

Neova® Night Therapy Combats Photodamage with DNA Repair and Copper Peptide Technologies

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Abstract

Neova® Night Therapy treatment now combines a blend of Copper Peptide Complex® technology with advanced DNA repair. The DNA repair is in the form of Endosomes, a liposome encapsulated enzyme (UV-Endonuclease) prepared from *Micrococcus luteus*. Night Therapy continues to provide the protection and regeneration properties of the advanced ceramides of Skinmimics® to fight the signs of aging and help restore skin's youthful texture. These functions are supplemented by enhanced moisturization action provided by Sodium hyaluronate.

Introduction

Wrinkles are not very desirable features for most people despite the fact that they are the inevitable results of aging and environmental stress and damage. Wrinkles, of course, are caused in part by the natural slowdown of repair of the underlying extracellular matrix (ECM) of the skin. The resulting accumulation of fine lines, wrinkles, sagging skin can add to an increased appearance of age.

Night Therapy now combines Copper Peptide Complex technology with DNA repair and the regeneration properties of the advanced ceramides present in Skinmimics, in a paraben free, nighttime treatment formula.

DNA damage is a critical aftermath of UV irradiation due to sunlight exposure and contributes to many visible aspects of photoaging. Exposure to UVB causes the formation of thiamine dimmers. DNA damage can also come about during the normal process of cellular metabolism and respiration.

DNA repair refers to a collection of processes used by a cell to identify and correct damage to the DNA from either normal cellular processes or UV radiation. The DNA repair process is constantly active as the cells respond to damage in the DNA structure. The rate of DNA repair is dependent on many factors such as the type of cell, the age of the cell, and the cellular environment. If a cell accumulates a large amount of DNA damage with insufficient repair, it may become dormant (senescence), initiate programmed cell death (apoptosis), or start unregulated cell proliferation (cancer).

Copper Peptide Complex®

Copper is essential to vital cellular and enzyme processes required for human health, and is the third most abundant trace metal in the body, after iron and zinc. Since the 1830s, copper has been known to be an essential nutrient. It was found that copper plays a key role in several of the body's essential enzyme systems needed for tissue repair and other biological responses. These copper-based enzyme systems allow tissue to repair itself, blood vessels to form, wounds to close and inflammation to decrease. Copper is now known to be critical to the normal repair and healing process in all tissue, including connective tissues that comprise human skin, internal organs and bones.

The Copper Peptide Complex in Night Therapy is a tripeptide (glycyl-L-histidyl-L-lysine) complexed with copper. The tripeptide was originally isolated from the albumin fraction of human serum¹. It was subsequently shown that the peptide existed as the copper complex and enhanced the uptake of copper by cells²⁻⁴. The glycyl-L-histidyl-L-lysine peptide sequence is found in several proteins associated with the extracellular matrix including the large extracellular matrix protein termed SPARC and may be liberated by endogenous proteolysis or cleavage of these proteins during the repair and regeneration processes⁵⁻⁸. These small peptides liberated from the extracellular matrix were termed matrikines.

Skin health, dermal wound healing, and general soft tissue repair requires many of the same biological processes such as reconstitution of an extracellular matrix and increased blood flow (angiogenesis). Copper is utilized by essentially every cell and organ; resulting in the formation of important copper-dependent enzymes - including

cytochrome C oxidase (energy production), superoxide dismutase (antioxidation) and lysyl oxidase (cross-linking of elastin and collagen in skin)^{9,10}.

In numerous studies, copper peptides have been shown to promote new blood vessel growth, enhance the expression of growth factors, activate matrix metalloproteases, and stimulate the formation of new collagen, elastin, and glycosaminoglycan components of tissue to accelerate the repair process¹¹⁻¹⁷.

More importantly, Copper Peptide Complex formulated in a wide variety of cosmetic preparations has shown to both stimulate collagen production and to reduce the visible signs of aging, improve skin laxity, clarity, and appearance, reduce the appearance of fine lines and wrinkles, and to increase skin density and thickness both on the face and eye area¹⁸⁻²¹.

As shown below, the activities of copper and copper peptide are all essential to maintaining skin health and reversing the signs of aging.

Activities of Copper and Copper Peptide Scientific Studies	
Collagen	Enhance
Glycosaminoglycans	Enhance
Elastin	Enhance
Angiogenesis	Enhance
Growth Factors	Enhance
Matrix Metalloproteases	Enhance
Performance Evaluations	
Collagen	Enhance
Skin Laxity	Improve
Skin Clarity	Improve
Skin Appearance	Improve
Fine Lines & Wrinkles	Reduce Appearance
Skin Density	Increase
Skin Thickness	Increase

Endosomes

Endosomes are liposomes that contain an enzyme extract prepared from *Micrococcus luteus*, which was discovered after a complete search for an organism very resistant to UV radiation. The resistance of *Micrococcus luteus* is largely due to the presence of the enzyme UV endonuclease, which recognizes UV induced DNA damage

and initiates its repair. The liposome delivery system has been specifically engineered for the transference of DNA repair enzymes across the stratum corneum and into the epidermal cells to enhance DNA repair of UV irradiated skin. Delivery of these enzymes is well known to enhance removal of sun damage and increase cell survival, and to protect the immune system²².

The enzyme activity stimulates the recognition and elimination of damage to skin that has been most closely linked to the long term effects of sun exposure, Figure 1.

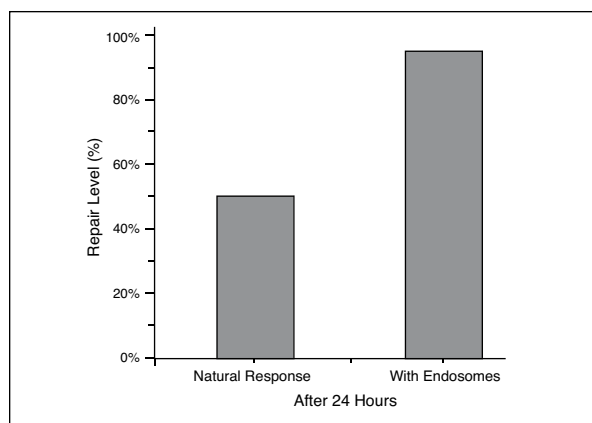


Figure 1. Endosomes Enhance DNA Repair in Human Cells

Application of Endosomes has also been shown to reduce the production of inflammatory mediators following UV-B exposure of an in vitro model of human skin, Figure 2.

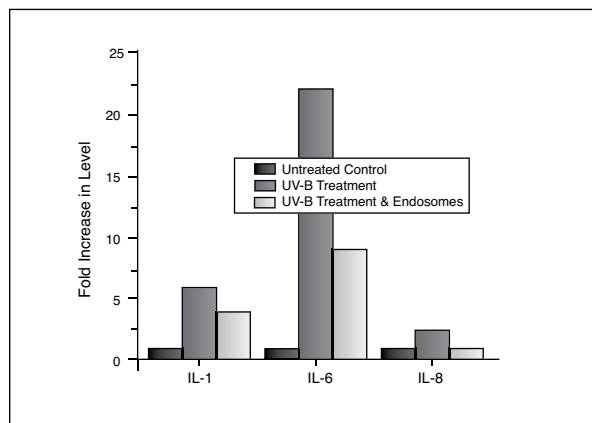


Figure 2. Endosomes Reduce Inflammatory Mediator Release in Human Cells

Skinmimics®

Skinmimics was designed to provide a combination of protection, prevention, and regeneration cosmeceutical actives in the form of ceramide technology²³. It is a mixture of long chain ceramides, cholesterol, and Sphingokines® signaling molecules. It has been reported that the mixture of Caprooyl-Phytosphingosine and Caprooyl-Sphingosine, components of the Skinmimics mixture, trigger the expression of genes for late-stage epidermal differentiation to enhance the synthesis of key sphingolipids in cultured keratinocytes. Similar results have been reported in studies with volunteers following application of the Skinmimics formulation. A significant reduction in TEWL (Transepidermal Water Loss) and an increase in skin elasticity has been measured.

These evaluations confirm that the application of Skinmimics will help mature skin be revitalized through the combination of protection, prevention, and regeneration.

Sodium Hyaluronate

Sodium hyaluronate is the sodium of hyaluronic acid. Hyaluronic Acid (HA) is the naturally occurring and widespread component found within the extra-cellular matrix within bodily tissues, especially those of the face. Its water-binding and water-attracting attributes fill up the spaces between the connective fibers collagen and elastin in the dermis.

Sodium hyaluronate has a smaller molecular size than HA (making it especially penetrative), and is able to hold more water than any other natural substance—up to 1,000 times its weight in water.

Summary

Night Therapy is formulated to combat the effects of photoaging on the skin. The treatment now combines Copper Peptide Complex technology with a new and powerful therapy—advanced DNA Repair Endosomes, liposome encapsulated enzymes (UVEndonuclease) prepared from *Micrococcus luteus*. Night Therapy continues to provide the protection and regeneration properties of the advanced ceramides of Skinmimics to fight the signs of aging and help restore skin's youthful texture. These functions are supplemented by enhanced moisturization action provided by Sodium hyaluronate.

References

- Pickart L, Thayer L, Thaler MM. Synthetic tripeptide which increases survival of normal liver cells, and stimulates growth in hepatoma cells. *Biochem Biophys Res Commun* 1973;54:562-6.
- May PM, Whittaker J, Williams DR. Copper complexing by growth stimulating tripeptide, glycyLhistidyllysine. *Inorg Chim Acta* 1983;80:L5-L7.
- Pickart L, Thaler MM, Millard M. Effect of transition metals on recovery from plasma of the growth-modulating tripeptide glycyLhistidyllysine. *Journal of chromatography* 1979;Vol.:73.4. Huang PJ, Huang YC, Su MF, 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;25: 183-90.
- Pickart L, Thaler MM. GlycyLhistidyllysine (GHL) facilitates uptake of copper by hepatoma cells. *Fed.Proc.* A2312-p.668. 1979.
- Maquart F, X, Simeon A, Pasco S, Monboisse JC. [Regulation of cell activity by the extracellular matrix: the concept of matrikines]. *Regulation de l'activite cellulaire par la matrice extracelulaire: le concept de matrikines. Journal de la Societe de Biologie* 1999;193:423-8.
- Reed MJ, Sage EH. SPARC and the extracellular matrix: implications for cancer and wound repair. *Current topics in microbiology and immunology* 1996;Vol.:81-94.
- Sage E Helene, Reed M, Funk SE, Truong T, Steadele M, Puolakkainen P et al. Cleavage of the matricellular protein SPARC by matrix metalloproteinase 3 produces polypeptides that influence angiogenesis. *The Journal of biological chemistry* 2003;Vol.:57.
- Oddos T, Jumeau-Lafond A, Ries G. Requirement Of Copper And Tripeptide Glycyl-L-Histidyl-L-Lysine-Cu (GHK) Complex Formation For Collagen Synthesis Activity In Normal Human Dermal Fibroblasts. *American Academy of Dermatology 60th Annual Meeting February 22-27, 2002 New Orleans, LA.* 2002.
- Jackson EM. The Importance of Copper in Tissue Regulation and Repair: A Review. *Cosmetic Dermatology* 1997;10 (10):35-6.
- Milne DB. Copper in clinical practice. *Clin Lab News* 1993;19:80-1.
- Buffoni F, Pino R, Dal Pozzo A. Effect of tripeptide-copper complexes on the process of skin wound healing and on cultured fibroblasts. *Archives Internationales de Pharmacodynamie et de Therapie* 1995;Vol.:60.
- Huang PJ, Huang YC, Su MF, 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;25: 183-90.
- Maquart FX, Bellon G, Chaqour B, Wegrowski J, Patt LM, Trachy RE et al. In vivo stimulation of connective tissue accumulation by the tripeptide-copper complex glycyL-L-histidyl-L-lysine-Cu²⁺ in rat experimental wounds. *J Clin Invest* 1993;92:2368-76.
- 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-copper(2+). *FEBS Lett* 1988;238:343-6.

15. McCormack MC, Nowak KC, Koch RJ. The effect of copper tripeptide and tretinoin on growth factor production in a serum-free fibroblast model. *Arch Facial Plast Surg* 2001;3:28-32.
16. Oddos T, Jumeau-Lafond A, Ries G. Requirement Of Copper And Tripeptide Glycyl-L-Histidyl-L-Lysine-Cu (GHK) Complex Formation For Collagen Synthesis Activity In Normal Human Dermal Fibroblasts. American Academy of Dermatology 60th Annual Meeting February 22-27, 2002 New Orleans, LA . 2002.
17. Pollard JD, Quan S, Kang T, Koch RJ. Effects of copper tripeptide on the growth and expression of growth factors by normal and irradiated fibroblasts. *Arch Facial Plast Surg* 2005;7:27-31.
18. Abdulghani AA, Sherr A, Shirin S, Solodkina G, Tapia EM, Wolf B et al. Effects of Topical Creams Containing Vitamin C, a Copper-Binding Peptide Cream and Melatonin Compared with Tretinoin on the Ultrastructure of Normal Skin. *Disease Management and Clinical Outcomes* 1998;1(4):136-41.
19. Finkey MB, Appa Y, Bhandarkar S. Copper peptide and skin. *Cosmetic Science and Technology Series* 27, 549-564. 2005. Marcel Dekker, Inc.
20. Leyden JJ, Stevens T, Finkey MB, Barkovic S. Skin Care Benefits Of Copper Peptide Containing Facial Cream. American Academy of Dermatology 60th Annual Meeting February 22-27, 2002 New Orleans, LA . 2002.
21. Leyden JJ, Stevens T, Finkey MB, Barkovic S. Skin Care Benefits Of Copper Peptide Containing Eye Creams. American Academy of Dermatology 60th Annual Meeting February 22-27, 2002 New Orleans, LA . 2002.
22. Barnett Products Corporation Brochure. *Ultrasomes Activity*. 2009.
23. Skinmimics. 2008. Goldschmidt/Degussa Brochure.
24. Arch Personal Care Products. *Biodynes TRF Data Sheet*. 2009.

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