Antiaging Effects of a Skin Repair Active Principle

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ABSTRACT: A particular extract of DNA from the gonadic tissue of male sturgeons is shown to have cell renewal effects with possible antiaging benefits for skin moisture, thickness, elasticity and a reduction in skin wrinkledness.

Sodium DNA is an ingredient with activity at the cellular level. This fact has led to its incorporation in numerous high-end antiaging skin care products. An explanation of that activity and results of several tests of one sodium DNA material are presented in this article.

The Many Levels of Aging

The slow, inevitable skin aging process is characterized by a progressive degeneration of the skin tissue as well as by a variety of attendant visible changes in the skin surface. The skin acquires a new appearance as wrinkles form and become increasingly conspicuous, the epidermal layer thins, and the skin decreases in firmness and elasticity. These changes show the passage from youth to adulthood to old age.

Such visible effects can be seen well before the age of 30 in humans and result from major changes in skin cells and the structures supporting the tissue. They are caused by a variety of genetic, metabolic, hormonal, biological and environmental factors.

The first and most notable sign of aging is a decrease in the skin’s water retention capability and the resultant decrease in dermis elasticity. This is visible when facial muscles are contracted and face wrinkles become deeper.

Moreover, as the years pass, biological and environmental damage accumulates and will not be repaired naturally. The most important changes concern collagen and elastin fibers, the basic constituents of the connective tissue. The amount of collagen, which is synthesized by the fibroblasts, tends to decrease as the activity of the fibroblasts is modified; this adds to the effects of the sun radiation and the fall in estrogen during menopause.

Action is necessary on different levels to slow down the skin aging process.

During menopause the elastin fibers atrophy as the dermis thins and their production is altered; thus, the dermis loses its viscoelastic properties. In addition, the epidermis becomes less efficient in performing its barrier function because of a loss of keratinocytes and a reduction in the thickness of the hydrolipid film thickness on its surface.

The skin tends to look dull, becomes dry and dehydrated, less firm and not homogeneous, grows thin and slackens. This is caused by a number of factors. On the one hand, the input of biological nutrients becomes poor due to reduced skin vascularization and slow cell renewal; on the other hand, the progressive degeneration of the dermal connective tissue and the structural changes in the epidermis play their role. Environmental stress must also be considered. Skin cells are exposed daily to UV rays, infrared (IR), osmotic stress and poor moisturization; therefore, they become an easy target for thousands of free radicals. Furthermore, psychological stress weakens the body’s defense system, making it more vulnerable to their attacks.

In conclusion, it seems clear that action is necessary on different levels to slow down the skin aging process.

Extracted DNA to Stimulate Cell Repair

More than 30 years ago in Russia, experiments were performed with the aim of developing an effective treatment for diseases related to ionizing radiation. Among the biologically active materials tested was deoxyribonucleic acid (DNA) extracted from the gonadic tissue of male sturgeons. The extract was carefully purified, depolymerized and neutralized with sodium hydroxide according documented procedures. The extract later received the INCI name Sodium DNA.

Positive feedback on sodium DNA was obtained in 1986, when it was employed to treat diseases related to the Chernobyl nuclear disaster, however the results were never precisely quantified. Indeed, in animal studies carried out some years later, the same com-
Sodium DNA acts to stimulate cell repair activity.

The most likely explanation of this ingredient's antiaging effect is based on the fact that some segments of DNA act as donors of uridine and cytidine bases, which are key molecules for the vitality of all cells. Sodium DNA passes through the cell membrane by pinocytosis (Figure 1), an endocytosis method of transport facilitated by sodium ions, which are combined with the polydeoxyribonucleotides. Therefore, the cells presumably use the acquired amount of sodium DNA both as a structural base to synthesize the nucleic acids and their cofactors and to metabolize their own DNA. These processes occur very easily in cells that are under metabolic conditions or extreme stress. This is the case of altered keratinocytes or fibroblasts, both of which are typical in aged skin. Thanks to the cell integration process, sodium DNA acts to stimulate cell repair activity, regenerate epithelial and granulation tissues and reduce the symptoms of inflammation, thus accelerating the healing of skin microlesions.

**In vitro Tests**

In vitro tests were used to assess the regenerating and photo-protective property of sodium DNA toward two cell types—keratinocytes and fibroblasts. The particular form of sodium DNA used in these tests was a highly purified commercial product with molecular weight was shown to protect and repair γ-radiation-induced lesions. In the following years, many clinical tests proved its efficacy at treating different types of skin lesions and illnesses. Scientists looked at its nucleotides, the basic units of nucleic acids. They found that nucleotide segments of DNA with a molecular mass from 250 to 500 kD were able to control the formation of wrinkles. Moreover, intradermal administration of DNA fragments in aesthetic surgery patients accelerated wound healing. This paved the way to research on sodium DNA as an antiaging active in cosmetics.

**Figure 1. Pinocytosis as a method of transport of exogenous molecules in the cell**
weight in the range 250–500 kD. This product will be called DNA-Na in the following discussion.

Keratinocytes and fibroblasts were obtained from two healthy donors by biopsy. Both specimens were grown in culture and incubated on plates containing DNA-Na at different concentrations.

The skin’s cell renewal rate decreases naturally as the years go by. This is the cause of skin aging. As a measure of the regenerating power, the growth rate of the cells treated with DNA-Na was determined at 24, 48 and 72 h after incubation and compared to the untreated cells used as controls.

To assess the property of protecting the cells exposed to radiation, the vitality of the cells treated with DNA-Na was tested 24 h after exposure to a UV source and compared to the untreated cells used as controls. Test results showed that DNA-Na stimulated cell proliferation and proved effective in protecting them.

In detail, it stimulated the growth of keratinocytes. Moreover, increased cellular growth was recorded 72 h after exposure at 1% concentration of DNA-Na (Figure 2). DNA-Na also improved the vitality of fibroblasts, whose growth was increased 24 h after exposure (Figure 3). Furthermore, phototoxicity tests suggested that DNA-Na had no harmful cytotoxic effects and carried out a protective function from the damage induced by UV rays toward fibroblasts.12,13

**In vivo Tests**

To assess the efficacy of an emulsion (Formula 1) containing DNA-Na aimed at increasing moisturization, elasticity and thickness and reducing wrinkledness, a test was performed after prolonged use and its results were compared to results from a placebo emulsion.14 This double-blind study enrolled 20 Caucasian female volunteers aged 30–60, with an average age of 49 years. These volunteers applied the test products on the two periocular zones, twice daily for eight weeks.

Numerous instrumental measurements of skin properties were taken before the first application and on the day following the final application.

- Moisturization level (in arbitrary corneometric units) was measured15 by a
It is related to the modification of conductance as measured by the probe applied to the skin surface.

- Elasticity was measured\(^{16}\) by a cutometer\(^{1}\). Its probe exerts a cycling suction on the skin surface and the consequent skin deformation is measured by electrical means.

- Skin wrinkledness was measured\(^{17}\) on skin imprints that are prepared with a quick-hardening resin\(^{4}\) and image analysis\(^{5}\) of skin replicas.

- Skin thickness measurements\(^{18}\) used scanning software\(^{6}\) and an ultrasound scanner at high resolution, with high frequency (320 MHz) ultrasound emission. This frequency allows skin scanning to a depth of 3 cm, with an axial resolution of 50 \(\mu\)m and a lateral resolution of 350 \(\mu\)m.\(^{18}\)

During the eight-week product application period, the test subjects were not allowed to use emulsions other than the ones being evaluated and were asked to abstain from prolonged exposure to UV rays.

The resulting instrumental data revealed that the emulsion containing the active principle had induced an increase in the mean basal values of skin moisturization from 60.9 corneometric units before treatment to 63.7 corneometric units after treatment, whereas the placebo values were essentially unchanged. The data also revealed a significant \((P<0.05)\) decrease of 4% in the mean basal values of maximum wrinkledness (Figure 4). However, the best results were recorded for biological elasticity and skin thickness. In the site treated with the active emulsion, the mean basal values of elasticity and skin thickness showed a highly significant \((P<0.01)\) increase of 25.6% and 8.7%, respectively.

Formulas 2–3 are given as guidance for an optimized use of sodium DNA.

**Conclusions**

Epidermal keratinocytes and skin fibroblasts of human origin were tested for cell vitality and phototoxicity. Within

\(^{4}\) Model CM 825 Corneometer, Courage & Khazaka, Germany

\(^{5}\) Cutometer 575, Courage & Khazaka

\(^{6}\) Silflo-Flexo Ltd., UK

\(^{7}\) Quantilines, Monaderm

\(^{8}\) Dermascan C Version 3, Cortex Technology, Denmark.

Dermascan C is a registered trademark of Cortex Technology.
the bounds of in vitro models, the test results suggested that nucleotide segments of sodium DNA in a proprietary material called DNA-Na in this article had a protective and regenerating effect on the skin. In vivo tests of a formulation containing DNA-Na showed a significant effect on increasing the basal values of moisturization, elasticity and skin thickness as well as in reducing skin wrinkledness.

The best results were recorded for biological elasticity and skin thickness.

Even if it is well-known that nucleotides, nucleosides, purine bases and pyrimidine bases enhance cell proliferation in vitro, the mechanisms involved in these actions are still controversial. These compounds are reported both to synergize with growth factors and to act directly on purinergic receptor A2 inducing per se a proliferative response. Moreover, they could stimulate the skin's photoprotective mechanisms and an immediate action against free radicals.19 Indeed, when cultured fibroblasts were incubated with radioactive amino acids in the presence of oligonucleotides, the incor-

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**Formula 2. Body cream for dry skin**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Water (aqua)</td>
<td>71.00% wt/wt</td>
</tr>
<tr>
<td>Betaine</td>
<td>1.00</td>
</tr>
<tr>
<td>Panthenol</td>
<td>0.20</td>
</tr>
<tr>
<td>Allantoin</td>
<td>0.10</td>
</tr>
<tr>
<td>Disodium EDTA</td>
<td>0.05</td>
</tr>
<tr>
<td>Glycerin</td>
<td>4.00</td>
</tr>
<tr>
<td>B. PVP/VA copolymer</td>
<td>0.20</td>
</tr>
<tr>
<td>C. Ammonium acryloyl-dimethyl taurate/VP copolymer</td>
<td>1.40</td>
</tr>
<tr>
<td>D. Olivol hydrolyzed wheat protein (and) ceteryl alcohol (and) glyceryl oleate (and) glyceryl stearate (and) potassium hydroxide</td>
<td>2.00</td>
</tr>
<tr>
<td>Butylene glycol dicaprylate/dicaprate</td>
<td>6.00</td>
</tr>
<tr>
<td>Phenoxyethanol</td>
<td>0.80</td>
</tr>
<tr>
<td>Salicylic acid</td>
<td>0.20</td>
</tr>
<tr>
<td>Tocopherol acetate</td>
<td>0.30</td>
</tr>
<tr>
<td>E. Potassium azeloyl diglycinate</td>
<td>1.00</td>
</tr>
<tr>
<td>Alcohol (and) water (aqua) (and) Plantago lanceolata (and) Berberis aquifolium</td>
<td>2.00</td>
</tr>
<tr>
<td>Arctium lappa (and) propylene glycol</td>
<td>1.00</td>
</tr>
<tr>
<td>Hedera helix (and) propylene glycol</td>
<td>1.00</td>
</tr>
<tr>
<td>Urtica dioica (and) propylene glycol</td>
<td>1.00</td>
</tr>
<tr>
<td>Water (aqua)</td>
<td>4.00</td>
</tr>
<tr>
<td>Sodium DNA</td>
<td>0.15</td>
</tr>
<tr>
<td>Diazolidinyl urea</td>
<td>0.30</td>
</tr>
<tr>
<td>Fragrance (parfum)</td>
<td>0.30</td>
</tr>
<tr>
<td>Silica</td>
<td>2.00</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100.00</td>
</tr>
</tbody>
</table>

**Procedure:** Prepare A in the main mixer under vacuum. Add B; after complete dispersion, add C, then mix and homogenize until complete swelling. Heat to 70°C. Melt D at 70–75°C; then add D to the main mixer. Homogenize ABCD for 10 min. Cool to 40°C while mixing; then add E in order. Cool to RT under vacuum.

**Characteristics:** White-ivory creamy emulsion; pH 5.3; viscosity (Brookfield RVT): 23000 mPa.s 5 rpm, 25°C.

**Comment:** Gel-cream easy to spread. The synergy between sodium DNA and the epithelizing, soothing, anti-inflammatory activity of the other actives protects and moisturizes, thus making the product especially suitable for dry skin.
poration of the tracer into secreted proteins increased significantly. In conclusion, regardless of the protection and repair mechanism involved, cell proliferation after contact with DNA-Na takes place, and the tested protection and repair mechanism proteins increased significantly.9

involved, cell proliferation after contact prohibited. is related not only to improved water appearance of age signs. This activity active principle proved in vivo to have a of skin thickness and elasticity. Action of drugs based on native DNA against RNA and DNA containing viruses, Klin Med (Mosk) 73(6) 3 (1995) 12. F Marzatico, Study concerning the in-vitro effects, in synergy with actives of vegetable origin, with antioxidant molecules and age signs at different skin levels. The principles include sodium DNA with antiaging

Comment: With emollient and rich texture, this emulsion is effective in controlling the age signs at different skin levels. The principles include sodium DNA with antiaging effects, in synergy with actives of vegetable origin, with antioxidant molecules and soothing, moisturizing, protective actives having firming and moisturizing properties.

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