

**miniHA™**

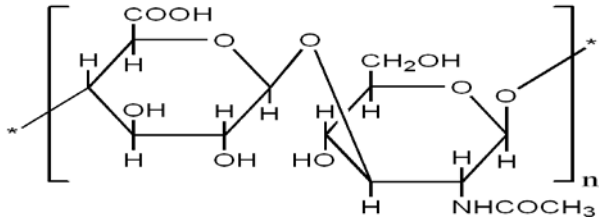
**High Activity, Extremely Low Molecular weight  
Hydrolyzed Sodium Hyaluronate**



# Content

- ❑ Concept of Oligo sodium hyaluronate
- ❑ Production process of Oligo sodium hyaluronate
- ❑ Advantage of miniHA
- ❑ Effects of miniHA in cosmetics

# 1. Concept of Oligo sodium hyaluronate



Oligo sodium hyaluronate (HA-Oligo)

$n < 25$ ;  $M_w < 10000\text{Da}$

molecular weight (Da)

1.8M

1M

10K

High Mw HA

Middle Mw HA

Low Mw HA

**Physical property:**

moisture retention

viscoelasticity

lubricity

**Physical property:**

moisture retention

**Bioactivity:**

promoting cell proliferation

initiating wound healing

antioxidant activity

## 2. Production process of Oligo sodium hyaluronate

**Traditional method**—  
Chemical degradation

- Hydrochloric acid
- Sodium hydroxide
- Hydrogen peroxide

Common  
HA-Oligo

**Innovative method**—  
Enzymatic degradation

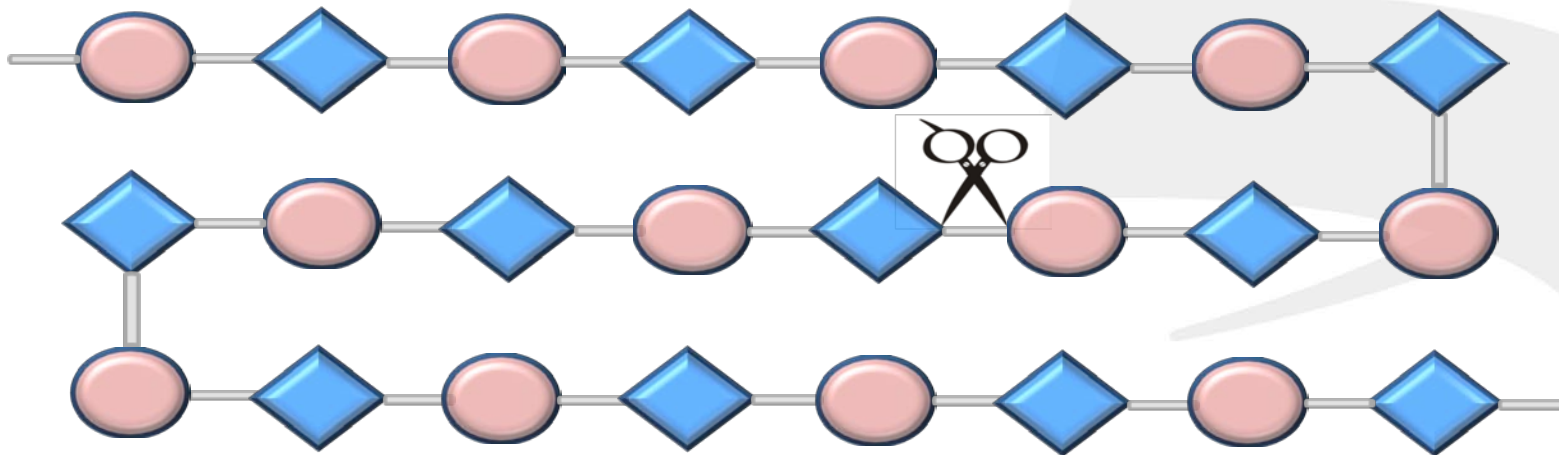
- Hyaluronidase

miniHA

# Enzymatic degradation



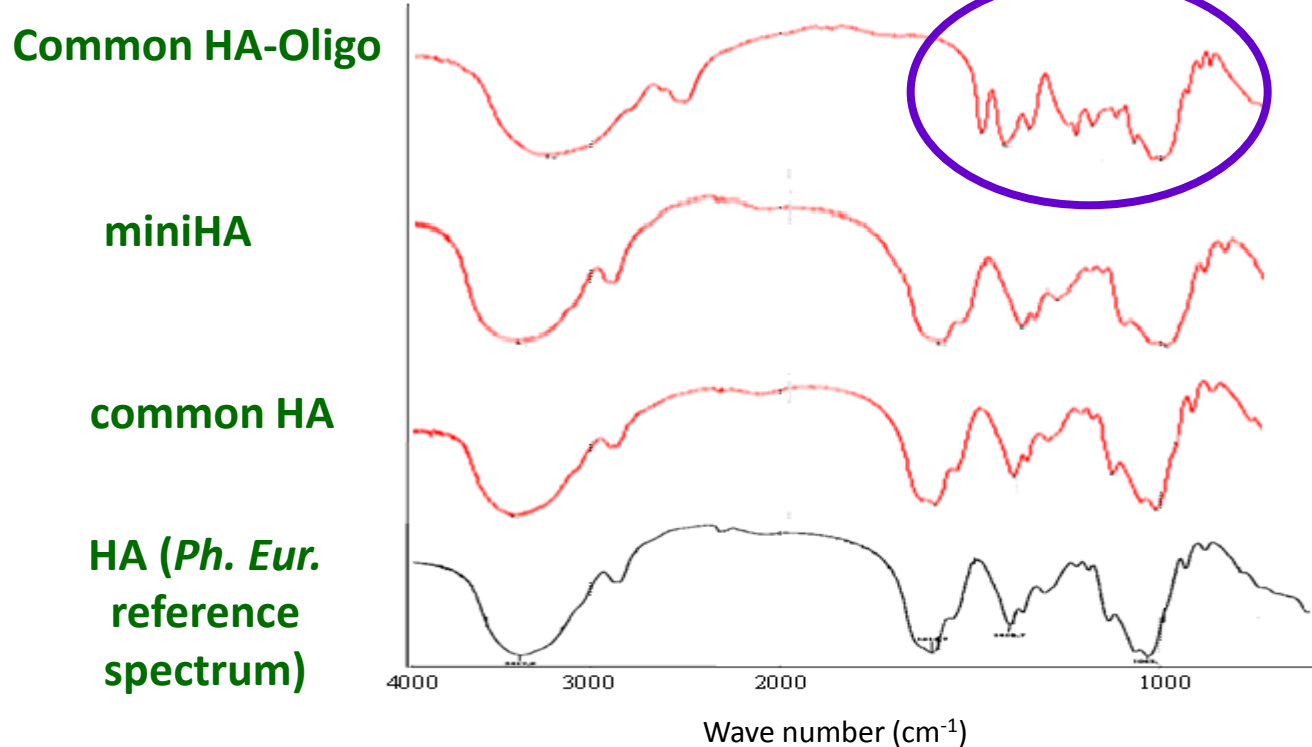
High specific cleavage of glycosidic bonds



Bloomage Freda is the first and only manufacturer in the world to use enzymatic degradation in large scale production of HA-Oligo.

# 3. Advantage of miniHA

## 3.1 Comparison of IR spectrum

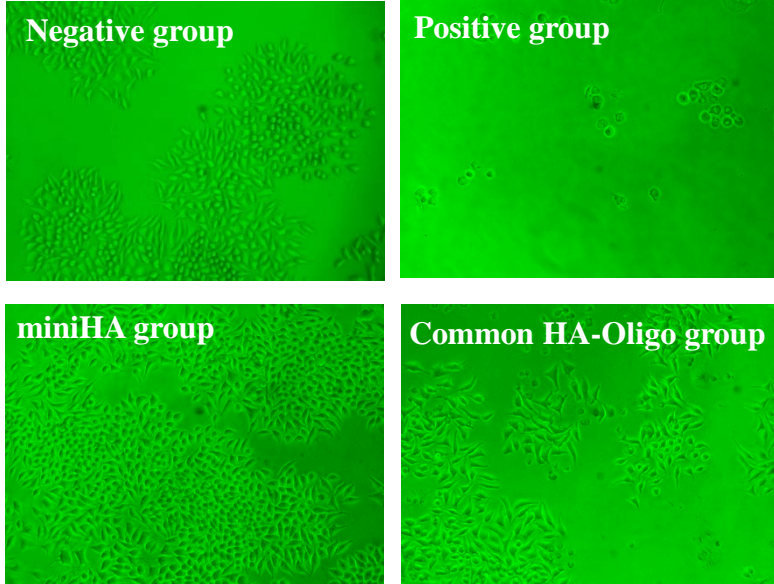


The infrared spectrum of miniHA was conformed with Ph. Eur. reference spectrum of sodium hyaluronate, while that of common HA-Oligo was obviously different.

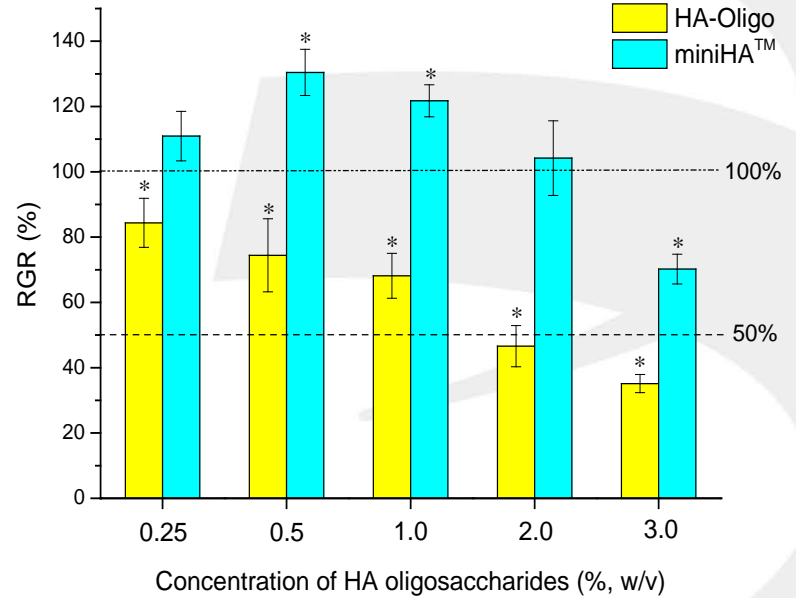
## 3.2 Assay by HPLC

Sample	Production method	Purity /%
miniHA-1	Enzymatic degradation	97.66
miniHA-2	Enzymatic degradation	98.02
miniHA-3	Enzymatic degradation	98.52
miniHA-4	Enzymatic degradation	97.79
Common HA-Oligo 1	Chemical degradation	62.35
Common HA-Oligo 2	Chemical degradation	67.65
Common HA-Oligo 3	Chemical degradation	63.23

### 3.3 Cytotoxicity test



Micrographs of cytotoxicity test



Relative growth rate (RGR) of the cell



## 3.4 Skin patch test

Degree	Grade	Cutaneous reaction	Volunteers
-	0	Negative	30
±	1	Weak erythema、Xerosis cutis、Wrinkle	0
+	2	Erythema、Edema、Papula、Wheal、Desquamation 、Cracks	0
++	3	Obvious erythema、Edema、Phlycten	0
+++	4	Severe erythema、Edema、Bleb、Erosion、 Hyperpigmentation or hypopigmentation、Acne kind change	0

This test was carried out according to Hygienic Standard for cosmetics (2007).

The cutaneous reactions of 30 volunteers were negative.

**Complete  
structure**

**Higher  
purity**

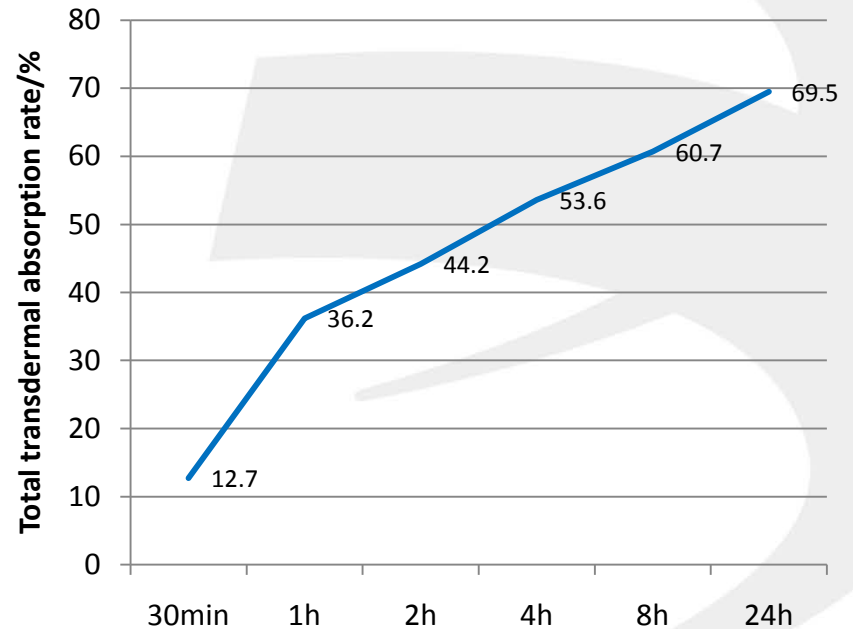
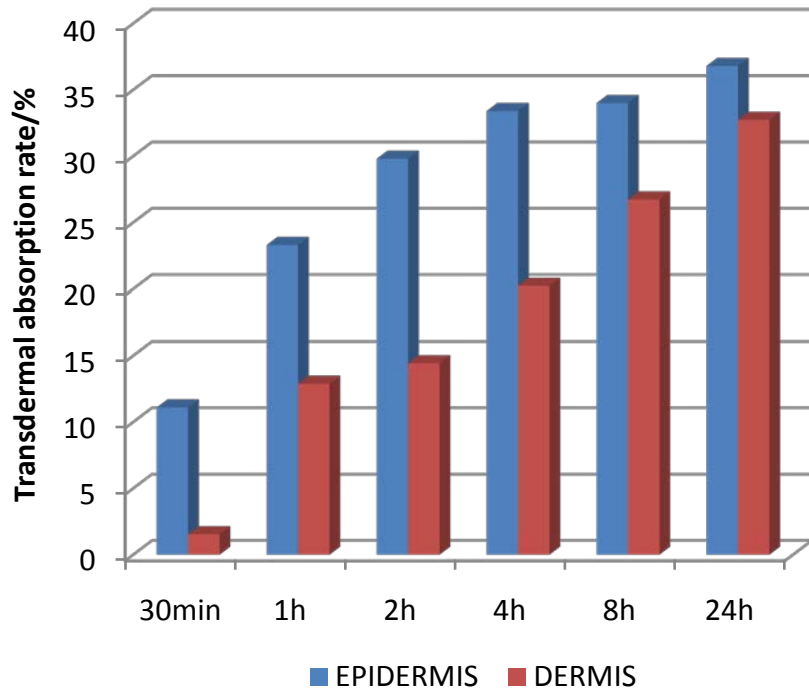
**No  
cytotoxicity**

**No skin  
irritation**

**miniHA is a safe cosmetic ingredient**

# 4. Effects of miniHA in Cosmetics

## 4.1 Transdermal absorption



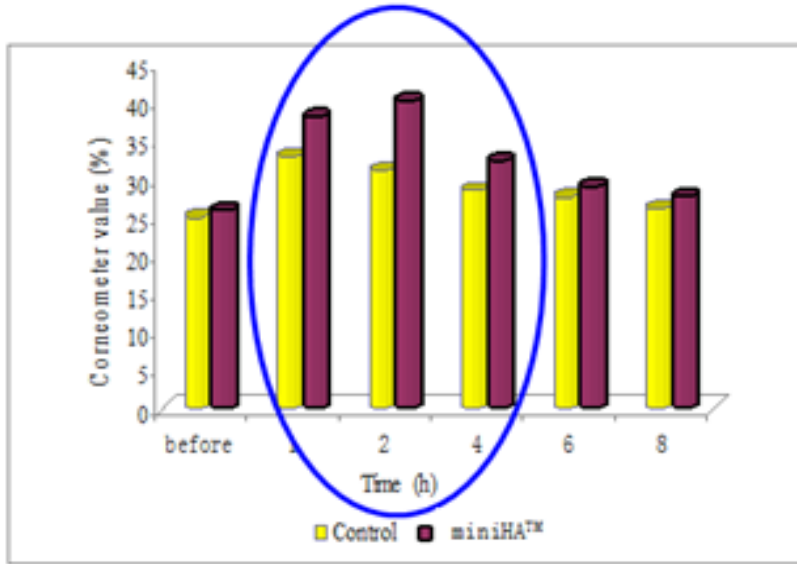
Sample: 0.5% miniHA solution Material: Reconstructed human skin

Farcoderm srl (Italy)



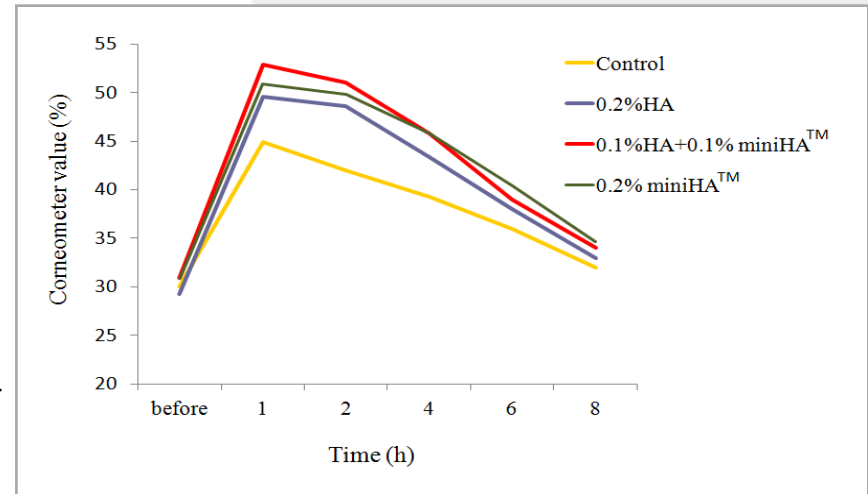
## 4.2 Moisturizing effect

- ◆ miniHA has significant moisturizing effect.

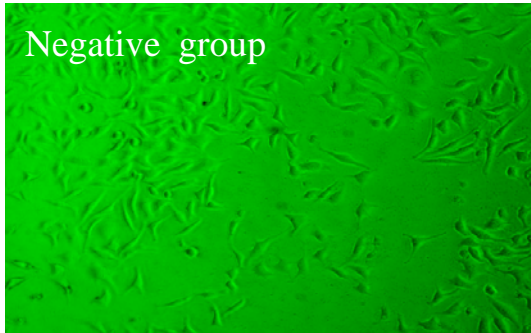


- Sample: The only difference between control and test samples is the formula of test creams containing 0.2% miniHA.
- Instrument: Corneometer CM825
- 30 healthy volunteers.

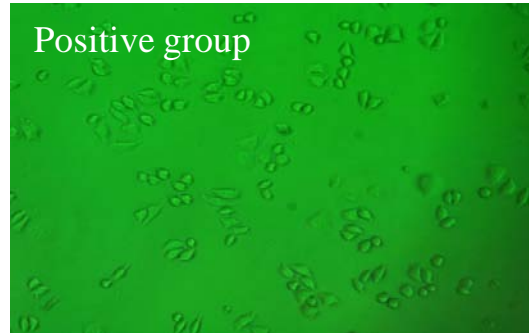
- ◆ When miniHA is used in cosmetic formulation together with HA, the moisturizing capacity is higher because of their synergetic effect.



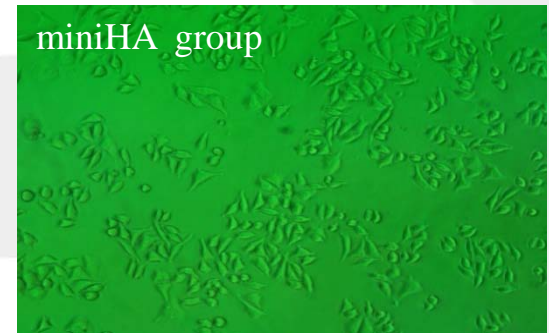
## 4.3 Repairing damaged cells



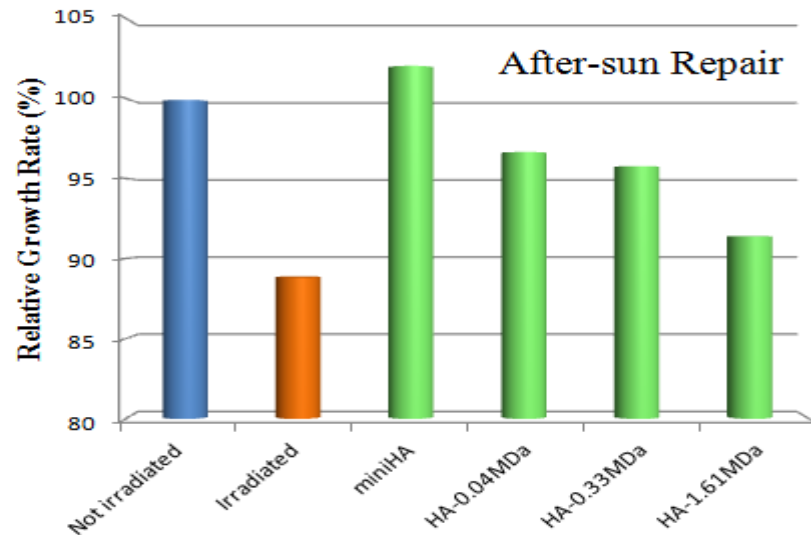
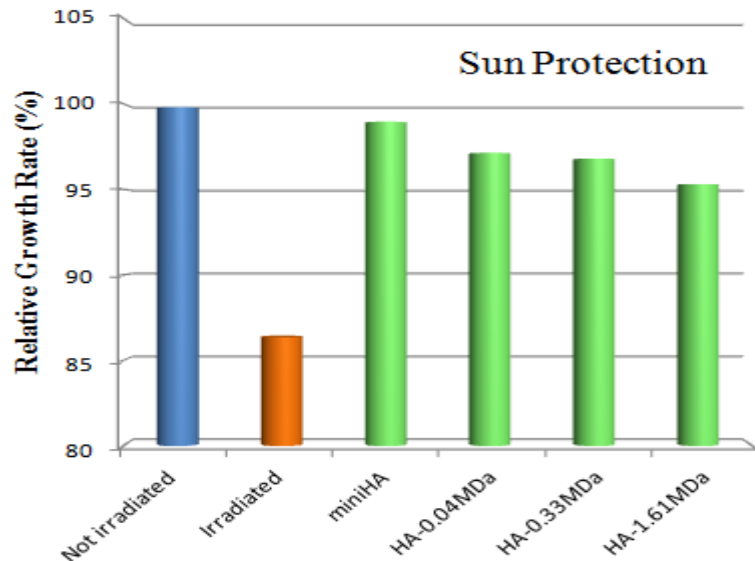
The count and morphology of cells were normal for the negative group.



The cell count was decreased and the cell shape was significantly changed for positive group.



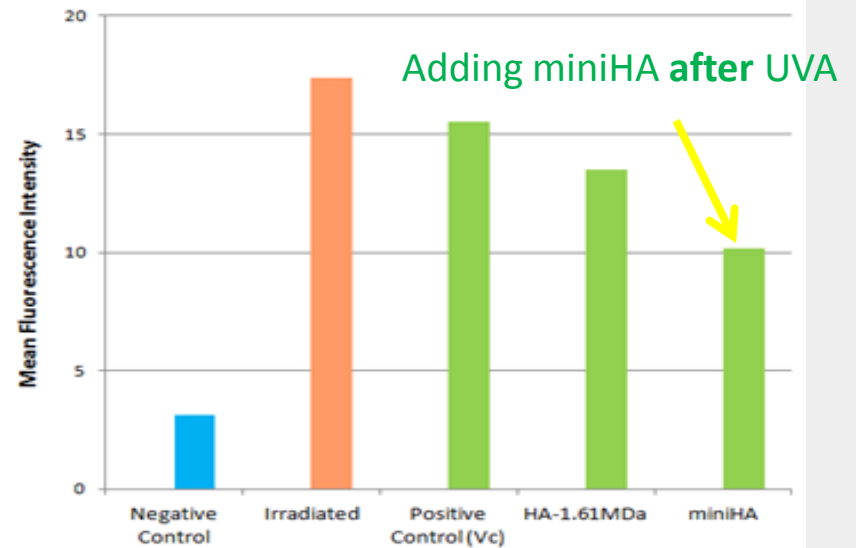
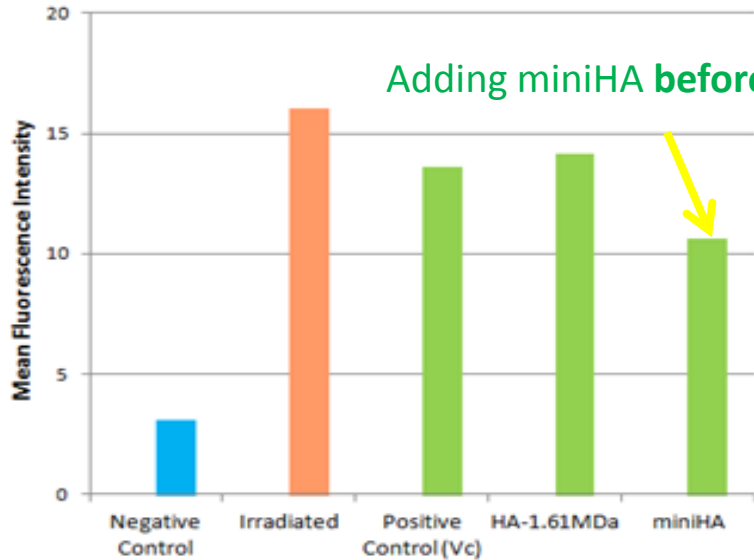
The cells count increased and cell shape returned to normal after adding miniHA.



Sample: 0.06% miniHA solution Material : Fibroblasts Method: MTT

Cells RGR of miniHA group was higher than other irradiated groups in both experiments, which indicated miniHA had good abilities of sun protection and after sun repair.

## 4.4 Anti-oxidation activity



Sample: 0.06% miniHA solution    Material : Fibroblasts    Instrument: Flow Cytometer

Whether adding miniHA before or after UVA, the average fluorescence intensity of miniHA group was much lower than positive control.

ROS: Reactive Oxygen Species, induced by UVA irradiation

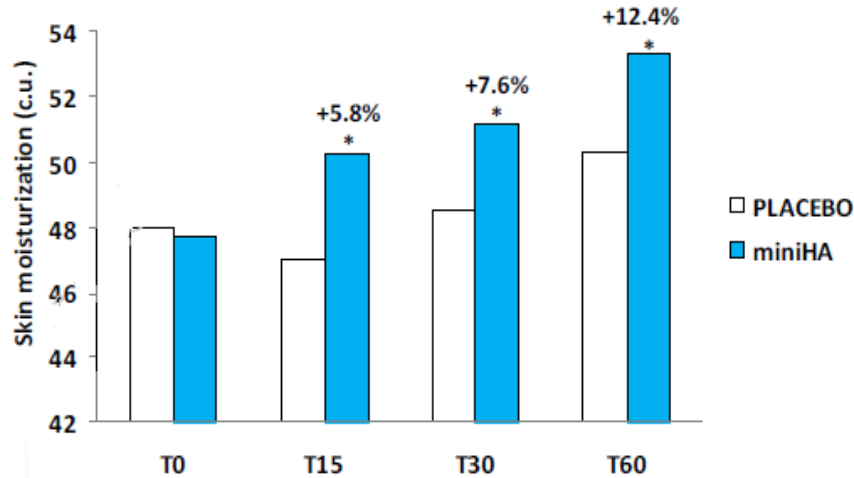
## 4.5 Anti-aging effect

- Double-blind, randomized, placebo-controlled clinical/instrumental evaluation of miniHA has been finished by Farcoderm srl (Italy).
- The active formulation is the same as the base cream + 0.5% miniHA.
- 20 healthy volunteers of 35-65 years old.

**miniHA anti-aging** effect is greater than placebo. The difference between the two products is statistically significant at all monitored experimental checks. These effects, instrumentally and clinically recorded, were also perceived by the majority of the subjects participating in the study.



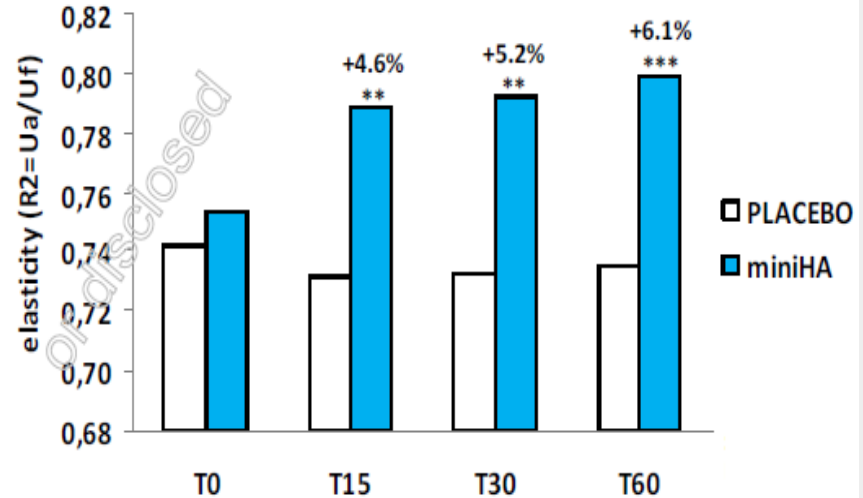
## SKIN MOISTURIZATION



Instrument : Corneometer (Courage+ Khazaka)

The skin moisturization increased 5.8%, 7.6% and 12.4% after applying miniHA cream 15d, 30d and 60d respectively.

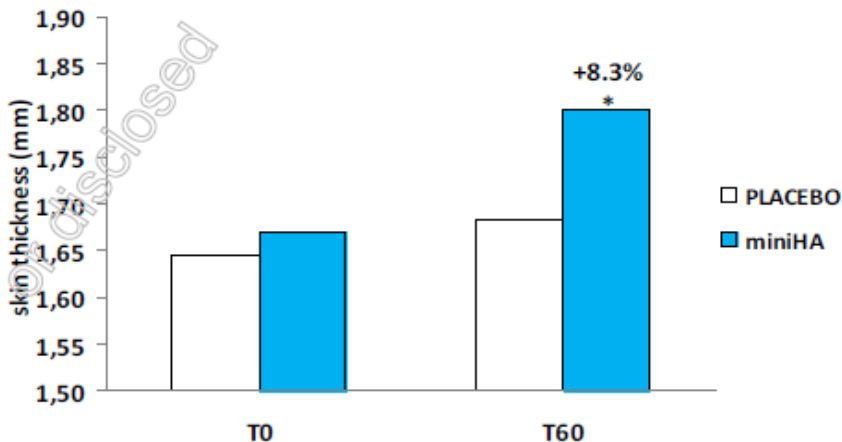
## SKIN ELASTICITY (R2)



Instrument : Cutometer MPA 580 (Courage+ Khazaka)

The skin elasticity increased 4.6%, 5.2% and 6.1% after applying miniHA cream 15d, 30d and 60d respectively .

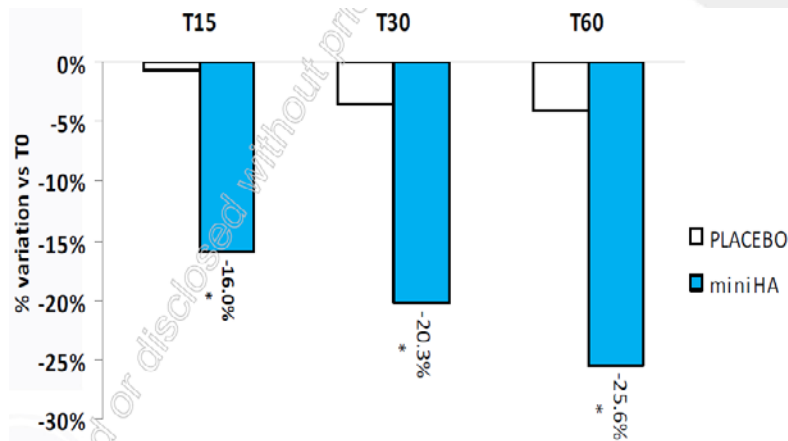
## SKIN THICKNESS



Instrument : Aloka pro-sound α6).

The skin thickness increased 8.3% after applying miniHA cream 60d.

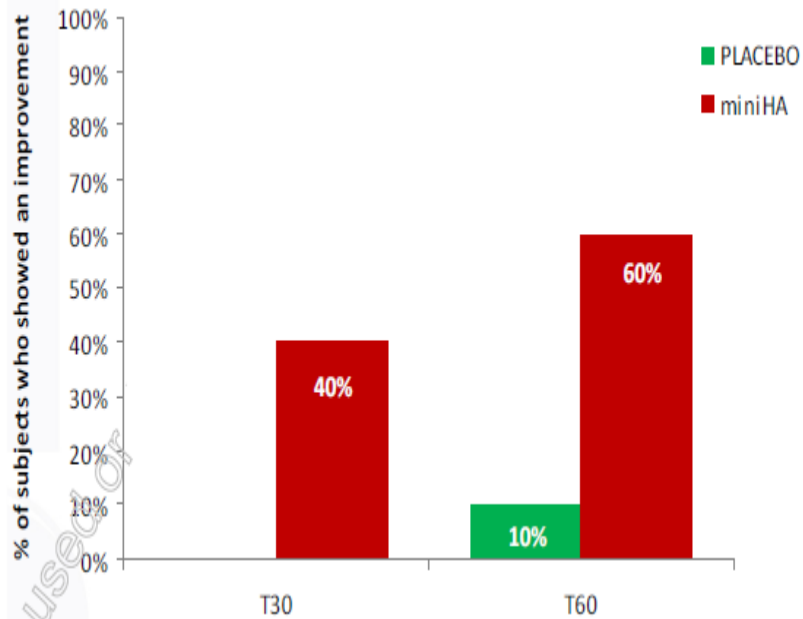
## SKIN PROFILOMETRY



Instrument : Primos 3D (GFMeStechnik)

The skin wrinkle depth decreased 16.0%, 20.3% and 25.6% after applying miniHA cream 15d, 30d and 60d respectively.

## CLINICAL ANALYSIS (SKIN WRINKLEDNESS)



The wrinkle depth decrease was also confirmed by the dermatologist that shows a reduced wrinkles appearance by 60% of the enrolled subjects.

miniHA is a multifunctional active ingredient

Moisturizing

Repairing

Anti-oxidation

Anti-aging

# Summary

Innovation



Safe



Multifunction

- 3000-10000Da
- Enzymatic method
- First one in the world
- Innovation Award

- Ecocert certified
- Complete structure
- High purity
- No cytotoxicity

- Moisturizing
- Repairing
- Anti-oxidation
- Anti-aging

# Instruction

## Application

Moisturizer, anti-aging agent, sunblock.

## Dosage form

Aqueous solution, gels, cream, emulsion, etc.

## Recommended usage

0.1~0.5%.

Much better efficacy when combined with common HA.

## Use method

Good solubility, good stability in any process of manufacture.



# Thanks

