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COPPER PEPTIDES FOR HAIR GROWTH AND REGENERATING COLLAGEN AND ELASTIN (SAGGING SKIN)

Regenerative and Protective Actions of the GHK-Cu Peptide in the Light of the New Gene Data*

The human peptide Gly-(L-His) -(L-Lys) or GHK, has a copper 2+ (Cu (2+)) affinity similar to the copper transport site on albumin and forms GHK-Cu, a complex with Cu(2+). These two molecules activate a plethora of remodeling related processes: (1) chemoattraction of repair cells such as macrophages, mast cells, capillary cells; (2) anti-inflammatory actions (suppression of free radicals, thromboxane formation, release of oxidizing iron, transforming growth factor beta-1, tumor necrosis factor alpha and protein glycation while increasing superoxide dismutase, vessel vasodilation, blocking ultraviolet damage to skin keratinocytes and improving fibroblast recovery after X-ray treatments); (3) increases protein synthesis of collagen, elastin, metalloproteinases, anti-proteases, vascular endothelial growth factor, fibroblast growth factor 2, nerve growth factor, neurotropism 3 and 4, and erythropoietin; (4) increases the proliferation of fibroblasts and keratinocytes; nerve outgrowth, angiogenesis, and hair follicle size. GHK-Cu stimulates wound healing in numerous models and in humans. Controlled studies on aged skin demonstrated that it tightens skin, improves elasticity and firmness, reduces fine lines, wrinkles, photodamage and hyperpigmentation. GHK-Cu also improves hair transplant success, protects hepatic tissue from tetrachloromethane poisoning, blocks stomach ulcer development, and heals intestinal ulcers and bone tissue. These results are beginning to define the complex biochemical processes that regulate tissue remodeling.

The human peptide GHK (glycyl-l-histidyl-l-lysine) has multiple biological actions, all of which, according to our current knowledge, appear to be health positive. It stimulates blood vessel and nerve outgrowth, increases collagen, elastin, and glycosaminoglycan synthesis, as well as supports the function of dermal fibroblasts. GHK's ability to improve tissue repair has been demonstrated for skin, lung connective tissue, boney tissue, liver, and stomach lining. GHK has also been found to possess powerful cell protective actions, such as multiple anti-cancer activities and anti-inflammatory actions, lung protection and restoration of chronic obstructive pulmonary disease (COPD) fibroblasts, suppression of molecules thought to accelerate the diseases of aging such as NFκB, anti-anxiety, anti-pain and anti-aggression activities, DNA repair, and activation of cell cleansing via the proteasome system. Recent genetic data may explain such diverse protective and healing actions of one molecule, revealing multiple biochemical pathways regulated by GHK.

Skin's ability to withstand damage and repair itself is highest in children and young individuals because of well-functioning repair and protective mechanisms. However, with age, skin's ability to repair damage declines. GHK content is highest in the plasma of young, healthy individuals. At age 20, the plasma level of GHK is about 200 ng/mL (10^{-7} M), and by the age of 60, it declines to 80 ng/mL.

A number of experiments established that GHK stimulates synthesis of collagen, selected glycosaminoglycans and small proteoglycan decorin. It also modulates activity of key metalloproteinases, which are enzymes that facilitate breakdown of proteins of extracellular matrix, as well as activity of anti-proteases. This suggests a general regulatory effect on protein breakdown in skin, helping to prevent both buildup of damaged proteins and excessive proteolysis. Since excessive breakdown of the dermal matrix as well as inadequate removal of damaged proteins can negatively

affect skin's health and appearance, GHK's ability to regulate both metalloproteinases and their inhibitors can support skin regeneration and improve its appearance.

GHK also demonstrated beneficial effects on skin fibroblasts, which are considered key cells in the skin regeneration process. Fibroblasts not only synthesize structural elements of the dermal matrix but also produce a wide range of growth factors essential for skin repair. GHK, in combination with LED irradiation (light emitting diode irradiation, 625–635 nm), compared with the LED irradiation alone increased: cell viability 12.5-fold, production of the basic fibroblast growth factor (bFGF), 230%, and collagen synthesis, 70%.

GHK-Cu has been found to stimulate epidermal basal cells, markedly increasing integrins and p63 expression. The cells' shape became more cuboidal, which indicates an increase in their stemness.

GHK-Cu at 0.01, 1 and 100 nM incubated with human adult dermal fibroblasts increased production of elastin and collagen. GHK also increased gene expression of MMP1 and MMP2 at the 0.01 nM. All concentrations increased TIMP1. The effects of GHK-Cu were also investigated in a randomised, double–blind clinical trial. Female volunteers applied GHK-Cu, encapsulated in nano-lipid carrier twice a day in the course of 8 weeks using either carrier alone or the commercially available peptide Matrixyl® 3000 as controls. Compared to Matrixyl® 3000, GHK-Cu produced a 31.6% reduction of wrinkle volume. Compared to control serum, GHK-Cu reduced wrinkle volume 55.8% and wrinkle depth 32.8%.

Reference: Badenhorst T., Svirskis D., Merrilees M., Bolke L., Wu Z. Effects of GHK-Cu on MMP and TIMP Expression, Collagen and Elastin Production, and Facial Wrinkle Parameters. J. Aging Sci. 2016; 4:166. doi: 10.4172/2329-8847.1000166.

GHK-Cu applied to thigh skin for 12 weeks improved collagen production in 70% of the women treated, in contrast to 50% treated with the vitamin C cream, and 40% treated with retinoic acid [16].

Reference: Abdulghani A., Sherr A., Shirin S., Solodkina G., Tapia E., Wolf B., Gottlieb A.B. Effects of topical creams containing vitamin C, a copper-binding peptide cream and melatonin compared with tretinoin on the ultrastructure of normal skin—A pilot clinical, histologic, and ultrastructural study. Dis. Manag. Clin. Outcomes. 1998; 1:136–141. doi: 10.1016/S1088-3371(98)00011-4

In addition to improving skin laxity, clarity, firmness and appearance, reducing fine lines, coarse wrinkles, and mottled pigmentation, and increasing skin density and thickness, GHK-Cu cream applied twice daily for 12 weeks also strongly stimulated dermal keratinocyte proliferation.

Reference: Finkley M., Appa Y., Bhandarkar S. Copper Peptide and Skin. In: Elsner P., Maibach H., editors. Cosmeceuticals and Active Cosmetics: Drugs vs. Cosmetics. Marcel Dekker; New York, NY, USA: 2005. pp. 549–563.