⁸

The poet Marie von Ebner-Eschenbach coined the following key phrase that also applies to the subject "studies": "Who doesn't know a thing has to believe everything."

Dr. Hans Lautenschläger

¹⁸ Lautenschläger H, Präparate mit besonderen Ansprüchen, Ästhetische Dermatologie (mdm) 2015;4:36-39