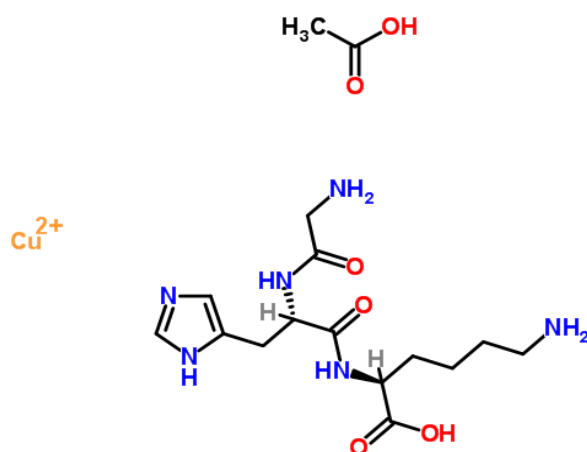


## Medical Professional Monograph

### GHK-Cu



Sequence - Gly-His-Lys( $\text{Cu}^{2+}$ )

Molecular Formula –  $\text{C}_{28}\text{H}_{52}\text{CuN}_{12}\text{O}_8$

Molecular Weight – 748.346 g/mol

#### Indication and Usage Summary

- Wound Healing
- Infection Control



- Hair Growth Restoration
- Facial Cosmetic Use
- Anti-Cancer Effects
- Cognitive Health

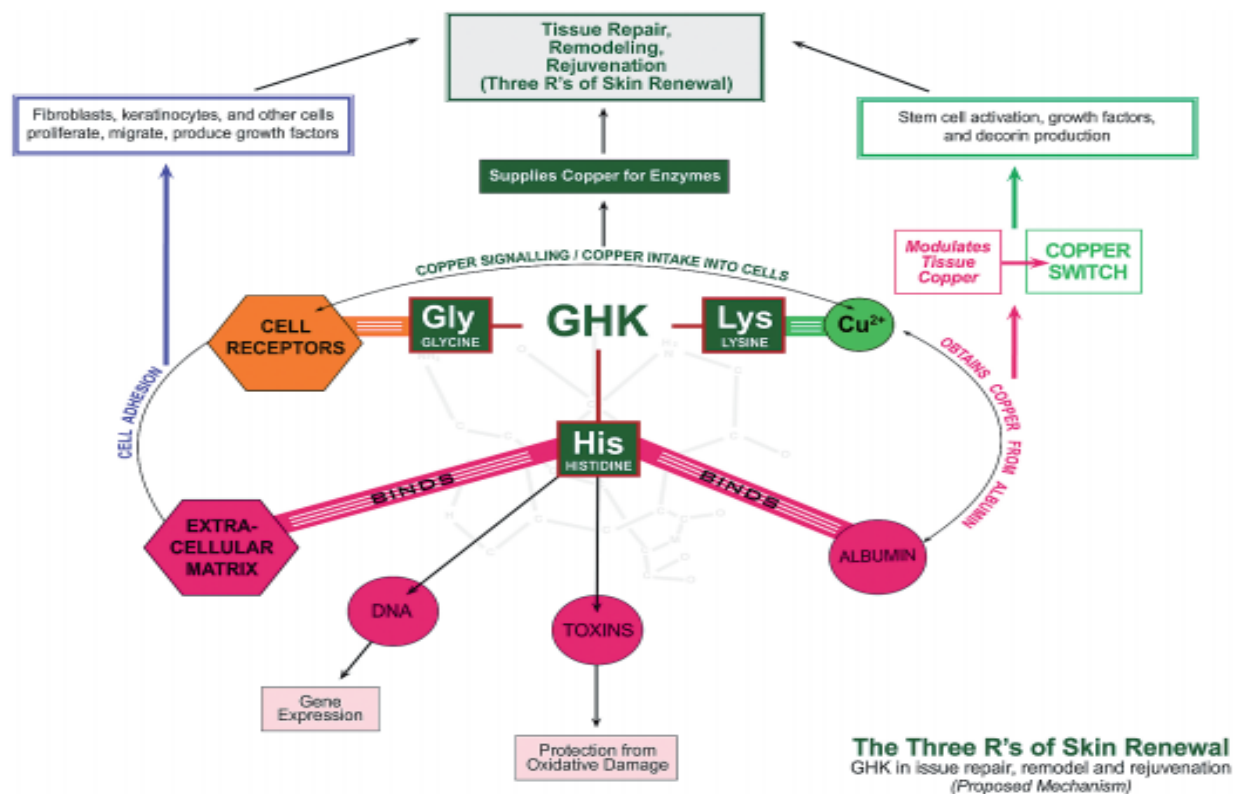
### Description/Classification:

GHK-Cu is a naturally occurring copper complex that was first identified in human plasma, but has hence been found in multiple locations such as saliva and urine. Copper peptides are small, naturally occurring protein fragments that have high affinity for copper ions, which are critical to normal body function. GHK-Cu has a variety of roles in the human body including, but not limited to, promoting activation of wound healing, attracting immune cells, anti-oxidant and anti-inflammatory effects, stimulating collagen and glycosaminoglycan synthesis in skin fibroblasts, and promoting blood vessel growth.<sup>1</sup> There has been evidence that has shown that it acts as a feedback signal that is generated after tissue injury. First, it seems to act as a potent protector of tissue and anti-inflammatory agent that controls the oxidative damage that occurs post-tissue injury. Further, it then plays a big role in signaling tissue remodeling which removes damaged/scarred tissue and generates new, healthy tissue. However, these positive effects decline with age because the concentration of GHK-Cu in the body decreases with age. Thus, there is an increase in inflammation, cancerous activity, and tissue destruction.

### Mechanism of Action

GHK-Cu exerts its action on a variety of pathways in the human body due to the peptide sequence and copper's ability to promote various functions. At the site of tissue injury, GHK-Cu acts as a potent chemoattractant for mast cells, macrophages, amongst others which promote the release of proteins that stimulate the growth and repair of tissue. As stated before, GHK-Cu acts in a dual manner to remove scar tissue from injured locations and replace it with new tissue. Primarily, it acts directly on fibroblasts by increasing production of mRNA and protein for collagen, elastin, proteoglycans, glycosaminoglycans, and decorin; all of which are critical components in tissue repair and maintenance. Further, it acts to stimulate the production of metalloproteases and protease inhibitors which function to remove damaged tissue proteins. It also reduced the secretion of TGF-beta from fibroblasts during this process as TGF-beta acts to induce scar formation (Pickart).

GHK-Cu also acts to increase collagen synthesis by chondrocytes within the bone. This leads to an increase in growth of human marrow stromal cells and attachment of osteoblastic cells which promote bone growth and formation. It also provides a source of copper for blood vessels in the process of angiogenesis in tissues. Because angiogenesis can not occur without a proper copper depot, GHK-Cu being present in the growing tissue is essential for survival. It has also been shown that GHK-Cu has the ability to increase differentiation and proliferation of axons within neurons, indicating it has an effect on the nervous system to ensure proper functionality. GHK-Cu blocks ferritin channels and the release of tissue damaging free (oxidative) iron after tissue injury, thus blocking iron catalyzed lipid peroxidation that occurs after injury. This mechanism of copper-peptide induced tissue repair appears to function for skin, hair follicles, the stomach lining, the intestinal lining, bone tissue, and hooves and fingernails.





## Dosage

- SubQ General Dosage\*
  - 50 mcg/kg SubQ daily

## Clinical Indications

### Wound Healing and Infection Control

There have been multiple studies that have shown the profound effects of GHK-Cu on the healing of wounds. In the process of healing wounds, it causes better wound contraction, faster development of granular tissue, and improved angiogenesis to restore blood flow to damaged tissue.<sup>ii</sup> It has also been shown that systemic injection of GHK-Cu can also cause enhancement of the healing process. Injection of GHK-Cu into the muscle can promote tissue repair at distant locations. A study was performed and showed that injections of GHK-Cu caused significant, systemic increases in collagen production, angiogenesis, and wound closure.<sup>iii</sup> There has been a clinical trial in diabetic patients suffering from ulcerations.<sup>iv</sup> When given a gel that contained 2% GHK-Cu, wound closure of ulcers increased by 40% and the percent of infection decreased by 27%, showing extremely promising results for the treatment of skin injuries that can be difficult to treat due to infection. In line with this, GHK-Cu could potentially be a valuable therapy given to individuals after surgery to promote wound healing, aid with pain and prevent infection.

### Anti-Inflammatory

GHK-Cu also tends to have anti-inflammatory properties. A study was performed on GHK-Cu and its interaction with TNF-alpha along with pro-inflammatory cytokines such as IL-6 in human fibroblasts. The study indicated that GHK-Cu was able to significantly decrease the amount of inflammation.<sup>v</sup> So, there is a strong indication that GHK-Cu could possibly be used as either a systemic injection or topically applied therapy in the treatment of inflammatory skin conditions such as psoriasis. It was also shown that it can reduce erythema caused by UV sunlight.

### Hair Growth Restoration

It has also been found that GHK-Cu stimulate hair growth. It was even shown that the efficacy of GHK-Cu for hair growth was comparable to that of 5% minoxidil, which is one of the most commonly used medications in the restoration of hair growth.<sup>vi</sup> It is commonly being put in hair gels and shampoos, along with other copper peptides, to restore hair growth. In fact, a commercial product known as GraftCyte, which contains GHK-Cu, was clinically evaluated and



proven to improve the outcome of hair transplantation surgeries and healing.<sup>vii</sup> Within the hair follicle, GHK-Cu has been shown to promote collagen production and strengthen already existing hair by stimulating growth in areas that are lacking thickness.

### **Facial Cosmetic Use**

The use of GHK-Cu for anti-aging cosmetics has been extensively researched and is used widely throughout the United States in a large portion of the population. When applied to the skin, GHK-Cu can cause firming of the skin, anti-aging, and anti-wrinkle activity. There have been multiple clinical studies done to determine the efficacy of GHK-Cu for treatment to the face. One study was done on 20 females and confirmed that GHK-Cu outperformed vitamin C and retinoic acid in increasing collagen in photoaged skin.<sup>viii</sup> Another clinical study was performed for 12 weeks on 67 women, and it showed that GHK-Cu significantly improved aged skin appearance, increased thickness, reduced wrinkles, and strongly induced proliferation of keratinocytes in the dermis.<sup>ix</sup>

### **Cognitive Health**

It has also been shown that GHK-Cu could potentially benefit cognitive health by playing a role in nerve regeneration. A study was performed on the effect that GHK-Cu had on axons within neurons and it showed that it has the ability to increase migration of hematogenous cells into collagen tube, produce nerve growth factors, increase expression of integrins and increase the rate of regeneration of myelinated nerve fibers. Schwann cells and axon count were also increased.<sup>x</sup> A human gene expression analysis was done to determine the effects of GHK-CU in gene expression due to the fact that the molecule declines with age. It was shown that it induces a 50% or greater change of expression in 31.2% of human genes affecting multiple biochemical pathways in organs and tissues including the nervous system. If levels of this important peptide go down in the body as you age, so will expression of necessary genes. Thus, treatment by GHK-Cu may not only directly impact physical nerve regeneration, but it could impact the expression of fundamental proteins in your body.<sup>xi</sup>

### **Anti-Cancer**

GHK-Cu has been recommended as a treatment for metastatic cancer. A study was performed to determine gene expression of normal and cancerous cells, and figure out what substances could silence genes involved in metastasis.<sup>xii</sup> They used a database of 7000 genome expression profiles, and after treatment with 1309 bioactive substances, it was found that only 2 were effective in turning down the genes over expressed in tumor spreading; 1 of those was GHK-Cu. Gene control is an exciting area of medicine, especially in the realm of cancer therapy. Higher



tissue copper may be the key to keeping cells younger and GHK-Cu seems to be a fantastic mediator of this system.

### **Lungs**

It has been postulated that GHK-Cu could play a key role in the protection of the lungs from acute injury and fibrosis. Numerous studies have been performed to try and determine what role it plays, and the findings have been fairly significant. One study was able to show that it protects lung tissue from damage by being able to reduce reactive oxygen species (ROS) production, increased superoxide dismutase (SOD) activity while decreased TNF- $\alpha$  and IL-6 production through the suppression of NF- $\kappa$ B p65 and p38 MAPK signaling in vitro and in vivo model of ALI. Moreover, GHK-Cu attenuated LPS-induced lung histological alterations, suppressed the infiltration of inflammatory cells into the lung parenchyma in LPS-induced ALI in mice.<sup>xiii</sup> Taken together, these findings demonstrate that GHK-Cu possesses a protective effect in LPS-induced ALI by inhibiting excessive inflammatory responses; accordingly, it may represent a novel therapeutic approach for Acute Lung Injury and Respiratory Distress Syndrome. Further, it was shown that treatment of GHK-Cu reduces inflammatory cell infiltration and interstitial thickness in subjects with pulmonary fibrosis. It significantly improves collagen deposition, imbalances in lung tissue, and reduces TNF-alpha and IL-6 in alveolar fluid.<sup>xiv</sup> Thus, GHK-Cu shows a strong indication for the treatment of a variety of lung diseases.

### **Conclusions**

GHK-Cu is a small peptide with big physiologic effects on the human body. It is widely used as a hair growth and cosmetic agent, but it is clear that there are many more indications for it in the clinic. Harnessing the ability to incorporate a natural peptide with copper into therapy can be significant in improving infection, wound healing, hair growth, cognition, amongst many others for patients.

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