There are several different parameters that influence the aspect and attractiveness of skin in an important way, such as moisturization, firmness or wrinkles. However, one of the concepts that has most influenced the different standards for beauty throughout history is skin pigmentation, or tone.

A radiant complexion is associated with beauty. The pigment distribution, melanin, and skin texture vary according to health status and age. An irregular coloration is an indicator of the age of the skin, since the aging is associated with the presence of dark spots.

When the body generates too much melanin to protect itself from this aggressions, or simply because of aging, accumulations can be created causing blemishes or changes in skin tone**. This disorder is called hyperpigmentation and can affect all skin types.**

Hyperpigmentation is the third major cosmetic concern, as it is one of the obvious signs of the decline of youth. For this reason, the cosmetic goal is to reduce blemishes and age spots, and to improve the skin tone.

- ✓ It allows to recover the luminosity and light lost as a result of the chronological aging, or an undue exposure to the UV rays (photo-aging), as well as numerous aggressions to which our skin is exposed daily (pollution, cold , tobacco, poor diet, lack of sleep, stress, ...).
- ✓ With a continuous use, it manages to homogenize skin tone and reduce unwanted pigmentation.
- ✓ Contributes to reduce wrinkles and lines of expression through the synthesis of collagen and elastin.
- ✓ It increases skin's the face lack of firmness, smooth and elasticity by stimulating the synthesis of collagen which contributes to regenerate the tissue support dermal matrix.

BIOACTIVE:

1) VITAMIN C

CORUM 9515 Corum 9515 is a new generation of stable vitamin C derivative that provides superb whitening effects, serves to promote collage synthesis and protects DNA damage.

- ✓ **Effective and stable skin lightening agent**
- ✓ **Balance the skin tone**
- ✓ **Reduce dark spot**
- ✓ **Prevent photoaging**
- ✓ **Increase collagen synthesis**
- ✓ **Excellent anti-oxidation properties**
- ✓ **Scavenge radical**
- ✓ **DNA protection**

Vitamin C, or L-ascorbic acid, acts as a cofactor for collagen synthesis. It has a high regenerating ability, by its collagen synthesis stimulating activity.

Vitamin C is essential for the proline hydroxylation, therefore in the development and maintenance of collagen integrity. In addition, vitamin C inhibits the synthesis of Extracellular Matrix Metalloproteinase enzymes of, enzymes which stimulates collagen degradation in the dermis.

Vitamin C's collagen stimulating properties provides it with wound healing properties, caused by trauma, cuts, burns, or surgery. It is also suitable for the formation of new tissues.

Vitamin C belongs to the group of water soluble vitamins, and like most of them, it is not stored in the body for a long period of time, but in small quantities which are eliminated through urine. For this reason, Vitamin C daily administration is important in order to provide sufficient antioxidant protection.

Its chemical structure is similar to that of glucose (in many mammals and plants, this vitamin is synthesized from glucose and galactose). All compounds which possess the biological activity of ascorbic acid are known as Vitamin C. We should note that the only active form of Vitamin C is L-Ascorbic Acid.

As Vitamin C is a water-soluble substance, it is rapidly eliminated from the organism. Our body

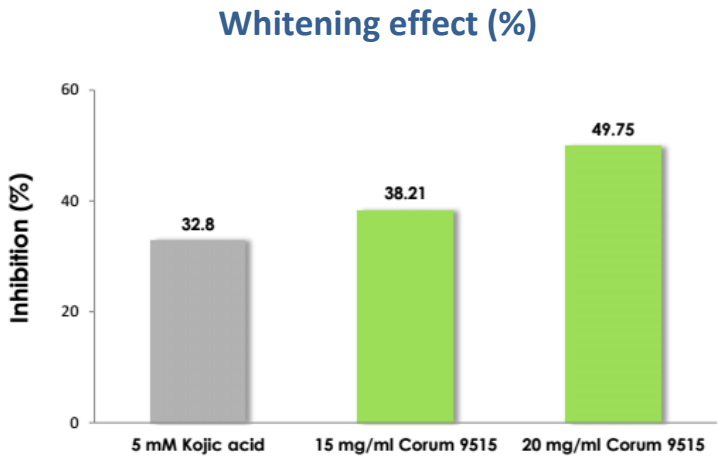
tends to protect vital organs, so any vitamin deficiency is felt primarily in the skin (less vital organ), which explains the importance of its topical application.

Clinical Efficacy Studies

1- In-vitro whitening activity study - melanin assessment on human melanocytes:

Theophylline was incubated with melanocytes in order to increase melanin production. Subsequently, Ethyl Ascorbic Acid was added at concentrations of 15 mg / ml and 20 mg / ml respectively, and comparing with kojic acid, a known anti-pigment ingredient.

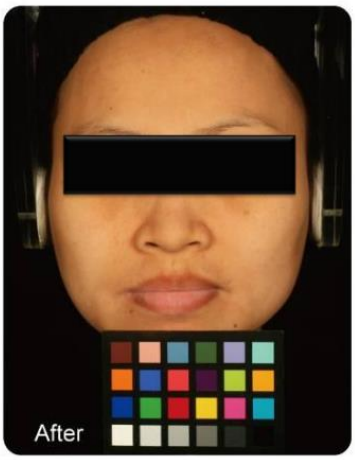
At both concentrations of Ethyl Ascorbic Acid clear depigmentation effect was observed, obtaining 49.75% whitening effect with 20mg/ml Ethyl Ascorbic Acid:



2- In-vivo whitening efficacy

A study on the in-vivo whitening capacity of Vitamin C (as Ethyl Ascorbic Acid) for 28 days in 20 healthy Asian women aged 25 to 40 years old with skin type III was performed.

A significant improvement in the skin lightening measured by chromatography observed:

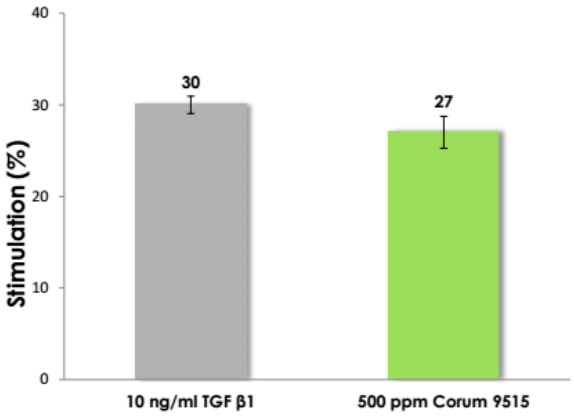


3- Stimulation of natural collagen synthesis:

The Stimulation of natural collagen synthesis activity was evaluated on human fibroblast culture.

After 24 hours of culture, the collagen was quantified using a Sircol Quantification Kit. Vitamin C had a similar effect on collagen synthesis that of TGF β1 (growth factor which stimulates collagen synthesis):

Stimulation of natural collagen synthesis:

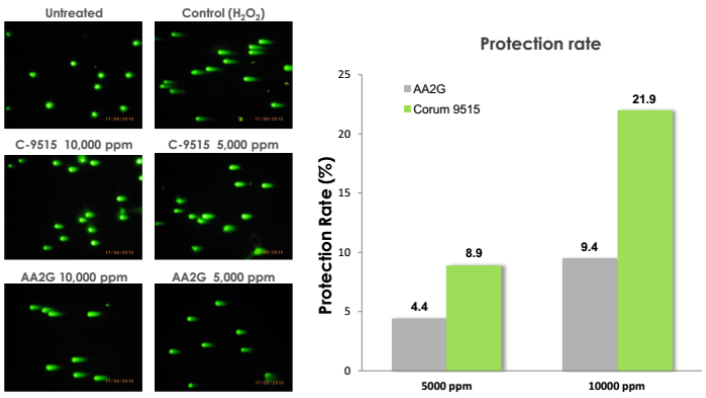


4- DNA protection by Comet assay in human fibroblasts:

The comet assay is a technique used to detect DNA damage and cell repair capacity. It is based on the DNA labile alkaline lysis at sites where damage has occurred.

When DNA is in good condition, it has a highly organized association with matrix proteins in the cell nucleus. When damaged, this organization is interrupted. The single DNA strands losing their compact structure and relaxes, expanding out.

Human fibroblasts were treated with Vitamin C (Ethyl Ascorbic Acid) for 24 hours, and then exposed to 100 mM H2O2. It was shown that Vitamin C at concentrations of 5000 ppm and 10,000 ppm, was able to protect DNA:



Vitamin C Mechanisms of action:

Vitamin C anti-aging action is exerted through several ways:

1. Synthesis and repair of dermal collagen

Deficiency of ascorbic acid (AA) produces significant alterations in connective tissue, since Vitamin C is essential for collagen synthesis.

Vitamin C is essential for the transformation of proline in hydroxyproline and lysine in hydroxylysine (essential constituents of collagen). Consequently Vitamin C offers stability to the extracellular matrix.

The local increase of vitamin C means therefore significantly promote collagen production; therefore improved skin elasticity and greater resistance in wall capillaries are assessed.

2. Antioxidant activity

Vitamin C protects cells from free radicals. From all the scientific publications regarding Vitamin C, the most interesting are those related to the photoprotective effect of ascorbic acid when topically applied.

In mouse and pig it showed that when ascorbic acid is applied before UV radiation exposure, the negative consequences it causes in the skin (erythema, histological changes, "burned cells", wrinkles ...) decreased significantly .

A study published by the Journal of Investigative Dermatology in May 1996, describes how topical application of vitamin C, vitamin E and Selenium protects rats skin cells from damage caused by exposure to UVB rays.

In parallel, the British Journal of Dermatology some years before, evidenced this protective effect of vitamin C, when used topically, on pig skin damaged by ultraviolet radiation.

The Spanish Journal of Physiology published a study showing how direct application of vitamin C protects, and thus prevents the aging in human skin cells in culture subjected to a strong oxidation stimulus with hydrogen peroxide.

One might think that its photoprotective effect was physical, that is to say, topical vitamin C behaves as a sunscreen, and however, its absorption spectrum has nothing to do with the emission of UV radiation. Later it was found that UV radiation produced a significant decrease in the levels of ascorbic acid in the skin.

All this goes to show that the UV light, after exhausting all the vitamin C present in the skin, cause an increase in free radicals, making manifest the neutralizing action of vitamin C.

3. Anti-inflammatory action

Vitamin C inhibits NFkB, which is responsible for the activation of a number of pro-inflammatory cytokines. Therefore, Vitamin C has a potential anti-inflammatory activity and can be used in conditions like acne vulgaris and rosacea. It can promote wound healing and prevent post-inflammatory hyperpigmentation.

4. Vitamin C as a whitening agent

When choosing a whitening agent, it is important to differentiate between substances that are toxic to the melanocyte and substances that interrupt the key steps of melanogenesis. Vitamin C falls into the latter category of depigmenting agents. Vitamin C interacts with copper ions at the tyrosinase-active site and inhibits action of the enzyme tyrosinase, thereby decreasing the melanin formation.

FERULIC ACID

- ✓ Reduces melanin pigmentation by inhibition of tyrosinase and by chelation of Cu2+ at the level of melanocytes.
- ✓ Reduces melaninisation of melanosomes.
- ✓ Promotes desquamation of the superficial horny layers and the melanin pigmentary residues contained therein.

1. decrease the pigmentation of skin (uncovered areas),
2. help lighten the skin.

It is a phenolic compound, antioxidant of vegetal origin with free antiradical properties, protector against UV radiation and chelating of metals. Its mechanism of action includes, on the one hand, the inhibition of tyrosinase and the chelation of copper in melanocytes (by these two mechanisms melanin synthesis is reduced), and on the other hand it accelerates the desquamation of the corneous layer, eliminating the present.residues of pigmentation

Helps to slow down the oxidative stress of cells and DNA. If applied after sunbathing accelerates the recovery of the skin.

DEPIGMENTING EFFECT (CLINICAL TEST)

The depigmenting efficacy of an emulsion containing 2% DERMAWHITE® NF LS 9410 was compared to that of a placebo emulsion and a benchmark emulsion containing 2% Arbutin.

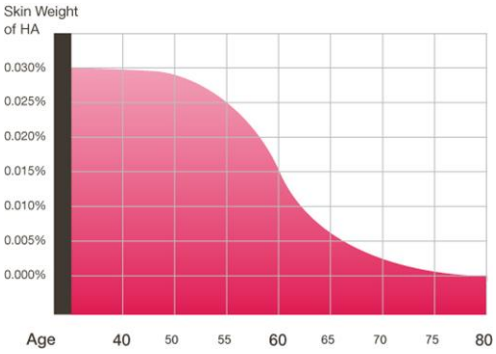
• Double-blind study on 42 Asian female volunteers, 18 to 45 years old, with dark or very dark skin on the upper side of the forearm.
• Bi-daily treatment for eight weeks.
• Skin pigmentation was measured using colorimetry (Mexameter®, Courage and Khazaka) before and after eight weeks of treatment

Only the emulsion containing 2% DERMAWHITE had significant depigmenting efficacy after eight weeks of treatment.

2) HYALURONIC ACID:

Hyaluronic acid (HA) is a polysaccharide from the type β- 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.

3) ALOE VERA: Excellent moisturizer

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, β-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.

4) HAMAMELIS VIRGINIANA: Decongestant and antioxidant

El extracto de hamamelis se obtiene a partir de las hojas de Hamamelis virginiana L. Hamamelis tiene propiedades medicinales sobradamente conocidas. Entre sus propiedades cosméticas se encuentran las siguientes:

- **Activity on blood circulation**

This activity is due to the flavonoids content of hamamelis extract.
Several tests demonstrated that hamamelis flavonoids
have phlebotonic, vasoprotective and capillarotropic effects, and that they reduce blood capillaries permeability. These effects are reinforced by the hamamelis leucoanthocyanidins.

- **Antimicrobial activity:** Due to its content in tannins and proanthocyanidins, it possesses bacteriostatic and antiviral properties (Alonso, J., 2004).

- **Antioxidant activity:** Its content in tannins, especially hydrolyzable tannins, and flavonoids inhibit lipid peroxidation.

5) CALENDULA EXTRACT: Re-epithelizing and healing

Calendula is one of the best-considered plants for treating sensitive skin.

It is one of the most recognized plants in medicinal treatments. It is composed of flavonoids and triterpenes whose properties are beneficial to treat the different conditions of the skin.

It is ideal for the dry and scaly skin as it moisturizes, rejuvenates the skin, improving its elasticity.

Los extractos de las flores de C.officinalis muestran un amplio espectro de acciones farmacológicas, de ahí la gran importancia de los extractos de caléndula en la cosmetología moderna [1].

- **Reepithelizing and wound healing activity**

This is one of the most extensively used actions of calendula. It is due to the presence of polysaccharides (mucilage), flavonoids (especially quercetrin-3-O-glycoside), triterpenes and carotenes. These substances act on the metabolism of glycoproteins and on the collagen fibers. Creams containing calendula floral extract 5% in combination with allantoin,

promoted remarkable epithelization with especial intensity on the metabolism of glycoproteins and collagen fibers during tissue regeneration.

More recent research suggested that the water extracts of calendula flowers, applied on skin wounds, play a role as micro-vascularization inducing agents, thus contributing to speed up healing [1].

According to ESCOP, calendula (flower) is recommended for the local treatment of skin inflammation, and as a co-adjuvant in wound-healing [2].

The calendula extract polysaccharides have concentration-dependant adhesive effects (absorption effects) on the epithelial tissue of the oropharyngeal mucosa. This action contributes to its therapeutic effects to treat oropharyngeal mucosae inflammation (www.fitoterapia.net).

For these reasons, the Calendula extract is highly recommendable to formulate cosmetic products with tissue regeneration action.

- ### Moisturizing activity

This activity of calendula is due to its saponin and mucilage content. These active principles have moisturizing properties (water retention and water release to the medium).

Due to its moisturizing activity, Calendula is ideal for formulating cosmetic products for the dry, irritated or delicate skin.

Anti-inflammatory activity

The topical use of calendula preparations is rather extensive in cosmetics as well as in dermatology because of its **anti-inflammatory activity**. The clinical efficacy of this plant has been long demonstrated. In vivo studies using rats evidenced the anti-inflammatory activity (on inflammation induced by carrageenan and prostaglandin E1) and the inhibitory action on leukocyte infiltration.

Thus, Calendula is highly recommended to formulate cosmetic products for sensitive and/or irritated skin.

6) ASIAN CENTELLA EXTRACT: Dermoprotectorr

Asian centella (Hydrocotile asiatica), contains an essential oil, triterpene saponins (asiaticosides, brahmosides), alkaloids (hidrocotilina), tannins, phytosterols, vitamin K and mineral salts (magnesium, calcium and sodium).

Highlights include its astringent, antiseptic, anti-inflammatory and dermoprotective virtues.

The triterpene derivatives stimulate the formation of fibroblasts, cells indispensable for repairing damaged tissues. In addition, they regulate the incorporation of collagen to the skin.

Collagen synthesis stimulating activity

The active ingredients of the selected triterpenes of Centella asiatica have shown to have modulating properties on the development and metabolism of connective tissue.
Centella asiatica has been documented to aid wound healing in several scientific studies. One of the primary mechanisms of action of this plant appears to be the stimulation of type-1 collagen production.

Triterpenes of Centella asiatica may help to improve wound repair with a better reepithelialisation and a normalisation of perivascular connective tissue allowing an improvement of the venous wall tone and elasticity.

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[1] Kasuga, 2010

[2] Alonso J., 2004

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[4] **Potential of herbs in skin protection from ultraviolet radiation.**

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[6] **Dietary Aloe Vera Supplementation Improves Facial Wrinkles and Elasticity and It Increases the Type I Procollagen Gene Expression in Human Skin in vivo.**

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