Neova® DNA Repair Factor Nourishing Lotion Stimulates Collagen and Speeds Natural Repair Process

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Abstract
Neova® DNA Repair Factor Nourishing Lotion is a light weight moisturizer that combines the restorative action of copper peptide with advanced DNA repair. Copper peptides have been shown to enhance the deposition of new extracellular matrix. DNA protection is provided by Helimoduline, a mixture of peptide factors from cotton which increase the surveillance of the DNA to identify damage and speed the natural repair process. These two functions are supplemented by enhanced moisturization action provided by a component similar to the skin's natural moisturization factors.

Introduction

The natural aging process normally begins in the mid-20s. In the skin, the synthesis of collagen and other components of the extracellular matrix is slower and elastin, the substance that enables skin to be flexible, is less functional. The dead skin cells at the surface do not shed as quickly and the production of new skin cells decreases. One of the main causes of the visible signs of aging skin is sun exposure. Freckles, age spots, spider veins on the face, rough and leathery skin, fine wrinkles that disappear when stretched, loose and dry skin, a blotchy complexion, actinic keratoses, and skin cancer can all be attributed to sun exposure.

Photoaging also occurs over a period of years. With repeated exposure to the sun, the skin loses the ability to repair itself. Studies have shown that repeated ultraviolet (UV) exposure breaks down collagen and other matrix components and impairs the synthesis of new collagen while DNA damage accumulates leading to increasing incidences of skin cancer and lower rates of cell renewal.

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. 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.

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)[1,2].

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 process[3-9].

DNA Repair Factor Nourishing Lotion contains the copper peptide L-Alanine-L-Histidyl-L-Lysine Copper (INCI Alanine/Histidine/Lysine Polypeptide Copper HCl) or AHK-Cu. This is a multifunctional copper peptide which both increases dermal cell proliferation and viability while increasing the deposition of collagen to renew the extracellular matrix.

Dermal fibroblasts are the main cells responsible for the production of collagen and other proteins essential for healthy skin. The response of human dermal fibroblasts to AHK-Cu has been investigated using cultured cells. The results

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show that AHK-Cu increases the growth and viability of dermal fibroblasts while stimulating the production of collagen[10].

Normal human dermal fibroblasts were seeded into a 96-well cell culture plate and grown to confluence in high glucose media supplemented with 10% fetal calf serum for three days. They were then placed in low glucose media with 2% serum and various amounts of AHK-Cu complex. After an additional three days, the cells were incubated with neutral red to assess their viability and stained with sulforhodamin B and counted to determine the number of cells.

The results in Figures 1 and 2, show that the addition of AHK-Cu complex stimulated the proliferation of the normal human dermal fibroblasts and increased their viability.

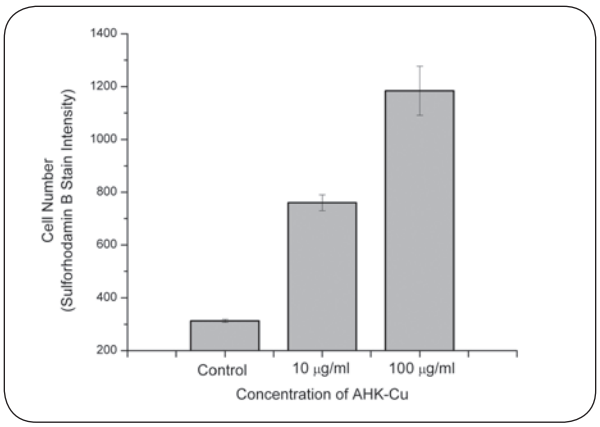

Figure 1. Effect of AHK-Cu on Dermal Cell Proliferation.

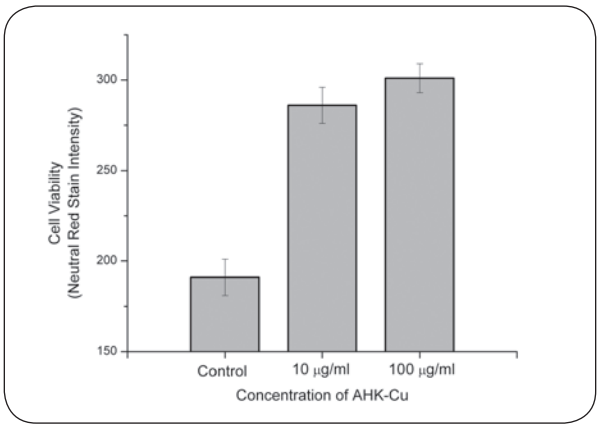

Figure 2. Effect of AHK-Cu on Dermal Cell Viability.

The effect of the AHK-Cu copper peptide complexes on collagen formation was determined by isolating the amount of collagen type I produced by human fibroblasts in cell culture. Normal human dermal fibroblasts were seeded into a 96-well cell culture plate and grown to confluence in high glucose media supplemented with 10% fetal calf serum for 3 days. They were then placed in low glucose media with 2% serum and various amounts of AHK-Cu complex. After 3 days, the culture media was collected and analyzed for collagen type I content by a sandwich ELISA assay using purified antibody to collagen type I.

The results below in Figure 3 show that the addition of AHK-Cu complex stimulates the formation of collagen type I by 300% over the control.

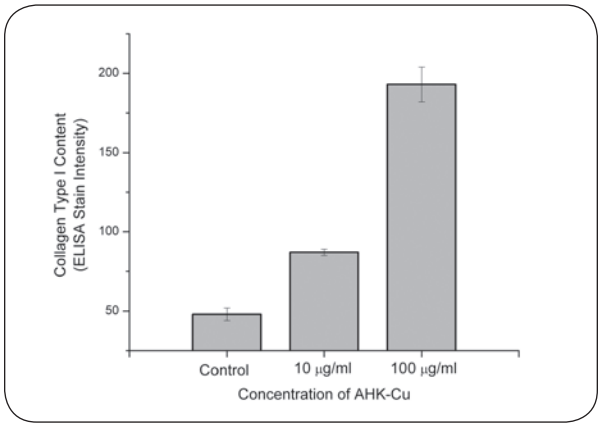

Figure 3. Effect of AHK-Cu on Dermal Cell Collagen Production.

Heliomoduline®

DNA damage is a critical aftermath of UV irradiation due to sunlight exposure and contributes to many of the visible aspects of photoaging. The DNA structure is constantly monitored by cellular mechanisms and repaired as needed to maintain healthy cells. DNA repair is a collection of processes in which the cell identifies and corrects damage to the affected DNA molecules. One of the important aspects of the ongoing DNA repair process is the recognition of the damage. Heliomoduline[11] (INCI name Gossypium Hirsutum (Cotton) Extract) is a mixture of peptides from cottonseed selected to prime the initial phase of DNA repair through the stimulation of the production of the protein termed XPC (the Xeroderma Pigmentosum group C protein). Rich in peptides purified from cotton seeds, Heliomoduline stimulates the natural DNA repair system and eliminates the damaged fragments. Skin-aging and inflammatory reactions are therefore reduced. XPC is an important DNA

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damage recognition protein involved in nucleotide excision repair[12,13]. The XPC targets the elimination of cyclobutane pyrimide dimers (CPD) by the repair enzymes, which in turn protect the cell from the mutagenic effects of UV radiation.

When tested on human fibroblasts irradiated with UVA, Heliomoduline significantly stimulated the expression of the XPC protein by 91 per cent above the control level (Figure 4).

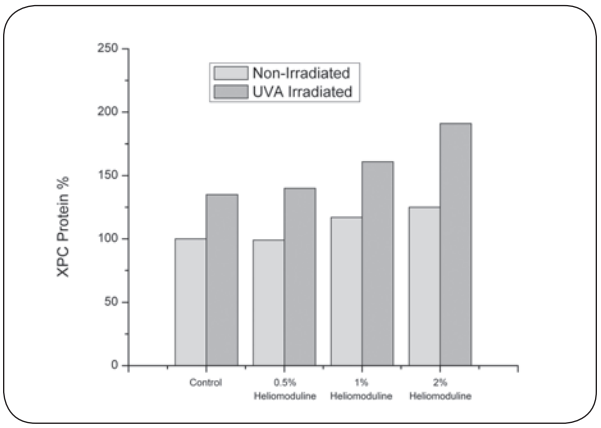

Figure 4. Enhanced Expression of XPC by Heliomoduline.

In other tests, Heliomoduline at a 2% concentration on cultured keratinocytes, it significantly reduces the level of cyclobutane pyrimide dimmers (CPDs) by 45%, thereby protecting the cell from the damaging mutagenic effects of UV irradiation (Figure 5).

In vivo tests in volunteers have shown that Heliomoduline limits inflammation and erythema. Tested at 4%, Heliomoduline leads to a significant reduction in the quantity of interleukins-1a induced by a UV radiation (-18%), and reduces the appearance of erythema by 7% in comparison to a placebo.

Prodew Amino Acid Moisturizer

Prodew is a moisturizer formulated to mimic the natural moisturization components of human skin[14]. Skin contains a number of natural moisturizing factors which consist of a combination of free amino acids, along with other physiological chemicals such as lactic acid, urea and salts. These are present primarily in the stratum corneum. Together these components are called "natural moisturizing factors"[15-18] and are responsible for keeping the skin moist and pliable by attracting and holding water—a property called hygroscopic.

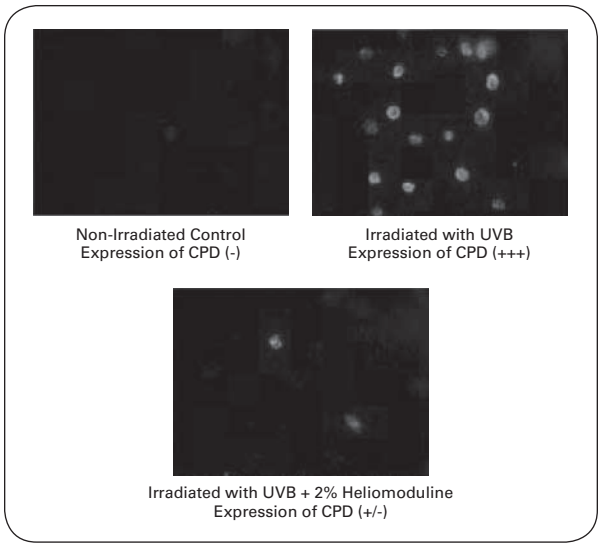

Figure 5. Reduction of CPDs by Heliomoduline in Keratinocytes.

The natural moisturizing factor is composed of approximately 40% of a mixture of amino acids, 12% PCA (pyrrolidone carboxylic acid), sodium lactate and a mixture of minor components. The amino acid composition of the ProDew component is modeled after that of the natural moisturizing factor and contains the same mix of basic, neurtal, and acidic amino acids. It also contains the PCA (pyrrolidone carboxylic acid).

In addition to providing enhanced moisturization by the mimicking of the natural moisturizing factor of skin, the Prodew amino acid mixture contains a combination of glycine, proline, and alanine similar to that found in collagen. Like any other protein, collagen consists of amino acids. Altogether there are 20 different kinds of amino acids in human cells. However, collagen is unusually rich in a few particular amino acids, among them glycine, proline, and alanine. Their presence enhances the available precursors in the skin to aid in the production of new collagen.

The Prodew moisturizer also contains the amino acid arginine which, in addition to providing moisturization as a component of the natural moisturizing factor is known to provide protection for skin cells and to aid in collagen production[19-21].

Collagen

Additional collagen precursor amino acids are provided by the addition of hydrolyzed collagen which contains all the necessary amino acids needed for optimization of collagen production.

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Summary

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