



COPPER TRIPEPTIDE-1

Dr. Charlene DeHaven, M.D.

Clinical Director, INNOVATIVE SKINCARE®

DEFINITION

Copper tripeptide-1 is a small protein composed of the three amino acids (protein building blocks) glycine, histidine, and lysine combined in a specific geometric configuration with the physiologically beneficial mineral copper. It is sometimes abbreviated GHK-Cu, indicating the chemical symbols for the four molecules composing it. These three amino acids have a very high affinity (attraction) for copper and are often found in association with this mineral in biologic systems. Within the body, Copper tripeptide-1 may be found both complexed with or without copper, although the form including copper is more beneficial. Since 1973 when Copper tripeptide-1 was discovered to cause aged liver cells to behave like young liver cells, a large body of scientific evidence has accumulated regarding the safety and beneficial effects of this fascinating compound.

LOCATION IN THE BODY

Injured tissues of all types contain Copper tripeptide-1, which acts as a signaling agent for processes of repair and regeneration, assisting damaged tissue to return to normal non-injured function. Copper tripeptide-1 was first found in human plasma, the liquid portion of blood minus the blood cells, and found to have helpful effects for liver cells. Soon, it was also found in saliva, urine, and collagen and then discovered to have important effects in repairing and maintaining all tissue types. Copper tripeptide-1 is bio-identical in that it has the exact chemical structure of molecules found naturally in the human body. Since it is a small molecule, it is able to move easily within tissue and around cells. Much of its benefit relates to its ability to efficiently bind and transfer copper ions. Copper tripeptide-1 is a member of a large family of copper-containing enzymes helpful in tissue repair, inflammation, metabolism, and synthesis of vital molecular structures.

ACTIONS

Copper tripeptide-1 belongs to a group of emergency response molecules which are released during injury and come to the body's aid when the processes below are activated.

Wound Healing

A huge body of scientific evidence supports the essential role of Copper tripeptide-1 in acceleration of wound healing. This compound is released during any tissue injury to signal repair processes to begin. Research has documented its benefit when used in various types of wounds, including surgical, post-laser, ischemic, burns, skin transplants, hair transplants, and diabetic ulcers. Diabetic wounds healed three times faster in the presence of Copper tripeptide-1. Time to re-epithelization is shortened.

Tissue Remodeling

Furthermore, Copper tripeptide-1 is active not only for primary healing but also for tissue remodeling, which is the return of injured tissue to normal architecture and function. It increases keratinocyte proliferation and normal collagen synthesis, improves skin thickness, skin elasticity and firmness, improves wrinkles, photodamage and uneven pigmentation, improves skin clarity, and tightens protective barrier proteins. Through effects on decorin, new collagen made in injured tissue assumes the correct anatomical configuration and structure rather than a disorganized scar. Matrix support structures of the dermis, including Collagen I, Collagen III, and glycosaminoglycans, are increased in the presence of Copper tripeptide-1 as normal tissue configuration is restored after injury. Scar-forming processes are minimized and protein synthesis increases through direct effects on fibroblasts. Copper tripeptide-1 blocks the effects of toxins on liver cells. It improves surgical outcome of joint replacements by increasing bonding strength and new bone formation between hardware and native bone. It also encourages healing of all types of gastrointestinal ulcers, including



those secondary to inflammatory bowel disease.

Anti-Tumor Effect and DNA Repair

Copper tripeptide-1 has a strong anti-tumor effect, partly mediated via decorin. It protects DNA from damaging effects of radiation, including radiation for cancer treatments and photoaging from sun exposure. Tumor cell lines died in the presence of Copper tripeptide-1 while healthy cell lines were encouraged. This compound is therefore not only biologically safe, but actually protective.

Stem Cell Anti-Senescence

By modulating integrins and p63, Copper tripeptide-1 promotes the survival of stem cells in the basal epidermis. This suggests it could have an important anti-aging role and, in fact, the anti-senescent effects of Copper tripeptide-1 have been demonstrated on a number of tissue types. Radiation severely damages DNA and induces aging but fibroblasts exposed to radiation were able to restore their function to that of intact cells in the presence of Copper tripeptide-1.

Anti-Inflammatory and Antioxidant Effects

Many of the body's intrinsic antioxidant systems, including superoxide dismutase, are induced by Copper tripeptide-1. Vitamin C and other antioxidant levels are increased in healing wounds. Its strong anti-inflammatory effect has been demonstrated during wound healing, photodamage, and wrinkle improvement.

Anti Microbial Effects

Copper tripeptide-1 lessens the risk of infection developing in a wound or in remodeled tissue. This partly relates to inhibition of ferritin ion release, a pro-oxidant.

Nerve Cell Maintenance

Copper tripeptide-1 has been suggested to have a potential therapeutic role in age-related neurodegeneration and cognitive decline. It improves axon survival and maintenance of nerves.

REFERENCES

- Pickart L. Published studies on tissue and skin remodeling copper-peptides: copper peptide studies on skin renewal, wound healing, and hair growth. Skinbiology.com. 2014.
- Choi HR, Kang YA, Ryoo SJ, Shin JW, Na JI, Huh CH, Park KC. Stem cell recovering effect of copper-free GHK in skin. J Pept Sci. 2012 Nov. 18(11):685-90.
- Pickart L, Vasquez-Soltero JM, Margolina A. The human tripeptide GHK-Cu in prevention of oxidative stress and degenerative conditions of aging: implications for cognitive health. Oxid Med Cell Longev. 2012. 2012:324832.
- Matalka LE, Ford A, Unlap MT. The tripeptide, GHK, induces programmed cell death in SH-SY5Y neuroblastoma cells. J BiotechnolBiomater. 2012. 2:144.
- Hong Y, Downey T, Eu KW, Koh PK, Cheah PY. A 'metastasis-prone' signature for early-stage mismatch-repair proficient sporadic colorectal cancer patients and its implications for possible therapeutics. ClinExp Metastasis. 2010 Feb 9. (Epub ahead of print).
- Gorouhi F, Maibach HI. Role of topical peptides in preventing and treating aged skin. Int J Cosm Sci. 2009. 31:327-45.
- Pickart L. The human tripeptide GHK (glycyl-L-histidyl-L-lysine), the copper switch and the treatment of the degenerative conditions of aging. Anti-Aging Therapeutics Volume XI. Klatz R, Goldman R (eds). American Academy of Medicine:Chicago IL. 2009. 301-3012.
- Kang YA, Choi HR, Na JI, Huh CH, Kim MJ, Youn SW, Kim KH, Park KC. Copper-GHK increases integrin expression and p63 positivity by keratinocytes. Arch Dermatol Res. 2009 Apr. 301(4):301-6.



- Pickart L. The human tri-peptide GHK and tissue remodeling. *J BiomaterSciPolym Ed.* 2008. 19(8):969-88.
- Huang PJ, Huang YC, Su MJ, Yang TY, Huang JR, Jiang CP. In vitro observations on the influence of copper peptide aids for the LED photoirradiation of fibroblast collagen synthesis. *Photomed Laser Surg.* 2007 Jun. 25(3):183-90.
- Miller TR, Wagner JD, Baack BR, Eisbach KJ. Effects of topical copper tripeptide complex on CO2 laser-resurfaced skin. *Arch Facial Plast Surg.* 2006 Jul-Aug. 8(4):252-9.
- Finkley MB, Apa Y, Bhandarkar S. Copper peptide and skin. *Cosmeceuticals and Active Cosmetics*, 2nd edition. Eisner P, Maibach HI (eds). 2005. Marcel Dekker:New York. 549-63.
- Dart AJ, Dowling BA, Smith CL. Topical treatments in equine wound management. *Vet Clin North Am Equine Pract.* 2005 Apr. 21(1):77-89.
- Bevan D, Gherardi E, Fan TP, Edwards D, Warn R. Diverse and potent activities of HGF/SF in skin wound repair. *J Pathol.* 2004 Jul. 203(3):831-8.
- Kinsella MG, Bressler SL, Wight TN. The regulated synthesis of versican, decorin, and biglycan: extracellular matrix proteoglycans that influence cellular phenotype. *Crit Rev Eukaryot Gene Expr.* 2004. 14(3):203-34.
- Canappo SO Jr, Farese JP, Schultz GS, Gowda S, Ishak AM, Swaim SF, Vangilder J, Lee-Ambrose L, Martin FG. The effect of topical tripeptide-copper complex on healing of ischemic open wounds. *Vet Surg.* 2003 Nov-Dec. 32(6):515-23.
- Leyden J, Stephens T, Finkey MB, Appa Y, Barkovic S. Skin care benefits of copper peptide containing facial cream. *Amer Academy Dermat Meeting.* 2002 Feb. Abstract P68, P69.
- Simeon A, Wegrowski Y, Bontemps Y, Maquart FX. Expression of glycosaminoglycans and small proteoglycans in wounds: modulation by the tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu(2+). *J Invest Dermatol.* 2000 Dec. 115(6):962-8.
- Simeon A, Emonard H, Hornebeck W, Maquart FX. The tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu²⁺ stimulates matrix metalloproteinase-2 expression by fibroblast cultures. *Life Sci.* 2000 Sep 22. 67(18):2257-65.
- Simeon A, Monier F, Emonard H, Gillery P, Birembaut P, Hornebeck W, Maquart FX. Expression and activation of matrix metalloproteinases in wounds: modulation by the tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu²⁺. *J Invest Dermatol.* 1999 Jun. 112(6):957-64.
- Mulder GT. The role of tissue engineering in wound care. *J Wound Care.* 1999 Jan. 8(1):21-4.
- Abdulghani AA, Sherr S, Shirin S, Solodkina G, Tapia EM, Gottlieb AB. 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. *Disease ManagClin Outcomes.* 1998. 1:136-41.
- Mulder GD, Patt LM, Sanders L, Rosenstock J, Altman MI, Hanley ME, Duncan GW. Enhanced healing of ulcers in patients with diabetes by topical treatment with glycyl-L-histidyl-L-lysine copper. *Wound Repair Regen.* 1994 Oct. 2(4):259-69.
- Matsumoto K, Tajima H, Hamanoue M, Kohno S, Kinoshita T, Nakamura T. Identification and characterization of "injurin", an inducer of expression of the gene for hepatocyte growth factor. *ProcNatlAcadSci USA.* 1992 May 1. 89(9):3800-4.



Wegrowski Y, Maquart FX, Borel JP. Stimulation of sulfated glycosaminoglycan synthesis by the tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu²⁺. *Life Sci.* 1992. 51(13):1049-56.

Miller DM, DeSilva D, Pickart L, Aust SD. Effects of glycyl-histidyl-lysyl chelated Cu(II) on ferritin dependent lipid peroxidation. *AdvExp Med Biol.* 1990. 264:79-84.

West MD, Pereira-Smith OM, Smith JR. Replicative senescence of human skin fibroblasts correlates with a loss of regulation and overexpression of collagenase activity. *Exp Cell Res.* 1989 Sep. 184(1):138-47.

Maquart FX, Pickart L, Laurent M, Gillery P, Monboisse JC, Borel JP. Stimulation of collagen synthesis in fibroblast cultures by the tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu²⁺. *FEBS Lett.* 1988 Oct 10. 238(2):343-6.