

Neova® DNA Total Repair™ Targets Damaged DNA and Combats the Effects of Photoaging.

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Abstract

Neova DNA Total Repair is formulated to combat the effects of photoaging on the skin. DNA repair enzymes encapsulated in liposomes target damaged DNA, within cells in the upper layer of skin, for protection from the photodamage that results from UV irradiation.

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 UV 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.

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

DNA Repair

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).

Liposome Delivery System

Neova DNA Total Repair is formulated with a combination of *Photolysosomes*, *Endosomes*, and *Mitosomes* — all liposome encapsulated DNA repair enzymes. Liposomes are small bubbles or vesicles composed of a phospholipid bilayer membrane, the same materials and structure as cell membranes.

They can be made to contain and deliver a variety of ingredients; as in this case, the DNA repair factors (Figure 1). The liposomes carry the repair enzymes across the stratum corneum and into the upper layers of skin cells. They deliver their contents to supplement the normal cellular processes of DNA repair.

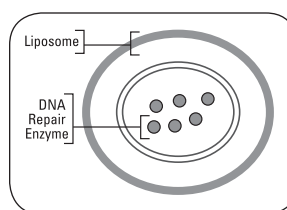


Figure 1. Liposome Delivery System.

Repair Ingredients

Photolysosomes:

Photolysosomes are liposomes containing a plankton extract which use visible light to reverse the damage caused by UV, in a process called photoreactivation.

Photolysosomes contain photolyase from the marine photosynthetic plant of the cyanobacteria group, called *Anacystis nidulans*.¹ The photoreactivating activity from these marine organisms is very efficient and is a key element in their defense against the high doses of solar UV in their natural environment.

Photolysomes by themselves reduce sunburn and have an “SPF” of about 3, using a modified SPF test. They also reduce UV immune suppression.^{1,2}

Comparable to chlorophyll, which also requires light activity, the mode of activation of photolyase absorbs visible light to directly cleave and reverse damage caused by shorter wavelength UV. Twelve human volunteers who have applied Photolysomes to UV-exposed skin had about a 52% reduction in UV damage. Photolysomes protects the cells of the skin’s immune system. In vitro tests demonstrate that Photosomes reduces the secretion of Interleukine-6 (IL-6).³

Photolysomes applied to skin which is then sun-or light-exposed, immediately reverse UV-induced DNA damage (Figure 2).⁴

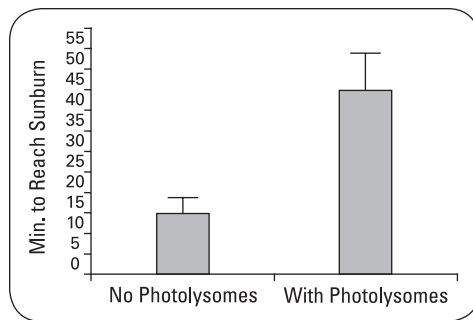


Figure 2. Photolysomes Plus Light-activation Protect Skin. Photolysomes plus light-activation protected skin from sunburn in 5 subjects. Results showed a 300% increase in protection in one hour.

Normal skin keratinocytes respond to the master immunity molecule interferon by displaying an important adhesion molecule (ICAM-1) on their surface. This adhesion molecule is necessary for proper communication with leukocytes. In UV exposed skin, ICAM-1 is not displayed; keratinocytes don’t respond to interferon. After treatment with Photolysomes, keratinocytes react appropriately and produce ICAM-1.^{1,4} In vivo tests were performed to demonstrate the reduction of “stress signals” by Photolysomes.

Endosomes:

Endosomes 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.

Delivery of these enzymes is well known to enhance removal of sun damage, increase cell survival and protect the immune system.⁵ In addition, it has shown to reduce the appearance of postsunburn Peeling (Figure 3).

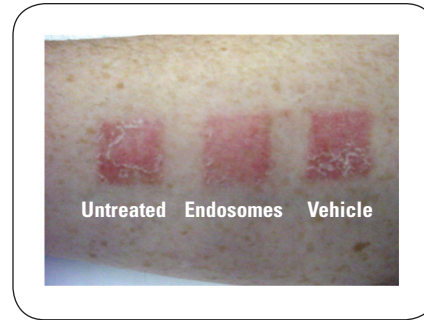


Figure 3. Endosomes Reduce Peeling. UV followed by Endosomes treatment for 3 days; peeling shown at day 8.

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.

Mitosomes:

Mitosomes contain a repair enzyme that recognizes the most common form of oxidative damage to DNA and initiates the repair process. Mitosomes contain an enzyme (named OGG1 for 8-oxoguanine DNA glycosylase) produced from the common plant *Arabidopsis* that recognizes this damaged base (8-oxo-guanine) and initiates its removal.^{6,7}

Mitochondrial DNA protection is also important to anti-aging activity. Damage from oxygen radicals is a main factor in aging. These reactive oxygen species come from pollutants in the environment, from UV-A induced reactions in skin, and from the body’s own stress responses. In addition, oxygen radicals are the inevitable side-effect of energy mitochondria. The accumulation of damage to mitochondria is considered an important element of aging.

These radicals damage DNA by oxidizing its nucleotide bases from to form 8-oxo-guanine. Mitosomes shorten the time for nucleus DNA repair from 24 hours to 2 hours (Figure 4). Mitosomes tested at 0.3% repairs 75% of the oxidative damage on

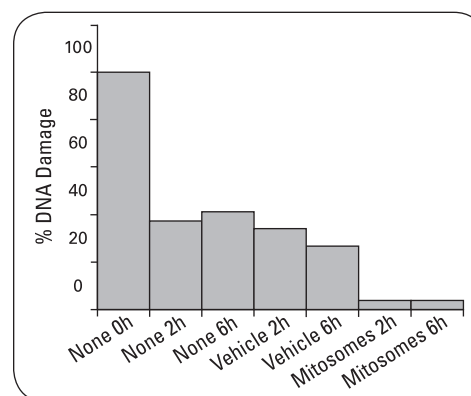


Figure 4. Mitosomes Increase DNA Repair. Engineered DNA repair enzyme from mustard plant *A. thaliana* and liposome delivery repairs oxidative damage to DNA.

DNA. In vitro testing at 0.5% shows that Mitosomes repair DNA in the mitochondria.

In vitro testing has shown that 1% Mitosomes completely repaired 8-oxo-guanine in cells in 2 hours, while 0.3% completed repair in about 3 hours⁶.

A vital feature of the Mitosomes enzyme is that it also protects mitochondria. The enzyme has a "mitochondrial localization signal" (MLS), which is recognized by the cells transport system, and guides it into mitochondria. This ability allows Mitosomes to repair the DNA in mitochondria after oxidative damage which occurs during normal cellular respiration.

L-Ergothioneine:

L-Ergothioneine is a natural amino acid found in human blood, liver and kidney. It is a powerful antioxidant that scavenges free radicals, including singlet oxygen and superoxide radicals, and exceeds other antioxidants, including idebenone, in neutralizing oxygen radicals.⁸⁻¹⁰

L-Ergothioneine is also suppresses the activity of both collagenase (MMP1)10 (Figure 5) and of elastase11 (Figure 6), both important to the prevention of photodamage to the extracellular matrix components.

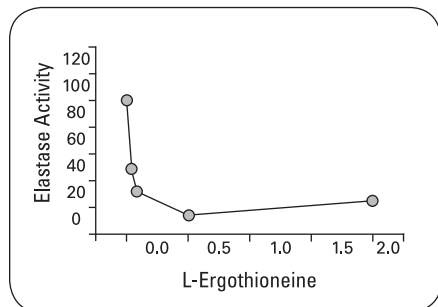


Figure 5. L-Ergothioneine Reduces Elastase Activity.

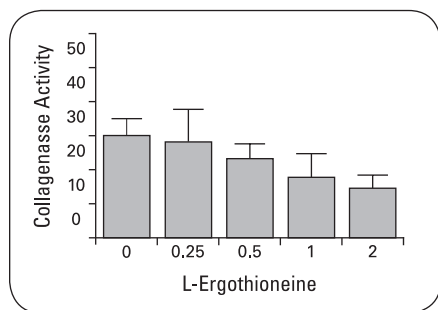


Figure 6. L-Ergothioneine Reduces Collagenase Activity.

Evodia Rutaecarpa Extract:

Another important ingredient is the Evodia Rutaecarpa Extract. This is a biometric (synthetic) mixture containing the same ingredients as the

natural form and is a potent inhibitor of UVB-induced PGE2 released by keratinocytes, thus decreasing associated erythema.¹²

Summary

DNA Total Repair is formulated to combat the effects of photoaging on the skin. DNA repair enzymes, encapsulated in liposomes, target damaged DNA within cells in the upper layer of skin, for protection from the photodamage that results from UV irradiation

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