

## Intensive Cell Regeneration and Cellular epigenetic rejuvenation



It combines the efficacy of ingredients from botanical and marine origin, with Epigenetic Science.

Futuristic cosmetics for clinically proven deep nutrition, regeneration and DNA rejuvenation.

### ACTIVE INGREDIENTS:

#### 1) **COBIOGENOL:**

**First active ingredient** focused on reducing the biological disorders produced by exposure to **Electromagnetic Radiation.**

Electromagnetic waves are a form of energy consisting in vibrations of electric and magnetic fields. We live in a sea of invisible electronic pollution, which is becoming toxic to our health.

We do not see or perceive them but are increasingly present in our domestic environment. Wherever we might be, non-ionizing radiation is all around us. We are constantly exposed to magnetic fields generated by appliances and domestic electrical installations: mobile phones, WIFIs, microwaves, television, radio, computers, etc.

As technology advances and the use of these devices increase, both at the workplace or private areas, our exposure to non-ionizing radiation is likely to intensify further.



### Special focus: Oxidative stress

The “digitization” of our world means that our cells are exposed to a continuously increased level of non-ionizing radiation, for which they have not adapted. In the last decade, EMR (Electromagnetic Radiation) levels have increased dramatically, and we are starting to realize its negative consequences. EMR is an environmental stress factor for human health, and skin

as a physiological barrier is the first objective of this radiation.



This exogenous stress leads to oxidative cellular stress, the formation of excessive reactive oxygen and nitrogen species and reaction products. It leads to a mitochondrial metabolic dysfunction: ROS causes a disruption of Mitochondrial function and cellular ATP Levels.

The massive oxidative cell stress leads to chronic inflammation. Several studies [1][1][3] have shown that skin exposure to cell radiation suffers several biological parameter alterations:

- ✓ Massive increase in free radical production (ROS)
- ✓ Massive Increase of pro-inflammatory cytokines
- ✓ Decrease in cell regeneration
- ✓ Reduction in structural proteins: key molecules involved in the stratification of the epidermis
- ✓ Lost in cohesion between keratinocytes
- ✓ TEWL increase: dehydration, the skin becomes more vulnerable and sensitive
- ✓ Stratum corneum weakening
- ✓ Disturbed skin refraction: lost in brightness, becoming dry and uncomfortable

**F**unctional ingredient proved to reduce the skin biological alterations, resulted from the exposure to EMR.

**It helps at the restoration process of the skin**, being a specific anti-stress agent. It is a **concentrated solution of purified marine glycogen**, ready to use at cosmetic skin care preparations.

Glucose is the most important sugar at the cellular level. It plays a very important role in the energetic metabolism of the cells. Its energy is used at the restoration process of the skin.

→ **Efficacy studies:**

- **Preventing and protecting from electromagnetic radiation-induced oxidative stress.**

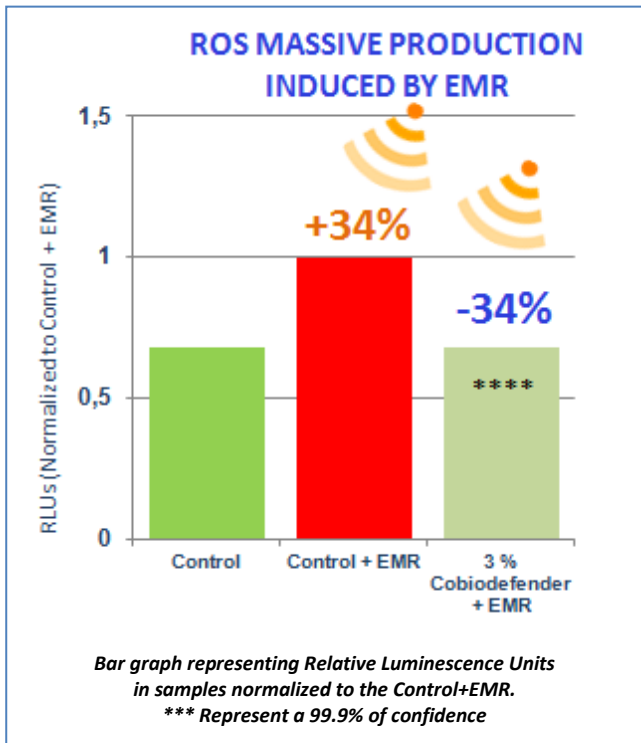
Several exogenous stimuli such as ionizing radiation, EMR, UV light, smoke, inflammatory processes and some human diseases trigger off free radicals production, causing severe damage in the mitochondrial membranes provoking the massive release of free radicals (ROS).

The goal of this study was to evaluate the capacity in protecting cells from the damage caused by induced electromagnetic radiation (EMR), by reducing oxidative stress (ROS).

To this end, Human keratinocyte cells were exposed to 6 hours of EMR

generated by a mobile phone to assess the response of skin cells to the induced oxidative stress and test the potential to prevent EMR-induced ROS.

After 6 hours exposition, EMR induced ROS accumulation  $34,26 \pm 3,13\%$  and treatment **reduced EMR-induced ROS production  $34,82 \pm 3,12\%$**  indicating a protective effect.



## Cellular epigenetic rejuvenation



### Epigenetics is a new paradigm in the Science of Anti-Aging.

It is the study of the mechanisms involved in the regulation of gene activity: the biological mechanisms that will switch genes on and off without altering their sequence.

Epigenetic change happens regular and naturally but can also be influenced by several factors including age, the environment (UV radiation, pollution...), lifestyle, emotions and diseases and much more that are yet to be discovered.

These factors discussed above, have the ability to "turn" or "turn off" certain genes, whose effects will be observed physically or physiologically.



The "on" or "off" effect of genes can be accomplished by three mechanisms:

- 1) MicroRNAs
- 2) Histone modification
- 3) DNA methylation

## What are miRNAs?

MicroRNAs (or "miRNAs") are chemical "switches". They are small fragments of RNA responsible for protein synthesis. These control mechanisms are key elements of epigenetic regulation. Its production is constantly modified by the environment and living conditions, including our emotions. MicroRNAs turn on and off numerous biological processes such as cell survival, skin repair, processes, hair growth...

## Epigenetics and the future of skin care



We can regulate microRNA expression to rejuvenate. miRNAs are involved in regulation processes such as cell cycles, DNA repair systems, reactions to oxidative stress, apoptosis, etc.

During aging and other external aggressions, chromatin ( the genetic material in the nucleus of our cells) becomes senescent and disorganized contributing to premature aging.

**Natural epigenetic active ingredient** that can regulate microRNA expression. This means that it has the ability to act on the expression of miRNAs and **"switch on" or " switch off" certain genes.**

• By **in vitro assays in human keratinocytes** (skin cells), been shown to have the ability to **rejuvenate cellular chromatin, making aging cells acquire characteristics of young cells.**

Increases the expression of miR-29b-3p, a miRNA that "**switch on**", or "activates" the synthesis of protein P53: **Protein guardian of genetic material**, which has a **potent antioxidant, anti-stress and anti-aging activity**.

• Under conditions of cellular stress induced by photo-oxidation (photo-aging) and oxidative stress, (by hydrogen peroxide), reduced the levels of **H3K79me3**, a miRNA considered as an **aging clock, inducing a cellular rejuvenation**.

### Summary of OXY-DEFENDER activity:

- ✓ Protection of oxidative stress caused by electromagnetic radiation
- ✓ DNA protection and rejuvenation
- ✓ Anti-aging activity
- ✓ Aged cells acquire characteristics of young cell

## 2) SYNERGISTIC COMBINATION OF SYNTHETIC PEPTIDES:

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3 synthetic peptides with the following functions:

• **A first peptide (Acetyl hexapeptide)** based on the transforming growth factor- $\alpha$  (TGF- $\alpha$ ), with a marked effect on skin rejuvenation.

This synthetic peptide based on the TGF- $\alpha$  has a very marked effect on the homeostasis of extracellular matrix (ECM). The technology used in obtaining this peptide makes it act as a mediator cell signaling certain cellular activities that are necessary to maintain the youthful and healthy appearance of the skin. Some researchers refer to TGF- $\alpha$  as essential for the production of collagen and elastin. They also believe that TGF- $\alpha$  may be the answer to maintaining youthful skin indefinitely.

• **A second synthetic biomimetic and sophisticated peptide (Acetyl hexapeptide)** with a similar action to the botulinic toxin type A one, in reducing facial gestural wrinkles due to the contraction of muscles during facial expression effect.

• **A third synthetic peptide (Palmitoyl hexapeptide) that prevents skin aging** by its potent inhibitory action against metalloproteases that are responsible for the destruction of the extracellular matrix.

With all these actives we achieve an extremely advanced ingredient in order to make a breakthrough in the aging technology, as both preventive treatment level is achieved.

This combination of peptides stimulates the ability of cells to repair the damage more efficiently and stimulates the synthesis of collagen and elastin.

Secondly, enhances the repair functions or "reconstruction" providing the cell with the precise signals so that they can interpret and follow the correct instructions as if they were young and healthy cells.



### 3) HOMEOSTATINE: *Enteromorpha compressa* marine pentasaccharide

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HOMEOSTATINE is a novel hydro-colloidal three-dimensional matrix of galactomannans of Andean origin, derived from the seeds of *Caesalpinia Spinosa* (Mol.) O.Kuntze, which sequentially releases, a marine pentasaccharide derived from the algae *Enteromorpha compressa* (L.) Nees.

This product helps recover and maintain **homeostasis in the dermal extracellular matrix**, which results in a **reduced amount of wrinkles**. The action of HOMEOSTATINE is aimed at preventing and/or fighting skin wrinkles. To that end, this product acts on the following processes:

- Increases the production of dermal collagen and other ECM components in fibroblasts.
- Inhibits the synthesis of metalloproteinases (MMP)
- Inhibits the synthesis of pro-inflammatory mediators

Thus, its application on the skin triggers a number of beneficial effects aimed at restoring the extracellular matrix homeostasis. The final outcome is a rejuvenated, less wrinkled, firmer, more elastic and better-moisturized skin.

#### → In-vivo clinical study: Evaluation of the anti-wrinkle effect

The anti-wrinkle effects of HOMEOSTATINETM were evaluated by FOITS (Fast Optical In vivo Topometry of human Skin). This technique allows for in vivo quantitative analysis of the skin surface topography by using an optical system (projection unit, measurement sensor, high-resolution digital camera, and software) designed to measure surface micro-relief.

The data recorded by this optical system on a 12 cm<sup>2</sup> surface yielded a “main wrinkle” value (SPt) and an “average area rugosity” (Spa) value, which were entered into a software designed to reconstruct the image of the analyzed surface.

This assay was conducted in the crow’s feet area of the face of 12 female volunteers, aged 44-58 years. The volunteers applied an HOMEOSTATINE 2%-containing cream on one side of the face and a placebo cream on the other side, twice a day for 8 weeks. Measurements were made at the beginning (T0) and at the end (T56) of the treatment.

Reduction in wrinkles size and depth can be observed for the HOMEOSTATINETM -treated area, while no change can be noticed for the placebo-treated area:

#### 4) COMBINED COENZYME Q10 + VITAMIN E:

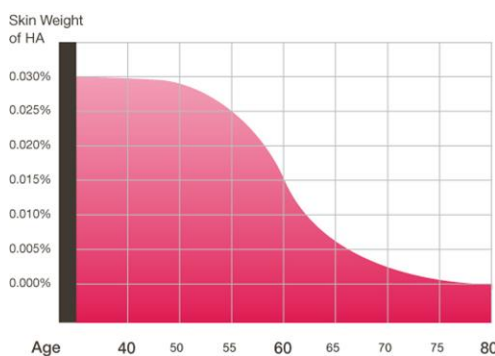
Coenzyme Q10 and vitamin E are the most important antioxidants in the skin. Both structurally closely interrelated, they are naturally contained in almost every cell of the body including the skin. CoQ10 is essential for energy synthesis (ATP). Together with vitamin E, they form a defense against oxidative attack. Studies by Quinn et al. showed that both antioxidants are integrated together in the lipid regeneration cycle. Once vitamin E is oxidized to its tocopheryl radical can be reduced by Ubiquinol regenerating Tocopherol.

Topical application of this combination of Coenzyme Q10 and vitamin E helps to balance the level of endogenous antioxidants.

#### 5) HYALURONIC ACID:



Hyaluronic acid (HA) is a polysaccharide from the type  $\beta$ -links glycosaminoglycans, having a structural function, such as chondroitin sulfates. It has the capacity to absorb more than 1000 times its volume in water. That is why it is used in epidermis moisturizing the as it reconstructs the fibers that hold skin tissues, giving a better shape. With a very high viscoelasticity, it is a natural component part of the skin and is essential to fight aging and wrinkles due to its high moisturizing power.



In the dermis, hyaluronic acid is the main component of the extracellular matrix (ECM). Fibroblasts are a cell type responsible for the production of collagen and elastin in the skin. ECM extracellular matrix is the space between the skin cells. This makes the skin soft, smooth and elastic.

Young skin (soft and elastic) contains high amounts of HA (Hyaluronic acid).

Hyaluronic acid contained in GOLD 24K FLASH, is of biotechnological origin, has a molecular weight of 50-110 kDa:

- ✓ Retains moisture and elasticity in the tissues (moisture retention in the extracellular matrix (ECM))
- ✓ Protects against environmental stress
- ✓ Helps to reduce the appearance of wrinkles and expression lines.

## 6) SQUALENE: Natural water balance

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It is a terpene with antioxidant properties naturally present in our skin, binding to the cell membrane, helping to eliminate toxins and disabling free radicals.

On the skin, it acts as an oxygen radical scavenger, thereby protecting the skin from lipid peroxidation due to exposure to UV rays and other sources of ionizing radiation.

With age, the production of this compound decreases and since it is one of the main constituents of our lipids, (25% approx), this reduction causes over the years that skin gets dehydrated more easily and become dryer.

It is an extraordinary emollient, keeps the skin hydrated also is non-comedogenic and quickly absorbed.

## 7) ALOE VERA: Excellent moisturizer

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Aloe juice is obtained from the pulp of its fleshy leaves by physical processes. It consists of a **complex mixture of more than 20 substances**, including mono and **polysaccharides, anthraquinones, enzymes, vitamins (A, B1, B2, B6 and B12), salicylic acid, saponins, sterols, and minerals [4]**. It's moisturizing, soothing, anti-inflammatory, anti-allergic and regenerative properties are well known.

**Fatty acids:** cholesterol, campesterol,  $\beta$ -sisosterol and lupeol. All have anti-inflammatory action. Lupeol also has antiseptic and analgesic properties.

It contains **phytohormones: auxins and gibberellins** that aid in wound healing and have anti-inflammatory action [5].

Aloe juice has been shown to **enhance the cellular structure of fibroblasts** and to **accelerate the process of collagen synthesis [6]**.

It is an excellent moisturizer, so it captures atmospheric water by moisturizing in depth as it acts on the three layers of skin: epidermis, dermis, and hypodermis.



## 8) CARROT OIL: Pro-vitamin A

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Carrot is one of the nature's products with the **highest percentage of beta-carotene (provitamin A)**. Carotenes are potent antioxidants that are applied to the skin, prevent cellular oxidation and therefore delay skin aging. This active principle stimulates the regeneration of the skin and is essential to synthesize vitamin A.

Carrot oil is also very rich in **vitamin E (tocopherol)**, essential for generating new skin. It favors the circulation in the small capillaries of the epidermis and therefore it reaches the nutrients that feed the cells giving them smoothness and elasticity.

- ✓ Carrot oil protects the skin from the harmful effects of the sun and stimulates the synthesis of melanin:

It is very beneficial to protect the skin in summer. On the one hand, it contributes to maintaining the dermoprotector mantle of the skin and prepare the skin for the exposure to solar radiation. It is soothing and acts effectively against dehydration and swelling produced by the heat accumulated in the skin, being ideal as a soothing after-sun. In addition, it stimulates the secretion of melanin and its continued use preserves for a longer time the tan tone that the skin has acquired in summer.

- ✓ Dermal Regenerator:

Its ability to stimulate cellular regeneration makes it effective in **treating wounds, scars**, skins affected by radiotherapy and to regenerate rough skin of elbows and knees. Vitamins A and E, as well as beta-carotene, are foods that have great conditioning properties. They are very useful in the conditioning of the skin.

## 9) MACADAMIA OIL: Elasticity and tone

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Macadamia oil is **very rich in monounsaturated fatty acids (palmitoléico and oleic acid)** so it helps to prevent the oxidation of cells, regenerates the skin in depth and helps to **fight the appearance of wrinkles** and also give it very properties Soothing and soothing. Returns elasticity, turgor, and tonicity to devitalized skin.

## 10) SHEA BUTTER: intense and lasting moisturizing power

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Shea butter is composed mainly of **palmitic acid (2-6%)**; **Stearic acid (15-25%)**; **Oleic acid (60-70%)**; **Linolenic acid (5-15%)**; **Linoleic acid (<1%)**, as well as an unsaponifiable fraction that confers it a **great moisturizing and emollient capacity**. It contains **antioxidants** such as **tocopherols (vitamin E)** and **catechins** (which are also found in green tea).

Other specific compounds have been detected as **triterpene alcohols, with anti-inflammatory properties**; **Esters of cinnamic acids, which have a limited ability to absorb ultraviolet (UV) radiation**, and **lupeol, which slows down the skin aging** phenomenon by **inhibiting enzymes** that degrade skin proteins. Shea butter also protects the skin by **stimulating the production of structural proteins by specialized dermal cells**. Its components give it an **intense and lasting moisturizing power**, improving the elasticity of the skin due to its nutritive properties and its high vitamin F content, a vital component of the cellular membranes. It is also an anti-irritant par excellence, very suitable for skins that redden easily, and with an allergic tendency.

## 11) SUNFLOWER OIL

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Sunflower oil is a vegetable oil of natural origin obtained from the seeds of the sunflower flower.

It is an oil especially rich in **vitamins, caffeic acid, and unsaturated fatty acids** which for the human are essential since it can not produce them being, therefore, a **natural antioxidant** that helps to keep the skin in good condition being very useful in the treatment of dermatitis.

## 12) SWEET ALMOND OIL: Skin barrier restoration

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It has a **powerful restorative activity of the barrier function of the skin**. Sweet almond oil is an oil with a **strong emollient power** that favors the regulation of the lipid phase of the skin mantle, due to its content in **unsaturated fatty acids**. By increasing the cutaneous levels of these essential fatty acids, increases the production of **beneficial eicosanoids with an anti-**

**inflammatory effect.**

The unsaponifiable fraction of the sweet almond, consisting mainly of **squalane, tocopherol, and phytosterols**, guarantees to the skin the contribution of **highly nutritive substances**, acting on the dermic connective tissue, **favoring the tone and the elasticity** of the skin.

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