BIOMOD LABS · RESEARCH PEPTIDE CO.

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GHK-Cu

Glycyl-L-histidyl-L-lysine copper(II) — an endogenous tripeptide-copper complex first isolated from human plasma albumin by Loren Pickart in 1973, characterised in preclinical models for effects on extracellular matrix remodelling, fibroblast biology, and copper-dependent enzyme regulation.

CAS REGISTRY	CATALOG REFERENCE	CLASS	DATE OF ISSUE
49557-75-7 (Cu complex) · 89030-95-5 (GHK peptide)	BM-LYO-013	Tripeptide-Cu(II) complex · 3 a.a.	May 2026

GHK-Cu is a tripeptide-copper(II) complex of sequence Gly-His-Lys (one-letter: GHK) chelating a single Cu(II) ion via the histidine imidazole nitrogen, the histidine α-amine, and additional coordinating ligands provided by the lysine and copper-bound water molecules. The molecule was first isolated by Loren Pickart in 1973 during work on a serum activity that caused old human liver tissue to synthesise proteins resembling those of younger tissue. Subsequent decades of preclinical investigation across multiple independent laboratories have characterised GHK-Cu in cell-culture and animal-model preparations as an extracellular-matrix-remodelling agent — modulating expression of matrix metalloproteinases (MMP1, MMP2) and their tissue inhibitors (TIMPs), stimulating collagen and elastin production by dermal fibroblasts, and engaging copper-dependent enzymatic systems including lysyl oxidase (essential for collagen and elastin cross-linking). **This monograph summarises published preclinical findings for laboratory research reference only.**

01 Compound Profile

COMMON DESIGNATION	GHK-Cu · Copper tripeptide-1 · Prezatide copper acetate (INN of related preparation)
PRIMARY SEQUENCE	Gly-His-Lys (G-H-K)
CAS REGISTRY	49557-75-7 (copper complex); 89030-95-5 (uncomplexed GHK peptide)
MOLECULAR FORMULA (GHK)	$C_{14}H_{24}N_6O_4$ · Cu(II) complex adds Cu^{2+}
AVERAGE MOLECULAR MASS	340.39 g · mol^{-1} (free peptide); ~404 g · mol^{-1} (Cu complex with acetate counterions)
CU(II) COORDINATION CHEMISTRY	Cu(II) chelated by histidine imidazole nitrogen, histidine α-amine, additional coordinating ligands; high binding affinity for Cu(II)[2]
PHYSICAL FORM	Blue / blue-purple lyophilised solid (the colour is the d–d electronic transition of the Cu(II) complex)
CRITICAL CHEMISTRY NOTE	**GHK-Cu MUST NEVER be reconstituted with acetic acid or bacteriostatic water**. The acidic environment disrupts the Cu(II) chelate, releasing free copper and destroying the chemistry of the complex. Sterile water for injection at neutral pH is the only acceptable reconstitution vehicle
SOLUBILITY (LAB RECONSTITUTION)	Soluble in sterile water for injection at neutral pH
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated, light-protected; reconstituted solution refrigerated 2–8 °C short-term in neutral aqueous conditions; aliquoted long-term at −18 °C
ANALYTICAL SPECIFICATION	≥ 98 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

Loren Pickart originally isolated the GHK-Cu activity during his doctoral research at the University of California, San Francisco, in 1973, observing that a fraction of human plasma albumin could induce old human liver tissue to synthesise proteins resembling those of younger tissue. Subsequent biochemical fractionation identified the active component as a tripeptide of sequence Gly-His-Lys, which under physiological conditions chelates Cu(II) with

high affinity to form the GHK-Cu complex. The molecule occurs naturally in human plasma (approximately 200 ng/mL in young adults, declining to approximately 80 ng/mL by the sixth decade of life), saliva, and urine.[1]

Chemically, the central feature of GHK-Cu is the Cu(II) chelation geometry. The histidine imidazole nitrogen and the histidine α-amine provide the primary coordinating ligands; additional coordination is supplied by the lysine side chain and (in solution) by water molecules. The blue-purple colour of the solid and concentrated solution arises from the d–d electronic transition characteristic of Cu(II) in a square-planar or distorted square-planar coordination environment. **This Cu(II) chelate is the source of the molecule's biological activity** — disrupting it by acidic reconstitution (e.g., with bacteriostatic water containing benzyl alcohol, or with acetic acid) releases free Cu(II) and produces a fundamentally different and biologically less-active chemistry.[2]

03 Proposed Mechanisms in Preclinical Models

The GHK-Cu literature documents multiple parallel preclinical mechanisms. **Matrix metalloproteinase and TIMP modulation** — Badenhorst et al. examined human adult dermal fibroblasts and reported that GHK-Cu at 0.01, 1, and 100 nM increased expression of MMP1 and MMP2 (at the lowest concentration) and increased TIMP1 expression across all tested concentrations.[3] **Collagen and elastin production** — the same study and earlier work by Maquart and colleagues reported increased collagen synthesis in fibroblast culture exposed to the peptide-copper complex. **Genome-wide transcriptomic effects** — Pickart and Margolina's 2018 review summarises Connectivity Map analyses indicating that GHK affects expression of approximately 4,048 human genes (about 6 % of the genome) in cell-line preparations, with the expression pattern in aged cells shifting toward profiles characteristic of younger tissue.[4] **Lysyl oxidase activation** — the Cu(II) of GHK-Cu serves as a cofactor for lysyl oxidase, the copper-dependent enzyme responsible for collagen and elastin cross-linking.[1] IN VITRO

04 Preclinical Findings

SYSTEM	PREPARATION	REPORTED OBSERVATION	REF.
MMP/TIMP regulation	Human adult dermal fibroblasts (HDFa)	↑ MMP1, MMP2 expression at 0.01 nM; ↑ TIMP1 across 0.01–100 nM	3
Collagen synthesis	Cultured rat & human fibroblasts	Stimulation of collagen synthesis (Maquart 1988)	5
Wound healing	Rat wound & skin transplant models (Pickart series)	Accelerated wound contraction; improved skin transplant uptake	1
Genome-wide effects	Connectivity Map analysis of cell-line transcriptomes	~4,048 genes modulated; aged cell profile shifts toward younger profile	4
Epidermal stem cell markers	Dermal skin equivalent preparations	↑ integrin and p63 expression in basal keratinocytes	1
MMP activation in wounds	Rodent skin wound preparations	Modulation of MMP expression and activation in wound tissue	6
Lysyl oxidase cofactor	Cell-free enzymology	Cu(II) of GHK-Cu serves as LOX cofactor for collagen/elastin cross-linking	1

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

GHK-Cu has one of the deepest published preclinical literatures of any cosmetic-research peptide, with consistent observations across MMP/TIMP regulation, collagen/elastin synthesis, fibroblast biology, and gene-expression profiling reported by multiple independent laboratories. The Pickart and Margolina Connectivity Map analysis (2018) is one of the more thorough transcriptomic characterisations of any small bioactive peptide. **For researchers, the principal experimental design consideration is preservation of the Cu(II) chelate** — the biological activity is the activity of the intact peptide-copper complex, not of the free peptide or free copper. Acidic conditions, reducing agents, and chelating buffer components (EDTA, EGTA, citrate at high concentration) will disrupt the chelate and destroy the active chemistry. Neutral aqueous vehicles are essential.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilised GHK-Cu is supplied under research-use specifications. **Critical handling requirement: GHK-Cu MUST be reconstituted with sterile water for injection at neutral pH only. Bacteriostatic water (containing benzyl alcohol, slightly acidic) and acetic acid solutions are NOT acceptable** — these disrupt the Cu(II) chelate and destroy the molecule's defining chemistry. Phosphate-buffered saline at neutral pH is acceptable. The lyophilised solid is held at −18 °C, desiccated and light-protected (Cu(II) complexes are mildly photo-reactive). Reconstituted solutions are held refrigerated 2–8 °C for short-term work and aliquoted at −18 °C for long-term storage. **Chelating buffer components (EDTA, EGTA, high-concentration citrate, DTT, β-mercaptoethanol) must be excluded from all vehicles, buffers, and laboratory glassware** — these compete with the GHK peptide for Cu(II) and destroy the active chemistry. Working concentrations are determined by the investigator's experimental design.

07 References

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