

The seeming and the real – What really works: Cosmeceuticals, Placebos & Co.

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The supply of products and promises are booming in the anti-aging beauty care. Not only consumers but also professionals have a hard time staying on top of things. In the following you will find a summary on reliable but also dispensable substances.

Skin and anti-aging – is that a subject that concerns all of us? If you enter the term “anti-aging” into Google Search and then scroll to the related pictures you certainly will be puzzled because there unfailingly pop up the faces of women aged 20-40 years. In other words, here you will find the most profitable target group regarding the supply of preparations, treatments, food supplements and medical services.

A more realistic consideration of our options against premature skin aging and also aging in general reveals completely other priorities that apply for both men and women, as for instance

1. exercise
2. balanced nutrition
3. balanced mind – stress reduction
4. physical skin protection – appropriate clothing
5. sustainable cosmetic skin care
6. instrument-based bio-engineering – instrument-based treatments and corrections
7. physician-guided medication, such as hormone- and hormone replacement therapy

Efficacy and costs in the above-mentioned listing are working in opposite direction, though. The options also are limited to the steps that can be taken and it still remains untold what we shouldn't do as for instance smoking cigarettes and drinking alcohol. It is a fact however, that up to the present day there is no remedy against intrinsic aging processes.

Sustainable skin care

The term “sustainability” is mentioned fifth in our list but it is an important issue in the panoply of cosmetic skin care.

- Skin protection against
 - physical impacts (radiation, mechanics and erosion)

- chemical impacts (household, workplace and environment)
- microbial impacts (individual microbiome and external microorganisms)
- cultural impacts (hygiene and overtreatment)
- Treatment and recovery of
 - barrier disorders
 - cornification disorders
 - disorders of the connective tissue and blood vessels
 - irritations, allergies and inflammations
 - pigment disorders
- Analysis and compensation of endogenous deficits, e.g. enzyme defects
- Preventive skin care
 - sustainable skin care (sustainable = no long-term adverse effects)
 - skin care with medical indications
- Optical treatments – camouflage with deco products

It hardly needs mentioning that reasonable components should be administered (“with”) and not beneficial or counterproductive components should be avoided (“without”). Resulting are the following five categories

- cosmeceuticals
- classical components
- placebos
- controversial components
- dispensable components

Cosmeceuticals

High standards are set on cosmeceuticals.¹ In order to provide high availability and efficacy in the targeted area (cell, tissue, blood vessel, enzyme, receptor) they must be able to pene-

¹ Lautenschläger H, Cosmeceuticals, medical Beauty Forum 2014 (4), 16-18

trate into and possibly also permeate the skin barrier.

The efficacy has to be clinically proven; measured in vitro activities are not sufficient for this purpose. In other words, there exist reproducible studies and causalities as well as significant effects. Activities should be localized and not systemic, though. Other requirements are the compliance with the German Cosmetic Directive (Kosmetikverordnung – KVO), documented safety in the safety report and the physiological compatibility. Substances that are banned in the KVO, as for instance hormones, should not be contained, pharmaceutical agents are allowed on a limited scale if they improve and stabilize the skin condition and eliminate skin disorders – examples are D-panthenol (provitamin B₅) in cases where the skin is prone to erythema; azelaic acid ≤ 1% (Federal Institute for Risk Assessment – Bundesinstitut für Risikobewertung, BfR) in the case of a tendency to blemished skin, acne, rosacea & perioral dermatitis; tranexamic acid for skin whitening purposes and reduction of erythema; clotrimazol in the case of dandruff. It should however be mentioned that according to the KVO advertising messages mentioning wound healing, acne treatment, fibrinolysis inhibition and antimycotic effects are not allowed in these cases.

Cosmeceuticals with anti-inflammatory effects² are

- 15-Lipoxygenase substrates – ω-3 and ω-6 fatty acids such as linoleic acid (gained from herbal oils, phosphatidylcholine³), γ-linolenic acid (evening primrose, borage) and α-linolenic acid (linseed, kiwi, rose hips, phosphatidylcholine)
- 5-Lipoxygenase inhibitors – caffeic acid (3,4-dihydroxy cinnamic acid), curcumin (curcuma alias turmeric rhizomes), hyperforin (St. John's wort alias amber), 3-O-acetyl-11-keto-β-boswellic acid (frankincense in vitro).
- 5-α-Reductase inhibitors – azelaic acid ≤ 1% (occurs in cereals).
- Protease inhibitors – boswellic acids (frankincense in vivo)
- Macrophage-activating substances - phosphatidylserine (soya, natural component of the body)

² Lautenschläger, Den Brand löschen – Entzündungshemmende Wirkstoffe, Kosmetik International 2014 (2), 26-29

³ Lautenschläger H, Cosmeceuticals: Phospholipide – Kraftvolle Klassiker, medical Beauty Forum 2018 (2), 14-18

Cosmeceuticals with regenerative activities:

- Retinoids⁴ – among other effects, they stimulate the growth factors: vitamin A (retinol) and ester, retinal (aldehyde), provitamin A (carotenoids, astaxanthin etc.). The effective metabolite is vitamin A acid which is not licensed for cosmetic use (INN: tretinoin). Applications: skin tightening, blemished skin (acne). The Federal Institute for Risk Assessment (BfR) recommends facial application only.
- Vitamin B series⁵ – among others, stimulation of growth factors. Examples: vitamin B₃ (niacinamide: anti-inflammatory, blemished skin respectively acne), provitamin B₅ (D-panthenol: irritated skin, soreness).
- Sphingosin-1-phosphate – inhibition of keratinocyte proliferation: skin care in the case of psoriasis.
- Zinc salts⁶ (≤ 1%) – substrate for oxidoreductases, among others superdismutase (SOD).
- Isoflavones – phytohormones⁷, bonding to oestrogen receptors.
- Gamma-linolenic acid – for delta-6-desaturase enzyme defects⁸ (atopic skin).
- Growth factors and messenger substances⁹ – various peptide structures.

Protective cosmeceuticals

- Linoleic acid – ceramide I substrate (vital for the elasticity of the skin barrier).¹⁰

⁴ Lautenschläger H, Retinoide und ihr Einsatz im kosmetischen Bereich, Kosmetik International 2015 (11), 148-151

⁵ Lautenschläger H, Wirkstoff-Klassiker – Vitamine in der Kosmetik, Teil 2, Beauty Forum 2014 (11), 38-42

⁶ Lautenschläger H, Spurenelemente – Kleine Lebenshelfer, Kosmetische Praxis 2011 (3), 13-15

⁷ Lautenschläger H, Flavone und Isoflavone – die Wirkstoff-Generalisten, Kosmetik International 2016 (10), 62-65

⁸ Lautenschläger H, Kettenreaktion – Hautenzyme & Enzymdefekte, Beauty Forum 2017 (1), 52-54

⁹ Lautenschläger H, Wachstumsfaktoren – körpereigene Peptide, die vielfältige Zellfunktionen steuern, medical Beauty Forum 2012 (2), 16-18

- Amino acids of the natural moisturizing factor (NMF) are natural radical scavengers¹¹ – cf. urea additives in the emission control of motor vehicles.
- UV filters^{12 13} convert radiation into heat. In various countries such substances belong to the medical skin care sector and thus are subject to particularly intense screening. Sun protection factors are calculated in such a way that they neutralize the radiation that is not eliminated by melanin. This ensures that the melanin formation still is stimulated to a minor degree and vitamin D can be formed. Additional antioxidants are counterproductive for the melanin formation, apart from the fact that in comparison with UV filters they are less durable under radiation and higher concentrations can support the radical chain formation.
- Tyrosinase inhibitors impede melanin formation¹⁴ – antioxidants are frequently administered against hyperpigmentation. Liposomal vitamin C phosphate ($\leq 1\%$) effectively impedes pigmentation during laser therapies and also supports the formation of collagen.
- Tranexamic acid ($\leq 2\%$) is an antifibrinolytic agent that stabilizes the superficial blood vessels (rosacea, erythema) and impedes melanin formation.¹⁵ It is a particularly popular active agent in the Asian skin care.

Skin diagnoses¹⁶ with appropriate probes, camera and documentation of the customer history, individualised treatments with a reduction of active agents to necessary substances, focussing on causality (causes & effects) and adequate dosage including the exemption of homeopathic formulations¹⁷, as well as the physiological composition of end products are significant elements in the administration of cosmeceuticals. In this context it is irrelevant whether natural or synthetic components are used.

Deciding factors are the purity of components, physiological compatibility, established and uncritical metabolism (no long-term adverse effects) and microbiome compatibility.¹⁸

In cases where a sustainable preventive skin care is accompanying or following the medical therapy – which actually occurs quite frequently – it is recommended using pharmacopoeia-compliant bases or bases that are in accordance with the German Ordinance on the Operation of Pharmacies (Apothekenbetriebsordnung – ApoBetrO) to avoid a change of system in the treatment. This ensures high compliance (“adherence”) and an optimal care accompanying the medical indication-based treatment.

Pharmaceutical and cosmetic active agents can also be effectively synchronized.¹⁹ Examples are

- Hormone treatments: oestrogens – isoflavones
- Atopic skin: corticoids – ceramides and hydrogenated phosphatidylcholine (Kligman’s Outside-in-Principle²⁰)
- Acne: vitamin A acid – vitamin A, 15-lipoxygenase substrates
- Psoriasis: vitamin D and derivatives – sphingosin-1-phosphate, free fumaric acid (liposomal)
- Rosacea: metronidazol – 5-alpha-reductase- and protease inhibitors
- Inflammations: antibiotics – AMP boosters (such as polyhexanide), 15-

¹⁰ Lautenschläger H, Hautbarrierestörungen – gezielte Prävention, Kosmetik International 2003 (9), 36-39

¹¹ Lautenschläger H, Wasserhaushalt der Haut – Moisturizer & Co., medical Beauty Forum 2014 (1), 18-20

¹² Lautenschläger H, Bestens geschützt – Filter, Lichtschutzfaktor & Sonnenschutzpräparate, Beauty Forum 2015 (2), 64-67

¹³ Lautenschläger H, Sonnenschutzprodukte - gezielt anwenden, medical Beauty Forum 2014 (2), 16-18 und Beauty Forum 2015 (2), 64-67

¹⁴ Lautenschläger H, Haut ohne Makel – Wirkstoffe und Wirkstoffsysteme, medical Beauty Forum 2014 (5), 32-35

¹⁵ Lautenschläger H, Bewährter Aufheller – Tranexamsäure wirkt gegen Pigmentflecken und Rötungen, medical Beauty Forum 2015 (3), 12-14

¹⁶ Lautenschläger H, Hautdiagnose – an Messergebnissen orientieren, Kosmetik International 2007 (10), 54-56

¹⁷ Lautenschläger H, Kosmetische Präparate mit besonderen Ansprüchen, Ästhetische Dermatologie (mdm) 2015 (4), 36-39

¹⁸ Lautenschläger H, Mikroorganismen – im und um den Körper, medical Beauty Forum 2017 (4), 12-18

¹⁹ Lautenschläger H, Gegenüberstellung – kosmetische und pharm. Wirkstoffe, Kosmetik International 2010 (10), 32-36

²⁰ Lübke J, Evidence-based Corneotherapy, Dermatology 2000;200:285-286

lipoxygenase substrates and protease inhibitors

- Itching: antihistamines – amides (urea, allantoin, secondary carboxylic acid amides)
- Scars: dermal needling – vitamin preparations
- Hyperpigmentation: medical peeling – tyrosinase-, PIH-, AGE-inhibitors)

Bases can be W/O- and O/W emulsions with biodegradable emulsifiers, emulsifier-free lamellar dispersions^{21 22} as well as additive-free, non-aqueous bases²³. Amides (D-panthenol, urea etc.), liposomes (water-soluble active agents)²⁴, biodegradable liquid (fat-soluble active agents) and solid nanodispersions (nearly insoluble active agents) facilitate the optimal penetration of active agents.²⁵

Extrapolating in-vitro studies to practical applications is not allowed. Just to mention the example of frankincense that in vitro is a 5-lipoxygenase inhibitor but in vivo is a protease inhibitor. Some effects only occur with the assistance of instruments and/or after injections as for instance lipolysis with phosphatidylcholine, caffeine, genistein.

Classical components

Belonging to this category are:

- Barrier-active components²⁶ such as long-chained fatty acids, cholesterol and phytosterols, ceramides, hydrogenated phosphatidylcholine, squalane/squalene.

- Moisturizers²⁷ such as glycerin, glycols, urea, amino acids, mineral salts and glycerophosphatidylcholine (GPC) in low concentration as well as topical-acting, filming polysaccharides such as hyaluronic acid, alginates and cellulose derivatives.
- Vitamins and provitamins – among others, vitamin E that improves epithelisation and the moisture retention capacity of the skin.
- Peptides, spilanthol, hyaluronic acid for wrinkle reduction²⁸
- Skin tightening extracts and active agents such as Centella asiatica, Kigelia, saponins, N-acetyl-glucosamine.
- Antioxidants: vitamins A, E, and C, isoflavones, polyphenols and derivatives in adequate (!) concentration. Strong antioxidants are counterproductive if they impede healing- and pigmentation processes that, without exception, are radical (!) processes.

Placebos

Placebos are permitted unless they cause (long-term) adverse effects. They obviously convey a feeling of wellbeing which, via psyche, also has its positive effects on the skin condition in general, as we all know. Placebos usually are sold as effective preparations and not just plain as placebos. In this context, it should be mentioned that most of the studies including proofs of efficacy are incorrect, artificial, not reproducible and not applicable in the field.²⁹ Even if the active agent may offer a good story to tell it needs to be said that using this story is not compliant with the regulations stipulated in the German Cosmetic Directive (KVO). Placebos can be detected by implementing double-blind studies. Typical placebos are preparations with 30 and more substances listed in the INCI including well-known active agents in homeopathic dosage. An essential requirement is that the substance contents come below the established allergy thresholds. Ineffective components can also unintentionally form by interaction of substances. Apart from that, protective- and healing processes

²¹ Lautenschläger H, Eine gute Basis – Pharmazeutische und kosmetische Basiscremes, medical Beauty Forum 2016 (5), 12-17

²² Lautenschläger H, Membranhaltige Barrierecremes – wie die Haut, so der Schutz, Kosmetische Praxis 2006 (4), 12-14

²³ Lautenschläger H, Vorteile von Produkten ohne Wasser und Hilfsstoffe, Kosmetik International 2017 (6), 56-58

²⁴ Lautenschläger H, Liposomes, Handbook of Cosmetic Science and Technology p. 155-163 edited by: A. O. Barel, M. Paye and H. I. Maibach

²⁵ Lautenschläger H, So klein, so fein – Nanopartikel von fest bis flüssig, medical Beauty Forum 2016 (2), 12-16

²⁶ Lautenschläger H, Regeneration der Hautbarriere, Kosmetik International 2000 (8), 100-103

²⁷ Lautenschläger H, Wasserhaushalt der Haut – Moisturizer & Co., medical Beauty Forum 2014 (1), 18-20

²⁸ Lautenschläger H, Kein Knitter-Look – Arsenal an Antifalten-Wirkstoffen, Kosmetik International 2012 (11), 22-25

²⁹ Ionannidis J, Why most published research findings are false, PLoS Medicine 2005(2);8:e124

can be impeded as shown in the following examples considering the use of antioxidants³⁰:

- The combination of strong antioxidants with coenzyme Q₁₀ leads to the formation of the (though active) hydroquinone form of coenzyme Q₁₀ while the antioxidants are consumed in the process.
- The treatment of sun burns with antioxidants is counterproductive for the healing process as it is a radical process.
- During blue light treatment of acne skin the resulting radicals influence the bacterial processes. Antioxidants reduce the effectiveness of the treatment. The same applies to the
- Red light used in the treatment of skin cancer and actinic keratosis in the context of the photodynamic therapy (PDT) with 5-aminolevulinic acid, as well as to
- Light- and O₂-induced dermatological therapies (psoriasis) with PUVA, dithranol etc.

In terms of the whole body it needs to be mentioned that chemotherapy and high antioxidant consumption neither are compatible. Apart from that, the immune responses to infections which mostly occur with rise of temperature and radical formation are counteracted by antioxidants.

Controversial components

Consequently, antioxidants as such are not necessarily counted among cosmeceuticals, with the exception of substances with multifunctional effects such as vitamins or phytohormones. Subject to controversial discussions also are cosmetic additives and active agents without causality, with positive but also negative features, or substances in which the efficacy depends on the presence of other substances. **Examples:**

- **Synthetic prostaglandins (eyelashes-growing substances): long-term adverse effects cannot be excluded due to their relationship with the natural prostaglandins of the body with local, hormone-like effects.**
- **Strong chelating agents bind heavy metal traces and thus impede the autoxidation of preparations, but they**

can also inactivate physiological heavy metals and possibly even antimicrobial peptides (AMP)³¹. This particularly applies to the persistent EDTA³².

- According to studies, low molecular hyaluronic acid^{33 34} stimulates the dermal, endogenous hyaluronic acid formation although it cannot penetrate through the skin – actually a contradiction. It is assumed that this effect is caused by not identified concomitant fragments such as glucosamine and N-acetyl-glucosamine³⁵. Another assumption is that the substances form with the breakdown of hyaluronic acid through microbiome activities of the skin.
- The lipid content of creams is used as a standard reference for the suitability of a cream. Without knowing the specific kind and concentration of the contained emulsifiers, this criterion is rather useless since the involved washout effect is unknown. A lamellar cream without emulsifiers and low lipid content thus is more beneficial in stabilizing the skin barrier than an emulsion with high lipid and emulsifier contents.
- The pH-value of a cream neither is qualified as a reference. In this case, the following principle applies: the skin easily tolerates unbuffered preparations in the range of pH 4-8. Buffered preparations however require a pH-value close to the local pH of the skin in order to avoid skin irritations.
- Novel active agents against environmental pollution: closer inspection reveals that effective occupational skin protection, skin care with barrier-active, non-occlusive components, the

³¹ Lautenschläger H, Antimikrobielle Peptide, Kosmetik International 2016 (7), 28-31

³² Lautenschläger H, Unerwünschte Nebenwirkungen, Ästhetische Dermatologie (mdm) 2016 (7), 50-55

³³ Kaya G, Tran C, Sorg O et al: Hyaluronate fragments reverse skin atrophy by a CD44-dependent mechanism. PLoS Med 3 (2006) e493

³⁴ Lautenschläger H, Hyaluronsäure – ein legendärer Wirkstoff, Kosmetische Praxis 2008 (4), 16-18

³⁵ Uitterlinden EJ, Koevoet JLM, Verkoelen CF, Bierma-Zeinstra SMA, Jahr H, Weinans H, Verhaar JAN, van Osch GJVM, Glucosamine increases hyaluronic acid production in human osteoarthritic synovium explants, BMC Musculoskelet Disord. 2008;9:120

³⁰ Lautenschläger H, Antioxidantien und Radikalfänger – zu viel ist zu viel, Ästhetische Dermatologie (mdm) 2015 (8), 12-16

moderate antioxidative action of amino acids (NMF) and mild skin cleansing preparations (tensides with low CMC) still are adequate and sufficient³⁶. Stress and strains – either due to PM10 (= max. 10 µm) but also due to PM2.5 (= 50% 2.5 µm; alveolar) have been declining for years.³⁷

Dispensable components

The sustaining skin care and thus related anti-aging preparations should completely avoid the following substance groups:

- Occlusive components – they impede the natural regenerative capacity of the skin³⁸
- Preservatives³⁹ – they affect the microbiome and cause resistances that in turn can trigger infections
- Dyes
- Emulsifiers & tensides – with the exception of cleansing products and tensides with low CMC⁴⁰
- Endocrine disruptors⁴¹
- Soothing substances⁴² that affect local nerve impulses – warning of the Federal Institute for Risk Assessment (BfR) of laureth-9 alias polidocanol (INN); 4-t-butylcyclohexanol is rated analogously
- Perfumes – they either naturally contain allergenic components or such components are formed during storage and use due to radiation and oxidation⁴³; they penetrate and permeate very fast into and through the skin because of their small molecular size.

³⁶ Lautenschläger H, Anti-Pollution-Kosmetik, medical Beauty Forum 2017 (3), 12-15

³⁷ Umweltbundesamt, Auswertung der Feinstaubwerte; Stand Dezember 2016, <https://www.umweltbundesamt.de/themen/luft/luftschadstoffe/>

³⁸ Lautenschläger H, Öle und Fette in kosmetischen Produkten, Kosmetische Medizin 2008 (2), 76-80

³⁹ Lautenschläger H, Konservierung von Kosmetika, Beauty Forum 2017 (11), 92-94

⁴⁰ Lautenschläger H, Mini-Kuppler - Von der Seife zum Hightech-Emulgator, Beauty Forum 2010 (11), 20-22

⁴¹ Lautenschläger H, Endokrine Disruptoren, Kosmetik International 2018 (1), 52-55

⁴² Lautenschläger H, Reizlindernde Stoffe, Kosmetik International 2017 (1), 114-116

⁴³ Lautenschläger H, Streifzug durch die Welt der Duftstoffe, Kosmetische Praxis 2010 (5), 10-14

Concluding remarks

The academic comment "Don't trust in studies that you didn't falsify yourself" does not apply to all the anti-aging actives and preparations. Studies shouldn't mislead into blocking out your own thinking, though. Marie von Ebner-Eschenbach's quote "Those who know nothing must believe everything" also is applicable in this context.

Information and sources for additional active agents can be found in the guideline "Dermocosmetics to fight skin aging" published by the Society for Dermopharmacy (GD – Gesellschaft für Dermopharmacy).

The parts coloured in blue were published online at www.beauty-forum.com.

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