

Abstracts

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A survey and analysis of the role of molecular chaperone proteins and imidazole-containing dipeptide-based compounds as molecular escorts into the skin during stress, injury, water structuring and other types of cutaneous pathophysiology

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Molecular chaperone, heat shock proteins (HSPs), stabilizes intracellular processes of cells under stress. Little is known about the role of molecular chaperone proteins in the skin pathology, rejuvenation and wound healing, or whether their expression is altered by environmental and physiological stress to the skin or systemic disease. The focus of this study was to examine the role of molecular chaperone proteins in the skin's local response to wounding, skin ageing and a range of skin diseases. Free radicals, one form of insult, induce or contribute to adverse effects on the skin, including erythema, oedema, wrinkling,

photoaging, inflammation, autoimmune reactions, hypersensitivity, keratinization abnormalities, preneoplastic lesions and skin cancer. A unified view of the molecular and cellular pathogenesis of the skin age-related pathology conditions has led to the search for molecular and chemical chaperones that can slow, arrest or revert disease progression. Specific alpha-crystallin domains and pharmacological imidazole-containing dipeptide chaperone molecules are now emerging that link our biophysical insights with developed skin therapeutic techniques. In this article, we discuss the molecular nature of the stress signals, the mechanisms that underlie activation of the heat shock response, the role of molecular chaperone proteins as skin protective molecules, and strategies for pharmacologically active chaperone molecules and their imidazole-containing dipeptide inducers as regulators of the skin stress response. We discuss how impairment in protein hydration may cause ultrastructural, mechanical and biochemical changes in structural proteins in the aged skin. We have pioneered the molecular chaperone protein activated therapeutic or cosmetic platform to enable simultaneous analysis of water-binding and structuring characteristics for biology of skin ageing and skin disease-related pathways. This cutting-edge technology has improved the way that proteins hydrate in photoaged skin. The mechanisms of skin diseases, ageing, cellular, and signalling pathways mediated by targeting with molecular chaperone protein(s) in patented formulations with imidazole containing dipeptide (N-acetylcarnosine, carbinine, carnosine) are also discussed within this review.

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Infant skin physiology and development during the first years of life: a review of recent findings based on *in vivo* studies

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Infant skin is often presented as the cosmetic ideal for adults. However, compared to adult skin it seems to be more prone to develop certain pathological conditions, such as atopic dermatitis and irritant contact dermatitis. Therefore, understanding the physiology of healthy infant skin as a point of reference is of interest both from the cosmetic as well as from the clinical point of view. Clinical research on healthy infants is, however, limited because of ethical considerations of using invasive methods and therefore until recently data has been scarce. Technical innovations and the availability of non-invasive *in vivo* techniques, such as evaporimetry, electrical impedance measurement, *in vivo* video and confocal microscopy, and *in vivo* fibre-optic based spectroscopy, opened up the field of *in vivo* infant skin physiology research. Studies incorporating such methods have demonstrated that compared to adult, infant skin continues to develop during the first years of life. Specifically, infant skin appears to have thinner epidermis and stratum corneum (SC) as well as smaller corneocytes at least until the second year of life. The water-handling properties are not fully developed before the end of the first year and infant SC contains more water and less amounts of natural moisturizing factors. Such findings re-evaluate the old notions that skin is fully matured at birth. Armed with this knowledge, we are in a position not only to better understand infant dermatological conditions but also to design better skin care products respecting the distinct qualities of infant skin.

Temperature as a moisture cue in haptics on hair

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A mechanism for giving a moisturized or dried-out feeling to hair was investigated. A two-step approach was conducted in order to elucidate the issue. First, we have reviewed previous studies that are related to the sensory perception of materials not only in cosmetic industry but

also in other fields, such as textile and architecture industries, and established a hypothesis. Second, we have verified the hypothesis derived from the first step and identified the mechanism for the moisturized or dried-out feeling that people feel by measuring the heat transfer characteristic, q_{max} . The results revealed that the moisturized or dried-out feeling that people feel at the moment of contact with hair was highly related to the temperature drop at the skin surface. The results also revealed that the moisturized or dried-out feeling strongly depends on the hair shape (meandering and diameter), surface damage and the water content of hair fibres which constitute the hair swatch. The moisturized feeling, however, was not related to the water content of hair fibres at a constant relative humidity (RH), as the differences in the water content of the hair fibres at a constant RH were too small for the recognition of the difference in the moisturized feeling.

Cream or foam in pedal skin care: towards the ideal vehicle for urea used against dry skin

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The aim of this study was to evaluate different urea-containing cosmetic preparations designed for foot care regarding skin occlusion. The primary aim was therefore to screen the short-term transepidermal water loss (TEWL) as a parameter for skin barrier function and skin occlusion and to characterize the relative role of the vehicle, i.e. cream or foam in the context of cosmetics containing urea in the 2–10% range addressing the cosmetic products urea 2% cream (GEHWOL FUSSKRAFT blau), petrolatum containing cream (GEHWOL med Schrundensalbe), urea 10% cream (GEHWOL med Lipidro-Crème), urea 10% foam (Allpresan Fuss Schaum) and vaseline (positive control) compared with an untreated area on the volar forearms of volunteers. Moreover, the short time (24 h) kinetics regarding the moisturizing effect of cream and foam formulations in diabetic patients were compared. The

efficacy of a cream on reduction of skin thickness of hyperkeratotic skin in the heel region before and after a period of product application was also evaluated. In some of the trials, healthy individuals and in others, diabetic patients (type I and II) were enrolled. TEWL was determined before product application, as well as at given points of time thereafter. In this study, no excessive occlusion effects comparable with a blockage of the skin's natural water evaporation could be observed for any of the test products. To the extent to be expected, this was found neither for the cream products nor for the foam product. Slightly lowered TEWL values after application of the 10% urea cream can be interpreted as a beneficial effect in terms of an improved barrier function. Regarding skin moisture, the urea-containing cream formulation appeared equal or slightly superior to the foam formulation. The thickness of the horny layer was found reduced after application of 10% urea-containing cream. At present it looks as if cream vehicles would still be vehicles of choice in general, when it comes to the formulation of skin care preparations for not only dry skin but also in the context of pedal skin care.

On the effects of a plant extract of *Orthosiphon stamineus* on sebum-related skin imperfections

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Overproduction of sebum is very common and results in an undesirable oily, shiny complexion with enlarged pores. Sebum secretion is basically under the control of 5- α -reductase, and more particularly under that of type I isozyme. But it is also highly sensitive to environmental factors such as temperature, humidity and food. Moreover, in Asia, the edicts of a flawless facial skin turn oily skin into a major concern for Asian women. We identified *Orthosiphon stamineus* leaf extract as an interesting ingredient for reducing the oily appearance of skin thanks to its ability to reduce 5- α -reductase type I expression in normal human epidermal keratinocytes *in vitro*. This was confirmed *ex vivo*, where *Orthosiphon stamineus* leaf extract was shown to reduce 5- α -reductase activity as well as the production of squalene, one of the main components of sebum that was used as a tracer of sebum. To evaluate the efficacy of *Orthosiphon stamineus* leaf extract at reducing sebum-related skin imperfections *in vivo*, we performed two different clinical studies, one in France on a panel of Caucasian volunteers and the other one in

Thailand on a panel of Asian volunteers. Using instrumental techniques as well as clinical evaluation and self-evaluation, we could highlight that an O/W cosmetic formula containing 2% of *Orthosiphon stamineus* leaf extract could visibly reduce the oily appearance of skin as well as the size of pores, thus leading to a significant improvement of complexion evenness and radiance. Overall, the results obtained were better than those observed with the same formula containing 1% of zinc gluconate, an ingredient frequently used in oily skin care products.

Lavender, tea tree and lemon oils as antimicrobials in washing liquids and soft body balms

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The aim of this study was to evaluate the antimicrobial activity of commercial essential oils: lavender, tea tree and lemon, antimicrobials in washing liquid and O/W soft body balm. The inhibition efficacy of essential oils in washing liquid (1% alone or in mixtures), in soft body balm (0.5% alone), as well as combined with the synthetic preservative DMDM hydantoin and 3-iodo-2-propynyl butyl carbamate mixture (0.1 and 0.3%), was tested against *S. aureus* ATCC 6538, *P. aeruginosa* ATCC 9027, *Candida* sp. LOCK 0008 and *A. niger* ATCC 16404 in compliance with the European Pharmacopoeia standards. The components of the system preserving soft body balm were supplemented with a solubilizer. Washing liquids containing only essential oils met Criterion A E.P. only for *S. aureus*, *Candida* sp. and *A. niger*. In soft body balm formulations, oils at a concentration of 0.5% did not reveal any preserving activity. The introduction of a solubilizer to a system containing 0.5% tea tree oil led to a substantial increase in the bacteriostatic activity of the formulation, but did not significantly affect its fungistatic properties. A combination of 0.5% tea tree oil, 5% solubilizer and 0.3% synthetic preservative ensured the microbiological stability of soft body balm in accordance with Criterion A E.P.

A novel anti-ageing mechanism for retinol: induction of dermal elastin synthesis and elastin fibre formation

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Dermal elastic fibres are extracellular matrix protein complexes produced by fibroblasts and involved in skin elasticity. Elastin fibres decrease with age as a result of reduced synthesis and increased degradation, resulting in skin sagging and reduced skin elasticity. In this study, we show that retinol (ROL), known to enhance dermal collagen production, is also enhancing elastin fibre formation. ROL induced elastin gene expression and elastin fibre formation in cultured human dermal fibroblasts. Topical treatment of cultured human skin explants with a low dose (0.04%) of ROL increased mRNA and protein levels of tropoelastin and of fibrillin-1, an elastin accessory protein, as documented by QPCR and immunohistochemistry staining. Luna staining confirmed the increased elastin fibre network in the ROL-treated skin explants, as compared with untreated controls. These data demonstrate that ROL exerts its anti-ageing benefits not only via enhanced epidermal proliferation and increased collagen production, but also through an increase in elastin production and assembly.

Formulation of sunscreens with enhancement sun protection factor response based on solid lipid nanoparticles

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Solid lipid nanoparticle (SLN) was regarded as new topical delivery systems for pharmaceutical and cosmetic active ingredients. The purpose of this study is to develop carrier systems for organic and inorganic sunscreens based on a matrix composed of carnauba wax and decyl oleate. Formulae (F1–F7) were prepared using butyl methoxydibenzoylmethane and octyl methoxycinnamate as organic components, and titanium dioxide (TiO₂) was used as inorganic component. Both types of sunscreens were incorporated into SLN formulations using classical method of preparation. To evaluate the effect of the pigments on the nanoparticles, particle size was measured using Mastersizer particle size analyser. UV-protection abilities of formulations were investigated by the in vitro sun protection factor test (SPF). Further parameters determined

were spreadability as well as viscosity. The rheological behaviour of the formulations was also carried out. From the plot of log of shear stress vs. log of shear rate, the slope of the plot representing flow index and ontology of the y-intercept indicating consistency index was calculated. The formulae showed a flow index of 0.2074–0.4005 indicating pseudoplastic flow behaviour. Significant increases in SPF values up to about 50 were reported after the encapsulation by using organic and inorganic filters in Canada wax and decyl oleate. So, SLN could be appropriate vehicles to carry organic and inorganic sunscreens. The rational combination of cinnamates, titanium dioxide and Zinc oxide has shown a synergistic effect to improve the SPF of cosmetic preparations

Stratum corneum free amino acids following barrier perturbation and repair

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Modulation of the skin environment after stratum corneum (SC) perturbation has profound effects on the rate and effectiveness of barrier repair. Intermediate water exposure, e.g. moderate relative humidity, may provide the optimum water gradient for SC repair. More rapid recovery with semipermeable (SP) films in vivo was associated with increased hydration measured as moisture accumulation rate. We hypothesized that (i) damaged SC recovering under the high water exposure of full occlusion (FO) would have lower free amino acids (FAA) than sites with low hydration (no occlusion, NO) and semi-occlusion (SP, semipermeable film, intermediate hydration) and (ii) SC under semi-occlusion would have higher FAA than with low hydration. Volar forearm sites in 15 healthy adults were perturbed via cellophane tape stripping and treated with SP, FO and NO for five days. Barrier recovery rate, hydration, dryness and erythema were determined. Serial SC samples (n = 15) were collected on day 5 and FAA quantified using reverse-phase HPLC and fluorescence detection. The cumulative protein removed was higher for SP than the control, NO and FO. FAA as total, individual amino acids and citrulline were consistently higher in the control than the three damaged sites. Generally, FAA was

higher in NO than FO. Citrulline was higher for NO than SP and FO over the sampled SC. Levels were higher for SP than FO in certain, but not all of the FAAs. FAA was inversely correlated to barrier integrity. Skin hydration was relatively constant at the external microenvironment of the SP site, whereas the NO and FO had a reduction, i.e. a gradient, over the time. Overall, barrier recovery under conditions of a decreasing hydration gradient produced SC with higher levels of FAA than did conditions of full occlusion.

Effective prevention of stress-induced sweating and axillary malodour formation in teenagers

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Emotional sweating and malodour production represent a relevant challenge to today's antiperspirant (AP) and deodorant products as stress in everyday life increases continuously. The aim of this study was to investigate stress-induced sweating in teenagers who are known to experience various stressful situations, e.g. exams at school or job interviews. To induce emotional sweating in 20 female and 20 male adolescents (16–18 years of age), we applied the Trier Social Stress Test (TSST), considered today to be the most reliable and standardized stress protocol. In this study, we demonstrate that the TSST induces high amounts of sweat and strong axillary malodour in the tested age group. Notably, male teenagers showed significantly higher stress-induced odour scores than female subjects, although no gender differences were detected concerning other physiological stress markers. Testing of a novel deodorant/AP product developed to specifically address the needs of adolescent consumers revealed excellent deodorant and AP efficacy under the challenging conditions of the TSST.

