

HA-PLANT

new generation of anti-wrinkles
system designed to improve
skin elasticity and to decrease
deep wrinkles



HA-PLANT

HA-PLANT is a new generation of anti-wrinkles product made by short hydrolyzed hyaluronic acid molecules (50000 daltons) and Kaempferol (an effective hyaluronidase inhibitor) encapsulated into niosomal vesicles to increase permeation of both through the skin.

HA-PLANT is an innovative and multifunctional active ingredient **that** improve viscoelastic properties of skin and to decrease deep wrinkles.

Cosmetic Use

- Anti-wrinkle
- Moisturizing
- Structuring and firming
- Regenerating and repairing

Main Components

Active components	Origin	Skin Benefits
Hydrolyzed Hyaluronic acid	Biotechnology	Reduce wrinkles and hydrates
Kaempferol	Botanical	Inhibitor of hyaluronidase

INCI/CTFA-Declaration

Hydrolyzed Hyaluronic Acid, Kaempferol, Magnolol, Honokiol, Polyglyceryl-10 Oleate, Polyglyceryl-6 Oleate, Apricot Kernel Oil Polyglyceryl-6 Esters, Sorbitan Palmitate, Aqua/Water.

Formulating with HA-PLANT

- DOSAGE: 1-3%
- SOLUBILITY: soluble in water, insoluble in oil or fats
- MODE OF INCORPORATION: dilute in a part of water before you embed inside of the cosmetic product. Do not heat it above 50° C.

HYALURONIC ACID AND SKIN AGING

Skin is the organ which contains most of the body's hyaluronic acid (50% of the total body HA). In normal skin HA is found in the intercellular spaces of epidermis except in the upper granular layer and in the stratum corneum. In the dermis, HA is present uniformly with a higher concentration at below of the basement membrane and around the skin appendages. Several studies have demonstrated that HA has many functions in skin in particular it can immobilize water in the intercellular matrix and thereby change the dermal volume and compressibility. This capacity to work as a water

reservoir contributes significantly to regulate the skin elasticity. HA is also involved in many others functions as: tissue repair, cell proliferation, differentiation, inflammation etc.

With increasing age, a reduction of HA quantity and a progressive reduction of its degree of polymerization occurs in the skin. Both these two processes occur into epidermis after activation of hydrolytic enzymes known as hyaluronidases. In the elderly, HA is only present in the upper dermis and this explains the dryness, the loss of elasticity and formation of wrinkles.

A treatment that can rejuvenate the skin by significantly reducing wrinkles must necessarily increase HA in the epidermis and/or inhibits the activity of hyaluronidases.

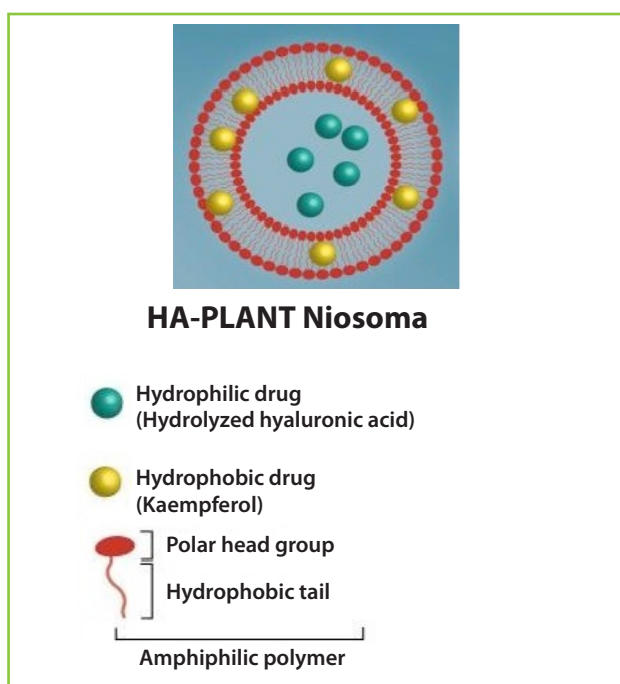
HA-PLANT is the association of short hydrolyzed HA molecules and Kaempherol, a strong anti-hyaluronidase inhibitor, both encapsulated into very small niosomal vesicles able to enhance the penetration in the deeper layers of epidermis

HA-PLANT represents an exciting way, without resorting to injectable dermal fillers, to treat wrinkles restoring the natural content of hyaluronic acid in the skin. The skin will return firm, hydrated and elastic in a very short time.

Niosoma as a potent skin delivery system for effective cosmeceuticals

HA-PLANT is a special ingredient for skin care formulation in which the oligo hyaluronic acid and Kaempherol are contained into very small vesicles (150-250 nm) known as niosomes. Niosoma is an effective drug delivery system particularly suitable for pharmaceutical and cosmeceutical. It consists of vesicles formed by the self-assembly of non-ionic surfactants in aqueous media in which the active compounds are trapped inside. The niosome is made of a surfactant bilayer with its hydrophilic ends exposed on the outside and inside of the vesicle, while the hydrophobic chains face each other within the bilayer. Such as liposomes, niosomes are able to increase drug stability, enhance the effectiveness, prolong circulation time and promote uptake of the entrapped drugs into the target site. However, respect liposomes, niosomes has additional important advantages such as:

- ability to entrap both hydrophilic and hydrophobic drugs
- greater chemical stability
- no problems related to phospholipids purity
- low toxicity due to non-ionic nature
- no requirement of special precautions and conditions for formulation
- production without the use of unacceptable solvents.



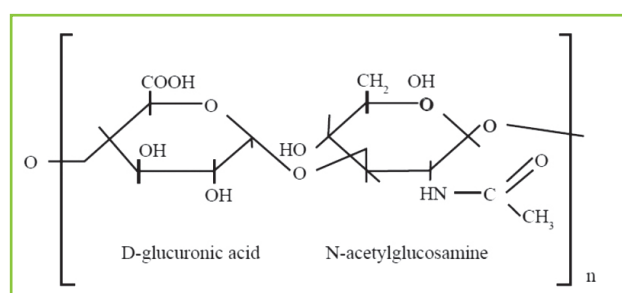
HA-PLANT increases the stability of entrapped active agents, improved bioavailability of poorly absorbed ingredients and enhanced skin penetration improving percutaneous passage of biologically active molecules through human stratum corneum which is known to be a highly impermeable protective barrier.

HA-PLANT: an innovative and powerful active for improvement each skin layer.

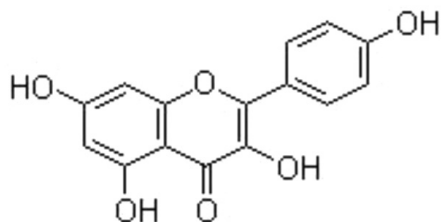
HA-PLANT is a niosomal active ingredient especially designed to reduce wrinkles and dryness. It consists of a complex of short hydrolyzed hyaluronic acid molecules of about 50000 Dalton and kaempferol a strong

hyaluronidases inhibitor. **HA-PLANT** is fast and easily absorbed in the deeper layers of skin.

- **Hyaluronic acid** is a linear polysaccharide composed by two regularly alternating monosaccharides, D-glucuronic acid and N-acetylglucosamine. It is estimated that the total amount of HA in all tissues of the human body is about 15g, of which about half is present in the skin. HA is the main component of extracellular matrix and it has the ability to bind 1,000 times its volume in water. This water-binding capacity contributes significantly to the elasticity of the skin and makes it the perfect substance for hydrating and for adding volume to the skin. However, all these potential beneficial features are limited by the molecular size of HA, which can reach up to 2000 kD interfering with the efficient skin penetration. To overcome this limitation, **we** used a dual strategy: 1) developed a short hydrolyzed hyaluronic acid molecules of about 50 kD; 2) encapsulated them into very small and skin penetrating vesicles known as niosomes.



- **Kaempferol** is a flavonoid widely distributed in the plant kingdom. Numerous edible plants contain kaempferol. Numerous studies support a role of kaempferol in the prevention of many diseases, including skin infectious and allergies. Recently many studies have demonstrated that kaempferol inhibits hyaluronidases, the enzymes that hydrolyzes glycosaminoglycans including hyaluronan (HA) in the extracellular matrix during tissue remodeling, inflammation, and skin aging.



HA-PLANT: Efficacy test: IN VIVO: Anti-wrinkles efficacy of HA-PLANT

The anti-wrinkle activity was demonstrated in a half face study with 15 healthy volunteers average age 51. An oil in water cream containing 3% of **HA-PLANT** and placebo consisting in the same cream without **HA-PLANT** were applied twice daily, once to each side of the face including the crow's feet area. The anti-wrinkle

activity of **HA-PLANT** was determined by evaluating wrinkle depth, the main wrinkle length, and wrinkle number using a light polarized camera connected to a software for the image analysis.

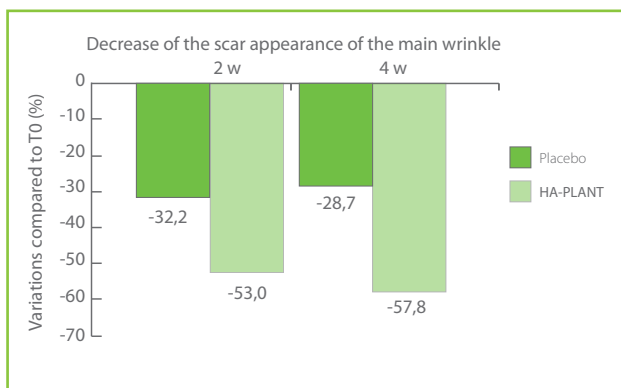
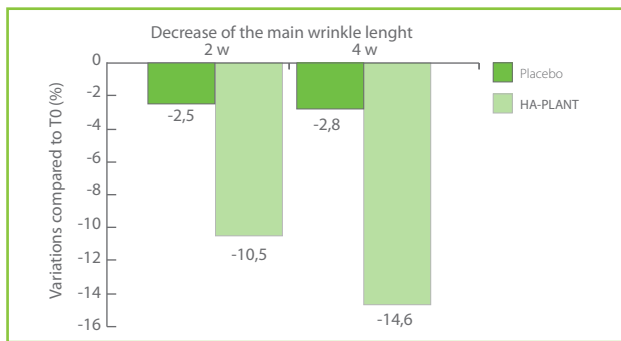


Placebo 2 weeks treatment

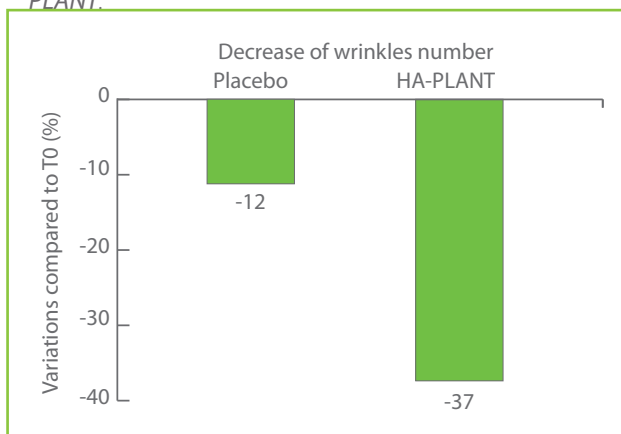


HA-PLANT 2 weeks treatment

HA-PLANT



Both at 14 and 28 day was observed a significant reduction of skin length (-14,6%) and a significant decrease of the scar appearance of the main wrinkle (-57,8%) in group treated with the cream containing 2,0% of **HA-PLANT**.



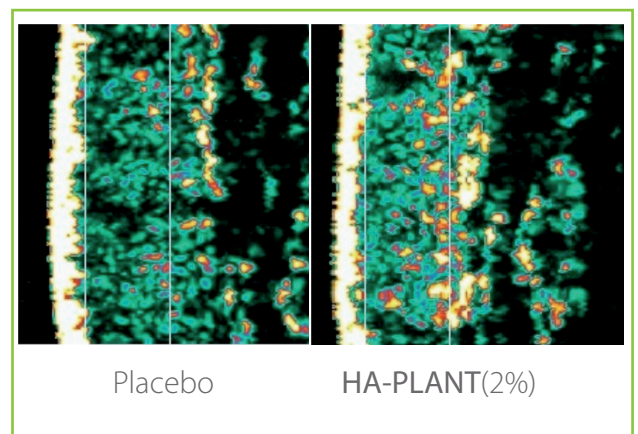
At 60 day was observed a significant reduction of wrinkles number (-37%) in group treated with the cream containing 2,0% of **HA-PLANT**. Panel composed of 10 Volunteers.

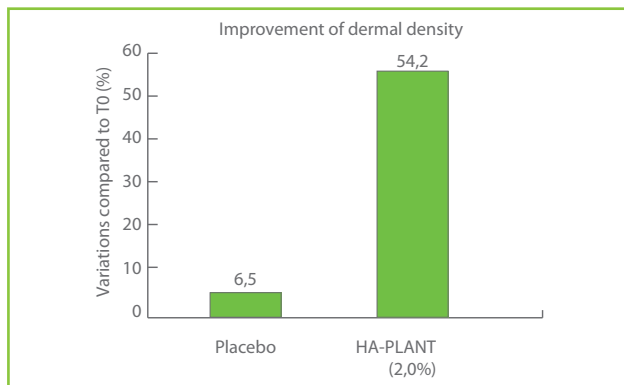
IN VIVO TEST: Clinical evaluation of HA-PLANT effect on dermal density

With aging the quantity of HA and its degree of polymerization decrease leading to loss of the three-dimensional fibers network, a reduction of the water content in the dermis and loss of skin elasticity.

All this changes determine a decrease of dermal density measured by High resolution Ultrasound Skin-Imaging (DERMASCAN CORTEX).

Treatments for four weeks with O/W cream containing 2% **HA-PLANT** significantly improved both dermal density and skin elasticity compared to the placebo.



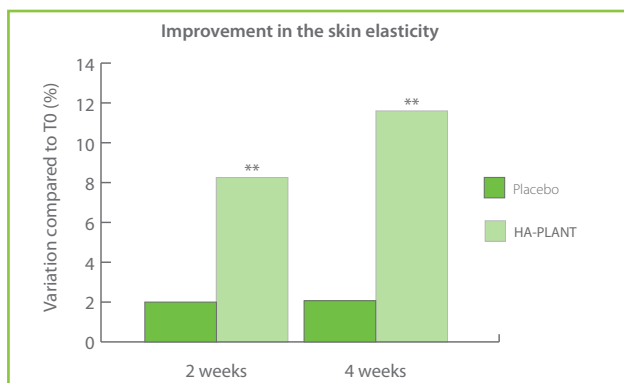


The study was carried out on 15 volunteers aged from 20 to 54 (average: 49,6). Everyone applied an oil in water cream containing 2% of **HA-PLANT** twice daily for 4 weeks.

In summary HA-PLANT:

- Decreases the main wrinkles length (-57%)
- Decreases of wrinkles number (-37%)
- Improves dermal density (+54%)
- Increases skin elasticity (+11%).

IN VIVO TEST: Clinical evaluation of HA-PLANT effect on elasticity



HA-PLANT was able to increase the skin elasticity of the crow's feet just after 14 days of treatment. At the end of the test, in the group treated with **HA-PLANT** the skin elasticity was increased of almost 12% respect to untreated skin indicating an effective role of **HA-PLANT** in the preventing of skin aging. ** $p < 0,05$ (ANOVA test)

The information contained in this publication is based on our current knowledge. **We** will not assume any expressed or implied liability in connection with any use of this information.