ALBION®
HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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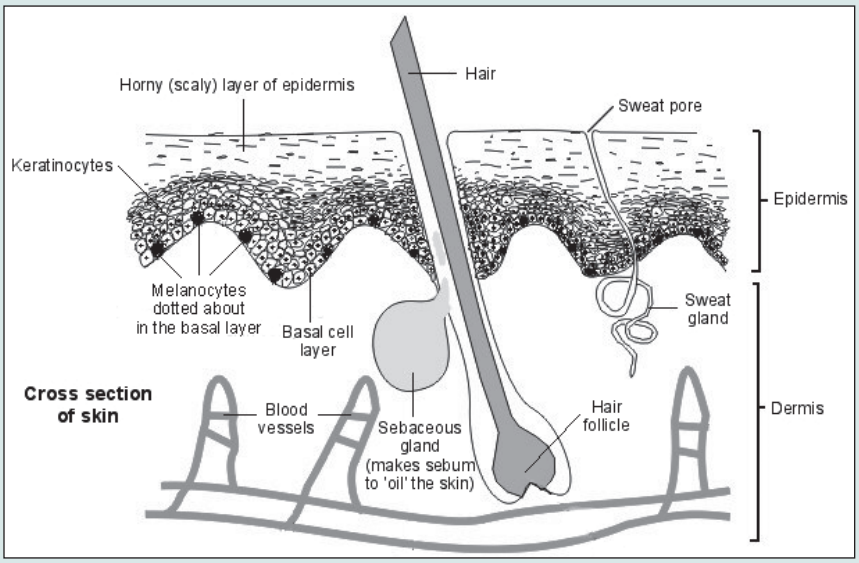
Minerals and the Skin

As the outermost covering of the body, the skin is our protector from the external environment. It consists of basically two layers. The outermost is an epithelium, of ectodermal origin, called the epidermis, the deeper layers of which are living cells, while the cells of the superficial layers are dead and impregnated by the fibrous protein, keratin. This keratin provides mechanical protection and contributes to the epidermal barrier which limits the movement of many substances, particularly water, through the skin. Melanin pigments, located in the epidermis protect against ultraviolet light. The epidermis is firmly attached to, supported and nourished by the dermis, a thick layer of fibrous connective tissue, derived from the mesoderm, which is responsible for most of the skins' mechanical strength and elasticity. The epidermis and dermis constitute the skin in the strict sense. Beneath these two layers, more or less firmly attached to it, is a layer of loose connective tissue called the hypodermis (superficial fascia), which contains abundant fat cells forming a layer of subcutaneous adipose tissue which is an important thermal insulator. The skin contains blood vessels and sweat glands which are also important in thermoregulation, and the nerves of the skin make it a major sense organ.

Figure 1.

Understanding the skin

The skin has two layers - the epidermis and the dermis. Beneath the dermis is a layer of fat and then the deeper structures such as muscles, tendons, etc.



The epidermis has three main types of cells.

- Basal cells. These are the bottom layer of cells in the epidermis.
- Keratinocytes. These cells are in layers above the basal layer. They make a substance called keratin which is a hard 'waxy' material. Keratinocytes are constantly dividing and a certain number are dying at any given time. The top 'horny' layer of the epidermis is made of dead keratinocytes which contain keratin. The top of the skin is constantly being shed and replaced by new dead cells which contain keratin.
- Melanocytes. These cells are dotted about at the bottom of the epidermis. They make a pigment called melanin when the skin is exposed to sun. The melanin is passed to the nearby skin cells to protect them from the sun's rays. Melanin causes the skin to tan in fair skinned people. Dark skinned people have more active melanocytes.

Nutrition is a key to the performance of the skin, and thus its ability to protect itself and the inner workings of the body. Minerals, particularly trace minerals, are very involved in the various protective properties of the skin. They have been shown to be essential in fighting the damages of excessive sun exposure, wrinkling, and maintaining the moisture of the skin.

Figure 1 shows the basic structure and functions of important epidermal cells.

Research Findings on Micronutrients and Skin Health

There are many studies on the impact of trace minerals on the condition of the skin. Manganese, zinc, copper, boron, and selenium have been shown to have dermatological impacts via a variety of mechanisms. Other nutrients, such as arginine, glucosamine, and creatine appear to be important as well. In the following published research studies, the roles that these micronutrients play in helping the skin are studied.

Evidence supporting zinc as an important antioxidant for skin.

Rostan EF, DeBuys HV, Madey DL, Pinnell SR.
Int J Dermatol 2002 Sep;41(9):606-611.

Antioxidants play a critical role in keeping skin healthy. The antioxidant benefits of vitamin C and E are well known, but the importance of the trace mineral zinc is often overlooked. This article offers a review of evidence that supports zinc's protection action against free radical-induced oxidative damage. Zinc protects against UV radiation, enhances wound healing, contributes to immune and neuropsychiatric functions, and decreases the relative risk of cancer and cardiovascular disease. In the skin, zinc is 5 to 7 times more concentrated in the epidermis than the dermis. It is an essential element in more than 200 metalloenzymes, including the antioxidant superoxide dismutase. There is abundant evidence showing the antioxidant role of zinc. Topical zinc has been demonstrated to provide antioxidant photoprotection for the skin. Two antioxidant mechanisms have been proposed for zinc. Zinc can replace redox active molecules, such as iron, at critical sites in cell membranes and proteins; additionally, zinc can induce the synthesis of metallothionein sulfhydryl-rich proteins that protect against free radicals. Regardless of mechanism, topical zinc provides important antioxidant defense for the skin.

The influence of L-arginine on the regulation of epidermal arginase.

Wohlrab J, Siemes C, Marsch WC.
Skin Pharmacol Skin Physiol 2002 Jan-Feb;15(1):44-54.

The topical use of urea is entrenched in dermatological therapy. However, despite ensured action, urea's irritating effect on erosive, exudative or strongly inflamed skin restricts its application. Endogenic urea is synthesized from L-arginine via extra-hepatic arginase in the keratinocytes. This enzymatic reaction is regulated by manganese, as well as the intracellular level of L-arginine. Incubating keratinocyte cultures in differing concentrations of L-arginine and manganese demonstrated an increase in the keratinocyte urea synthesis. In relevant concentrations, L-arginine and manganese do not exhibit any proliferation-inhibiting action, do not trigger apoptosis or necrosis, and are stable. The research found that applying L-arginine alone or in combination with manganese increases the endogenous intrakeratinocytic urea synthesis and thus can be an effective topical therapy for cases of dry skin conditions.

Stimulatory effect of boron and manganese salts on keratinocyte migration.

Chebassier N, Ouijja el H, Viegas I, Dreno B.
Acta Derm Venereol 2004;84(3):191-194.

Keratinocyte proliferation and migration are needed to rebuild the cutaneous barrier after skin injury. Thermal waters rich in boron and manganese have been seen to improve wound healing. This study investigates the mechanisms of this action. This in vitro study looks at the modulation of keratinocyte migration and proliferation caused by the boron and manganese present in high concentration in a thermal water (Sainte Gervais). Incubation of keratinocytes for 24 hours with boron and manganese accelerated wound closure as compared to a control medium. Since this acceleration was not related to an increase in keratinocyte proliferation, the researchers conclude that boron and manganese act on wound healing by increasing keratinocyte migration.

Overexpression of manganese superoxide dismutase suppresses tumor formation by modulation of activator.

Zhao Y, et al.
Cancer Res 2001 Aug 15; 61(16):6082-6088.

Manganese superoxide dismutase (MnSOD) is a nuclear encoded primary antioxidant enzyme localized in mitochondria. MnSOD is critical to maintaining cellular redox status, and reactive oxygen forms play a role in signal transduction and carcinogenesis. Based on this, the study was carried out to look

at the possible role for MnSOD in preventing cancer, using a 2-stage skin carcinogenesis model. The study contained two groups of female mice. One that was transgenic for the expression of MnSOD, and the other group was nontransgenic for this trait. (A transgenic animal is one that carries a foreign gene that has been deliberately inserted into its genome). The transgenic mice were seen to have a significant reduction in papilloma formation. A quantitive analysis of certain proteins exhibited a greater accumulation of oxidative damage in the nontransgenic mice, and this oxidative damage was present in the mitochondria and nucleus. In addition, a chemical induced (TPA) protein kinase activation which harkens tumor formation occurred within 6 hours in the nontransgenic mice, but was greatly delayed in the transgenic mice. These results indicate that MnSOD regulates both cellular redox status and modulates protein kinase and inhibits tumor promotion, leading to a reduction of dermal tumors in MnSOD transgenic mice.

Zinc, copper, and manganese enhanced keratinocyte migration through functional modulation of keratinocyte.

Tenaud I, Leroy S,
Chebassier N, Dreno B.
Ex Dermatol 2000 Dec;9(6):407-416.

Keratinocyte migration is important to the re-epithelialization of cutaneous wounds. Zinc, copper, and manganese are used in vivo for their healing properties, but their mechanism is only partially understood. They are known to promote keratinocyte proliferation and modulate integrins (family of integral membrane proteins involved in healing) expression. The study's goal was to see if these trace elements also cause keratinocyte migration, and if this is related to their modulation of integrins. Two independent migration assays were used to study keratinocyte migration. Inhibition studies using function blocking antibodies directed to alpha3, alpha6, alpha(v), and beta1 subunits were performed to elucidate the modulation effect of the trace elements on integrin function. Zinc and copper increased alph3, alpha(v), and beta1 integrin functions, while manganese modulated functions at alpha3 and beta1. None of them impacted alpha6. Zinc, copper, and manganese increased keratinocyte migration, and one of the mechanisms involves their modulation of integrin functions.

Adaptive antioxidant response protects dermal fibroblasts from UVA-induced phototoxicity.

Meewes C, et al.
Free Radic Biol Med
2001 Feb 1;30(3):238-247.

The skin has developed a complex antioxidant system to respond to the reactive oxygen species caused by UV irradiation. It has previously been shown that exposure to UV irradiation induces an increase in MnSOD activity. The researchers now find that single, and to a higher extent, repetitive low dose UVA irradiation causes a substantial upregulation of glutathione peroxidase (GPx) activity. The dual antioxidant enzyme response in the same detoxification path resulted in protection from high UVA dose cytotoxicity, after preirradiation UVA exposure. The adaptive response between low and high UVA exposure was effective for a 12 hour interval, but not for a 24 hour interval. A 12 hour interval saw an increased induction of MnSOD activity and under selenium supplemented conditions, an increased GPx activity, as well – causing definite cellular protection from UVA induced phototoxicity. In selenium deficient conditions, there were no UVA mediated increases in GPx activity, and thus the adaptive protection against cytotoxicity from high UVA doses was much lower as compared to selenium supplemented conditions. There was a 4.6 fold increase in MnSOD activity leading to specific resistance to UVA mediated photoxicity, as compared to selenium deficient conditions. These data show that the concomitant increase in MnSOD and GPx activity gives optimal protection from photoxidative damage. This adaptive antioxidant protection depends on interval of irradiation and selenium supply.

The creatine kinase system in human skin: protective effects of creatine against oxidative and UV damage in vitro and in vivo.

Lenz H, et al.
J Invest Dermatol
2005 Feb;124(2):443-452.

Detrimental changes in mitochondrial function caused by a decline in cellular energy metabolism is a cause for cutaneous aging. Things such as solar UV radiation leading to free radical generation can lead to these detrimental changes in mitochondrial function. The skin tries to compensate for the loss of mitochondrial energy capacity through other routes, such as glycolysis or the creatine kinase (CK) system. The latest studies are showing that there are cytosolic and mitochondrial isoenzymes of CK, as well as a creatine transporter found in the human skin. This study looks at cutaneous CK system and

cellular stressors involved with skin aging. In the study, it was observed that a stress-induced decline in mitochondrial energy in the human epidermal cells correlated with a decline in mitochondrial CK activity. The study also looked at the supplementation of creatine to human epidermal cells as a way to reinforce the endogenous energy supply to the skin. It was seen that the administered creatine was taken up by keratinocytes and increased CK activity, mitochondrial function, and protected against free radical stress. The study's new data clearly indicates that the administration of creatine energetically recharges human skin cells to protect against a variety of cellular stress conditions, such as oxidative and UV damage in vitro and in vivo. This could have further implications in a creatine role in preventing premature skin aging and skin damage.

The effect of an oral supplement containing glucosamine, amino acids, minerals, and antioxidants on cutaneous aging: a preliminary report.

Murad H and Tabibian MP.

J Dermatolog Treat

2001 Mar;12(1):45-51.

Alterations in collagen, elastin, and glycosaminoglycans lead to cutaneous changes associated with aging. In this study, an oral supplement containing glucosamine, amino acids, minerals, and other antioxidants was administered in a randomized, controlled, single-blind study on 53 female volunteers. After 5 weeks of intake of this oral supplement, the hydration properties of the skin, as well as a textural analysis of the fine lines and wrinkles of the women's skin, was performed. The researchers found a 34% reduction in the number of visible wrinkles and the same percentage reduction in the fine lines of the women who took the supplement. There were no significant changes in the skin hydration of either group. They concluded that the use of this oral supplement containing glucosamine, minerals and antioxidants can improve the appearance of visible wrinkles and fine lines.

Related Findings

There are many research findings that show the benefits of zinc for the treatment of skin conditions, from sunburn to acne and even decubital ulcers. Studies by Cama E., et al., from the University of Pennsylvania [Biochemistry 2003 Jul 1;42(25):7748-58 and Biochemistry 2004 Jul 20;43(28):8987-99], in addition to the one mentioned earlier [WohlrabJ, et al., Skin Pharmacol Appl Skin Physiol 2002 Jan-Feb;15(1):44-54] that show the role of manganese in the metalloenzyme arginase that takes arginine and splits it into ornithine and urea, and the importance that this has in the treatment of dry skin conditions. There are repeated studies that clearly show the antioxidant roles that the trace elements, boron, manganese, copper, zinc, and selenium play in the photoprotection of the skin. Some of the trace elements, like zinc and manganese have been demonstrated to have multiple mechanisms in either maintaining skin health or helping to heal skin disorders.

Concluding Remarks

Albion Advanced Nutrition has developed an advanced array of mineral ingredients that should be considered when looking to develop products for the skin. As shown, arginine, glucosamine, creatine, along with the trace elements selenium, boron, manganese, zinc, and copper have effective skin applications. There are several very unique chelates to consider in skin conditions available from Albion.

Items such as:

- Manganese Arginine Amino Acid Chelate
- Zinc Arginine Amino Acid Chelate
- Magnesium Creatine Chelate (Creatine MagnaPower™)
- Copper Chelazome®
- Selenium Amino Acid Complex
- Manganese Glucosamine Chelate (coming this Fall)

Albion also offers other forms of zinc, such as Zinc Chelazome® and Zinc Histidine Amino Acid Chelate. In addition to Manganese Arginine Amino Acid Chelate, Albion makes Manganese Chelazome®, and manufactures another form of copper – Copper Lysine Amino Acid Chelate.

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