

lymphatics, the extracellular matrix and the presence of excess subcutaneous fat that bulges into the dermis. It has been described as a normal condition that maximizes subcutaneous fat retention to ensure adequate caloric availability for pregnancy and lactation. Differences in the fibrous septae architecture that compartmentalize the adipose tissue have recently been reported in women with cellulite compared with men. Weight loss has been reported to improve the cellulite severity by surface topography measures although in obese subject's skin dimpling does not seem to change appreciably. However, histological analysis suggests that fat globules retract out of the dermis with weight loss. Cellulite has been treated with massage which decreases tissue oedema but it is also likely to have its effects at the cellular level by stimulating fibroblast (and keratinocyte) activity while decreasing adipocyte activity. In addition to massage, effective topical creams with a variety of agents were used to ameliorate the condition. Nevertheless, only a few studies are reported in the

scientific literature. Xanthines, botanicals, fragrances and ligands for the retinoid and peroxisomal proliferator-activated receptors appear to be giving some benefit. Reducing adipogenesis and increasing thermogenesis appear to be primary routes and also improving the microcirculation and collagen synthesis. Many agents are being investigated for weight management in the supplement industry [hydroxycitrate, epigallocatechin gallate, conjugated linoleic acid (CLA), etc.] and some of these agents seem to be beneficial for the treatment of cellulite. In fact, CLA was proven to ameliorate the signs of cellulite. One product, Cellasene, containing a variety of botanicals and polyunsaturated fatty acids also appears to provide some relief from these symptoms. Although more work is needed, clearly these treatments do improve the appearance of skin in subjects with cellulite. It is quite possible, however, that synergies between both oral and topical routes may be the best intervention to ameliorate the signs and symptoms of cellulite.

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Expression and Function of Neurotrophins and Their Receptors in Human Melanocytes

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Melanocytes and cells of the nervous system are of common ectodermal origin and neurotrophins (NT) have been shown to be released by human keratinocytes. We investigated the expression and function of NT [nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), NT-3, NT-4/-5] and their receptors in human melanocytes. Human melanocytes produce all NT in different amounts, whereas they only release NT-4. NT-4 release is downregulated, whereas NT-3 is upregulated by ultraviolet (UVB) irradiation. Melanocytes treated with phorbol 12-myristate 13-acetate (PMA) express TrkA and TrkB, but not TrkC. NT fail to stimulate melanocyte proliferation, whereas they stimulate the synthesis of tyrosinase and tyrosinase-related protein-1 (TRP-1). Finally, NT-3, NT-4 and NGF increase melanin production. Taken together, these results demonstrate an intriguing interaction between melanocytes and the nervous system. We speculate that NT could be considered the target of therapy for disorders of skin pigmentation.

Whitening Effect of a Dermocosmetic Formulation: A Randomized Double-Blind Controlled Study on Melasma

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Melasma is an endocrine-mediated facial hypermelanosis with epidermal and occasionally dermal components. We tested in a randomized double-blind design the effect of a whitening formulation (Thiospot intensive®) on this skin disorder. The product containing ethyl linoleate, thioctic

acid, octadecenedioic acid, lactic acid and ethylhexyl methoxycinnamate was applied twice daily for 3 months by 20 young women. Another control group of seven women received a non-skin lightening formulation. Clinical assessments were made at 1-month intervals. In addition, objective measurements of the hypermelanosis were performed using narrow-band reflectance spectrophotometry, image analysis of video-recorded ultraviolet light reflection (ULEV method) and photodensitometry of the comeamelanometry test. A significant lightening effect was evidenced beginning the second month of treatment with the whitening formulation. No significant effect was observed with the control product.

Protective Effects of Taurine on Human Hair Follicle Grown in Vitro¹

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Taurine is a naturally occurring β -amino acid produced by methionine and cysteine metabolism. It is involved in a variety of physiological functions, including immunomodulatory and antifibrotic. Taking advantage of the ability of human hair follicle grown in vitro to recapitulate most of the characteristic features of normal hair follicle in vivo, we studied (i) taurine uptake by isolated human hair follicles; (ii) its effects on hair growth and survival rate; and (iii) its protective potential against transforming growth factor (TGF)- β 1, an inhibitor of in vitro hair growth and a master switch of fibrotic program. We showed that taurine was taken up by the connective tissue sheath, proximal outer root sheath and hair bulb, promoted hair survival in vitro and prevented TGF- β 1-induced deleterious effects on hair follicle.

New Antiaxillary Odour Deodorant Made With Antimicrobial Ag-zeolite (Silver-Exchanged Zeolite)

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The causative substances for axillary osmidrosis, which are often found in apocrine sweat, are the decomposed/denatured products of short-chain fatty acid and other biological metabolite compounds produced by axillary-resident bacteria. Conventional underarm deodorants suppress the process of odour production mostly by the following mechanism: (1) suppression of perspiration, (2) reduction in numbers of resident bacteria, (3) deodorization and (4) masking. The most important and effective method to reduce odour is to suppress the growth of resident bacteria with antimicrobials, which have several drawbacks, especially in their safety aspect. To solve these problems, we focused on Ag-zeolite (silver-exchanged zeolite) that hold stable Ag, an inorganic bactericidal agent, in its structure, and therefore, poses less risk in safety. Its bactericidal effect on skin-resident bacteria was found to be excellent and comparable with that of triclosan, a most frequently used organic antimicrobial in this product category. The dose-response study of Ag-zeolite powder spray (0–40 w/w%) using 39 volunteers revealed that 5–40 w/w% Ag-zeolite could show a sufficient antimicrobial effect against skin-resident bacteria. The comparison study using 0.2 w/w% triclosan as the control and 10 w/w% Ag-zeolite indicated that: (1) one application of the powder spray containing 10 w/w% Ag-zeolite could show a sufficient antimicrobial effect against the resident bacteria and its effect continued for 24 h, (2) a powder spray containing 0.2 w/w% triclosan was unable to show a sufficient antimicrobial effect, and (3) no adverse event was observed. These studies show that Ag-zeolite has a superior antimicrobial ability that is rarely found in conventional antimicrobials used in deodorant products and a strong antiaxillary odour deodorant ability because of its long-lasting effect. During clinical study, patch tests with humans and other clinical studies of this product showed no adverse events related to the treatment with the Ag-zeolite product.

Induction of The Skin Edogenous Potective Mitochondrial MnSOD by Vitreoscilla Filiformis Extract

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Vitreoscilla filiformis (Vf), a filamentous bacteria living in fresh water is thought to contribute to the observed beneficial effects of Spa water on skin. An active fraction obtained from a Vf biomass was evaluated for its ability to modulate mRNA expression in cultured skin cells. cDNA array analysis was conducted first using a customized membrane including 1176 selected and fully identified genes involved in skin physiology and homeostasis then the newly developed full genome U133 plus 2.0 GeneChip from Affymetrix. The mitochondrial protective manganese superoxide dismutase (MnSOD/SOD-2) was identified as a preferentially induced mRNA target in both normal human

dermal fibroblasts and keratinocytes. Induction at the transcriptional level in both cell types was confirmed using quantitative real time/polymerase chain reaction and a kinetic analysis revealed a maximal increase in mRNA expression 20 h after stimulation with Vf extract (Vfe). Using immunofluorescent (fluorescent cell sorter) analysis, an induction of MnSOD protein in both normal human dermal skin fibroblasts ($\times 1.6$; $P < 0.01$) and epidermal keratinocytes ($\times 1.4$; $P < 0.01$) was confirmed. As MnSOD is a major inducible free-radical scavenger in skin, these results suggest that the Vfe could induce skin cells to produce their own endogenous protective defences in vivo against both exogenous environmental stressors such as UV irradiation or microflora as well as to combat endogenous sources of deleterious free radicals involved in skin ageing. Finally, in order to confirm the in vivo potential of this original extract in human, we evaluated its protective activity vs. placebo on the generation of sunburn cells in epidermis under UVB stress. As expected from in vitro profiling, Vfe was indeed found to significantly inhibit the appearance of sunburn cells in UVB-exposed areas, a signature of skin alteration which has been suggested to be linked to a defect in MnSOD protective activity. Altogether, those data suggest that the combination of a suitable protective UV filter together with this bioactive Vfe might improve skin protection through complementary pathways.

Stress and The Skin

J. Hosoi

'The skin is the mirror which reflects the state of the mind.' 'The skin is the window of the mind.' These have been proverbs since ancient times. It is the topic of this article. Our life became convenient with the information technology these days but too much information often drives us on. We suffer from mental stress rather than physical stress. Since Selye advocated stress reaction, various reactions in the body have been described. Skin is also a target organ of the stress reaction. What the effects of stress are and how stress affects the skin are summarized in this review. Possible use of fragrance for the regulation of the stress reaction is also introduced.

Artocarpus Lakoocha Heartwood Extract As a Novel Cosmetic Ingredient: Evaluation of The In Vitro Anti-Tyrosinase and In Vivo Skin Whitening Activities

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The heartwood extract of *Artocarpus lakoocha* Roxb. was evaluated for the in vitro tyrosinase inhibitory activity and the in vivo melanin-reducing efficacy in human volunteers. The IC₅₀ of the extract and oxyresveratrol, its major active ingredient, against mushroom tyrosinase was determined to be 0.76 and 0.83 $\mu\text{g mL}^{-1}$, respectively. The extract dissolved in propylene glycol was subsequently tested in female volunteers using a parallel clinical trial with self-control (n = 20 per group). The first group received the

0.25% w/v A. lakoocha solution as the test solution, whereas the second and the third group, respectively, received 0.25% licorice extract and 3% kojic acid as the reference solutions in the same solvent. The subjects in each group twice daily applied the test (or reference) solution in one of her upper arm, whereas the remaining arm was treated with only propylene glycol (self-control) for 12 weeks. The melanin content of each application site was measured using Mexameter every week and calculated as % reduction in melanin content relative to the initial melanin value (% whitening). The value of % whitening was then compared between the product-treated and the propylene glycol-treated arms within the same subject using paired t-test ($\alpha = 0.05$). The A. lakoocha extract was the most effective agent, giving the shortest onset of significant whitening effect after only 4 weeks of application ($P < 0.05$), followed by 3% kojic acid (6 weeks) and 0.25% licorice extract (10 weeks). The effect also increased with time with maximum whitening observed at week 12 for A. lakoocha extract. When the extract was formulated as an oil-in-water emulsion, its whitening efficacy was further enhanced. Daily application of 0.1% w/w A. lakoocha lotion to the upper arms ($n = 25$) and cheeks ($n = 15$) of volunteers produced significant whitening over the lotion base after 2 and 3 weeks, respectively ($P < 0.05$). Thus, the preliminary study suggested that the heartwood extract of A. lakoocha may have a promising potential for use as an effective and economical skin-whitening agent.

Heat Shock Proteins In The Skin

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Heat shock proteins (hsp) are expressed in all cells and organisms. Their expression is induced by heat shock (temperatures above 42°C) and other forms of pathophysiological stress. Elevated levels of hsp protect cells from further stress exposure. Hsp are expressed intracellularly. They are highly conserved throughout evolution indicating hsp being necessary for survival under potentially harmful environmental conditions. Hsp are divided into families according to their molecular weight. The majority of hsp function as molecular chaperones. Chaperone function is characterized by binding to other proteins and mediating their folding, transport and interaction with other molecules. In human epidermis hsp are abundantly expressed and have been linked with functions in cell differentiation and photobiology. Recent research has mainly focused on the 27 and 72 kD hsp that are constitutively expressed in human keratinocytes. ultraviolet radiation (UV)-induced cell death and sunburn cell formation can be inhibited by previous heat shock exposure and UV itself can induce hsp expression. The expression of the 27 kD hsp (hsp27) in epidermal keratinocytes in situ and in culture correlates with differentiation. Expression of hsp27 increases

simultaneously with keratinocyte differentiation. For that reason, hsp27 is described as a marker of epidermal differentiation. Changes in the expression and inducibility of hsp have been linked with ageing. In the skin, recent data indicate that hsp72 expression remains remarkably stable with intrinsic ageing. In contrast, levels of hsp27 have been found to be elevated in sun-protected aged skin indicating a link between hsp27 expression and age-dependent epidermal alterations. Regulation of hsp can be modified by pharmacological intervention and the development of safe topical and systemic treatments for the prevention of skin damage and disorders of keratinocyte differentiation can be expected for the future.

Histological Evaluation of Hyperpigmentation on Female Filipino Axillary Skin

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Females in South East Asia (Thailand, Indonesia and the Philippines) show concern about dark areas of skin which develop in their underarms, but little is known about the features differentiating pale and hyperpigmented axillary skin in the general population. To investigate this, a histology study was undertaken in the Philippines to define the aetiology of underarm darkening, which is postulated to be a mild form of postinflammatory hyperpigmentation (PIHP). Punch biopsies were taken from dark and light axillary skin sites of 20 female subjects, of whom seven had hyperpigmented underarms, based on an instrumental (Mexameter MX-18, Courage and Khazaka Electronic GmbH, Cologne, Germany) measure, and 13 had not. Histological and immunohistochemical analyses were undertaken using a range of stains and antibodies, including haematoxylin-eosin for general histopathology, Masson-Fontana for melanin, anti-CD68 for monocytes and macrophages, Van Gieson's technique for fibrosis, anti-proliferating cell nuclear antigen for cell mitosis, and the melanocyte-specific immunostains, anti-tyrosinase and anti-tyrosinase-related protein 1. In most cases, dark skin sites from hyperpigmented panellists had increased intensity of Masson-Fontana, anti-tyrosinase and/or anti-TRP1 staining, indicative of melanocyte stimulation and increased melanin production. Furthermore, hair plucking emerged as a key stimulus to increased pigmentation. The trauma of hair plucking slightly increased the number of infiltrating mononuclear cells and macrophages that ingested melanosomes leaking from the damaged epidermis, more so in the skin of hyperpigmented panellists; this, in turn, potentially increases pigmentation. However, cell infiltration was focal, mainly near the plucked follicles, and not indicative of diffuse inflammation. The results from this study support the hypothesis that axillary darkening is mild PIHP, characterized by increased epidermal melanin, following stimulation or mild irritation of skin, with hair plucking as a key factor in this process.