

COPPER TRIPEPTIDE-1

Dr. Charlene DeHaven, M.D.
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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-epithelialization 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

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.

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WHITE PAPER

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ADVANCEMENT IN DNA REPAIR ENZYMES: EXTREMOZYMES®

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EXTREMOZYMES AND EXTREMOPHILES

Extremozymes are enzymes developed by plants living in extreme environments that assist survival and adaptability. Organisms able to not only survive but thrive in harsh planetary locations are called “extremophiles”, a term that literally means “extreme loving.” Scientists have been fascinated with extremophiles for many years and have studied their adaptive mechanisms.

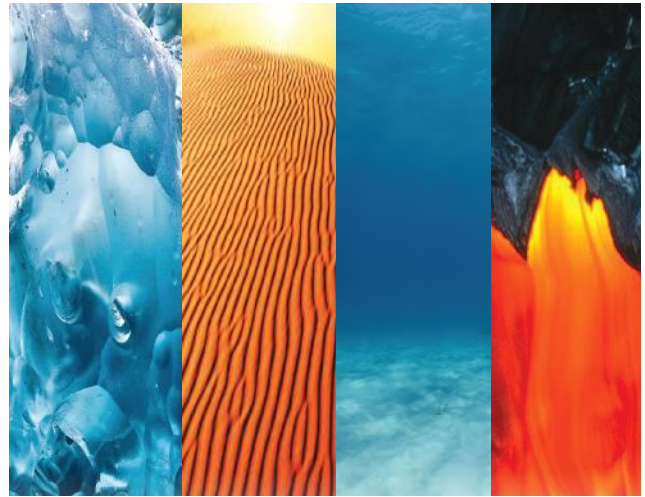
Many of these extremophiles are micro-organisms, but even more complex organisms, such as plants, have been able to adapt to the extent required to survive at planetary extremes. These organisms, some of which date back more than 40 million years, use powerful biologic processes to protect themselves against extreme cold, heat, salinity, pH balance, dehydration and radiation.

Varieties of extremophiles include hypoliths from cold, dry deserts; cryophiles found in polar ice; piezophiles from pressurized deep ocean trenches; thermophiles from very hot areas; and polyextremophiles from environments containing multiple adversities. A number of polyextremophiles originate from marine environments where there may be extremes of temperature, pressure, salinity and darkness.

EXTREMOZYMES IN NATURE

Extremophiles have developed a variety of ingenious survival strategies allowing them to regenerate, metabolize and reproduce in spite of very difficult environmental conditions. Their enzyme systems, Extremozymes, protect vital biological macromolecules, cells and chromosomal DNA from damage by external stresses. In addition to protein structural components, an organisms’s DNA genetic blueprint is one of the most important elements that every organism must conserve

for survival. Methods of protection include unique configurations of protein folding, protection from dehydration by incorporation of sugar molecules, and biochemical means of cushioning and shielding DNA. An example of this ability is prevention of thymine dimer formation when DNA is exposed to oxidative stress and radiation in these extreme environments. These unique, natural enzymes scavenge free radicals and destroy radical oxygen species.

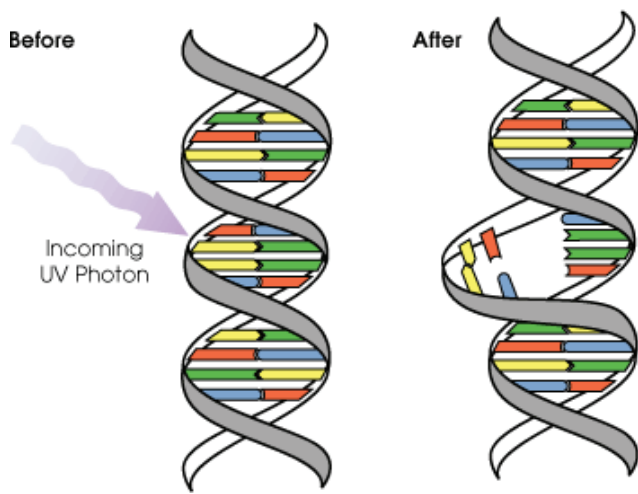


Some of the harsh environments in which extremophiles thrive include extreme cold, heat, dryness, and deep ocean trenches.

EXTREMOZYMES FOR SKIN

Human skin also experiences environmental extremes. The power of Extremozymes may be harnessed for skin protection against environmental damage including dryness, wind, radiation (solar UVA and UVB), heat, cold, salinity (saltiness from sweating) and irritation (e.g. from soaps). Exposure of structural proteins including collagen and elastin to moisture loss, radiation, heat, cold, and free radical damage as well as exposure of essential genetic DNA to environmental stresses causes aging with loss of elasticity, resilience, immune function, and cancer resistance.

Exposure of skin to solar rays causes photoaging. Thymine dimers form abnormal cross-bridges in DNA as intranuclear DNA experiences oxidative stress. Measurement of thymine dimers as well as other DNA damage markers such as sunburn cell formation can be measured scientifically. Quantification of thymine dimer and sunburn cell formation is a key parameter of sun damage. Just as Extremozymes® shield extremophilic organisms from damaging environmental radiation, the ravages of solar radiation on skin can be lessened by incorporating Extremozymes technology into skin care.



UV Radiation causes the formation of thymine dimers, a form of DNA damage.

The genetic adaptations of extremophiles and their Extremozymes have profound functional applications to skin care. Over time, environmental conditions have a very noticeable and disastrous effect on our skin. Nature's miracles of adaptation can also be used to protect human skin from damage caused by environmental extremes. INNOVATIVE SKINCARE® has drawn from the natural selection processes of specialized extremophilic organisms, pioneering the future of skin care in terms of ultimate protection for healthy skin.

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YOUTH SERUM™ COLLAGEN SYNTHESIS

Induction of collagen synthesis *in vitro* in human fibroblasts

SIT: Skin Investigation and Technology Hamburg GmbH

STUDY OBJECTIVE

YOUTH SERUM™ was evaluated for its ability to encourage collagen synthesis in aged human fibroblasts.

STUDY DESIGN

Fibroblasts with a biologic age of 50+ years were grown in cell culture both with and without exposure to YOUTH SERUM™. Wells containing fibroblasts without YOUTH SERUM™ treatment were used as the Control. The Sircol dye reagent assay with photo-colorimetric quantitation was used to measure collagen synthesis at timed intervals. Measurements from the various tissue culture wells were compared to evaluate the effectiveness of YOUTH SERUM™ in increasing collagen synthesis.

SIGNIFICANCE OF STUDY

With both photoaging and intrinsic aging, impairment of collagen synthesis occurs. Collagen is the most abundant human protein and most collagen is found in the skin. The aging process and photoaging in particular demonstrates visible changes related to loss of functional collagen, including wrinkling, sagging, decreased elasticity, and loss of resiliency to stress.

The synthesis of collagen occurs continuously throughout life to repair damaged tissue and build new cellular structures. Collagen synthesis progressively declines about one percent with each year of life and by the age of 60, about one-half of the functional collagen is synthesized compared to the age of 20. Aged fibroblasts both *in vitro* and *in vivo* are able to produce less collagen compared to younger cells. Aged fibroblasts were used for this study to present a stronger test for the product. Fibroblasts are the skin cells responsible for synthesizing collagen.

An increase in collagen synthesis in aged cells is even more significant than in youthful cells since older cells are functionally less able to produce collagen effectively and in amounts able to compensate for ongoing damage processes. Furthermore, popular interest in decreasing the visible signs of aging increases with advancing age, as these signs become more noticeable. Products able to encourage collagen synthesis are desired by persons wishing to minimize the signs of aging and maintain skin health throughout life.

Continued ...



RESULTS AND CONCLUSIONS

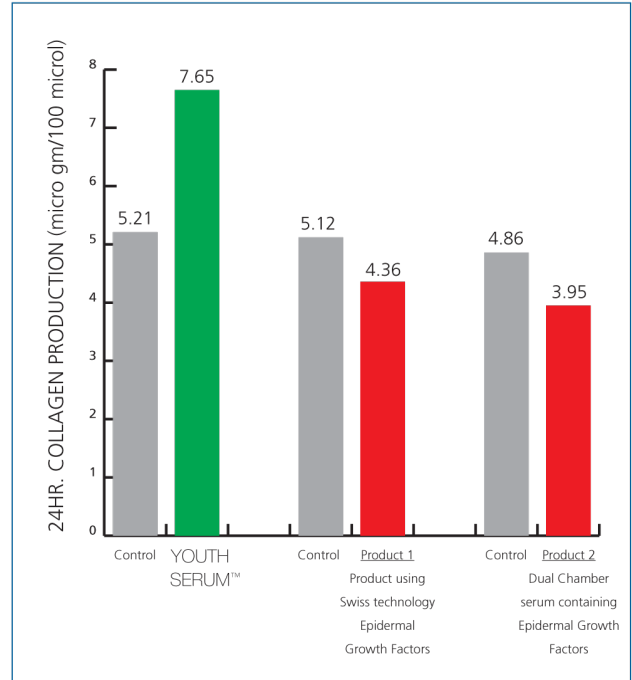
Older fibroblasts with equivalent age of 50 years were able to increase their collagen synthesis in the presence of YOUTH SERUM™. These results were compared to control values without YOUTH SERUM™ and evaluated for statistical significance. Collagen concentrations are shown in the bar graph on page 2.

Fibroblasts in the presence of YOUTH SERUM™ synthesized much more collagen compared to Control cells without YOUTH SERUM™. These results were statistically significant.

Fibroblasts in the presence of Product 1 were unable to synthesize more collagen than the Control cells without Product 1 when results were evaluated for statistical significance.

Fibroblasts in the presence of Product 2 were unable to synthesize more collagen than the Control cells without Product 2 when results were evaluated for statistical significance.

YOUTH SERUM™ clearly improved the synthesis of collagen by aged fibroblasts. Two other products in the marketplace were unable to improve collagen synthesis. These results have positive implications for using YOUTH SERUM™ to improve changes seen in the aging face associated with wrinkling, sagging, and loss of resiliency.





treat



treat
YOUTH SERUM™
5.4 pH +/- 0.5

IMMEDIATE SMOOTHING & TIGHTENING,
LONG-TERM WRINKLE REDUCTION,
RESTORATIVE

BENEFITS

- Clinically proven to increase collagen I synthesis
- Contains safe growth factors that shield skin from cancer development
- Helps prevent DNA damage (Extremozyme® technology)
- Immediately smoothes fine lines and wrinkles
- Provides immediate and long-term improvements
- Improves skin firmness and elasticity
- Excellent for use under makeup
- Safe around the eye area, passed ocular irritancy tests
- Paraben-free

COMMENTS

YOUTH SERUM™ is designed to give skin the best of both worlds: instant smoothing and tightening, with dramatic wrinkle reduction over time. Intelligent proteins target damaged sites, strengthen dermal structure, and instantly smooth fine lines for an immediately firmed complexion. Meanwhile, YOUTH SERUM™'s safe, bio-identical growth factors gradually rebuild lost collagen to reduce fine lines and wrinkles long-term. Our patented Extremozyme® technology, combined with a powerful blend of antioxidants, including vitamins A, C, E, and centella asiatica, encourage cellular health, provide UV photoprotection, and prevent environmental damage. The result is a more youthful, vibrant, and resilient complexion.

YOUTH SERUM™ can be applied all over the face and neck, and is even safe to use in the eye area, passing ocular irritancy tests.

INDICATIONS

- Normal, dry, oily, or combination skin
- Fine lines and wrinkles
- Rough skin texture
- Loose, sagging skin

APPLICATION; A little goes a long way. Apply enough for full face coverage but not so much it feels sticky

RETAIL
SIZE
30 mL e 1 fl. oz.
DOSAGE
Small amount per
application



treat
YOUTH SERUM™


5.4 pH +/- 0.5



treat

DESCRIPTION Straw to light amber, slightly opaque gel.

INGREDIENT FEATURES

KEY INGREDIENTS	DESCRIPTION
EXTREMOZYMES® 	A proprietary combination of extremophilic enzymes (Extremozymes®), clinically proven to protect and repair fragile proteins and DNA components.
AHNFELTIA CONCINNA EXTRACT	An intertidal seaweed algae extract from the Rhodophyta group containing proteoglycans, peptides, polypeptides and glycans. Contains a large quantity of 4-hydroxyproline, an unusual amino acid found only in collagen, which triggers the epidermis to begin the collagen repair process.
INTELLIGENT PEPTIDES & PROTEINS	Primarily pseudoalteromonas ferment extract, a glycoprotein from the Antarctic Sea, and hydrolyzed wheat and soy proteins. Clinically proven to identify and adhere to damaged sites, providing targeted regeneration.
COPPER TRIPEPTIDE-1 GROWTH FACTOR (Bioidentical)	Copper tripeptide-1 (bioidentical) has been clinically proven to stimulate the synthesis of collagen in skin fibroblasts and increase accumulation of total proteins, glycosaminoglycans (in a biphasic curve), and DNA in dermal wounds. The Copper tripeptide-1 sequence is present in collagen, and it is suggested that the Copper tripeptide-1 is released after tissue injury. ¹ Copper tripeptide-1 also increases synthesis of decorin: a small proteoglycan in the regulation of collagen synthesis, in wound-healing regulation, and in antitumor defense. ²
ASIATICOSIDE, ASIATIC ACID, AND MADECASSIC ACID (Sourced from Centella Asiatica)	Efficacious antioxidants that stimulate collagen synthesis and improve microcirculation, capillary flow, and vascular tone, to promote wound healing and reduction of scar tissue.
RETINYL PALMITATE (Vitamin A) TOCOPHERYL ACETATE (Vitamin E) ASCORBYL PALMITATE (Vitamin C)	Powerful vitamin antioxidant blend, encapsulated in a liposome for ease of penetration.

¹ 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;238(2):343-6.

² Siméon 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-Cu²⁺. *J Invest Dermatol.* 2000;115(6):962-8.

INGREDIENTS

Water, PVP, Caffeine, Glycerin, Disodium EDTA, Hydroxyethylcellulose, Ceratonia Siliqua (Locust Bean) Gum, Hydrolyzed Casein, Pseudoalteromonas Ferment Extract, Hydrolyzed Wheat Protein, Hydrolyzed Soy Protein, Tripeptide-10 Citrulline, Tripeptide-1, Lecithin, Butylene Glycol, Xanthan Gum, Carbomer, Triethanolamine, Caprylyl Glycol, Phenoxyethanol, Ahnfeltia Concinna Extract, Beta Vulgaris (Beet) Root Extract [Extrait de racine de betterave], Haberlea Rhodopensis Leaf Extract, Faex (Yeast) Extract [Extrait de levure], Acetyl Tyrosine, Proline, Hydrolyzed Vegetable Protein, AdenosineTriphosphate, Ergothioneine, Saccharide Isomerate, Hydrolyzed Wheat Protein/PVP Crosspolymer, VP/Dimethylaminoethylmethacrylate Copolymer, Phospholipids, Tocopheryl Acetate, Retinyl Palmitate, Ascorbyl Palmitate, Asiaticoside, Asiatic Acid, Madecassic Acid, 1,2-Hexanediol.

CAUTIONS For external use only. Avoid contact with eyes. Store in a cool place.