NANO VETORES® GROUP

NV RETINOL

FACIAL

Active Ingredient: Retinol

Benefits

- Anti-aging action;
- Promotes epidermal renewal;
- Standardizes skin tone;
- Reduces wrinkles and expression lines;
- Hydration;
- Acne vulgaris treatment.

Application

Primers, emulsions, masks, serums, gels, facial creams, liquid soaps, make up removers and products to standardize skin tone.

IN Harmony NANOVETORES

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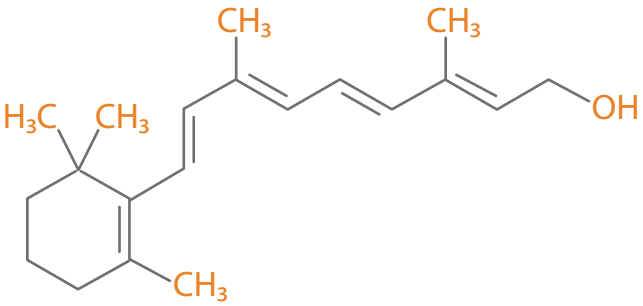
Description

Retinol is a derivative of vitamin A, widely used in skin care. Recognized as one of the most efficient vitamins with anti-aging potential, (Figure 1) retinol has the capacity of stimulating collagen production and normalizing skin keratinization, besides providing an antioxidant support which accelerates cell renewal rate. Its constant application significantly improves skin elasticity, softness, resulting in a younger, uniform and healthy skin[1].



Chemical name: Retinol CAS: 68-26-8
Molar mass: 286,45 g/mol

Figure 1: Chemical information and retinol molecular structure.

Action Mechanism

The biological retinol mechanisms are mainly based in its conversion into retinoic acid after entering the epidermis, being used in cell repair. Retinol can be converted in the skin by oxidative metabolism into retinaldehyde, followed by additional oxidation into retinoic acid (Figure 2)[2,3].

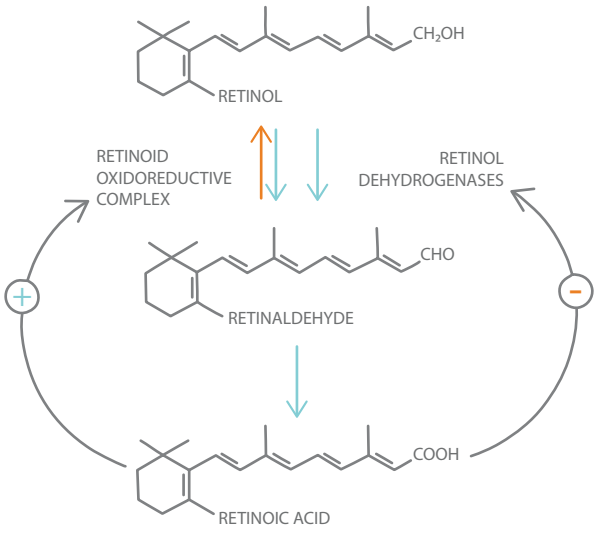


Figure 2: Retinol enzymatic conversion into retinoic acid in vivo (Adapted[3]).

Many benefits are observed with the topical use of retinol, it induces the expression of cell-binding proteins that result in several molecular changes. In photoaging, acts preventing the induction of metalloproteinases (MPP) involved in the process of extracellular matrix destruction. As result, we have the dermic structure restauration with the proliferation of keratinocytes and fibroblasts, the raise of corneocytes release, glycoproteins production, collagen and hyaluronic acid deposition. With the capacity to stimulate several biological receptors, Retinol also reduces melanin production, and has anti-inflammatory effects, being usefull in vulgaris acne treatment [5, 6].

Studies show that the major part of retinol applied in the skin remains in the stratum corneum, and a small compound part reaches the viable epidermis and the upper layers of the dermis, where it would perform its biological action[5]. For topical applications, Nanovetores encapsulation system offers effective and safe delivery of actives in skin regions where they play their biological role.

Retinol Encapsulation Advantages

The Retinol encapsulation through Nanovetores' Technology enables a smart and safe delivery of the active ingredient to the skin, with significant stability increase, ensuring greater cosmetics efficacy.

Conventional products containing Retinol require multiple applications to maintain the therapeutic effect, which can bring negative consequences such as: irritation, erythema and skin peeling. To overcome these challenges, the encapsulation of retinol provides a better biological performance, with high skin tolerance and better formula's chemical stability (Figure 3).

NV Retinol is composed by nanoparticles with average size superior than 200nm. The encapsulation system promotes safety and active protection against the oxidative degradation that happens once in the presence of air and light. NV Retinol also makes the ingredients' incorporation in cosmetic formulations easier, resulting in the improvement of its sensory and its compatibility with the other ingredients.

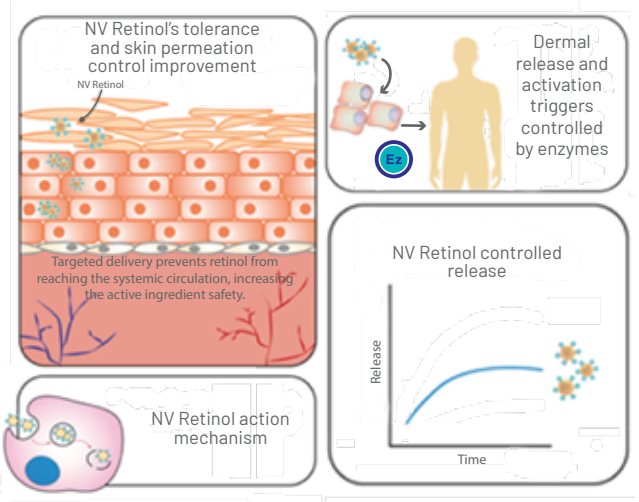


Figure 3: NV Retinol's action mechanism (Adapted[5])

14X More efficient in cellular longevity promotion

3,3X More powerful than free retinol in collagen protection

5X More chemically stable than free form

STABILITY

NV Retinol superior stability

To demonstrate the Nanovetores encapsulation system performance in the protection and maintenance of Retinol content, comparative accelerated stability studies were performed.

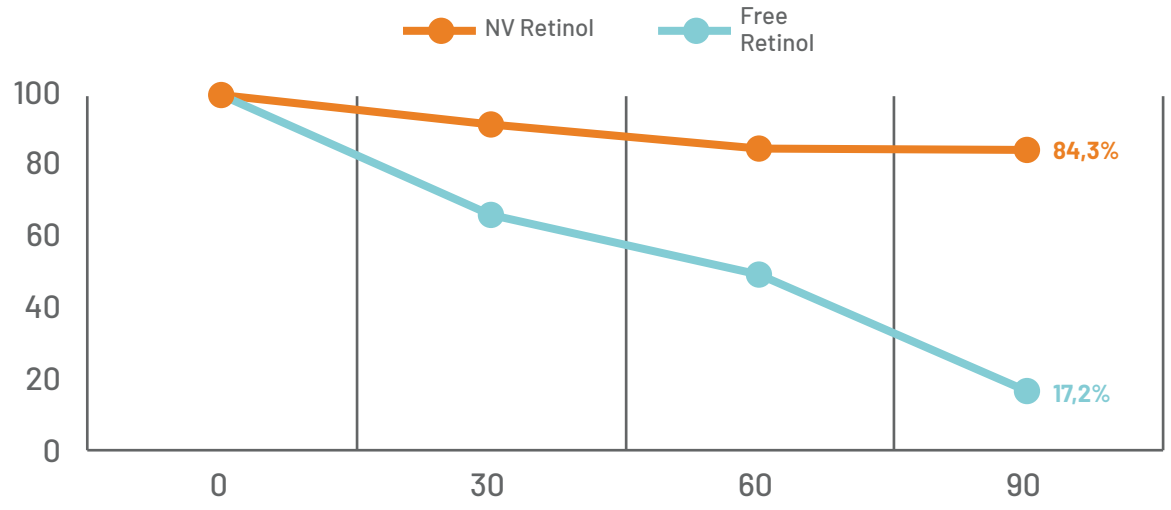
Methodology

Samples: Free Retinol and NV Retinol.
Test conditions: Exposure to light and temperatures of 5°C; 25°C; 40°C, for 90 days.
Retinol's content analysis: HPLC (High performance liquid chromatography) dosing, during the accelerated stability study in times 0; 30; 60 and 90 days.
Organoleptic and physical-chemical analysis: pH, sensory analysis and density.

Results

The NV Retinol shown a much superior stability when compared to the free form active. According to the obtained results, it was possible to conclude that NV Retinol was shown stable in the stress conditions not showing expressive variations in pH, color, odor, and density. Nanovetores encapsulation system ensures the active content maintenance, dispensing refrigeration, which makes the product's transport and storage easier. (Graph 1). Besides, NV Retinol performance makes its incorporation much easier in cosmetic formulations and grants all the ingredients benefits.

Graph 1 demonstrates the retinol content rate of decay highlighting the improved stability of the nanoencapsulated version. The NV Retinol presented a 15,7% of decay during the accelerated stability study, while free form retinol shown 82,8% in the same period. Therefore, NV Retinol was **5 times** more stable in the maintenance of vitamin A content when compared to free form retinol.



Graph 1: Retinol's Content analysis by HPLC, in samples of free form Retinol and NV Retinol exposed to temperatures of 25°C in times 0 day; 30 days, 60 days and 90 days.

Cell longevity evaluation

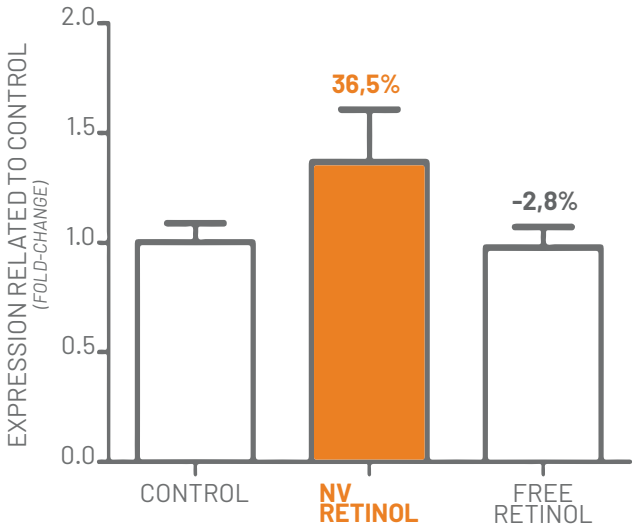
Samples: Free retinol and NV Retinol.
Objective: Evaluate the products' anti-aging potencial through the capacity to stimulate Fox03 markers related to cell senescence and longevity.
Methodology: Expression of Fox03 and SIRT1 markers by RTq-PCR, using human fibroblast cell culture. Products diluted from the concentration of 10% of sample in culture medium. Greenhouse incubation at 37°C and 5% of CO2 for 24 hours.

Senescence is a naturally occurring process and refers to a period in which the cells are uncapable to continue their cycle, even in the presence of growth factors, defining the lifetime of the mammalian cells and preventing unlimited proliferation. This process can be triggered by several types of cellular stress, including telomere shortening, the presence of free radicals and an oncogenic signaling, promoting aging. The FoxOs markers control an infinity of cellular functions, such as growth, survival, metabolism, regulating the expression of several related genes. The increase in Fox03 expression has the capacity to suppress cellular senescence by reactivating the transcription of the antioxidant and, therefore, inhibits free radicals' generation, and can be stimulated using anti-aging actives like Retinol[7].

Results

Graph 2 shows the Fox03 expression in human fibroblasts culture submitted to the contact with the control (culture medium), NV Retinol and free Retinol. The NV Retinol was tested at a 10 times lower concentration in retinol content when compared to the retinol version (pure).

The NV Retinol presented an increase of 36,5% while free retinol shown a reduction of 2,8% in the Fox03 expression. These results demonstrate the NV Retinol nanoparticles power with **14 times** greater activity when compared to free Retinol, even being at a 10x lower concentration of Retinol active. The NV Retinol superior results have demonstrated its anti-aging increased performance. With nanotechnology, less is more.



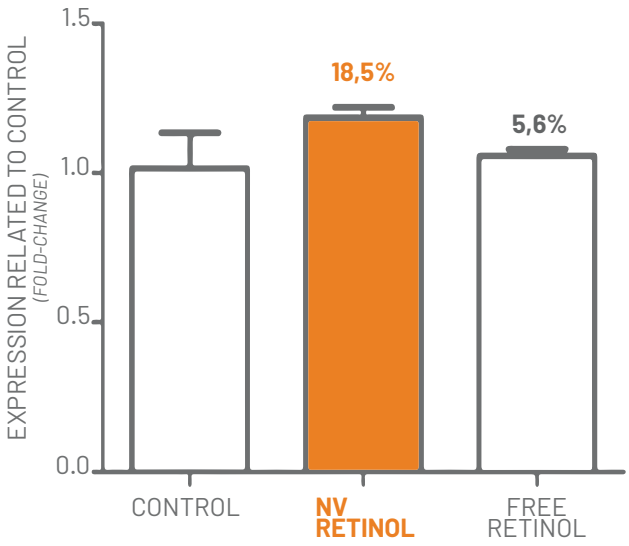
Graph 2: Result of the analysis of Fox03 relative expression of the samples when compared to the control group in human fibroblasts.

PROTECTION

Collagen protection evaluation

Samples: Free retinol and NV Retinol.
Objective: Evaluate the products collagen protection potential through the capacity to stimulate marker SIRT-1.
Methodology: Expression of the marker SIRT1 through RTq-PCR, using human fibroblasts cells culture. Diluted products from the concentration of 10% of sample in culture medium. Greenhouse incubation at 37°C and 5% of CO2 for 24 hours.

The SIRT-1 presence at the dermal fibroblasts is related to the diminished collagen degradation, due to its influence on the reduction of matrix metalloproteinases. As it can be observed bellow in Graph 3, the NV Retinol presented an increase of 18,5% in SIRT-1 expression, while Free Retinol has only presented 5,6%. That is, once again NV Retinol showed superior results, being **3,3x more efficient** when compared to Free Retinol. Bearing in mind that the retinol content in NV Retinol is 10x lower, indicating, therefore, that the encapsulation provides a more effective retinol delivery in its action target which ensures an increase in the collagen degradation protection when compared to free retinol.



Graph 3: Result of the analysis of SIRT-1 relative expression of the samples when compared to the control group in human fibroblasts culture.

NV RETINOL

Regulatory Information

INCI Name	Cas Number	EINCS Number
AQUA	7732-18-5	231-791-2
CAPRYLIC/CAPRIC TRIGLYCERIDE	73398-61-5	277-452-2
RETINOL*	68-26-8	200-683-7
LINOLEIC ACID	60-33-3	200-470-9
OLEIC ACID	112-80-1	204-007-1
POLYSORBATE 80	9005-65-6	-
POLYSORBATE 20	9005-64-5	-
PPG-15 STEARYL ETHER	25231-21-4	-
STEARETH-2	9005-00-9	500-017-8
STEARETH-21	9005-00-9	-
PHENOXYETHANOL	122-99-6	204-589-7
CAPRYLYL GLYCOL	1117-86-8	214-254-7
BHT	128-37-0	204-881-4
BHA	25013-16-5	246-563-8

*NV Retinol contains 150.000 UI/g of vitamin A.

Physical-Chemical Information

Aspect	Milky liquid
Color	Cream to yellow
Odor	Characteristic
Dispersibility	Dispersion of encapsulated actives in water
Relative Density	0,9 to 1,1 g/mL
Characterization	Blend
pH	3,5 to 6,5

Usage Mode
Add to the formulation bellow 40°C under moderate agitation.

Usage concentration
Up to 6,6%.

Storage
Keep it bellow 25°C in a ventilated place, protected from light and heat. After being opened, it is recommended to storage under refrigeration.

Compatibility
Anionic, non-ionic and cationic bases. For aqueous solutions of low viscosity, the use of a suspending agent is indicated.

Incompatibility
Enzymes, ethanol and other organic solvents.

Stability pH
2,0 to 7,0.

CLINICAL TESTS

The NV Retinol Perceived Efficacy Study was conducted with the product IN PEARLS RETINOL*, after 30 days of product use in standardized conditions.

Methodology: The products were used by the research participants during 30 ± 2 days according to the mode of use informed by the Sponsor.

Evaluated product: IN PEARLS RETINOL.
The product IN Pearls Retinol* contains 4.875 UI/g of Vitamin A, which corresponds to 0,325% of retinol.
Number of volunteers: 32 Participants.

After 30 days of use, the investigational product (IN PEARLS RETINOL) promoted wrinkles improvement in 64% in relation to baseline measures.

Dermatologically tested product.

*Retinol BP version

RETINOL BP

Regulatory Information

INCI Name	Cas Number	EINCS Number
AQUA	7732-18-5	231-791-2
RETINOL*	68-26-8	200-683-7
PEG-40 HYDROGENATED CASTOR OIL	61788-85-0	-
POLYSORBATE 20	9005-64-5	-
PHENOXYETHANOL	122-99-6	204-589-7
CAPRYLYL GLYCOL	1117-86-8	214-254-7
POLOXAMER 407	9003-11-6	-
ALGIN	9005-38-3	-
BHT	128-37-0	204-881-4
BHA	25013-16-5	246-563-8
CALCIUM CHLORIDE	10043-52-4	233-140-8

*NV Retinol BP contains 75.000 UI/g of vitamin A.

Physical-Chemical Information

Aspect	Milky liquid
Color	Yellow to slightly greenish
Odor	Characteristic
Dispersibility	Dispersion of encapsulated actives in water
Relative Density	0,9 to 1,1 g/mL
pH	4,0 to 7,0

Usage Mode
Add to the formulation bellow 40°C under moderate agitation.

Usage concentration
Up to 13 %.

Compatibility
Anionic, non-ionic and cationic bases.

Incompatibility
Ethanol.

Storage
Keep it bellow 25°C in a ventilated place, protected from light and heat. After being opened, it is recommended to storage under refrigeration.

Stability pH
4,0 to 7,0.

Our production process is based on Green Chemistry, being water-based and free of organic solvents, totally sustainable. We do not generate waste that could be harmful to users or the environment

We do not test on animals. All tests are conducted in trustworthy laboratories with human volunteers.

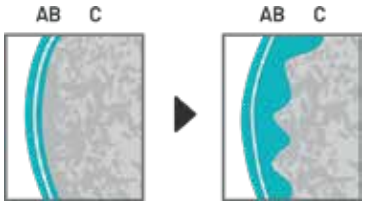
Essential oils, Vitamins, Acids and Natural Extracts are highly oxidative substances that degrade quickly and react constantly with the medium and other cosmetic compounds (light, oxygen, packaging, preservatives, fragrances, surfactants, etc.). By encapsulating it, we guarantee the stability of the active ingredients and protect them from potential reactions with the formulation or the environment.

References

1. Shields IV C.W. et al. Encapsulation and controlled release of retinol from silicone particles for topical delivery. Journal of Controlled Release, 28 (278): 37-48, 2018.
2. Yourick J. J. In vitro and in vivo percutaneous absorption of retinol from cosmetic formulations: Significance of the skin reservoir and prediction of systemic absorption. Toxicology and Applied Pharmacology (231) 117–121, 2008.
3. Belyaeva O. V. et al. Generation of Retinaldehyde for Retinoic Acid Biosynthesis. Biomolecules. 10, 5, 2020.
4. FISHER G. J. et al. All-Trans Retinoic Acid Induces Cellular Retinol-Binding Protein in Human Skin In Vivo. The journal of investigative dermatology. 05, (1), 1995.
5. Ferreira, R., Napoli, J., Enver, T. et al. Advances and challenges in retinoid delivery systems in regenerative and therapeutic medicine. Nat Commun. 11, 4265, 2020.
6 . VARANI J. et al. Molecular Mechanisms of Intrinsic Skin Aging and Retinoid Induced Repair and Reversal. The Society for Investigative Dermatolog, 08, (3), 1998.
7. Bourgeois B, Madl T. Regulation of cellular senescence via the FOXO4-p53 axis. FEBS Lett. 592(12):2083-20972018.

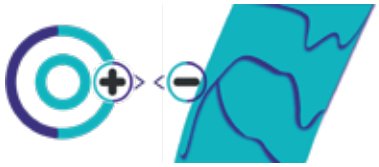
Nanovetores Encapsulation Technology

Active Ingredient Protection against oxidation resulted from interaction with external environment and other components of the cosmetic formulation.

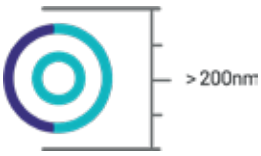


Greater Permeation on the contact surface due to the small size of the capsule.

Monodispersity, that ensures control of the particle size, providing adequate permeation to its proposed action.



Surface Charge Control of the particle, promoting greater affinity with the contact surface.



Secure particles larger than 200nm, biocompatible and biodegradable.

Water Base. Active ingredients are manufactured without the use of organic solvents, ensuring safety for users and the environment.

Use Encapsulated Active Ingredients and Ensure:

- Stability Improvement
- Increased compability in the formulation
- Occlusion of odors
- Increased skin permeation
- Reduced dose
- Use of sensitive active ingredients (without refrigeration)
- Increased Solubility
- Prolonged release
- Increased effectiveness

NANO VETORES® GROUP

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