



SCC Ontario Chapter



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“A retrospective and update on the emergence and evolution of Hyaluronic Acid in skin care”

Education Hour Presented by

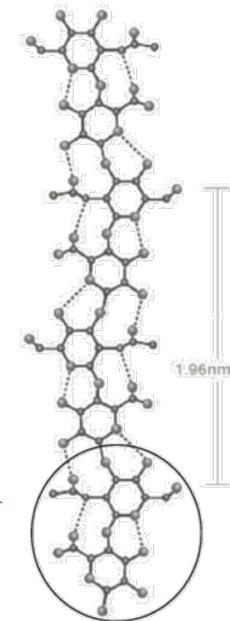
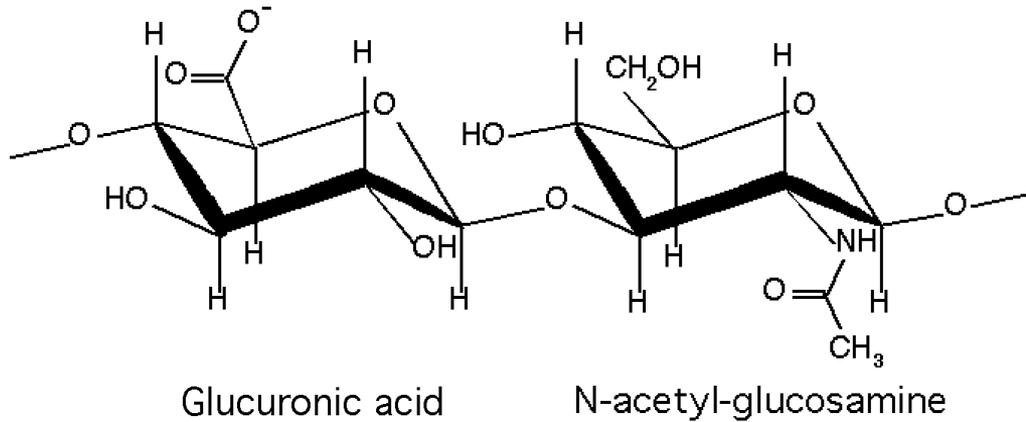
Dr. Giuseppe Calloni

Vice President Bloomage Biotechnology USA Inc.

5/28/2020

BLOOMAGE BIOTECHNOLOGY CORPORATION LIMITED

- Hyaluronic Acid (HA) is a naturally occurring LINEAR polysaccharides, widely known for its ability to form a highly viscous solution in aqueous media.
- The polymer chain of HA is composed of repeating DI-saccharide units of glucuronic acid and N-acetylglucosamine.
- The molecular weight can reach up to several million Dalton (Da), which represents the unit of molecular mass
- The number of disaccharides can reach about 10000 or more.



History:

HA was discovered in 1934 by Karl Meyer and John Palmer at Columbia University NY. They isolated the substance from a cow's vitreous body and derived the name hyaluronic acid from **hyalos** (the Greek word for 'glass') and the **uronic** sugar found in the substance.

In 1950 Alexander G Ogston and his collaborators at Oxford characterized a hyaluronan- protein complex from synovial fluid and found it had a molecular weight in the order of millions and extended over a large volume.

Initially it was believed that HA was an inert filling material between cells, without any biological activity. In 1972 Hardingham and Muir discovered that cartilage proteoglycans specifically bind to HA. Subsequently a number of extracellular proteins and cell surface receptors have been discovered that interact with HA.

Finally it was found that HA regulates many cellular functions and the development of HA field has accelerated in the last decades, showing it plays important role in areas like mitosis, embryological development, cellular motility but also inflammation, eye surgery, arthrosis, space filler in tissues.

Nomenclature:

Under physiological conditions, virtually all HA molecules are in their ionized form- Hyaluronate. As it is not feasible or necessary to define the counter ion (e.g. sodium, calcium) or the degree of dissociation of HA, it has been called more frequently “Hyaluronan”. HA now stands for hyaluronic acid, hyaluronate, hyaluronan, depending on the context in which it is mentioned.

Physical-Chemical characteristics:

1. Bovine vitreous contains lower MW HA, in the range of 10,000-100,000 Da
2. Streptococcal cultures produce HA with MW in the range of 100,000-1000,000 Da
3. HA from rooster comb, human umbilical cord and synovial fluid have MW in the range 1,000,000-10,000,000 Da

2 key properties of HA are closely associated, its high MW and the large hydrodynamic volume. In fact the MW is often derived from the intrinsic viscosity (a measure of hydrodynamic volume), as defined by the Mark-Houwink equation:

$$\eta = KM^\alpha$$

Where M is the MW. For HA $K=0.036$ and $\alpha = 0.78$ according to the study by T. Laurent. A 2 million Da HA has an intrinsic viscosity of approximately 3000 ml/g

The usefulness of HA as medical products is dependent on their unique biophysical properties, mainly "*viscoelasticity*" and "*pseudoplasticity*" (reduction of viscosity when subject to shear force)

Protective effect on tissue = ability to absorb water, fill extracellular space, coat and lubricate the tissue surface, and absorb the mechanical stress.

The fact that HA molecules from different sources have the same primary structure, explain the molecular basis for its natural biocompatibility.

Sources:

1. Human umbilical cord was the source of HA in many early researches
2. HA from animal tissues such as cock's comb and HA from microbial fermentation turned out to be the 2 major choices for the industry

Animal source

In 1949 Boas reported the identification of HA from cock combs. The isolation and purification procedure by Boas can be outlined as follows:

- Grinding freshly harvested combs
- Soaking combs material in acetone to remove fat
- Extracting HA using sodium acetate solution
- Adding ethanol to precipitate HA
- Adding chloroform and shaking the mixture to remove protein

The obtained product was pure white and fibrous, the yield of HA was approximately 0.1% weight of the combs processed. **1kg produces 1gr**

Industrial source

- The HA production by fermentation was first reported in 1937 by Forrest et al.
- In 1985 Bracke et al. produced HS from streptococcus bacteria by fermenting under anaerobic conditions, glucose was used as the carbon source. The separation of microorganisms (killing) with trichloroacetic was necessary.
- In 1988 Brown et al. developed a fermentation process that does not require the killing of microorganisms, that could cause the release of pyrogenic substances, which would be difficult to remove. The Brown method yielded a final HA product with low protein content.
- In 1988 Nimrod developed a novel method utilizing the streptococcus zooepidemicus. The microorganisms were treated with a suitable mutagen capable of producing mutants of the organism, like nitrosoguanidine. The mutants could produce an enhanced amount of HA and for the first time Nimrod produced high MW HA that exceeds 3.5million Da.
- Just recently (1996) the enzymes responsible for HA synthesis have been identified and used in large scale.
- In 1991, Dr. Xueping Guo first began the research of HA fermentation in China. Today the yield of HA fermentation can be 10-11 g/L.

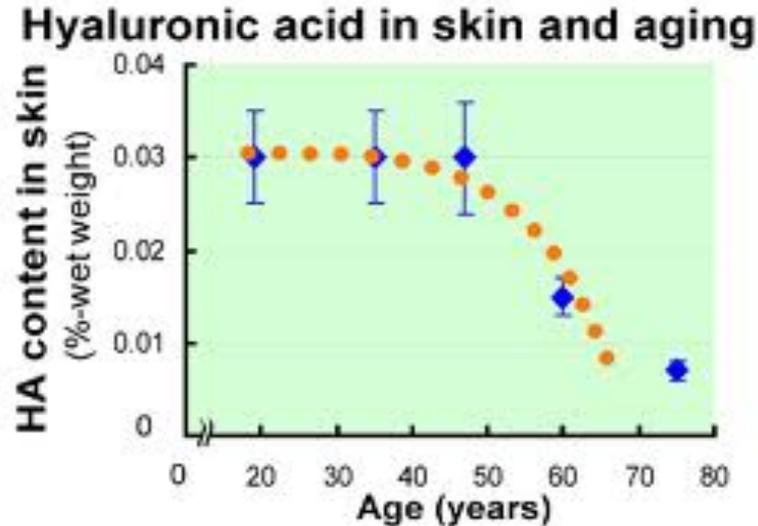
Comparison Fermented HA vs Animal source

Parameters	Fermented HA	Animal source HA
Content of HA	Min. 95%	About 65%
Pathogen	No risk	High risk from animal source
Supply	High yield rate	Very low yield rate, insufficient supply
Price	Acceptable	Expensive because of low yield rate
Regulation / Chemical name	Sodium Hyaluronate / Hyaluronic Acid	Cockscomb extract

Distribution:

HA can be found extracellularly in most human tissues. Skin, lungs and intestine contain more than 50% of the HA in the body.

With age, the amount of hyaluronic acid decreases in the skin, resulting in reduced dermal hydration and increased wrinkling.



Degradation:

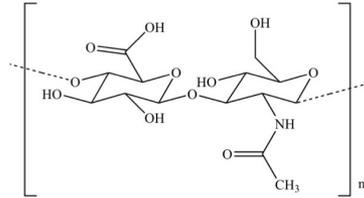
The physiological turnover of HA in circulation is very rapid; the daily turnover of HA in circulation is in the range of 170-700mg, almost 1/3rd of the total body content.

Influence on Cell Behaviour:

HA is not merely a structural component of connective tissue but plays an important role in the regulation of cell behavior as well, especially because of its ability to maintain the water balance in the extracellular matrix.

HA is strongly responsible for the cell migration, proliferation and wound healing (**protecting and repairing property**)

The presence of HA may greatly influence the quality of wound repair because of its influence on reepithelization, inflammation, angiogenesis, as well as ECM synthesis, deposition and remodeling



Native hyaluronic acid (HA)



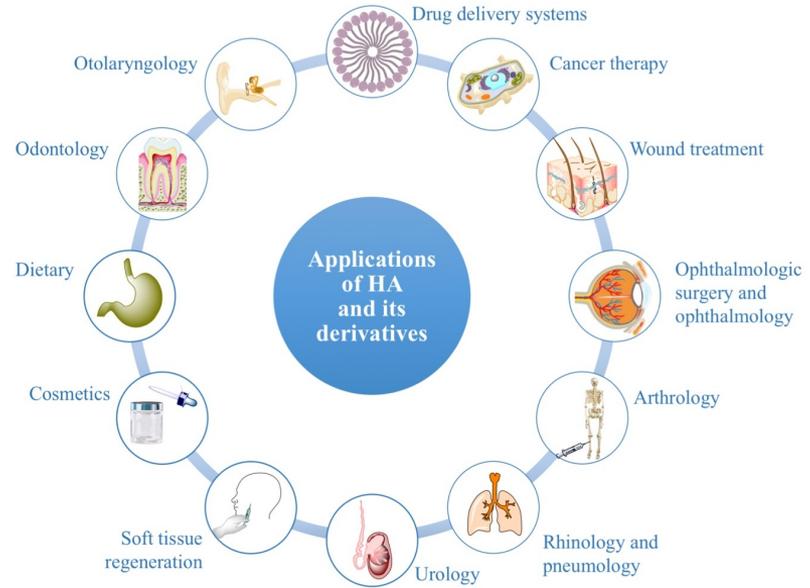
Native HA



Conjugated HA

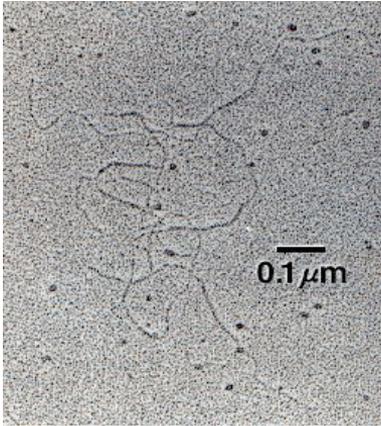


Crosslinked HA



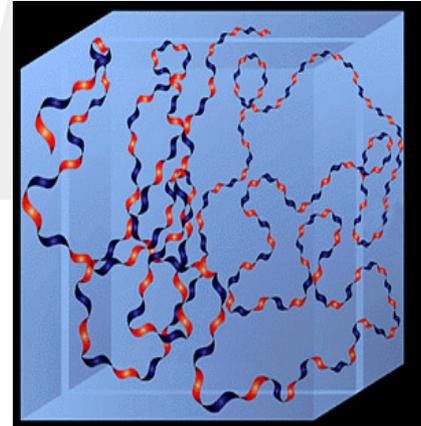
Structure

Polymer Structure



An electron micrograph a few intertwined HA molecules. One HA molecule of 10,000 repeat disaccharides could extend 10 μm if stretched from end to end.

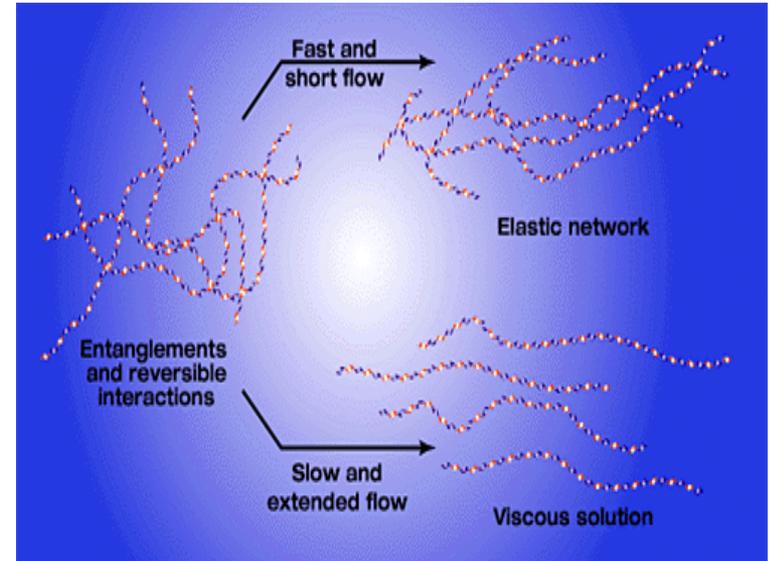
Solution Structure



One HA molecule assumes an expanded random coil structure in physiological solutions which occupies a very large domain.

Rheology: Response to applied shear-stress

- ✓ Through the network structure, HA can resist rapid, short-duration fluid flow, and exhibits elastic properties which can distribute load or shear forces within the network. (when we run)
- ✓ Slow, longer-duration fluid flow can partially separate and align HA molecules, allowing their movement and exhibiting viscous properties. (when we walk)



HA Used in Cosmetic Industry



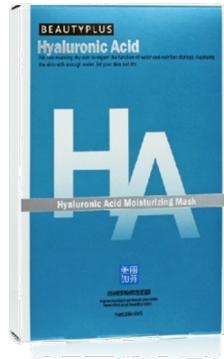
- Moisturizing
- Soothing
- Anti-aging, Anti-oxidant, Anti-pollution
- Protecting and repairing skin damage, wound healing
- Lubricity and film-forming properties
- Increasing emulsion stability

Slow-release of active ingredients-drugs

The active ingredients can be fixed in three-dimensional network structure of HA. Due to the natural enzymatic degradation of HA, the active ingredients will be slowly released.

Such as perfume, medical device, patch, face mask





Available HA materials

Small molecule:
High activity
Trans epidermal absorption
Deep moisturizing
Scavenging free radicals
Repairing damaged cells
Anti-aging

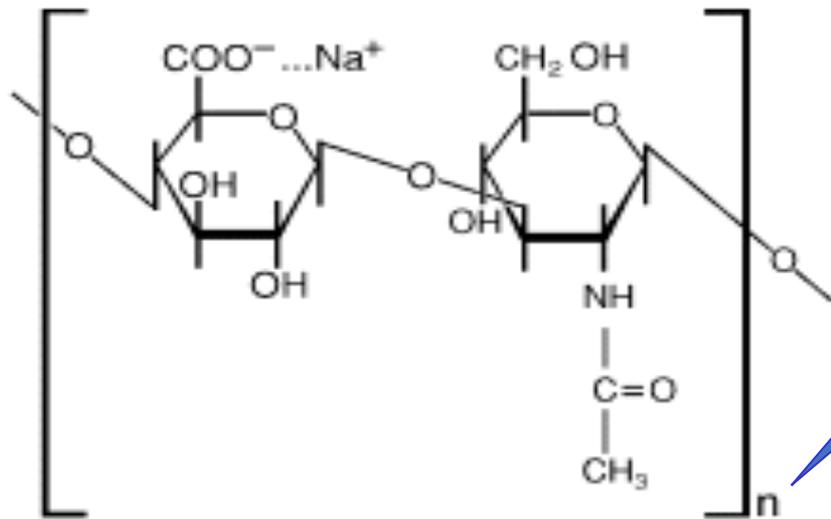
Encapsulate HA;
Bring HA into Color products
Moisturizing, repairing and lip-pumping



Quaternary HA;
Bring HA into Rinse off products
Moisturizing, improving barrier function of scalp

Large molecule- crosslinked HA;
Protective layer
Breathable network structure
Long-lasting moisturizing
Improving skin elasticity
Reducing skin roughness

HA with Different M_w



$N < 25$



Sensitive Skin

Sensitive Skin (SS) , refers to the skin in physiological or pathological condition of a state of high reaction, occurs mainly in the face.

Clinical manifestation is influenced by physical, chemical, spiritual stimulation factors such as skin prone to heat, stabbing pain, itching and subjective symptom such as tension, with or without erythema, descaling, chip, capillary expansion, objective signs.



The Cause of Sensitive Skin

Heredity



Age/Gender Hormone Level Stress



Physical Factor Chemical Factor Iatrogenic Factors

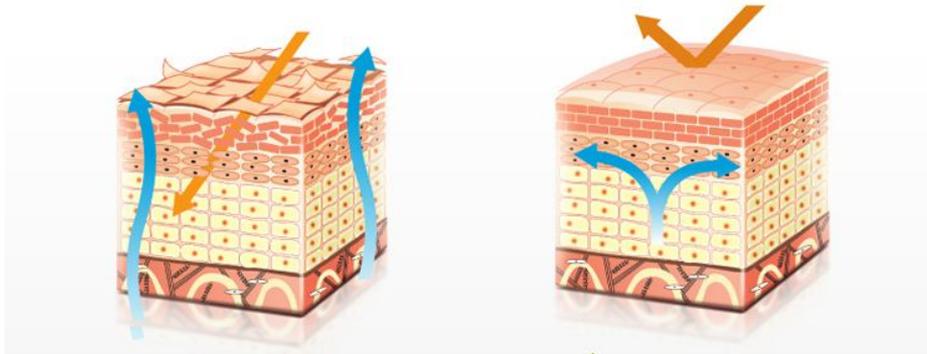


Intrinsic Factor

External Factor

Skin barrier system

The skin barrier system is composed of sebum membrane, keratin, lipid and GAG.



Damaged skin

Healthy skin

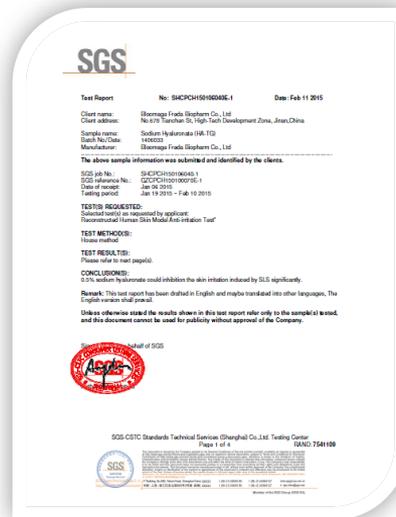
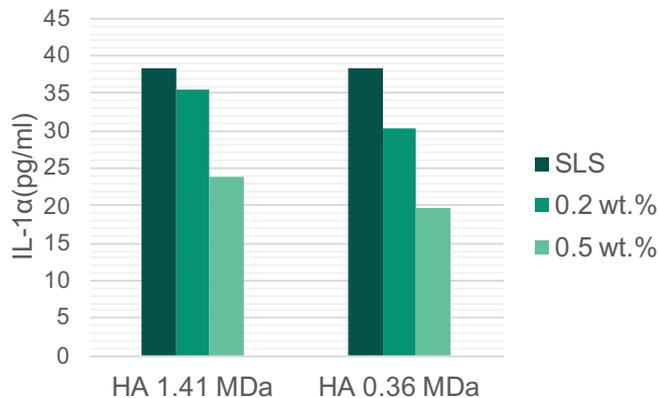
“After the skin is damaged, the bacteria, fungi or viruses symbiotic bacteria on the skin surface get into dermis and trigger autoimmune inflammatory response”.

Anti-inflammatory activity of HA

Test model: Reconstructed Human Skin Model (Episkin) ,

Samples: 0.5% sodium lauryl sulfate(SLS), 0.5wt. % and 0.2wt.% HA

Test method: ELISA



HA has a significant anti-inflammatory effect, the lower the molecular weight, the more significant the anti-inflammatory effect.

HA with MW<5k Da

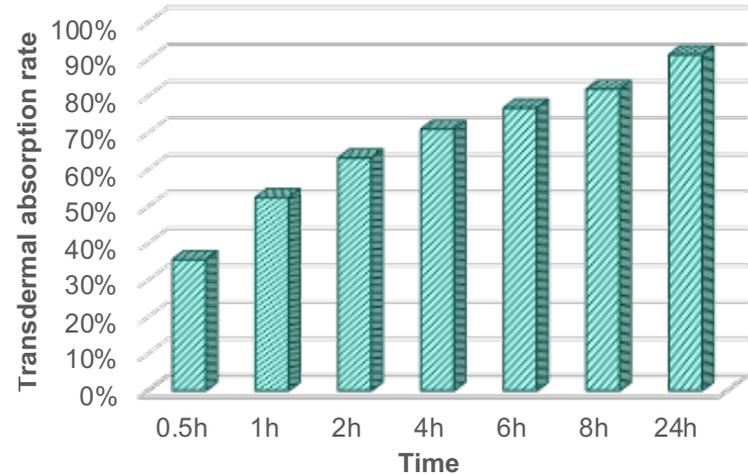
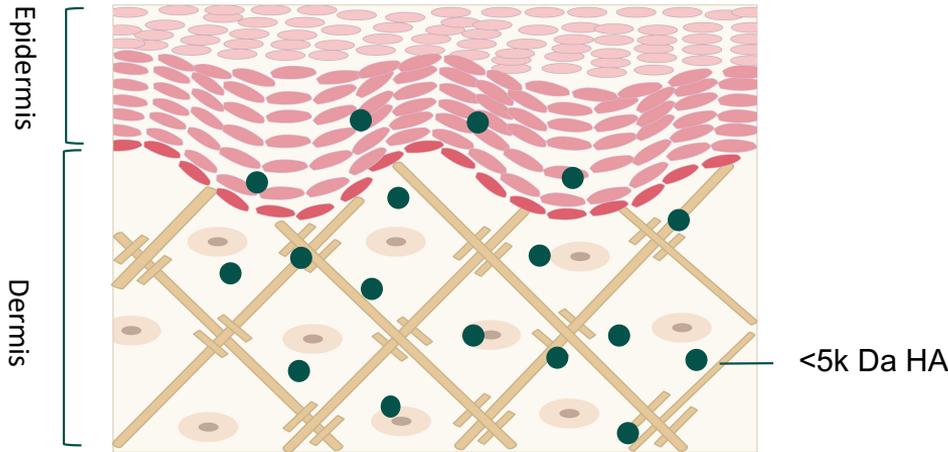
Super Active Hyaluronic Acid is a new low molecular weight active ingredient (<5k Da) produced by a unique enzymatic degradation technology with superb biological activity. It can quickly penetrate the epidermis and the dermis to scavenge free radicals, reduce inflammation factor activity, repair damaged cells, protect the skin against inflammation and sensitivity caused by various external stimulus.



Global patent : WO 2013/123791 A1

Excellent transdermal absorption

<5k Da HA is easy to penetrate into the epidermis and dermis of the epidermis due to its extremely low molecular weight. The results show that, the absorptivity of <5KDa HA was 35.6% after 0.5 hour , 52.5% after 1 hour, 81.9% after 8 hours, and more than 90% after 24 hours.



Significant immunomodulatory effects

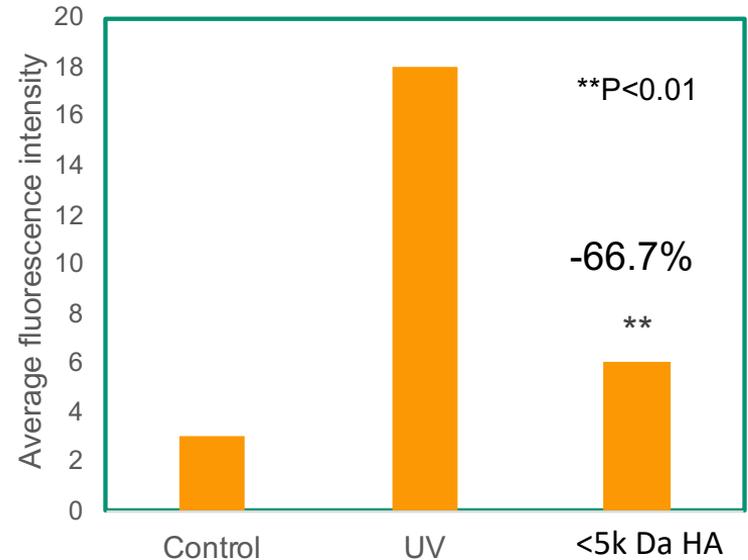
<5k Da binds to CD44 receptors on the cell surface and regulates immune cell activity.

- ◆ Increases the Self-Defense of Skin Epithelium by Induction of -Defensin 2 via TLR2 and TLR4
- ◆ Promote the function of the phagocytic cells and NK cells
- ◆ Can form a coat of cells that acts as a barrier against cytotoxic lysis
- ◆ Stimulate the migration and phagocytosis of macrophages and multinucleated granulocytes and reduce the inflammatory reaction

Ultra high antioxidant activity

When the skin cells are stimulated, they produce a large amount of oxygen free radicals, causing inflammation, thus resulting in skin damage and color spots. Since the 1940s, HA has been found to be degraded by various oxidation systems and ion radiation. Now research has found that HA can remove ROS through its own degradation, and it can also play an antioxidant role by increasing the activity of antioxidant enzymes in the body.

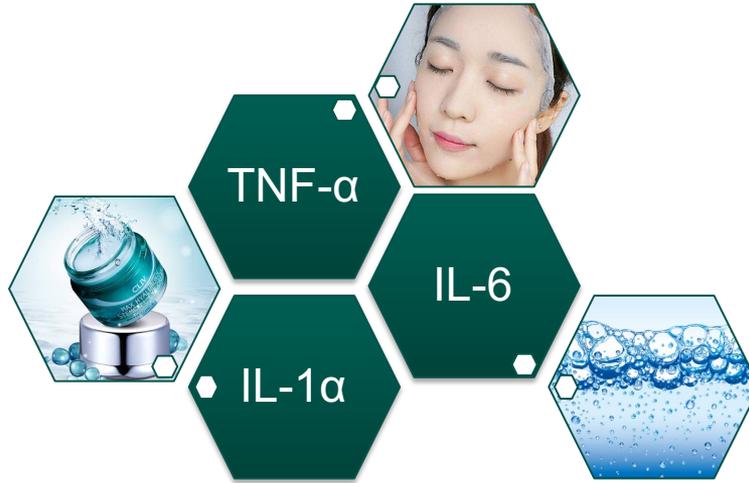
<5kDa HA can effectively remove the UV-induced reactive oxygen free radicals and reduce the inflammatory response. <5k DaHA could reduce the average fluorescence intensity by 66.7% and ROS clearance rate to 81%.



<5k Da HA (0.1%, m/m) , test model: "UVA-L929"

<5k Da HA --Anti-inflammation

Skin damage can lead to an immune response that triggers inflammation. Cytokines produced by immune cells amplify the skin inflammation cascade. To inhibit the release of inflammatory factors it is an effective measure to prevent the rise of inflammation.



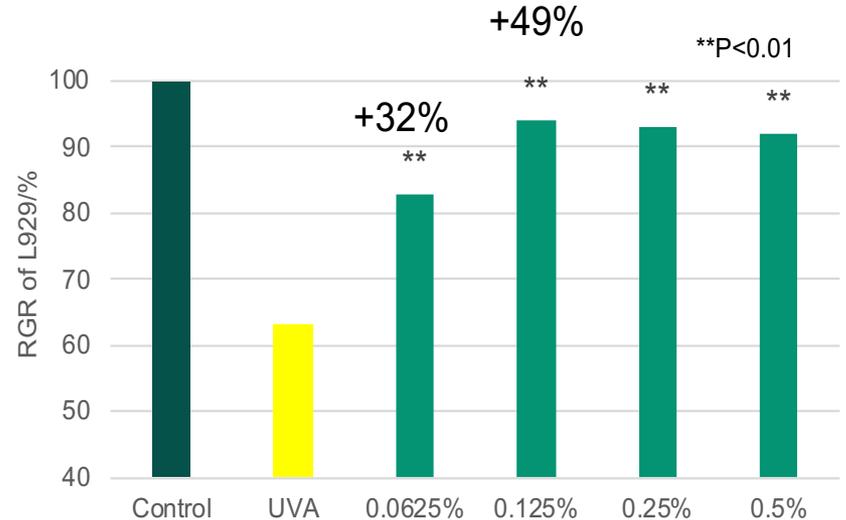
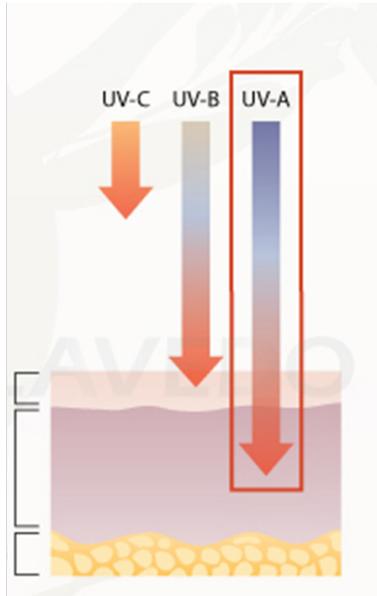
Inhibition of TNF- α release

Inhibition of IL-6 release

Inhibition of IL-1 α release

Repairing UVA-damaged fibroblast cells

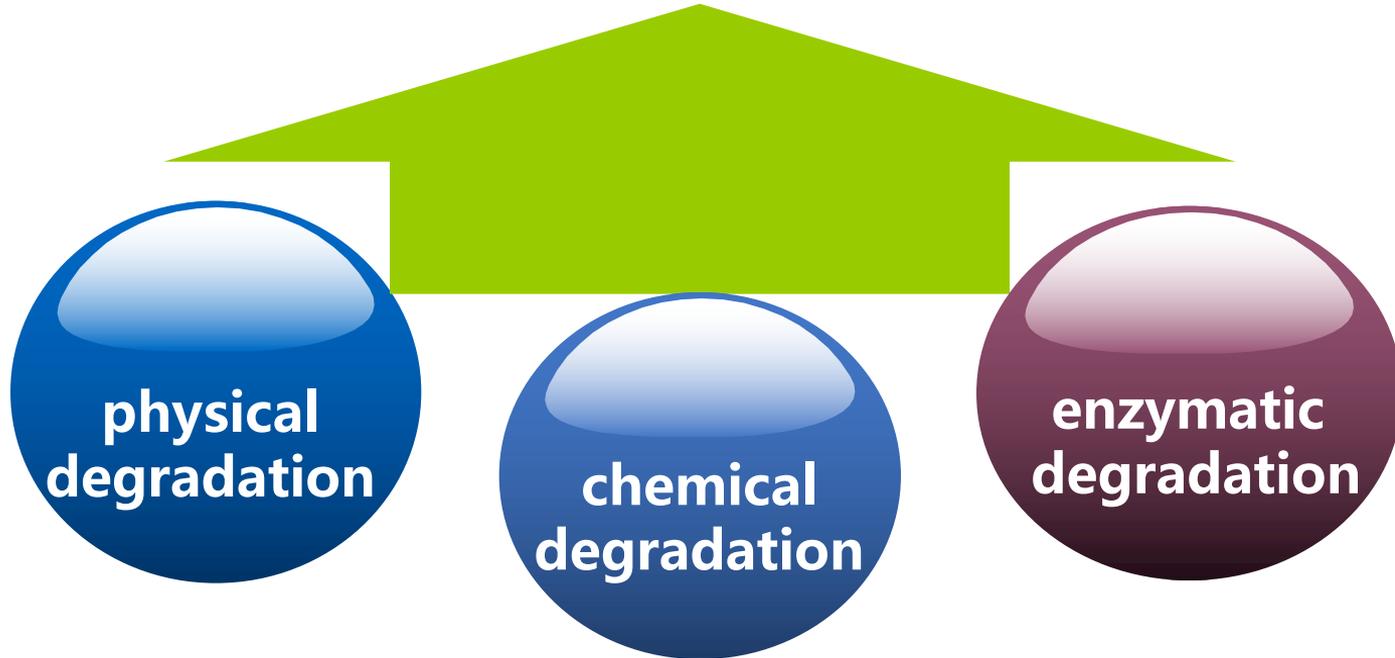
Results show that after UVA irradiation, RGR (relative growth rate) of L929 cells fell to 63%. With the addition of <5k Da HA, the cell proliferation rate increased significantly; 0.125% <5k Da HA can make the cell proliferation rate increase up to 94%.



<5kDa HA (0.0625%-0.5%, m/m) , test model: "UVA-L929"

HA with MW 5kDa-10kDa

low molecular weight HA and Oligo-HA

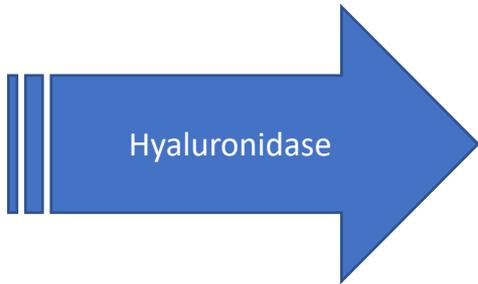


**Traditional Method
Chemical
Degradation**



COMMON OLIGO HA

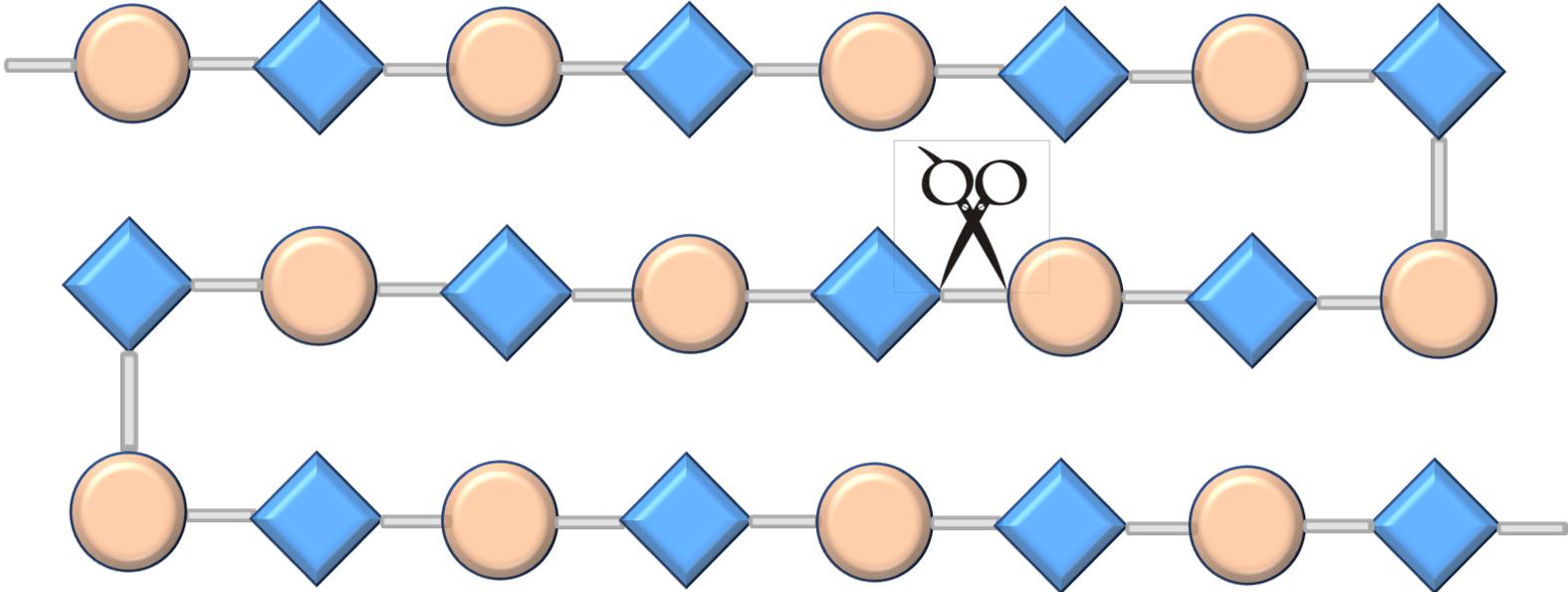
**Innovative Method
Enzymatic
Degradation**



HYDROLIZED SODIUM HYALURONATE

Enzymatic degradation

High specific cleavage of glycosidic bonds

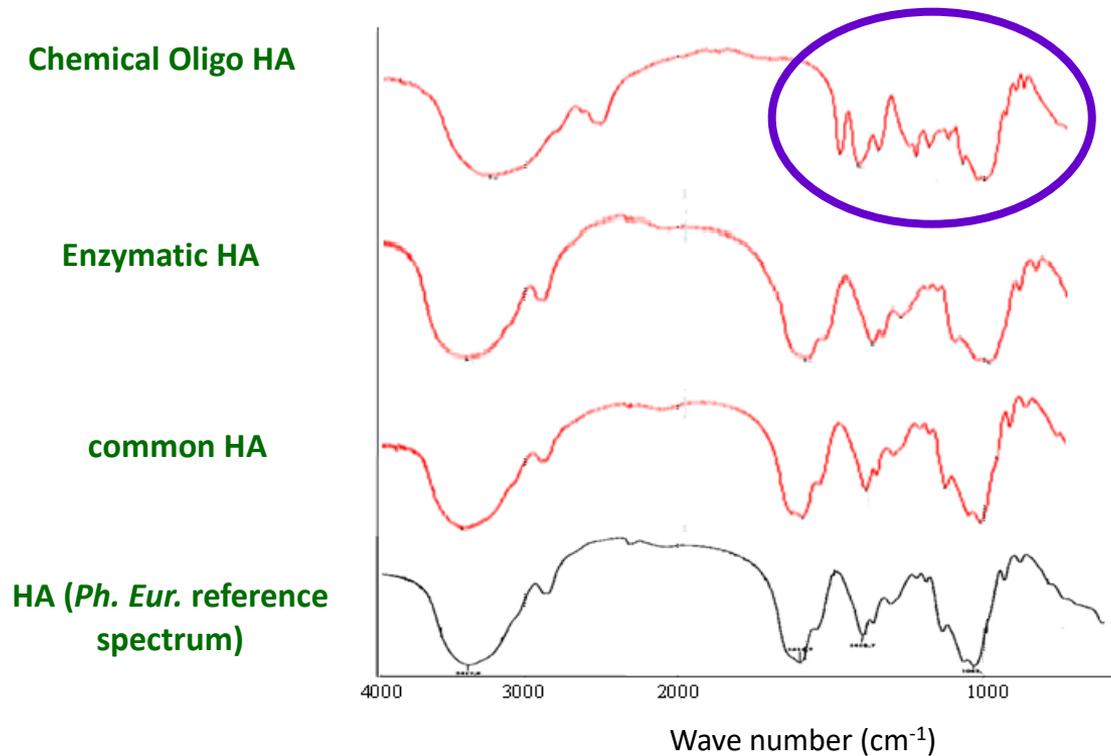


Advantage of enzymatic Oligo HA

Compared with Common HA-Oligo (chemical degradation)

- **Complete structure**
- **Higher purity**
- **No cytotoxicity**
- **Higher safety**

Complete structure — Comparison of IR spectrum



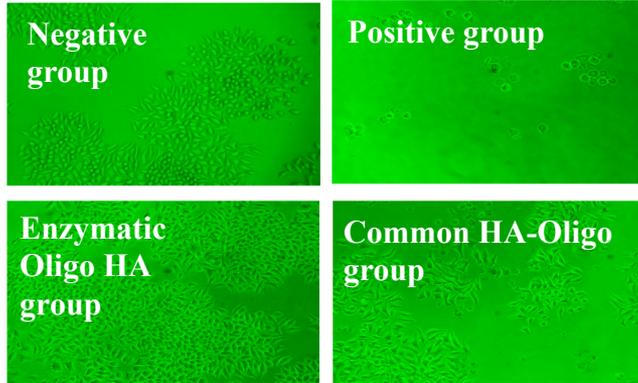
The infrared spectrum of Enzymatic HA is conformed with Ph. Eur. reference spectrum of sodium hyaluronate, while common Oligo HA is obviously different.

Higher purity—HPLC Assay

Sample	Production method
Sample 1	Enzymatic degradation
Sample 2	Enzymatic degradation
Sample 3	Enzymatic degradation
Sample 4	Enzymatic degradation
Sample 1	Chemical degradation
Sample 2	Chemical degradation
Sample 3	Chemical degradation

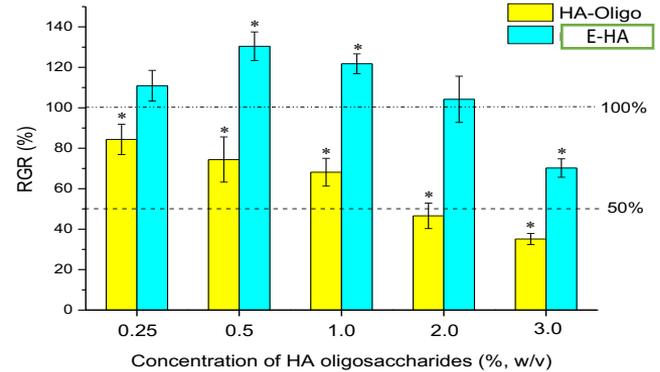
Purity /%
97.66
98.02
98.52
97.79
62.35
67.65
63.23

TOXICITY



Micrographs of cyto toxicity test

- The cells were almost killed for positive group. The cell counts of Enzymatic HA group are obviously more than that of the negative group. **The cell counts of common HA-Oligo are far less than Enzymatic HA group.**



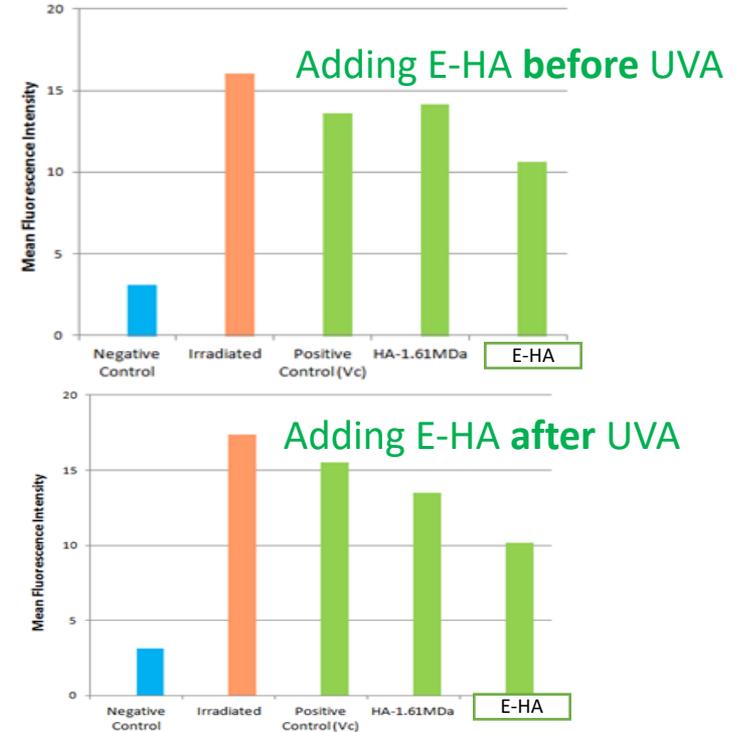
Relative growth rate (RGR) of the cell

- RGR of Enzymatic HA is greater than that of common HA-Oligo at each concentration. Especially when concentration is 1%, RGR of Enzymatic HA is almost the twice that of HA-Oligo. Even if the concentration is 3%, **Enzymatic HA can be considered as non-toxic.**

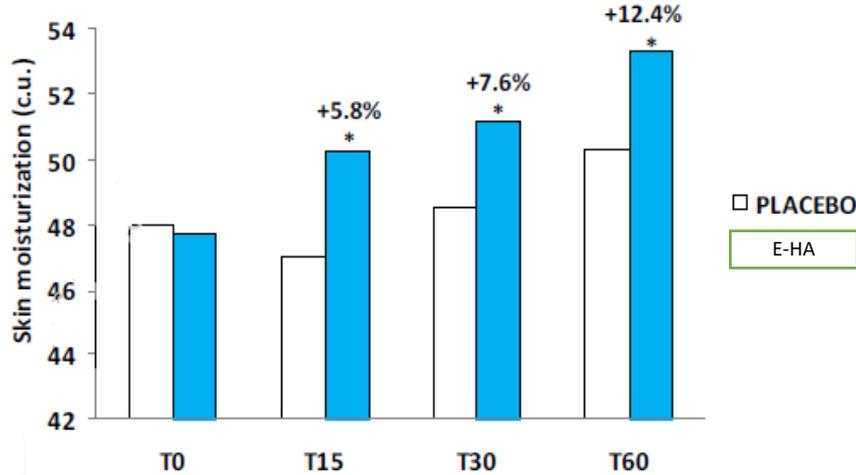
Anti-oxidation activity

ROS (reactive oxygen species) induced by UVA irradiation can accelerate skin aging.

This test was designed to prove the ROS scavenging capacity of E-HA. The lower the average fluorescence intensity was, the higher the ROS scavenging capacity. Whether adding E-HA before or after UVA, we could see the average fluorescence intensity of E-HA group was much lower than positive control. So E-HA has higher anti-oxidation activity.



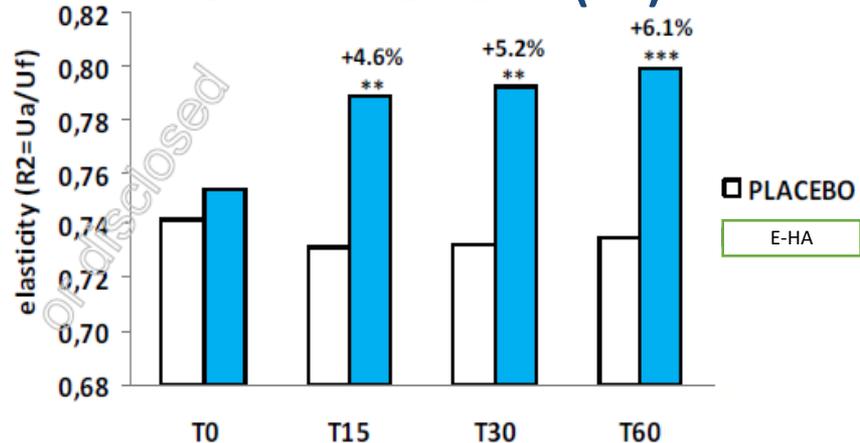
SKIN MOISTURATION



Compared to the placebo group, a statistically significant improvement of skin elasticity of E-HA group was determined. The skin elasticity increased 4.6%, 5.2% and 6.1% after applying E-HA cream 15d, 30d and 60d respectively.

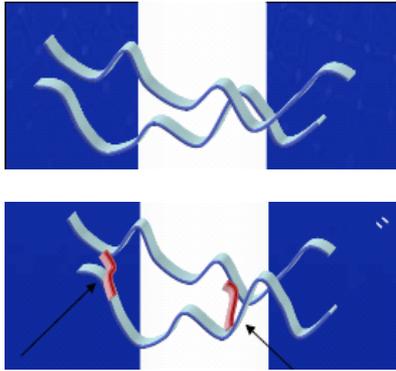
Compared to the placebo group, a statistically significant improvement of skin moisturization of E-HA group was determined. The skin moisturization increased 5.8%, 7.6% and 12.4% after applying E-HA cream 15d, 30d and 60d respectively.

SKIN ELASTICITY (R2)

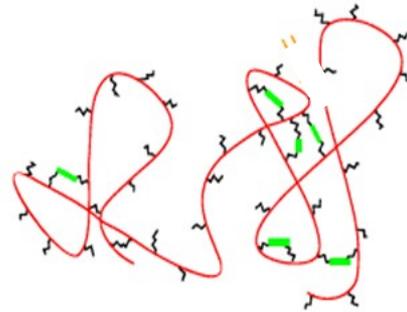


HA Elastomer, MW>3MDa

Hyaluronic Acid Elastomer is a cross-linked polymer derived from natural Hyaluronic Acid (HA). It appears like an elastic gel with high viscosity, able to form invisible biological film on the surface of the skin with various effects, such as moisturizing, protection, slow release, etc.



Cross-linking reaction

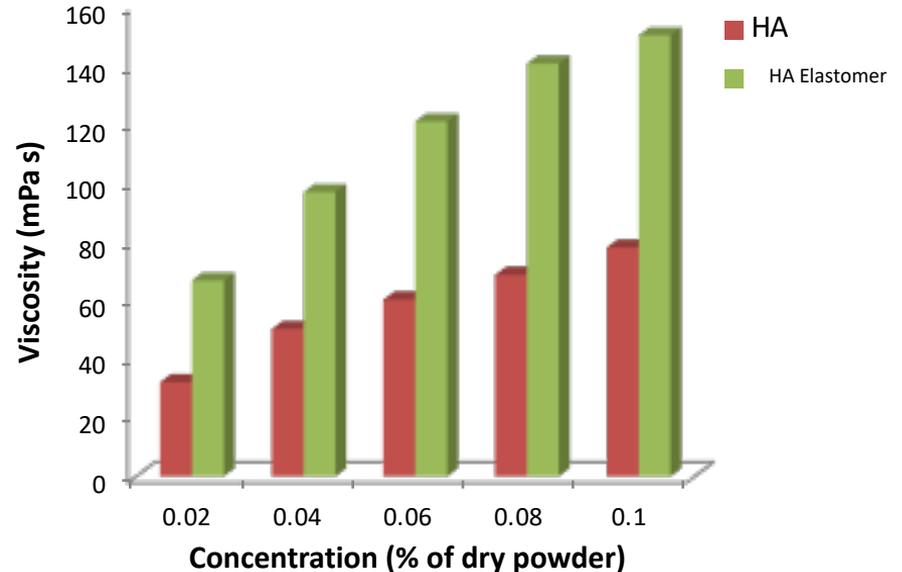


Structural diagram



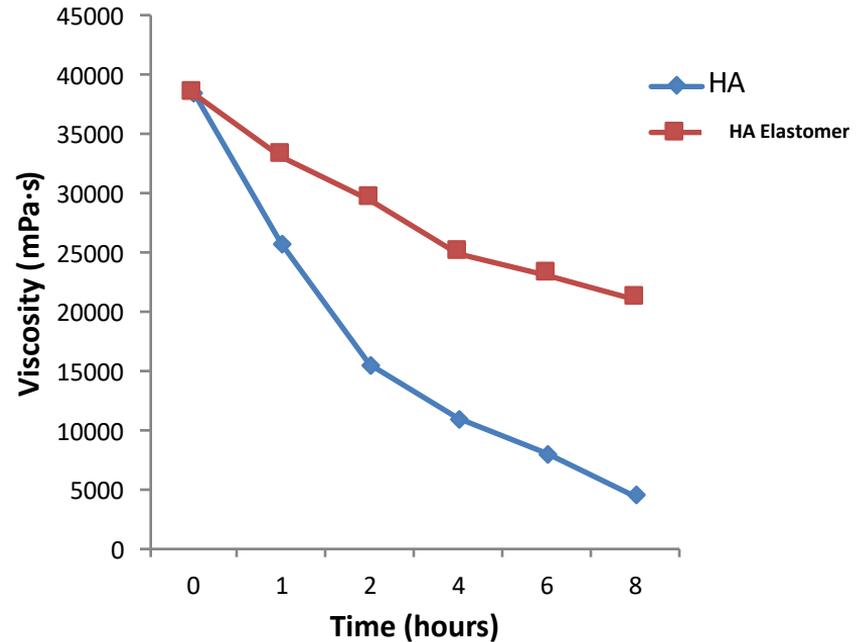
Excellent water binding capacity

The viscosity of a HA elastomer solution is 2-3 times that of an HA solution at the same concentration, which indicates that HA elastomer can bind with more water molecules, because of its cross-linked structure. HA elastomer behaves like a “micro reservoir” delivering continuous water to the skin.



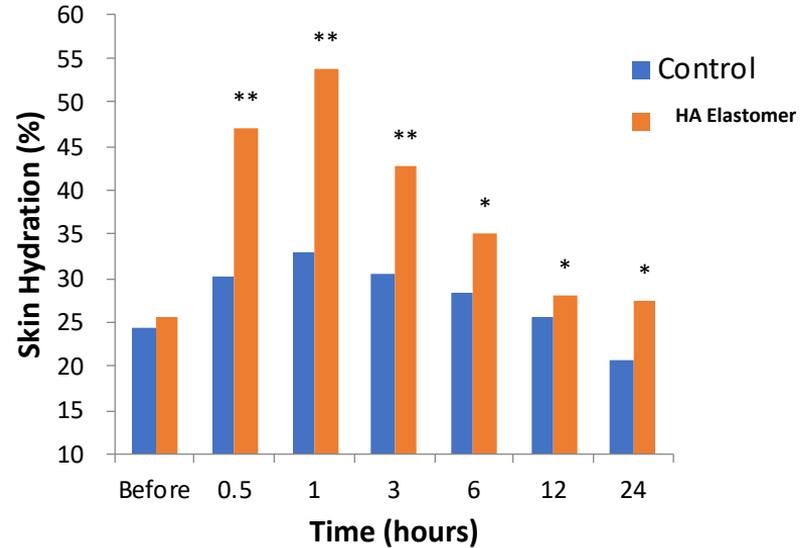
Good resistance to Hyaluronidase

HA Elastomer shows better resistance to Hyaluronidase than common Sodium Hyaluronate, therefore the film formed by HA Elastomer on the skin surface is more stable and durable.

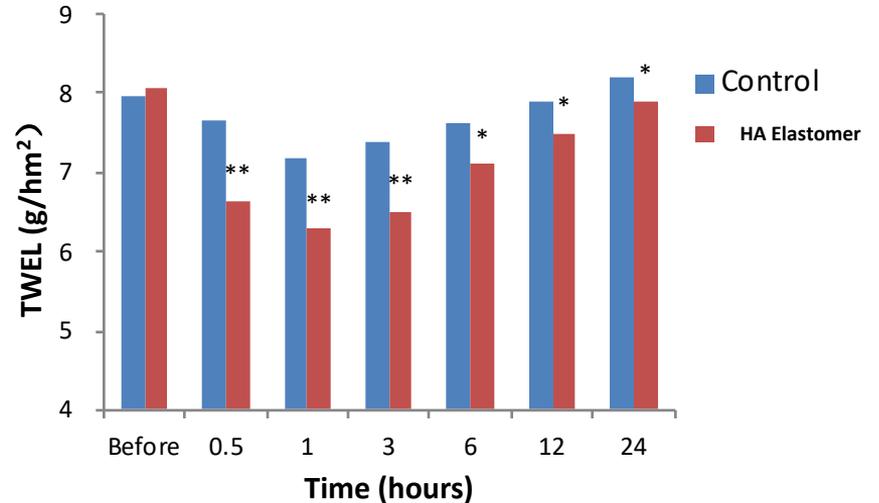


Long-lasting Moisturizer

Compared to the control group, the skin hydration of the HA Elastomer group was increased by 85% after 0.5h and 110% after 1h. HA Elastomer significantly increased skin hydration even after 24h.



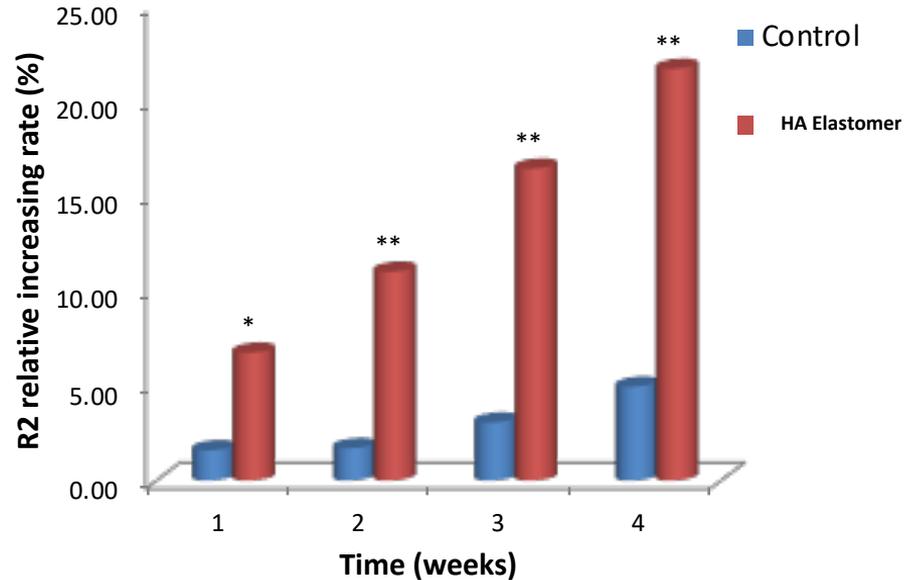
Compared to the control group, the skin TEWL of HA Elastomer group was reduced by 18% after 0.5h and by 22% after 1h. HA Elastomer significantly reduced skin TEWL even after 12h.



HA Elastomer can keep cuticles moisturized, because of the excellent water binding capacity and can also decrease the water evaporation of the deeper skin moisture by forming a dense film on the skin surface.

Improving skin elasticity

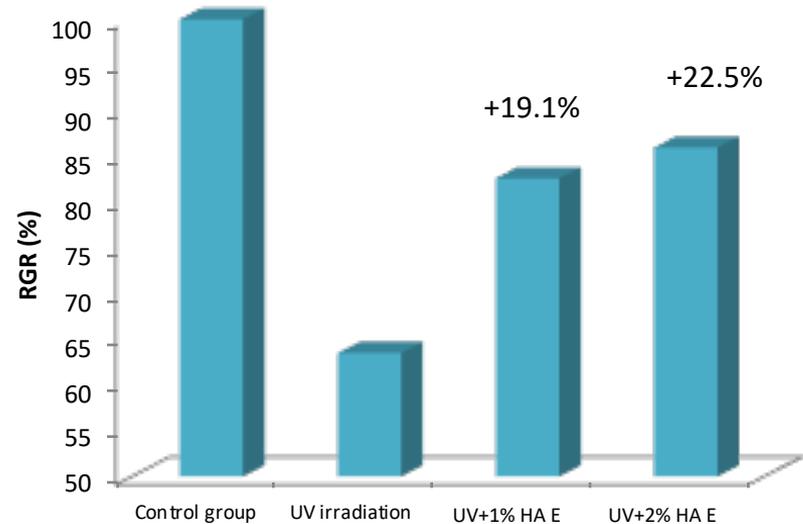
Compared to the control group, the skin elasticity of HA Elastomer group was significantly increased. After 4 weeks of application, the relative skin elasticity increasing rate for the HA Elastomer group reached 21.6%.



Protecting cells against UV

The relative growth rate (RGR) of HaCat cells was decreased sensibly after UV irradiation. While RGR increased 19.1% after 1% HA Elastomer pretreatment and 22.5% after 2% HA Elastomer pretreatment.

The results indicate that HA Elastomer has UV protection ability, and it can effectively reduce cell damage induced by UV irradiation.



Anti-pollution

Performed by: Korea Institute of Dermatological Sciences, KOREA

Subject: 3D Reconstructed Human Skin Tissue Model (Epidermal keratinocyte Progenitors)

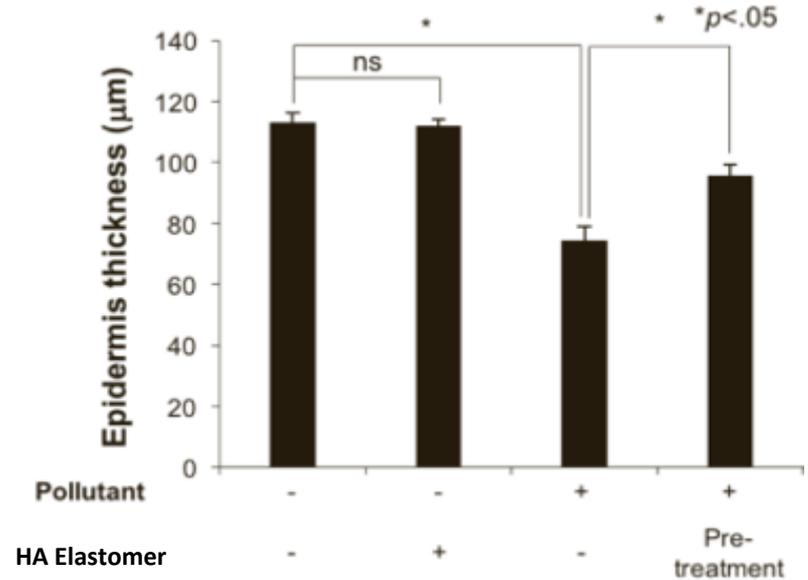
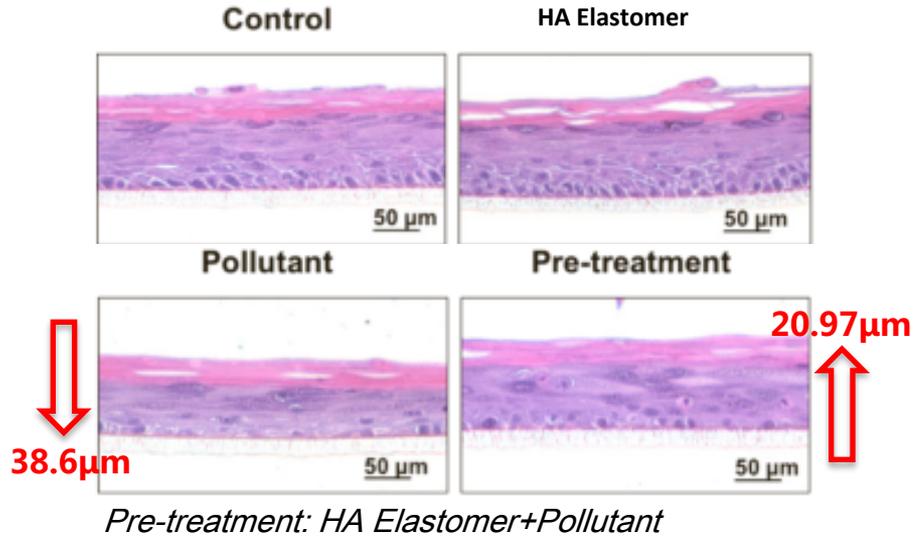
Pollutant: Particulate matter (*ISO 12103-1, A1 Ultrafine test dust, Power technology, USA*)

Method: 3D Reconstructed Human Skin Tissue Model was treated by pollutants and HA Elastomer (1 μ g/mL) respectively, observing the skin tissue and measuring skin thickness. 3 proteins related with skin barrier were analyzed by immunofluorescence method.

Conclusion: HA Elastomer shows the safety on skin, blocking efficacy on pollutant and functional effect of skin barriers.

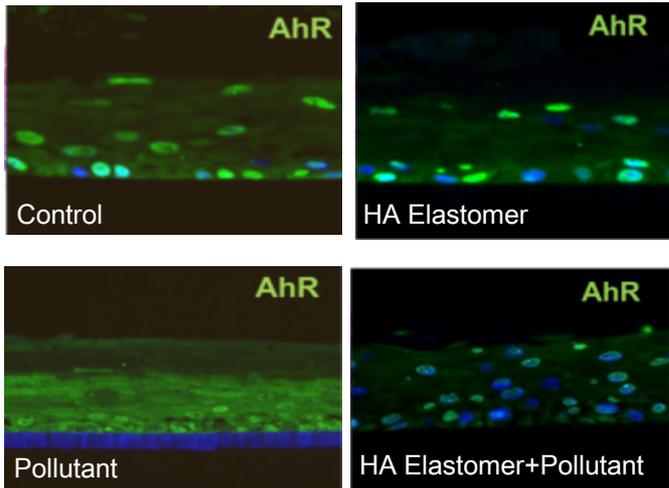


Morphology analysis

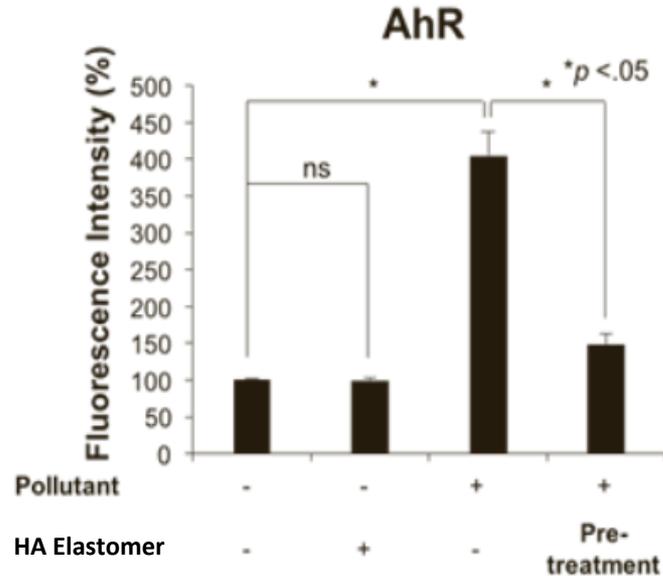


Compare with the control group, the skin tissue of the pollutant group showed abnormal morphology and the skin thickness decreased 38.6μm. On the other hand, the skin tissue damage was reduced by pretreatment with HA Elastomer and the thickness of skin tissue increased 20.97μm compared to the pollutant treated group.

Reducing AhR expression

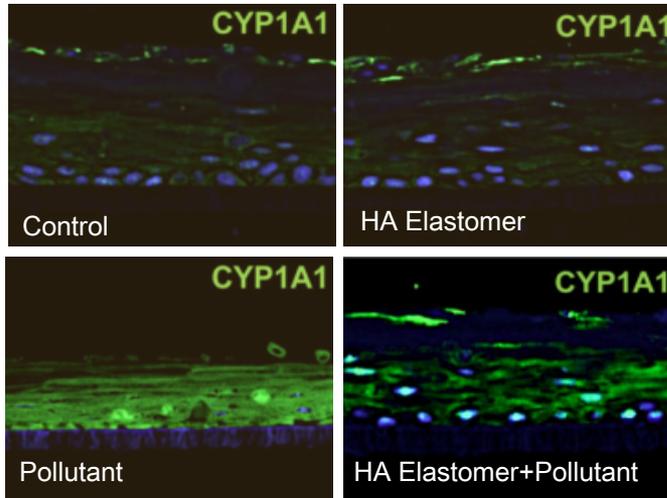


AhR (Aryl hydrocarbon receptor), Green



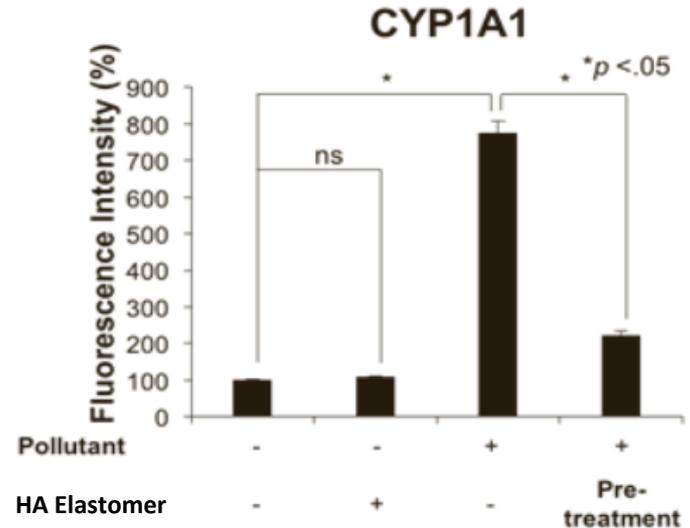
When HA Elastomer was pretreated 24 hours prior to the treatment of pollutant, and then cultured for 24 hours with pollutant treatment, the expression of AhR was reduced by 63.26%.

Reducing CYP1A1 expression

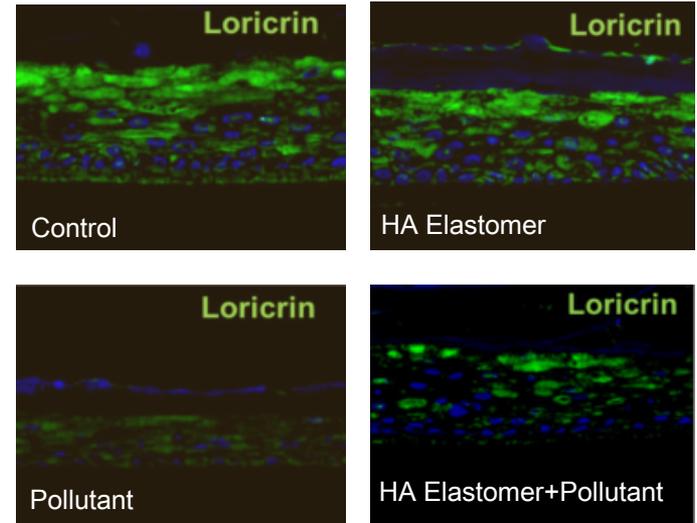
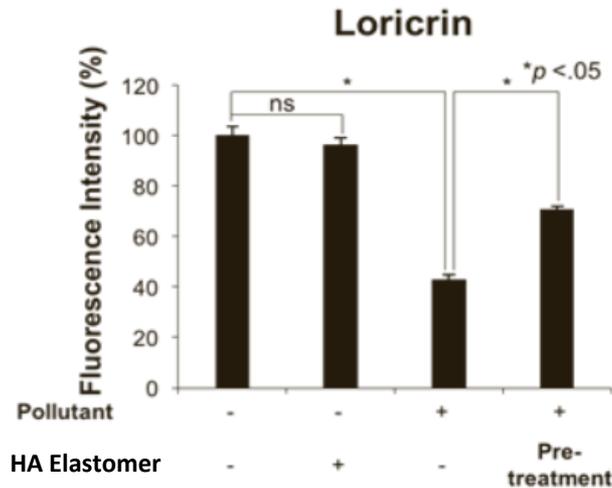


CYP1A1 (Cytochrome P450 1A1), Green

When HA Elastomer was pretreated 24 hours prior to the treatment of pollutant, and then cultured for 24 hours with pollutant treatment, the expression of CYP1A1 was reduced by 71.44%.



Increasing Loricrin expression



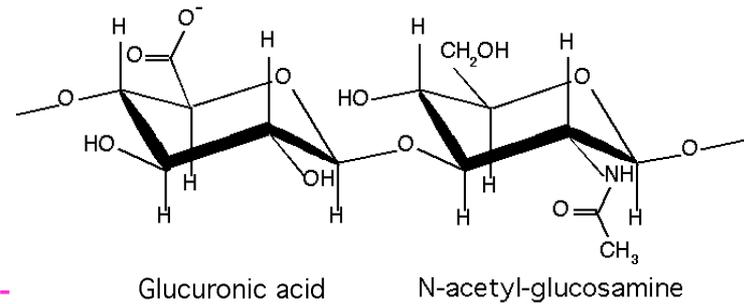
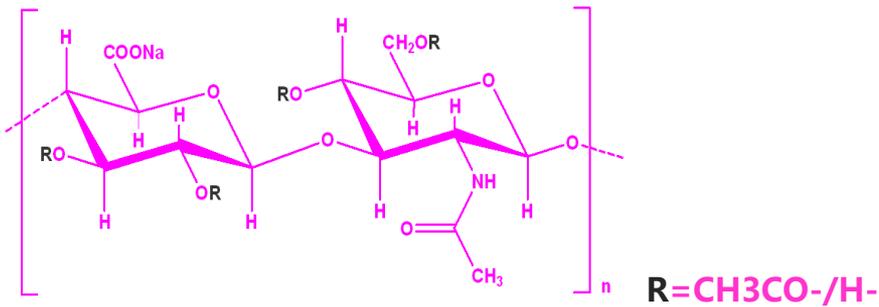
Loricrin, main ingredients of skin barrier, Green

The expression of Loricrin involved in the skin barrier function increased by 64.93% compared to the pollutant treated tissue group.

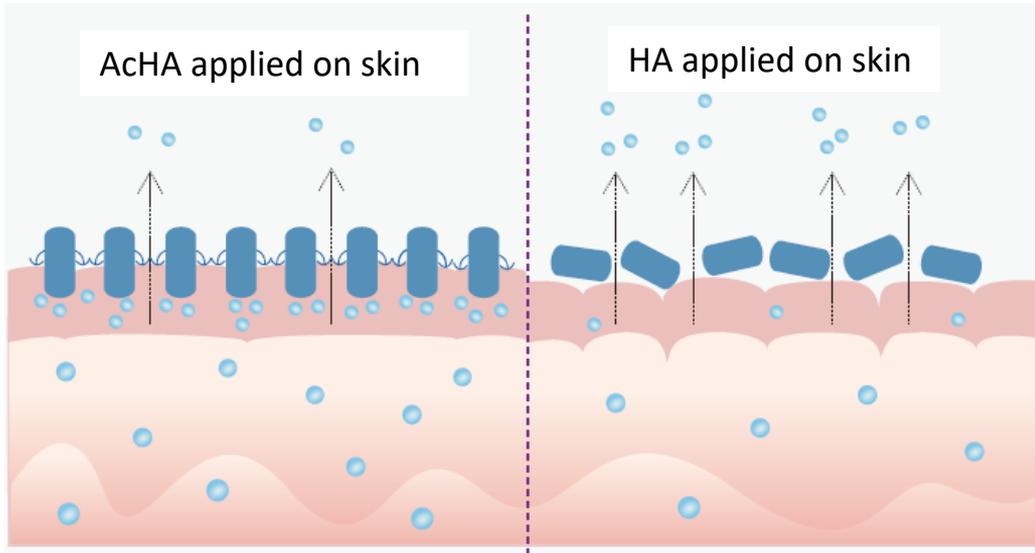
NEW HA DERIVATIVES

- Sodium Acetylated Hyaluronate
- Zn-Hyaluronate
- Sodium Anhydroformyl hyaluronate
- Sodium Azidyl hyaluronate
- Sodium Butanoyl
- Sodium Caproyl
- Sodium Linolenoyl Hyaluronate, modified by alpha linolenic acid
- Sodium Octanoyl formyl
- Sodium Oleyl
- Sodium Palmitoyl
- Dimethylsilanol Hyaluronate, by organic silicium and HM hyaluronic acid

Sodium Acetylated Hyaluronate (AcHA), is a specialty HA derivative which is synthesized from the Natural Moisturizing Factor Sodium Hyaluronate (HA) by acetylation reaction. The hydroxyl group of HA is partially replaced with acetyl group; it owns both lipophilic and hydrophilic properties. This helps to promote high affinity and adsorption properties for the skin. AcHA has a fresh and not-sticky feeling that can provide superb moisturizing, repair skin barrier, improve skin elasticity, and can leave skin smooth.



High affinity & adsorption



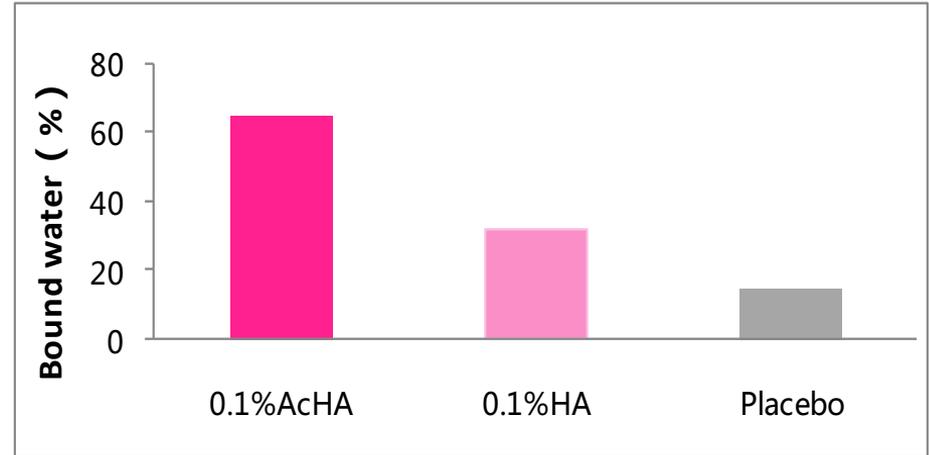
The acetyl group which is highly lipophilic, can help AcHA adhere firmly to the skin surface. Its small molecular weight allows AcHA to penetrate into stratum corneum rapidly. Thus, AcHA can stay on epidermis very tightly with a **semi-submerged structure**.

This prevents water evaporation and improves moisture accumulation from inside, while penetrating skin to bind water and softening stratum corneum. AcHA can remarkably reduce skin dryness and roughness and enhance the elasticity.

Superb moisturization

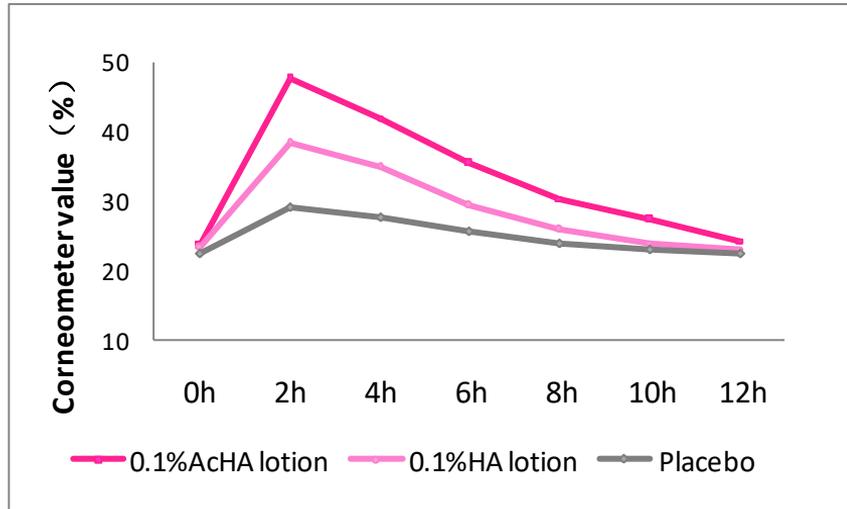
◆ Water-binding ability in stratum corneum

Compared to HA group, AcHA has higher water-binding ability and can provide a substantial hydrating effect to stratum corneum.



• *First treat skin materials with AcHA/HA aqueous solution, then test the amount of water bound in stratum corneum through measuring the loss on drying. Results show that, AcHA group has bound almost twice as much water as HA group.*

Increase skin hydration



•Instrument : Corneometer CM825

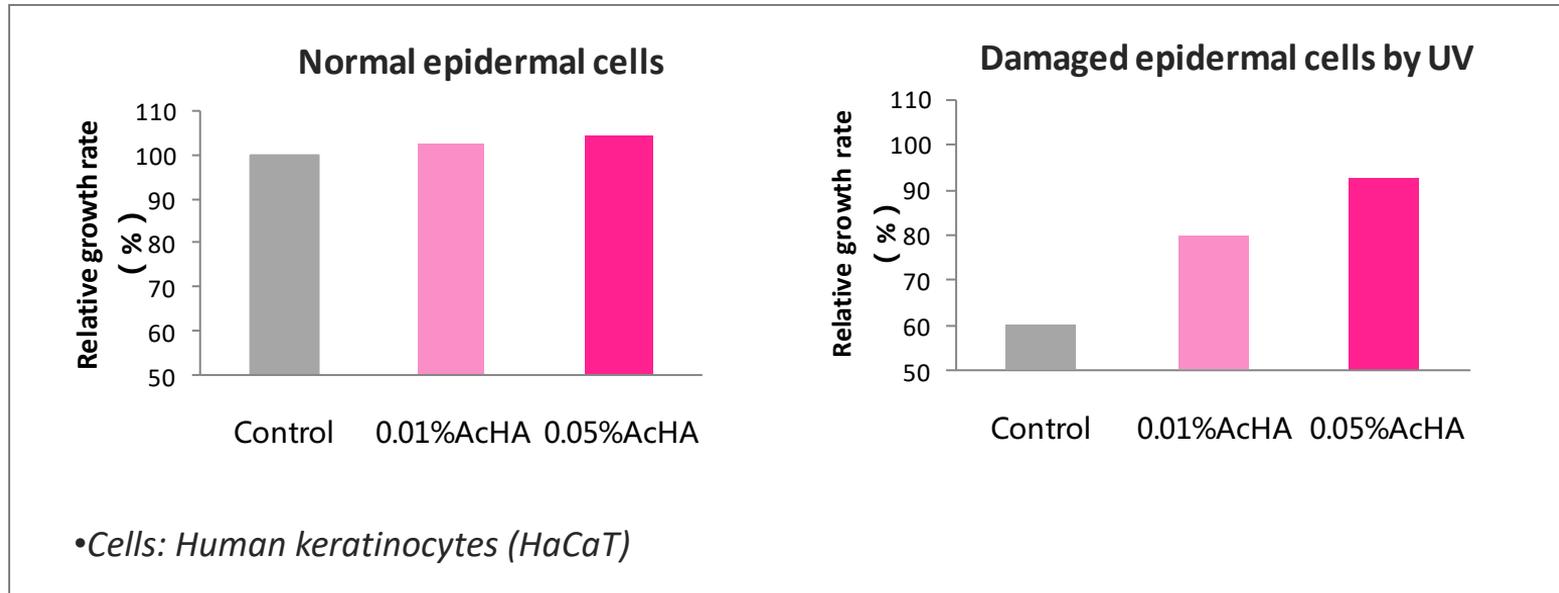
•Volunteers : 30 healthy women

AcHA binds water quickly to increase skin hydration while keeping the skin moisturized during the day.

•After 2hrs application, the skin hydration of AcHA group is increased quickly by 103.4%, compared with 65.3% of HA group and 29.6% of placebo group.

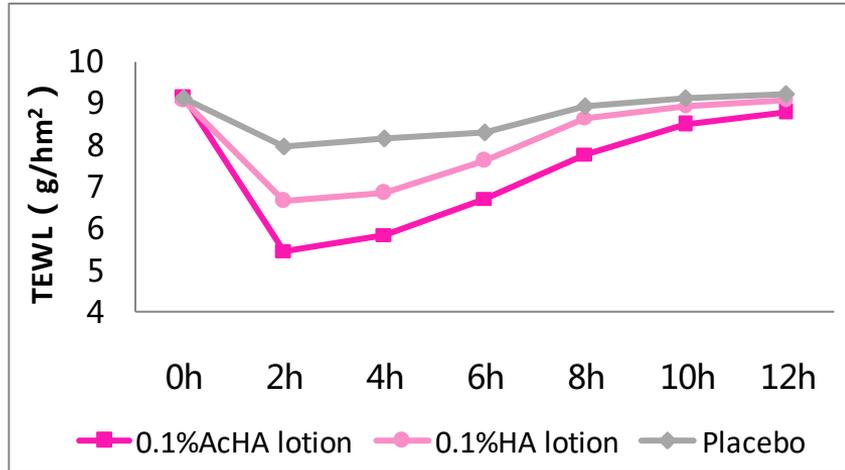
AcHA can keep skin moisturized and last for 12 hours.

Promote epidermal cellular proliferation



AcHA can promote cellular proliferation and repair damaged epidermal cells, thus strengthen the barrier function of stratum corneum.

Reduce water evaporation



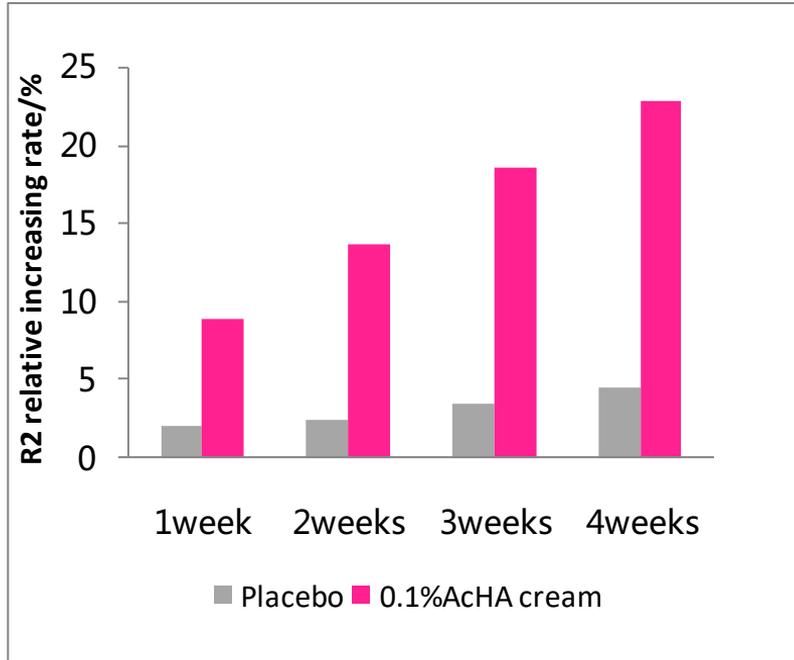
AcHA can repair skin barrier function and effectively reduce water evaporation from inside, thus improving the skin dryness and roughness.

- After 2hrs application, the skin TEWL of AcHA group is reduced by 40.5%, compared with 26.9% of HA group and 12.6% of placebo group.
- AcHA can reduce skin evaporation and last for 12 hours.

• Instrument : Tewameter TM300

• Volunteers : 30 healthy women

Improve skin elasticity

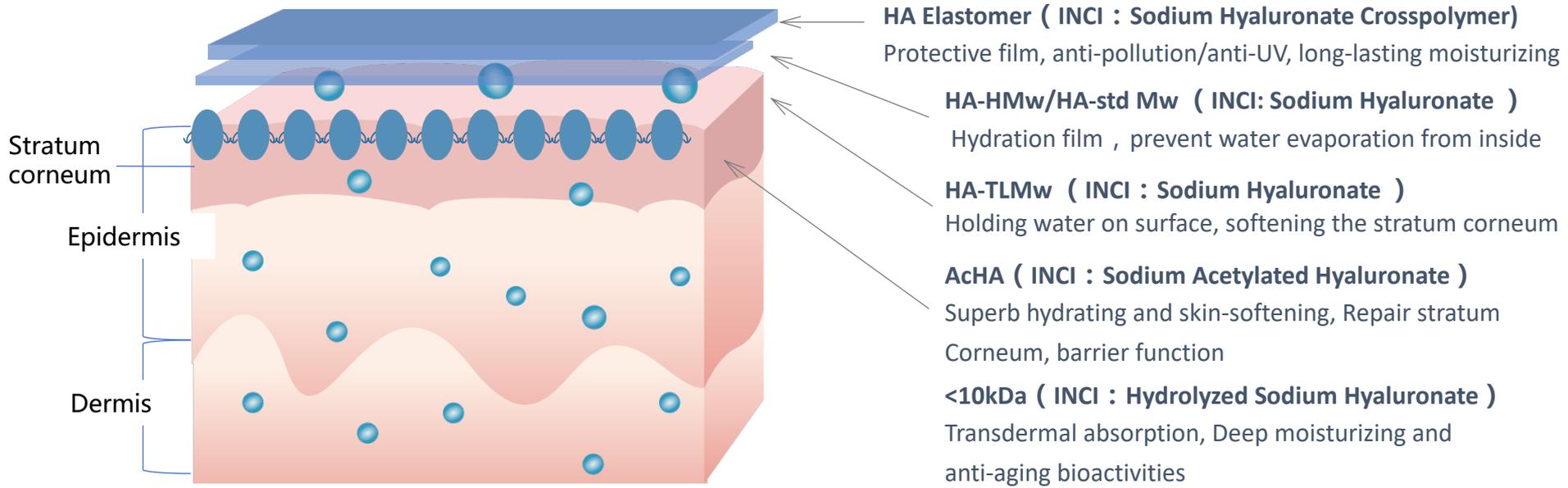


After 4 weeks of continuous application of a facial cream containing 0.1% AcHA, the skin elasticity of volunteers has significantly increased by 1.6 times and skin is softened.

•*Instrument : MPA580*

•*Volunteers : 30 healthy women*

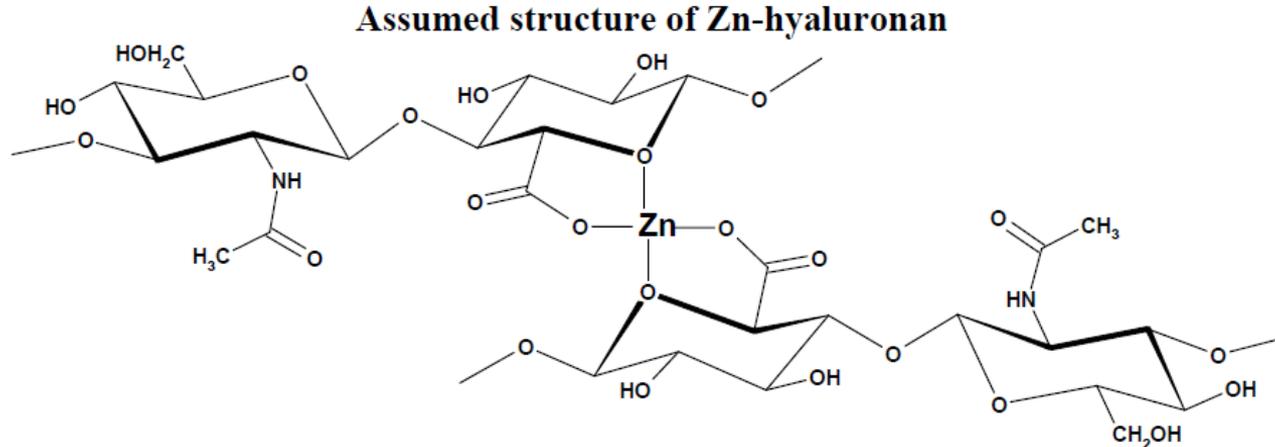
Full spectrum activity based on MW



Zn-Hyaluronate

An effective and outstanding raw material for Wound healing

Zinc can be used as an alternate cation to bind to HA, aim to enhance the therapeutic benefits of Sodium Hyaluronate (HA-Na), it is called **Zinc Hyaluronate (HA-Zn)**.

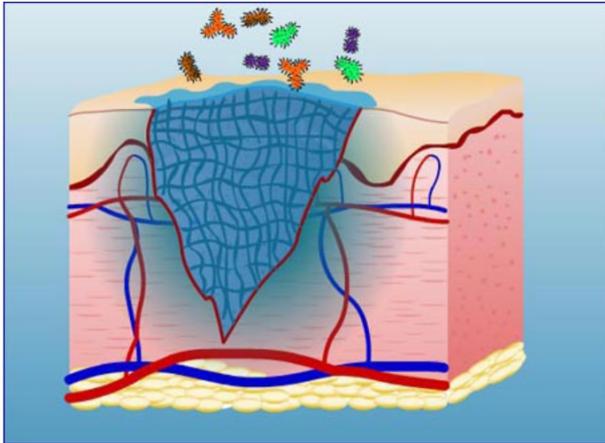


Zn-Hyaluronate

Functions

Moist & Repair

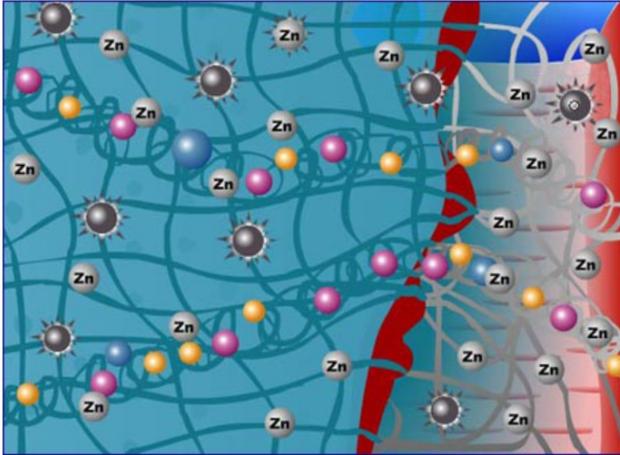
Infection prevention



Due to the molecular pore size of the zinc hyaluronan matrix acts as an antimicrobial filter against bacteria of airborne and contact origin, this shielding the healing wound from infection.

Zn-Hyaluronate

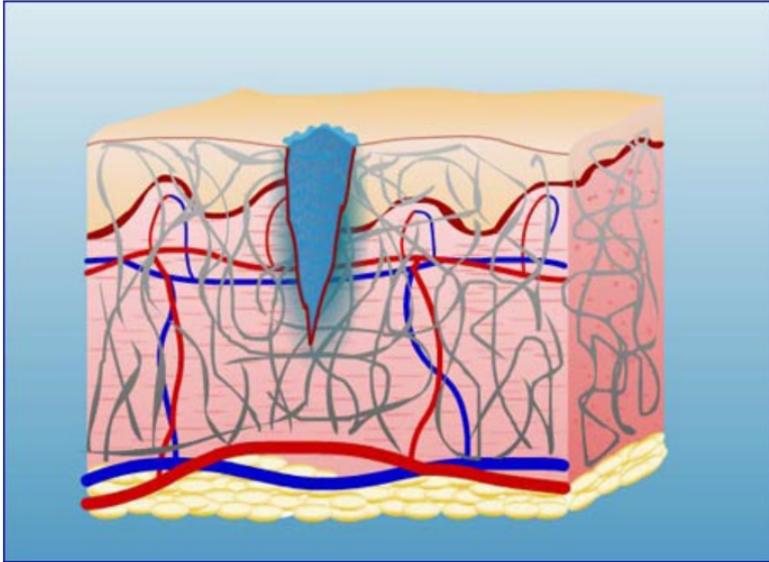
Anti-inflammation



- Being a constituent of the enzymes necessary for anti-inflammatory processes, zinc itself is an indispensable element of wound healing.
- In chronic wounds the zinc content of tissues is lower.

Zn-Hyaluronate

Scars healing



helps to restore the damaged skin to its natural condition and appearance...

Zn-Hyaluronate

Applications

Recommended in topical products for smoothing and healing efficacy

Acne vulgaris

Burns

Diabetic foot ulcer

Postoperative trauma

Novel HA designed for Color Cosmetics

Lip Structure

◆ Lips need more care

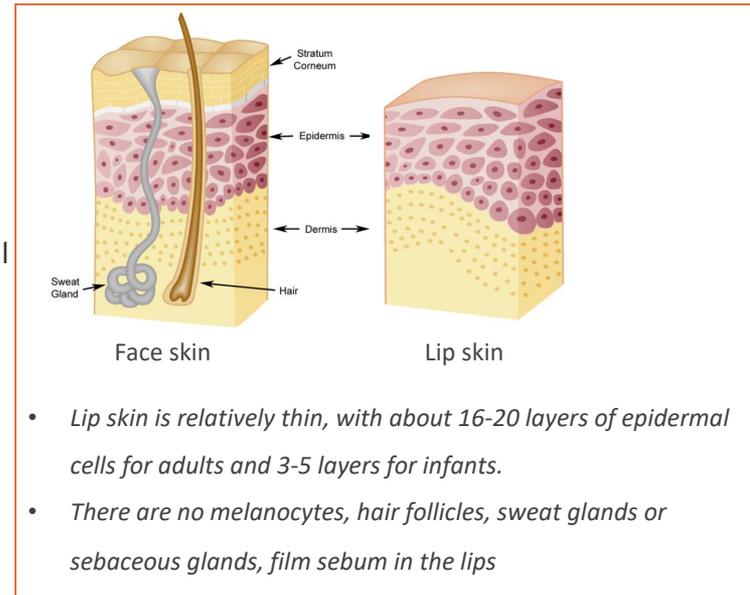
- Lips have the weakest resistance to environmental intrusions, compared to other parts of the body and they are most likely to show signs of aging.
- For lips, the cuticle is very thin, and in the absence of sebum and film protection, lip's skin evaporation is faster than normal skin, so it is prone to drying, peeling, lip wrinkles deepen and so on.



Drying



Peeling



- Besides color and texture, hydrating and nourishing are also very important for lip products.
- Lipstick with moisturizing ability becomes the first choice by consumers.



Dry lines



Moist and full

Popular lipsticks in the market

Sodium Hyaluronate (HA)

- HA, due to the highlights and differentiation factor of products, is popularly used in lipsticks which are not only the most popular products in 2017, but also new released products in 2018.



Estee Lauder



Givenchy



YSL



Dior



Guerlain



Revlon



Amani New Ecstasy Shine



CPB Lip gloss



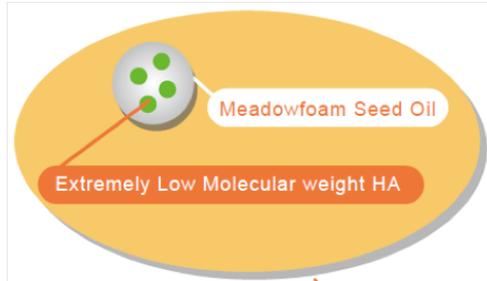
Nars Powermatte Lip Pigment



The lipstick of China's Palace Museum

Oil Dispersed HA

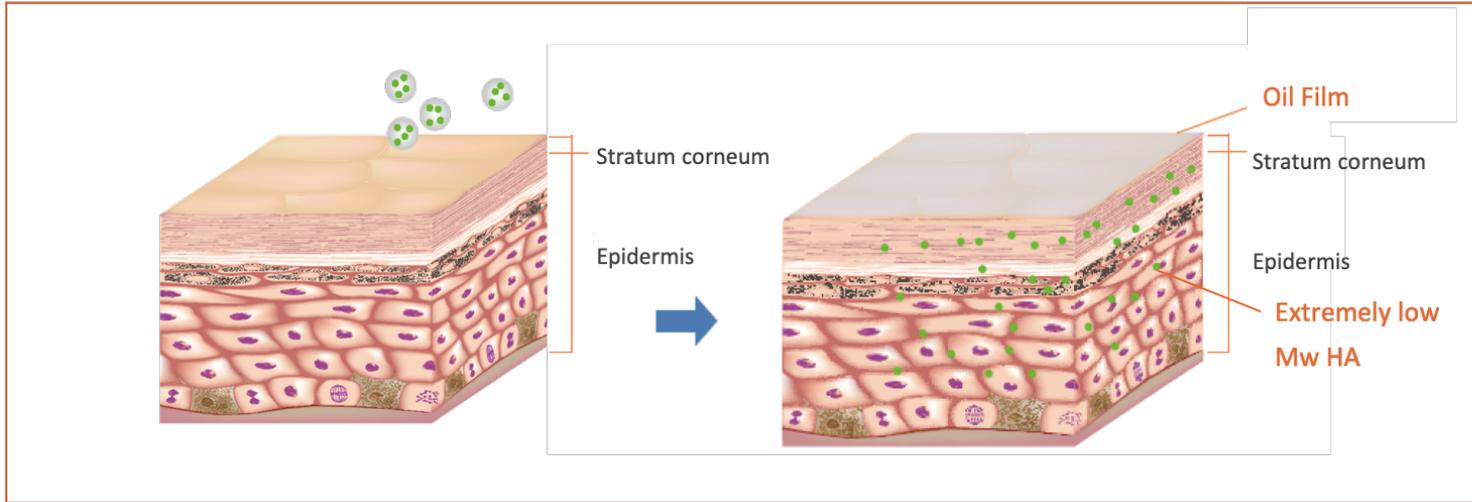
Oil-dispersed Sodium Hyaluronate, a new type of Sodium Hyaluronate (HA) designed for color cosmetics, is obtained by the combination of extremely low molecular weight HA and Meadow foam seed oil or Ricinus castor oil through the unique HA microsphere technology. This perfect combination of HA with botanical oil will permit water soluble-HA to be easily applied into the color cosmetic formulations which are mainly based on oily ingredients. It can provide significantly moisturizing ability, nourish the skin from inside out, then improve skin dryness and roughness.



- ◆ Vegetable oil, the outer component of Oil dispersed HA, owns excellent skin affinity and nourishing ability.
- ◆ The inside part is based on the extremely low molecular weight HA, which has good transdermal absorption, hydration and repairing ability.

The microsphere structure of Oil dispersed HA

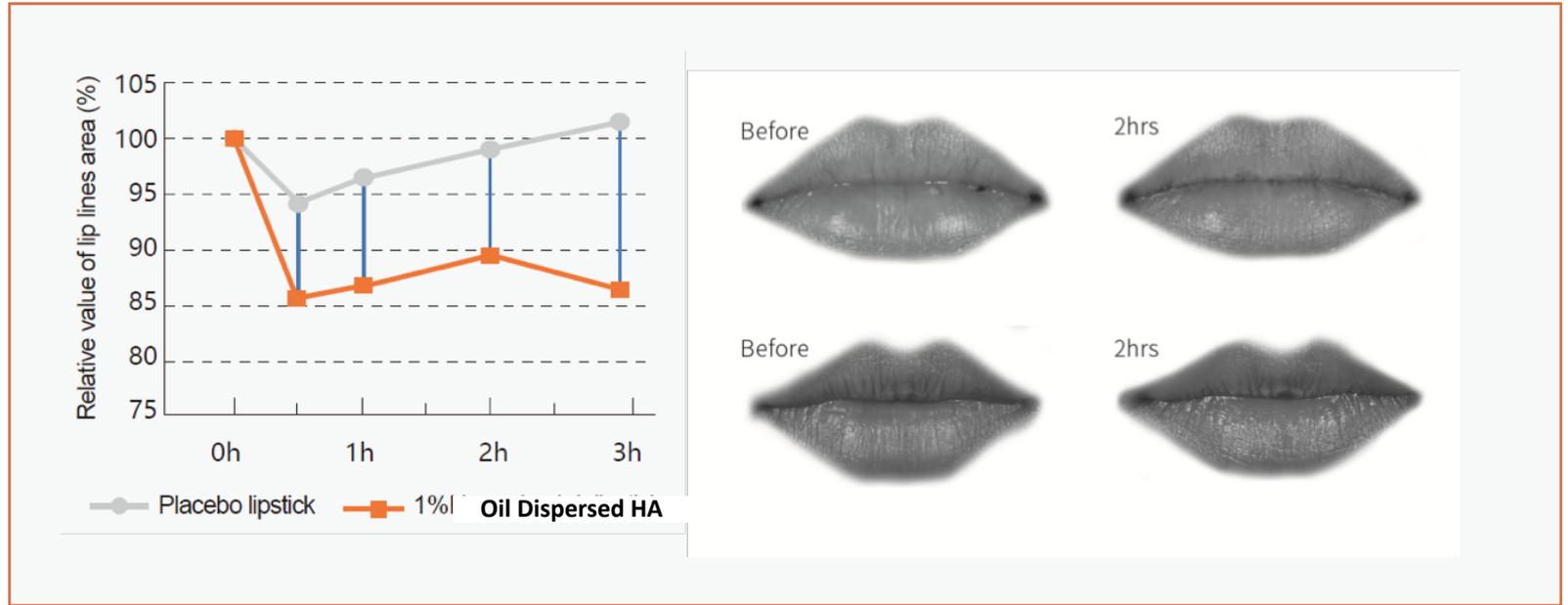
Action mechanism



When applied Oil dispersed HA onto the skin surface, the microsphere will easily break down, thus allowing the extremely low molecular weight HA to be released and penetrate into the skin quickly, for water-holding, water-locking and nourish the skin from inside. The outer layer of meadowfoam seed oil can form an oil film on the skin surface which prevents water evaporation and improve moisture accumulation from inside.

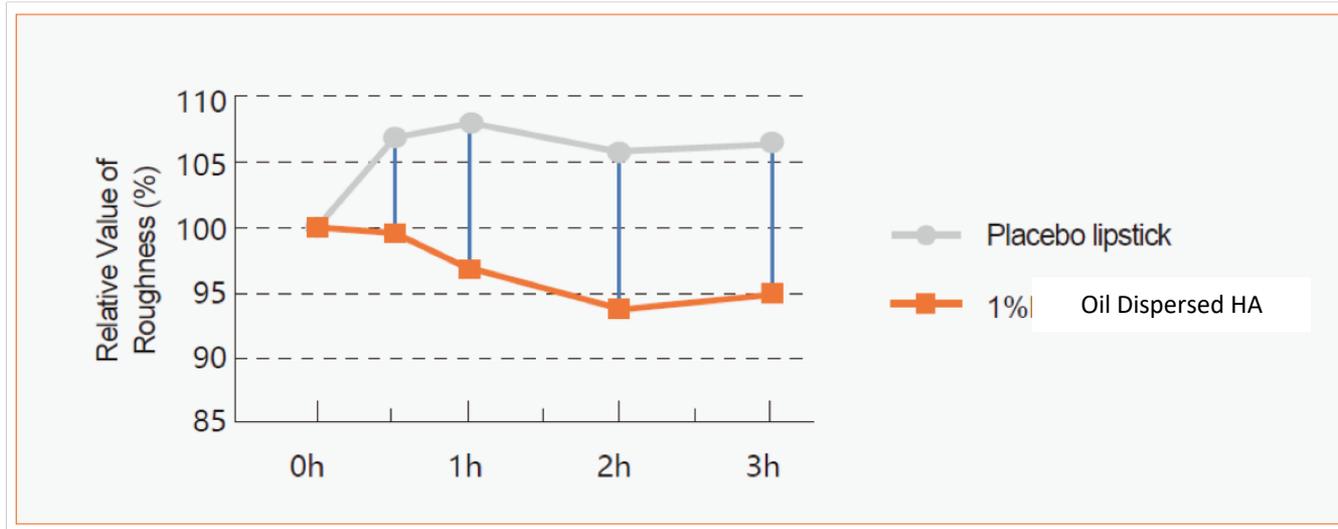
The double moisturizing efficacy of Oil Dispersed HA can hold water from outside, bind water from inside and improve skin dryness and roughness directly from within.

- **Texture evaluation**



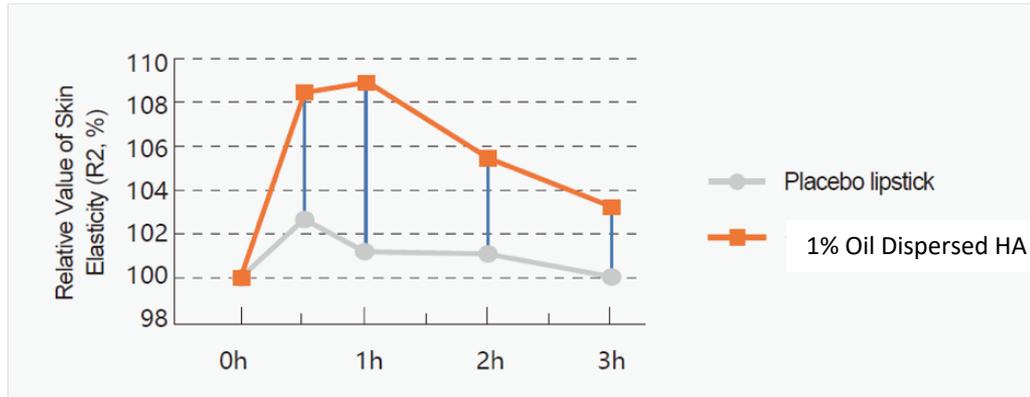
Results from the pictures and software analysis have shown a marked improvement of the lips texture in the test area and a significant lips fine lines reduction by the application of Oil Dispersed HA. The relative value of lips lines area is reduced by 14% after 30min application.

- Smoothness evaluation



Results show that Oil Dispersed HA can improve skin roughness and smooth the dry lips. The relative value of roughness is reduced by 6.1% after 2 hours application.

- Softness evaluation



Oil dispersed HA can provide instantly hydrating ability and improve the elasticity and softness of lips. The relative value of elasticity is increased by 8.3% after 1 hour application.

Oil Dispersed HA, due to its high content of extremely low molecular weight HA and meadowfoam seed oil, can hold water from outside and bind water from inside. The double moisturizing efficacy of Oil dispersed HA can improve the textures, smoothness and softness of dry and rough lips.

Thanks

华熙生物科技股份有限公司 BLOOMAGE BIOTECHNOLOGY CORPORATION LIMITED

地址 | 济南高新技术开发区天辰大街678号 (250101) 电话 | 0531 82685969 传真 | 0531 82685988
www.bloomagebioactive.com