Neova[®] Power Defense Combines Biomimetic Peptides with Copper Technology

Leonard M. Patt, Ph.D., Procyte, A PhotoMedex Company 147 Keystone Drive, Montgomeryville, PA 18936

Abstract

Neova® Power Defense is a serum that combines Copper Peptide Complex® technology with an advanced peptide targeted to support the Dermal-Epidermal junction. This unique combination of factors targets aging effects throughout the layers of the skin. These functions are supplemented by enhanced moisturization action provided by Sodium Hyaluronate and a combination of well known antioxidants including Sodium Carboxymethyl Betaglucan, Camellia Oleifera (Green Tea) Extract, Tocopheryl Acetate, Vitis Vinifera (Grape) Seed Extract and Ubiquinone (Coenzyme Q10).

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.

The skin is made up of 2 key layers - the epidermis and dermis. The epidermis is the outer layer and functions as a barrier to the external environment. The cells of the epidermis are keratinocytes which move from the bottom layer of the epidermis to the top layer building up a large amount of keratin which provides the protective outer layer. The second layer of skin is the dermis, which contains the structural part of the skin, the connective tissue or extracellular matrix. The dermis is composed of a variety of structural elements, among them collagen elastin, and the glycosaminoglycans.

The junction between these two layers, the dermis and the epidermis, is an important structure. The dermal-epidermal junction (DEJ) forms fingerlike projections called rete ridges. The cells of the epidermis receive their nutrients from the blood vessels in the dermis. The rete ridges unique structure increases the surface area of the epidermis and dermis contact area, this increasing the flow of vital nutrients.

Both the epidermis and dermis are affected by the aging process. The cells of the epidermis become thinner and less thick leading to a lowering of the barrier function of the skin. In the dermis the manufacture of essential structural components lessens leading to a less flexible and also thinner layer. Importantly, the rete-ridges of the dermalepidermal junction start to flatten out decreases the amount of nutrients available to the epidermis by decreasing the surface area in contact with the dermis.

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 Power Defense 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-Llysine peptide sequence is found in several proteins associated with the extracellular matrix including the large extracellular matrix protein termed SPARC and may 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 from (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, key components of the dermis to accelerate the repair process¹¹⁻¹⁷.

More importantly, Copper Peptide Complex formulated in a wide variety of cosmetic preparations has show 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.

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

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

ChroNOline

ChroNOline[™] is a biomimetic tetrapeptide that boosts the production of key components at the DEJ (Dermal-Epidermal junction) such as collagen VII, laminin-5 and fibronectin for optimal skin structural support²². The key ingredient in ChroNOline is caprooyl tetrapeptide-3, a peptide based on the structure of transforminggrowth factor (TGF-ß), a growth factor that plays an important role in maintaining the extracellular matrix. In research studies, caprooyl tetrapeptide-3 stimulated the production of laminin (+26%) and fibronectin (+60%), proteins that are important structural components of the DEJ.

In a model of corticoid-induced skin ageing, caprooyl tetrapeptide-3 stimulated the expression of collagen VII and laminin-5. These proteins are involved in the anchoring of the epidermis to the dermis at the DEJ.



Figure 1. Effect of ChroNOline on Collagen VII



Figure 2. Effect of ChroNOline on Laminin

In the same model, it also prevented the flattening of the DEJ caused by corticoid treatment. In performance evaluations, ChroNOline[™] provides outstanding reduction in the appearance of fine line and wrinkles.

Caprooyl tetrapeptide-3 was tested in a cream formulation for fine lines and wrinkle reduction. The study was a split face placebo-controlled clinical trial involving 27 women volunteers aged 40-65. The cream was applied on the crow's feet area and silicone replicas were taken at day 28 and day 56. An ultrasonographic study was also performed on volunteers to document the effects of caprooyl tetrapeptide-3 cream on skin structures.

In this study, the treatment reduced fine lines and wrinkles by as much as 27% after 56 days in in a subgroup aged 50-65 (Figure 3).



Figure 3. Effect of ChroNOline on Wrinkles

Consumers who tested a cream containing the material spontaneously reported rapid antiageing results such as increases skin smoothness, firmness and younger looking skin.

Sodium Hyaluronate

Sodium hyaluronate is the sodium the salt 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 1000 times its weight in water.

Summary

Neova Power Defense is formulated to combat the effects of photoaging on the skin. Power Defense continues to provide the known benefits of copper peptide to combat aging of the skin by enhancing the production of key components of the dermis. Supporting the actions of copper peptide is a biomimetic tetrapeptide that boosts the production of key components at the DEJ (Dermal-Epidermal junction) such as collagen VII, laminin-5 and fibronectin for optimal skin structural support.

These functions are supplemented by enhanced moisturization action provided by Sodium Hyaluronate and a combination of well known antioxidants including Sodium Carboxymethyl Betaglucan, Camellia Oleifera (Green Tea) Extract, Tocopheryl Acetate, Vitis Vinifera (Grape) Seed Extract and Ubiquinone (Coenzyme Q10).

References

- 1. 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.
- 2. 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 growthmodulating tripeptide glycylhistidyllysine. Journal of chromatography 1979;Vol.:-73.
- 4. Pickart L, Thaler MM. Glycylhistidyllysine (GHL) faciltates 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.
- 6. 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.
- Simeon A, Monier F, Emonard H, Wegrowski Y, Bellon G, Monboisse JC et al. Fibroblase-Cytokine-Extracellular Matrix Interactions in Wound Repair. Current Topics in Pathology 1999;93:95-101.
- 9. Jackson EM. The Importance of Copper in Tissue Regulation and Repair: A Review. Cosmetic Dermatology 1997;10 (10):35-6.

- 10. Milne DB. Copper in clinical practice. Clin Lab News 1993;19:80-1.
- 11. Buffoni F, Pino R, Dal Pozzo A. Effect of tripeptidecopper 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.
- 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.
- Finkey MB, Appa Y, Bhandarkar S. Copper peptide and skin. Cosmetic Science and Technology Series 27, 549-564. 2005. Marcel Dekker, Inc.
- 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. Diane Billdeau, Isabelle Lacasse. Drawing the line on wrinkles. Cosmetics & Toiletries 123[7], 39-47. 2010.

ChroNOline is a trademark of Unipex Group Inc.