< Hyalo-Oligo® >

for skin care

~High penetration・High moisture retentivity~

Kewpie Corporation
Fine Chemical Division

QPFC®

Features of <Hyalo-Oligo®>
(The differences from common hyaluronic acid)

<Common hyaluronic acid>

The skin is coverd by hyaluronic acid as if it is membrane.

⇩

Loss of skin moisture is prevented.

⇩

Skin moisture is kept.

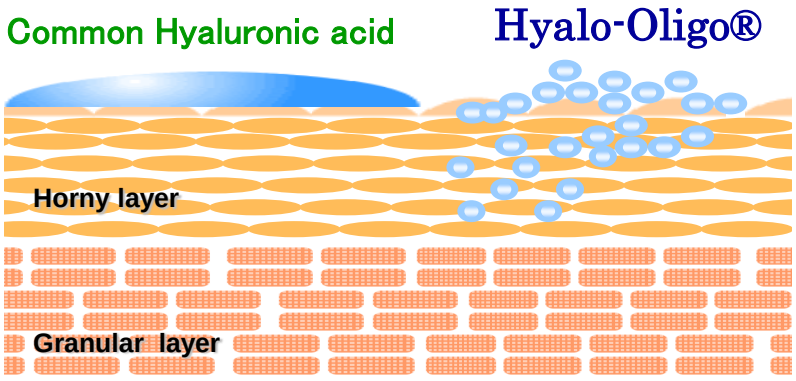
Common hyaluronic acid is easily washed away because it doesn't penetrate into the skin

<Hyalo-Oligo®>

It is quite a new hyaluronic acid with very low molecular weight (av.7,000 da).

①Since Hyalo-Oligo® covers the skin surface and also penetrates into horny layer, it keeps the skin moisture both inner and outer side of the skin.

②Hyalo-Oligo® which remains in horny layer of the skin is not washed away, thus unlike common hyaluronic acid ,it retains the skin moisture even after washing.



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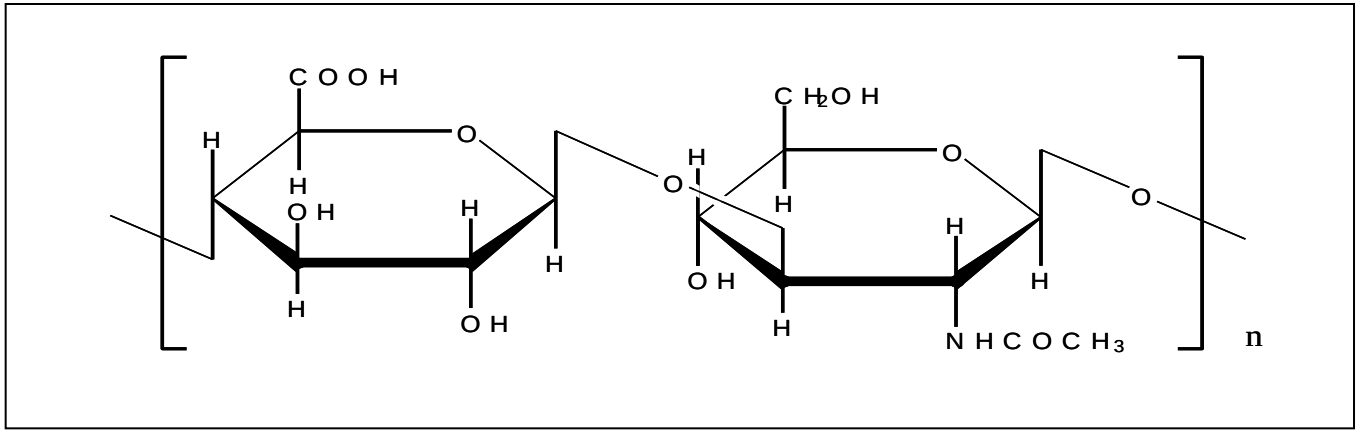
Chemical structure & Molecular size

- **Molecular weight : Less than 10,000 Da (Av.7,000)**
  (By conversion from intrinsic viscosity)
- **Average molecule size : About 15～25nm**



About 1nm*

n : 15～25

* Glyco forum,Hyaluronan Today
(http://glycoforum.gr.jp/science/hyaluronan/hyaluronanJ.html)

The gap among cells of human skin surface is studied ** as 40~50nm ,and there are pores and sweat glands on skin surface. Therefore it is no wonder that Hyalo-Oligo penetrates into human skin.

** [The journal of investigative dermatology] No.124 article titled ' Nanostructure of the epidermal extracellular space as observed by cryo-electron microscopy of vitreous sections of human skin' written by Ashraf Al-Amoudi, Jacues Dubochet, Laes Norlen.

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Feature1. Transdermal absorption

Hyalo-Oligo® penetrates into horny layer of the skin

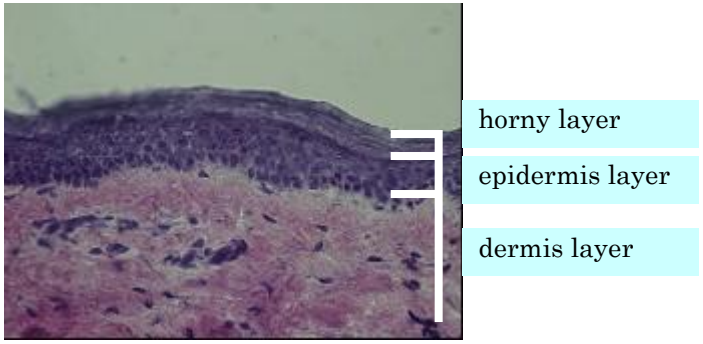


Fig.1 Hemato-xylin/eogin dying of skin

Note) Fig.2
1% solution of Hyalo-Oligo® labeled with fluorescent probe was applied to the surface of the test skin for **one hour.**
(*Franz Diffusion Cell)

Fluorescent colouring at the lower part of the Fig.2,3 are of elastinic protein which by nature exists in the skin cell.

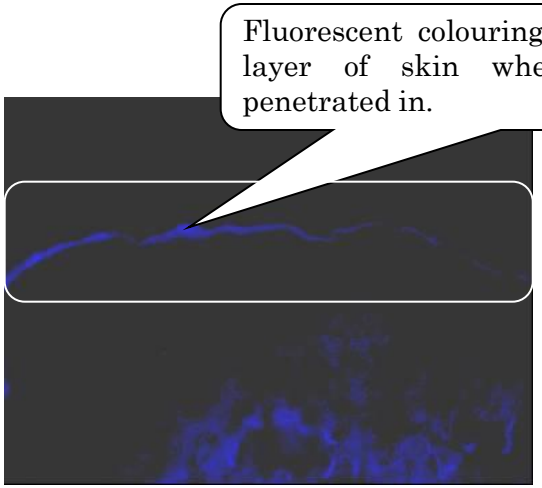


Fig.2 **Hyalo-Oligo®**

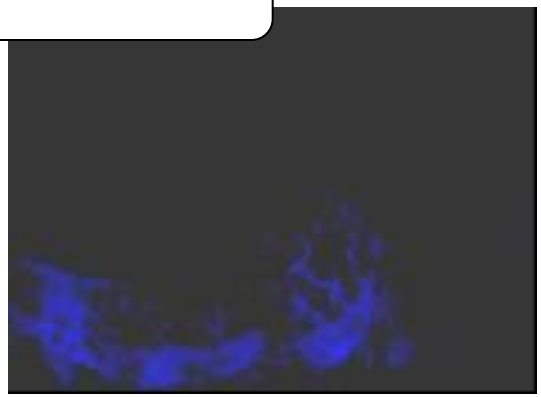
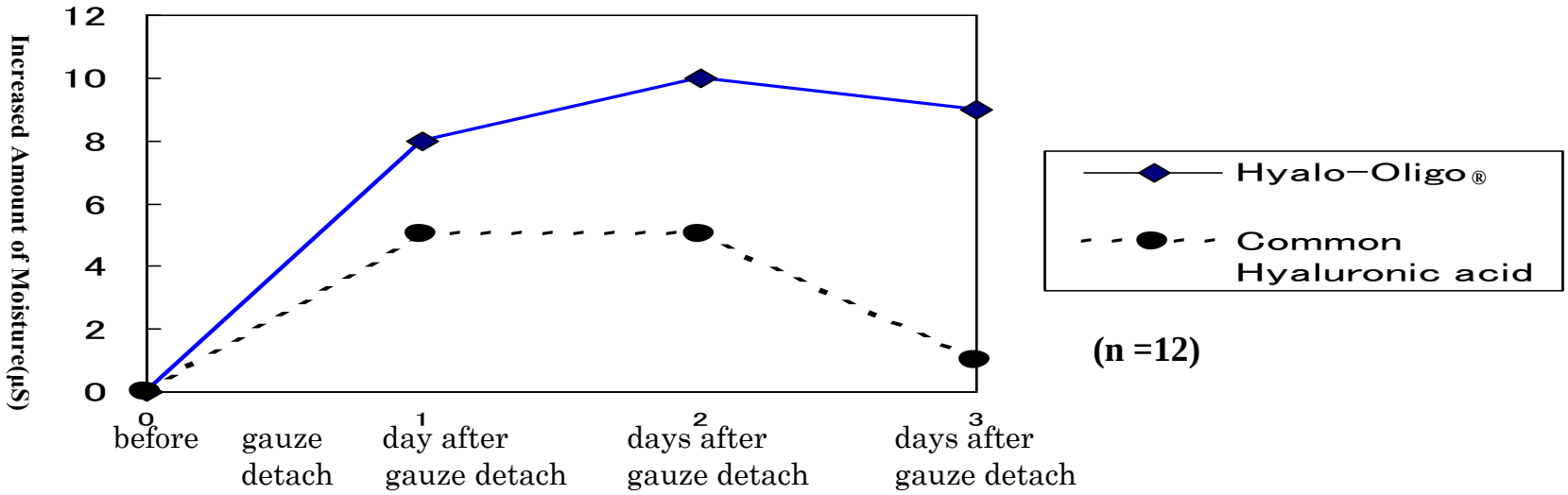


Fig.3 **Control**

Feature2. Skin moisture increase

Hyalo-Oligo® increases twice as much skin moisture as common hyaluronic acid.

(Presented at Annual Meeting of the Pharmaceutical Society of Japan, March 2006 by Takushi Yoshida Q.P.Corporation)



The gauze soaked in 1% solution of Hyalo-Oligo® was attached to the human skin for 24 hours. (Control: 1% solution of common hyaluronic acid).After the gauze was detached, the skin electric conductivity indicating the amount of skin moisture was measured at three points ,namely 1 day after detaching gauze(above 1), 2 days after(above 2), 3 days after (above 3).

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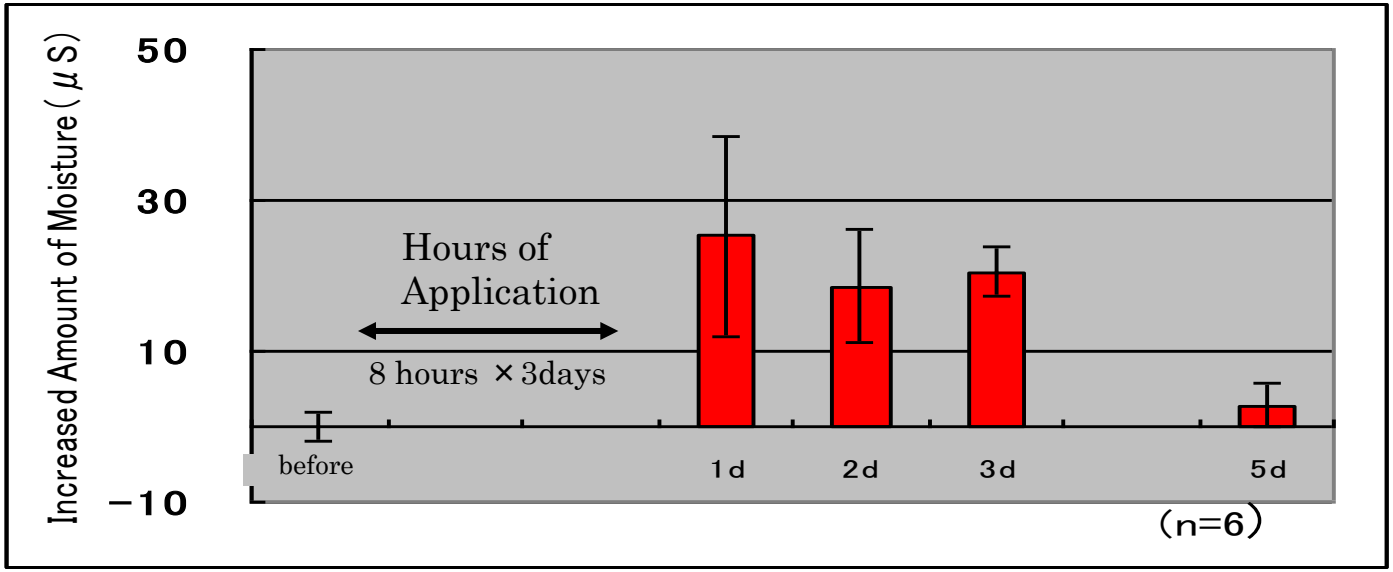
Feature3. High moisture retentivity-1

Hyalo-Oligo® keeps skin moisture during 3 days after application.

(Presented at Annual Meeting of the Pharmaceutical Society of Japan, March 2006 by Takushi Yoshida Kewpie Corporation)



The gauze soaked in 1% solution of Hyalo-Oligo® was attached to the human skin for 8hours × 3days. After this application, the skin electric conductivity indicating the amount of skin moisture was measured at four points,namely1 day after the application (above 1d), 2 days after (above 2 d), 3 days after (above 3 d),and 5 days after (above 5d).

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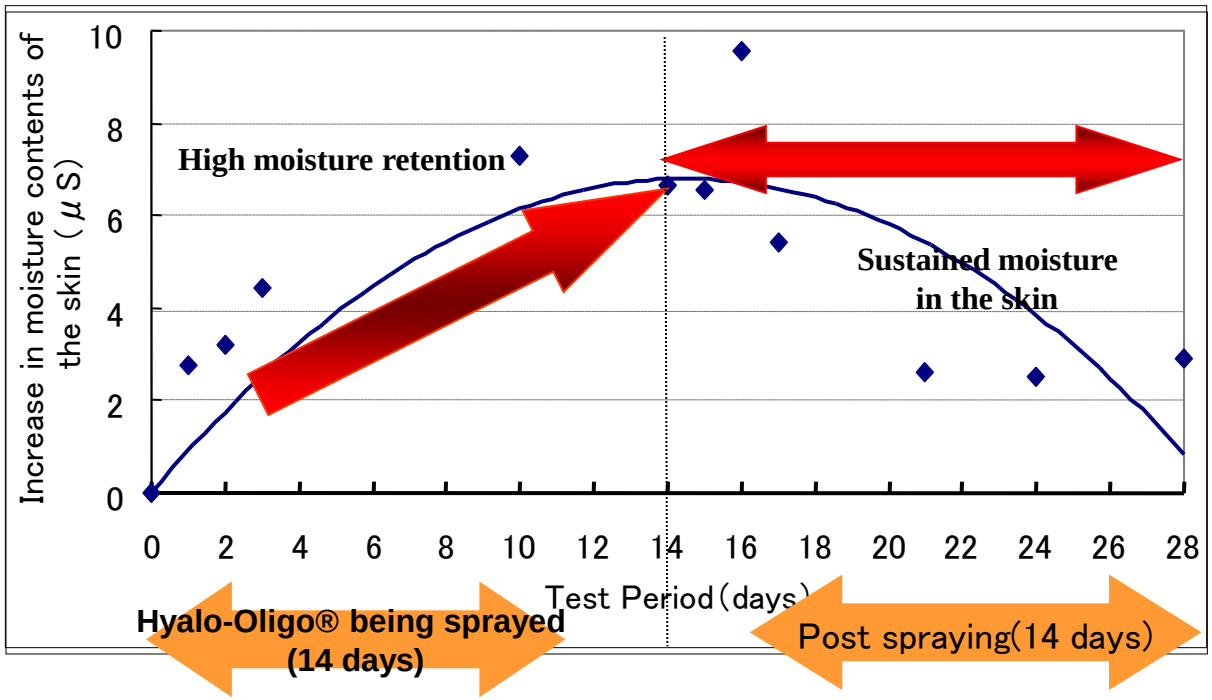
High moisture retentivity-2

Long period continuous application test

A confirmation of Feature 3. (High moisture retentivity) : Sustainability of moisture retention for a long time was confirmed.



1% solution of Hyalo-Oligo® was sprayed over forearm of 6 test subjects twice a day (in the morning and in the evening) for 14 days. Skin moisture increase was measured by electrical conductivity during the spraying 14 days and during the post period .

(Data by The Research Laboratory of Q. P.Corp.)

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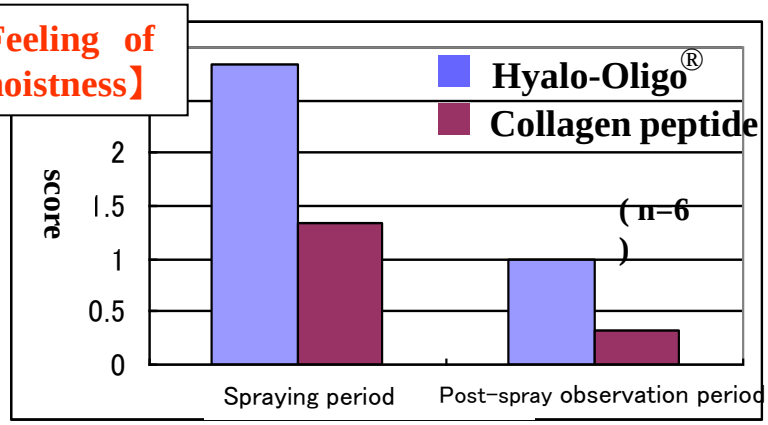
Comparison with collagen peptide

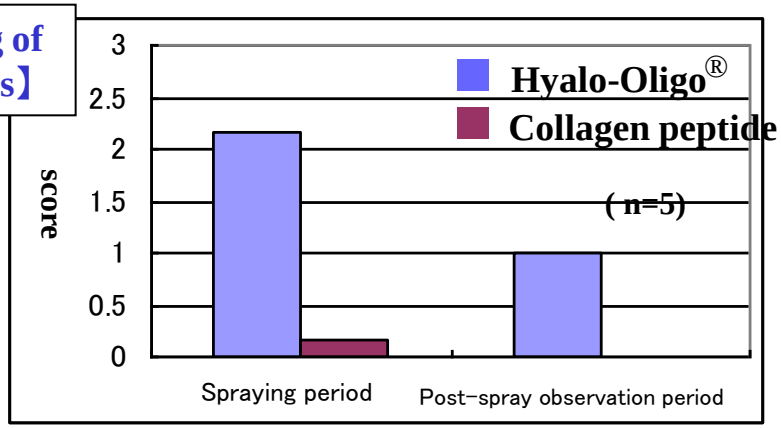
A trend was confirmed that Hyalo-Oligo® keeps skin moist and firm better than collagen peptide

<Post-use questionnaire>

【Feeling of moistness】



【Feeling of firmness】



1% solution of Hyalo-Oligo® and 1% solution of collagen peptide were sprayed over forearm of 6 test subjects and 5 test subjects respectively **twice a day (in the morning and in the evening) for 14 days.**

Questionnaires were replied at the end of the spraying period and during post-spray observation period respectively.

＜Digitalization of subjects' feeling by questionnaire research＞

Questionnaires were set in six levels of feeling as:

①Felt very strongly ②Felt strongly ③Felt positively ④Felt slightly ⑤Felt very slightly ⑥Did not feel

Then the above sensory judgments were digitalized as :

① 5-points、② 4-points ③ 3-points ④ 2-points ⑤ 1-point ⑥ 0-point

This means that the higher the score is the stronger the sensory valuation by the subjects.

(Data by the Research Laboratory of Q. P. Corp.)

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Sensory research – questionnaire to female user

Hyalo-Oligo®, 0.3% solution

Method

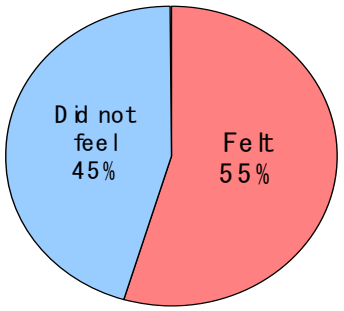
Applied the lotion sample to 11 females' one side of their faces , followed by washing and normal care, then compared the condition with non-applied side .

Result

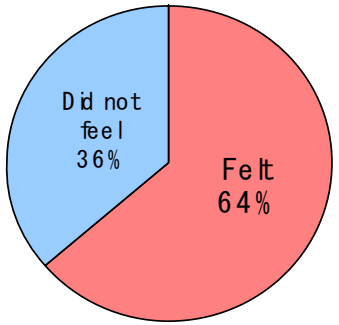
〈Smooth silky touch〉

- More than half of the subjects felt improvement in smooth silky touch.
- On the 20th day of use ,more subjects felt the touch.

＜survey on 10th day of use＞



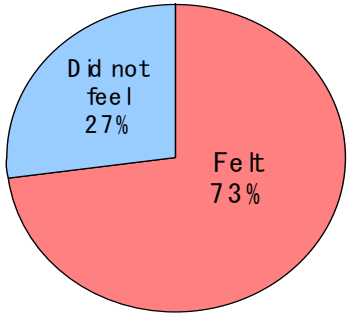
＜survey on 20th day of use＞



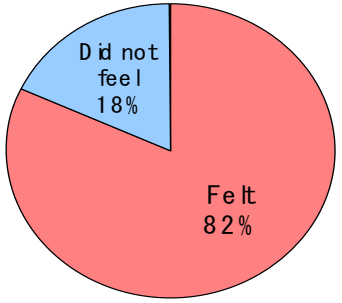
〈Softness〉

- More than 70% of the subjects felt softness.
- On the 20th day of use ,more subjects felt the softness.

＜survey on 10th day of use＞



＜survey on 20th day of use＞



Hyalo-Oligo® skin elasticity test
<test method>

Sample

①1% solution of Hyalo-Oligo®
②Purified water(as control)
*0.15% of methylparaben added to both ① and ②

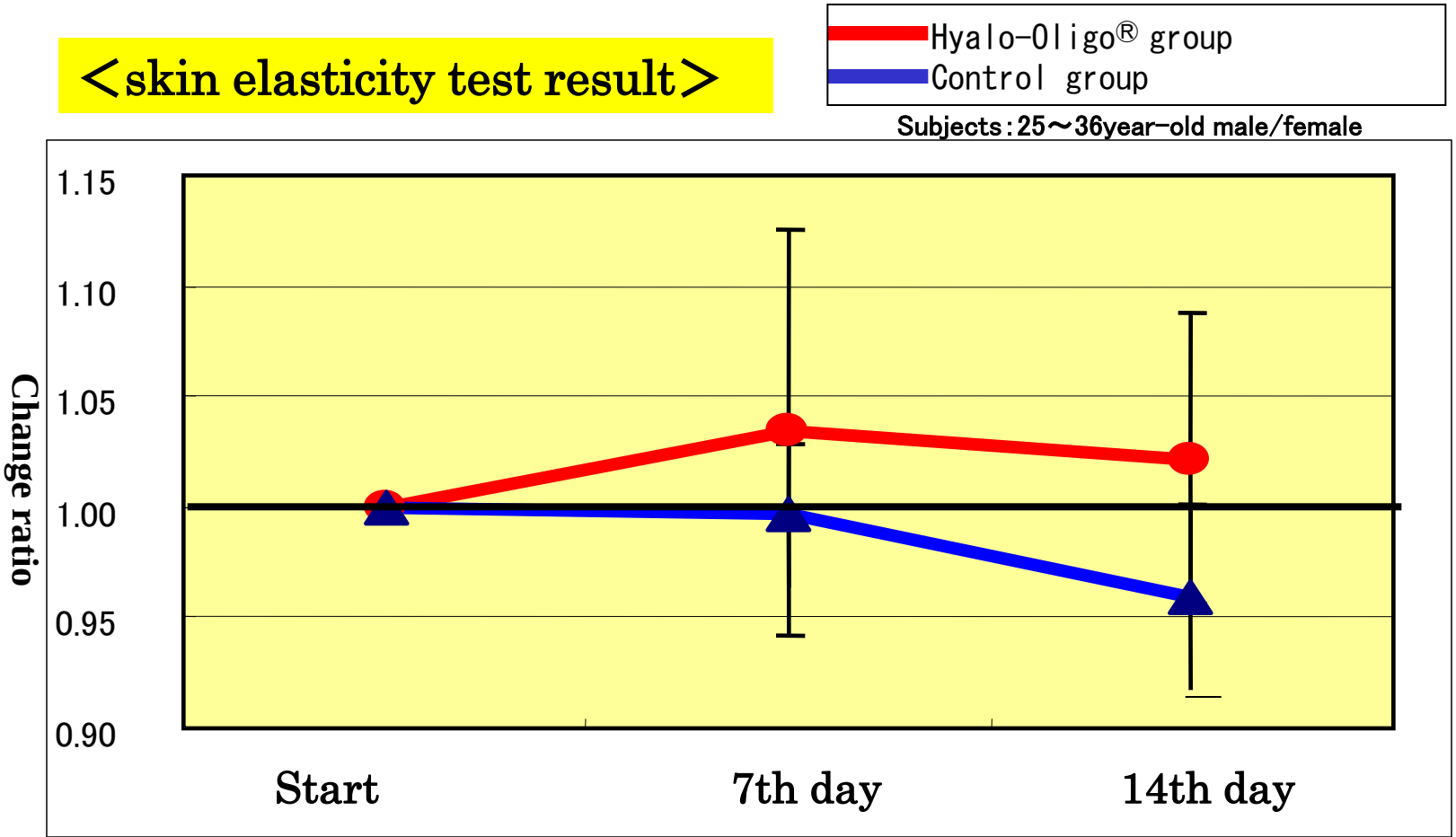
Flow-chart of the test

Applying sample to the corner of eye
(n=8) ↓
Applying twice a day (morning & night)
↓
<skin elasticity test>
measuring the change ratio of the skin after 3 seconds
(elasticity measuring device:
CUTOMETER MPA580)
(Reference)
< Moisturizing effect test>
measuring moisture of the skin
(skin moisture measuring device:
SKICON-200)

Hyalo-Oligo® improves skin elasticity

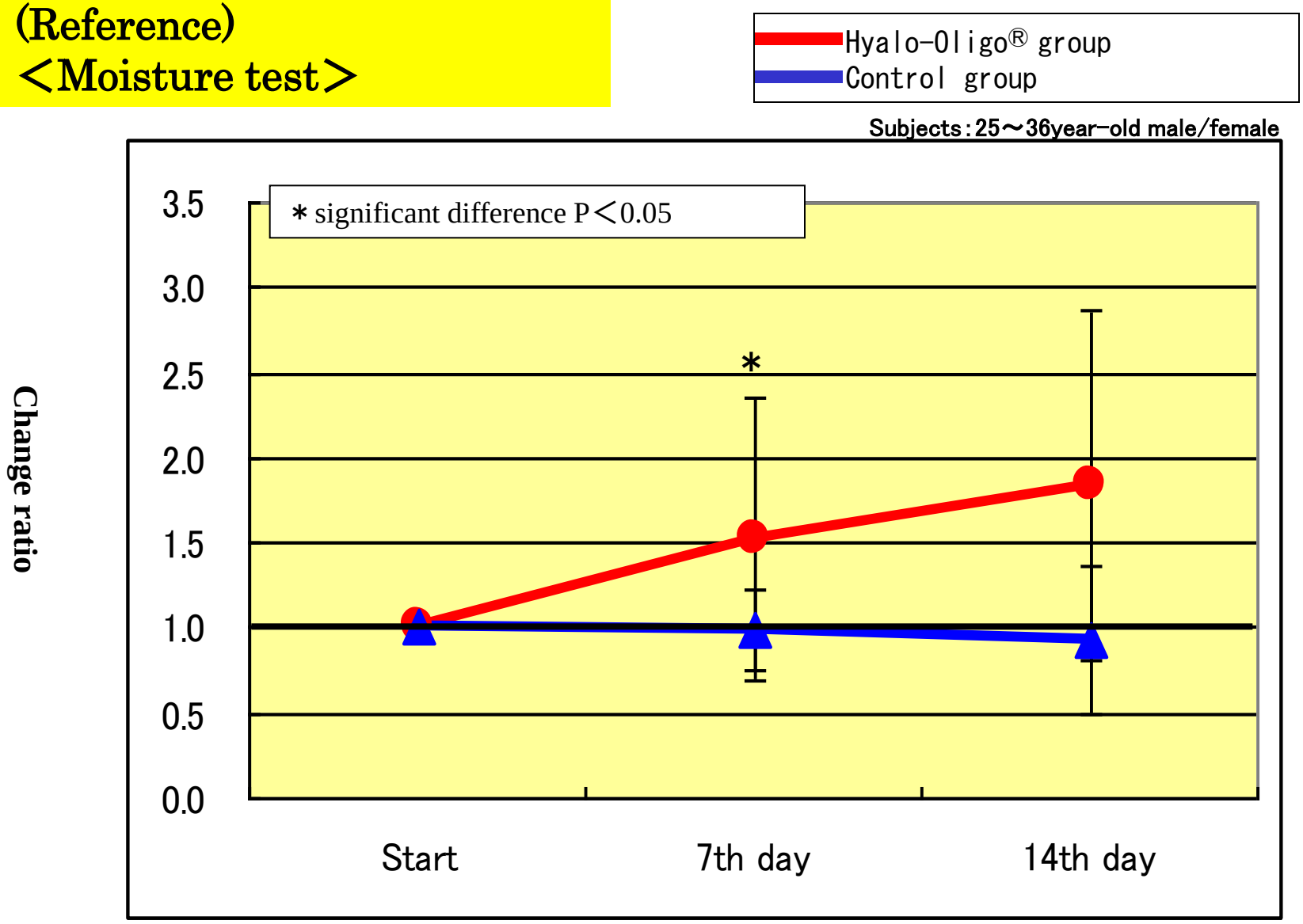
The test result confirmed that Hyalo-Oligo® improves skin elasticity. Hyalo-Oligo is an effective anti-aging ingredient to help diminishing the appearance of wrinkles caused by dehydration.

＜skin elasticity test result＞



Hyalo-Oligo® improves skin elasticity

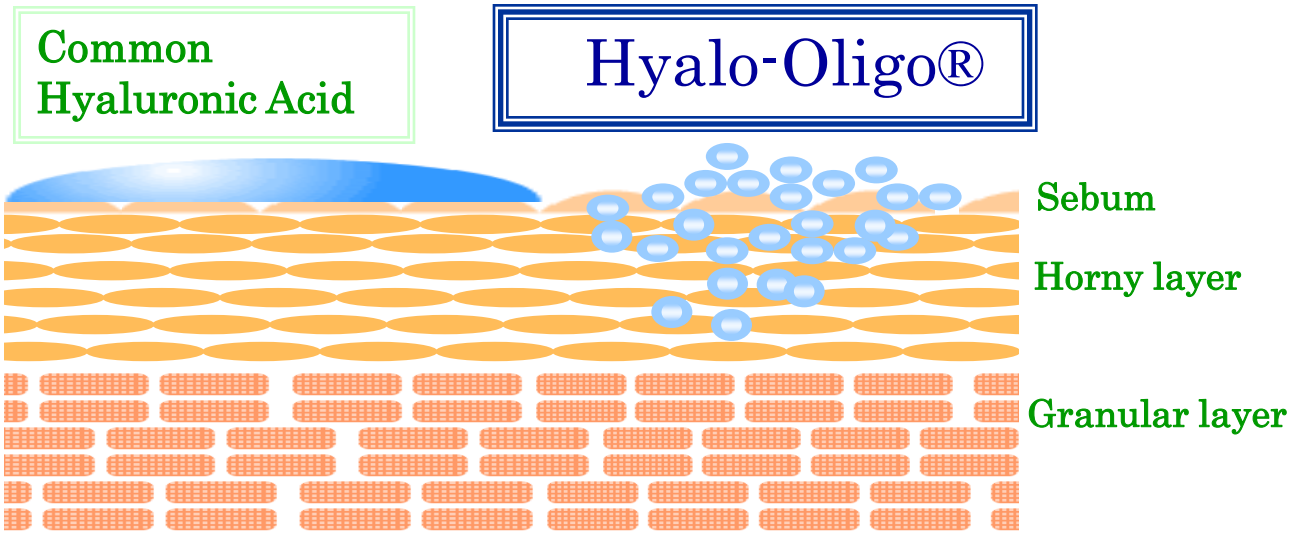
(Reference)
＜Moisture test＞



Application

So far features of Hyalo-Oligo was explained. Before going into actual application, we will look into application concepts.

Concept-1 : Penetration type HA



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Concept-2: Double moisturing effect

By using Hyalo-Oligo® together with common hyaluronic acid, skin moisture retention is doubly effective.

Hyalo-Oligo®

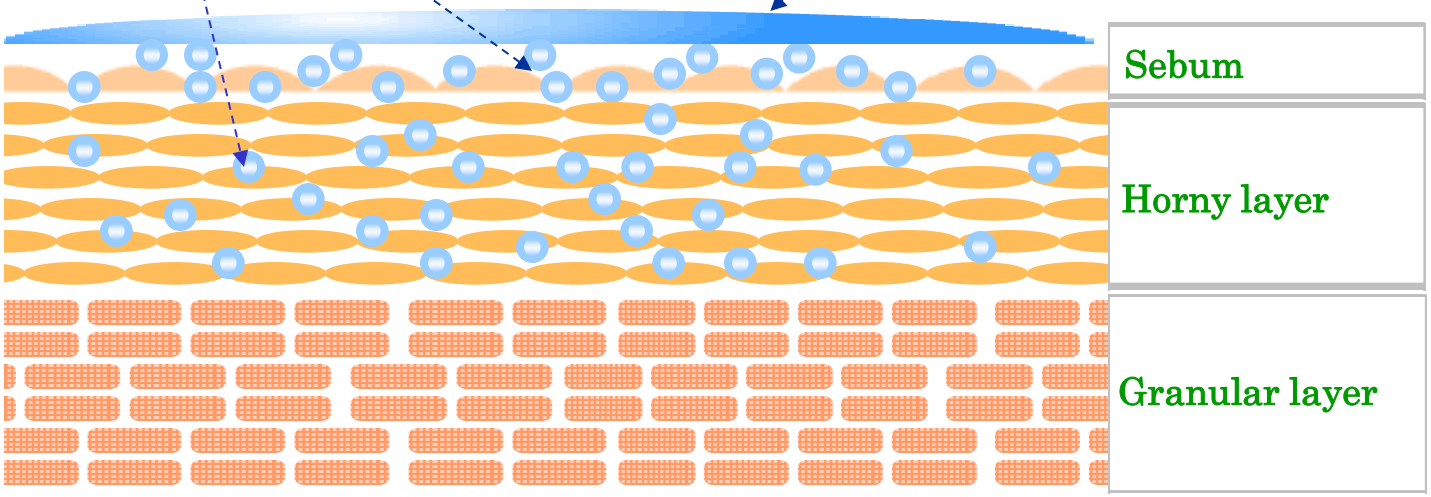
- Penetrates into the skin
- Increases moisture inside the skin

Double moisturizing effect

+ good visco-elastic touch

Common Hyaluronic Acid

- Gives good feelings due to high viscosity
- Prevents skin moisture from running out



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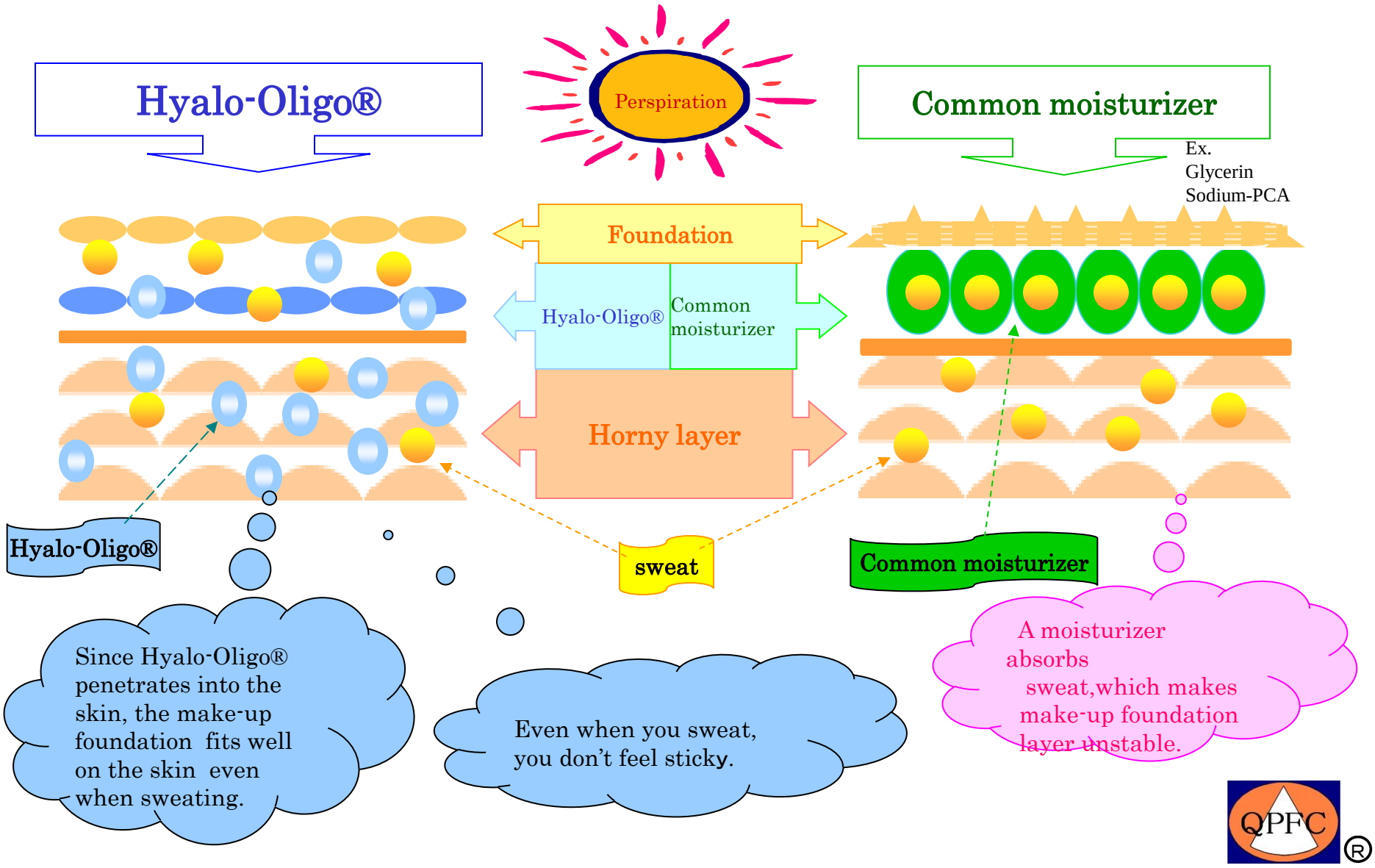
Concept-3 : Day time application-sweat proof



Application proposals

Concept-1 : Penetration type HA

Concept-2 : Double moisturing effect

Concept-3 : Day time application-sweat proof

Concept 1 &/or 3

◆Day type skin care
1% solution of Hyalo-Oligo®
The make-up cosmetics could be fit well on the skin

◆Spray mist as moisturizer
Natural water＋ 0.5 % solution of Hyalo-Oligo®
To persons who feel dry before and after the make-up

◆Body spray after bath
Natural water＋ 0.5 % solution of Hyalo-Oligo®
Keeps the skin moist after taking bath

◆Liquid foundation
by mixing Hyalo-Oligo®
You don't feel sticky but moist

Concept 2

◆Night type skin care
1% solution of (Hyalo-Oligo®＋Hyaluronic acid)
High moisture retentivity and high penetration

◆Face mask as moisturizer
1% solution of (Hyalo-Oligo＋Hyaluronic acid)
High moisture retentivity and high penetration

◆Lip moisturizer
Solution of (Hyalo-Oligo® 2%＋Hyaluronic acid 1%)
Gives the moisture to your lip

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< Hyalo-Oligo® >

for hair care

~High penetration・High moisture retentivity~

The effect of Hyalo-Oligo® for hair care

moisture

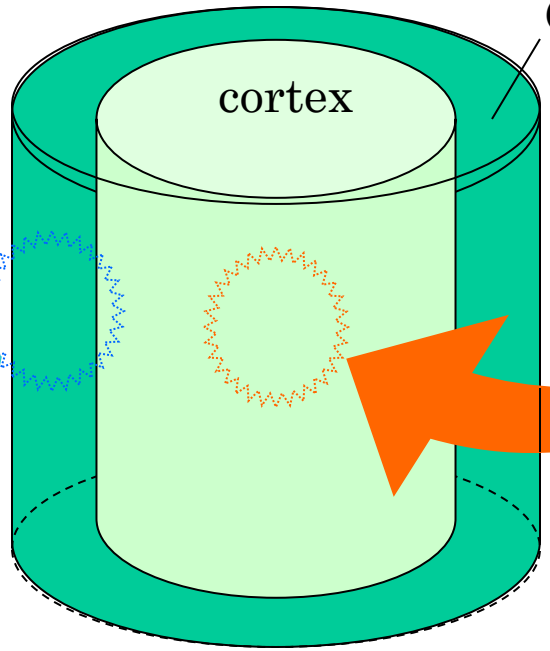
Shine

Feelings like a film

Improvement of feelings

Set of hair

The image of hair



Common hyaluronic acid acts only on the hair surface.

Hyalo-Oligo® penetrates into hair.

Verified by the experiment and the monitor test.

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The penetration test and the questionnaire survey

((The penetration test))

Sample ：Damaged hair (Bleached hair)

Treatment liquid ： 1% solution of Hyalo-Oligo®

Conditions ：40℃×5、10、15 minutes

Method

①Prepare 1% solution of Hyalo-Oligo® with the fluorescence label.

②Immerse damaged hair into 1% solution of Hyalo-Oligo® and warm under the above conditions.

③Wash and dry damaged hair

④Observe the section of damaged hair with a fluorescence microscope.

((The questionnaire survey))

Objects ：18 women aged from 20 to 50

Sample ：1% solution of Hyalo-Oligo® (spray)

Duration ：For 14 days

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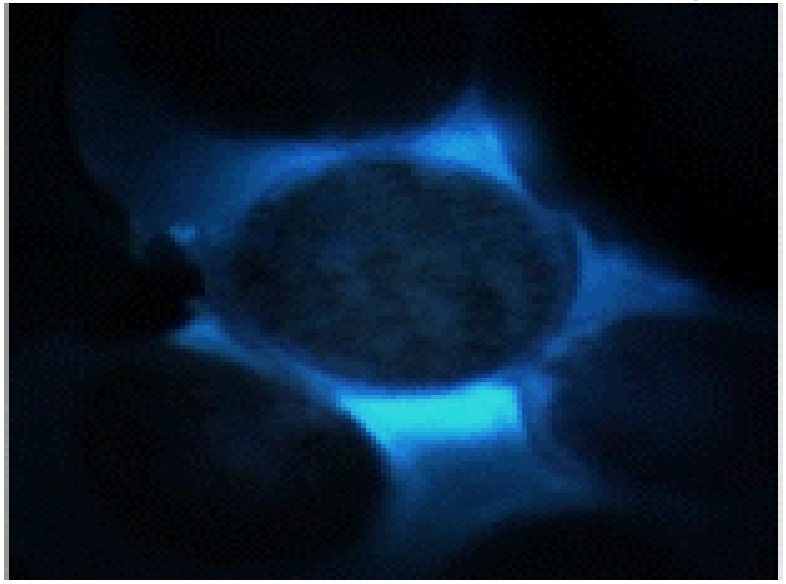
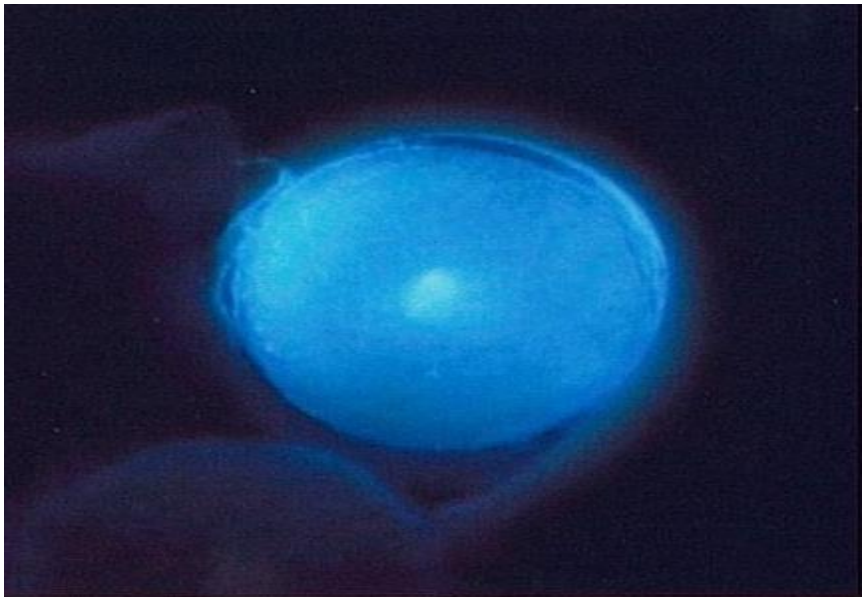
Proof of Hyalo-Oligo® penetration into hair

Bleached & damaged hair was soaked in 1% solution of LQH, 1%solution of Hyalo-Oligo both with fluorescence label at 40℃for 10 minutes, washed and dried. We compared shining degrees .



Damaged hair（treated with common HA: HA-LQH）



Damaged hair treated with Hyalo-Oligo®

The coloring degree shows the penetration of Hyalo-Oligo®

Under the conditions assuming daily shampoo (40℃×5 ~15 minutes), Hyalo-Oligo® penetrated into the center of damaged hair.

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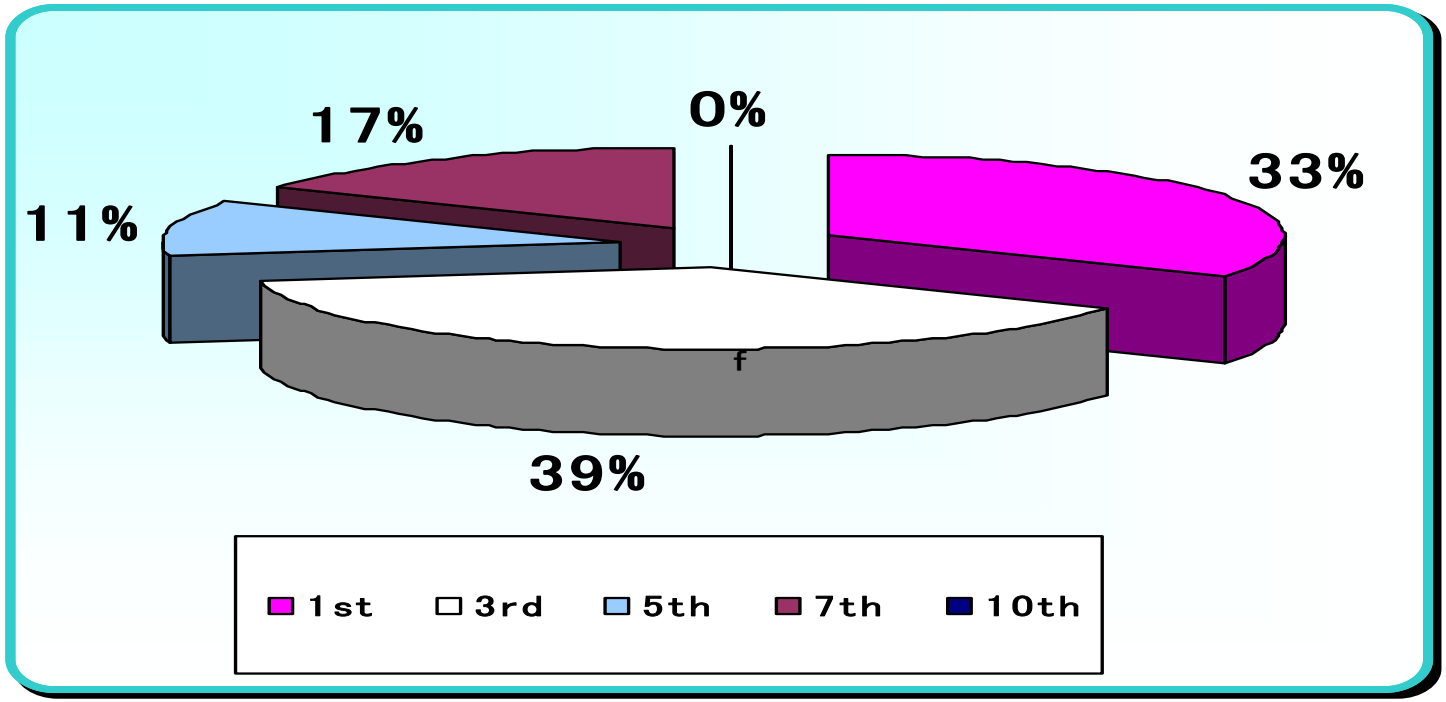
The results of the questionnaire survey

Times of usage till effectiveness was actually felt in terms of improvement of touch, unruly hair

n = 18 , age 20~50

1 % solution of Hyalo-Oligo® was sprayed.



72% of the people actually felt effectiveness by the 3rd usage.

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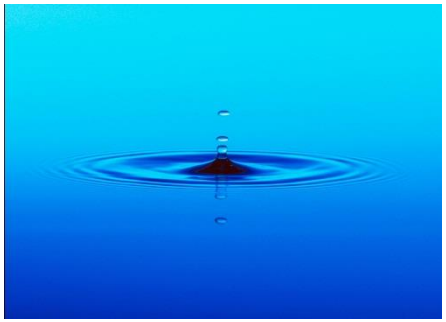
The proposal examples



Hyalo-Oligo® with high penetration ability makes your hair moist and flexible

- Spray mist

  0.5% solution of Hyalo-Oligo®

- Treatment

  Solution of (Hyalo-Oligo® 0.5% + Common hyaluronic acid 0.5%)

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Skin Related Gene Test of Hyalo-Oligo

Human Epidermal Keratinocytes

↓

Add
1) **Blank**
2) **Hyalo-Oligo 0.001μg/mL**
3) **Hyalo-Oligo 0.01 μg/mL**

↓ **6 hours later**

Extract RNA

↓

Measure Skin related-gene

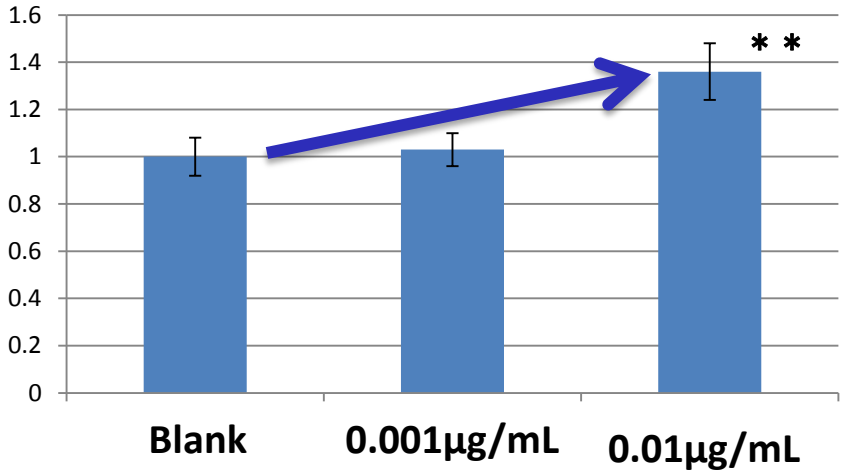
1. Aquaporin	2. Tight Junction
-Aquaporin3	-Occludin
	-Claudin1
	-JAM-1

Aquaporin
Exists in cell membrane, and Controls the movement of water in or out of cell.

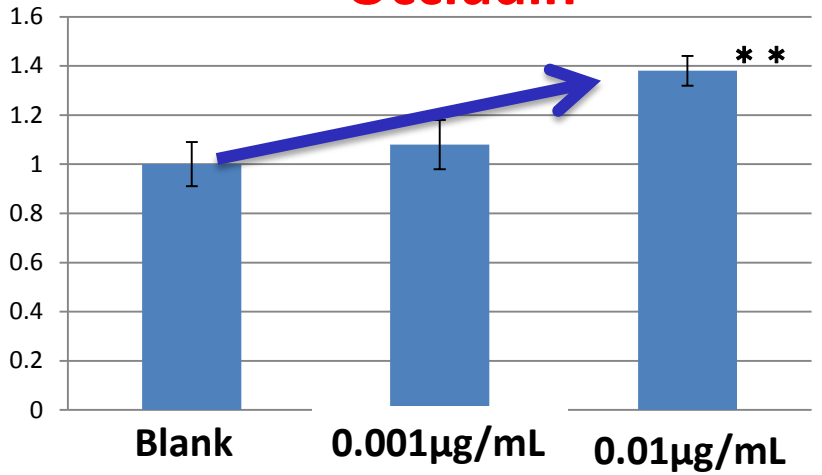
Tight Junction
Surrounds the cell in belt form, connects the cells together, and control intercellular transit of liquid.
Consists of protein such as Occludin、Claudin、JAM ant etc.

Increase of expression level of skin related genes by Hyalo-Oligo

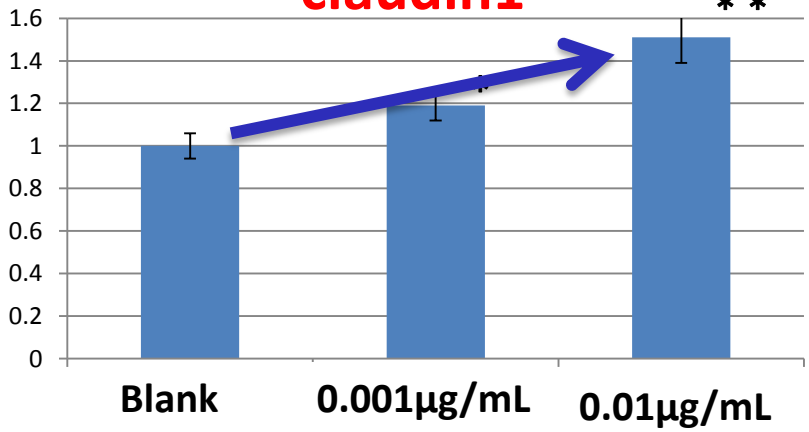
Aquaporin3



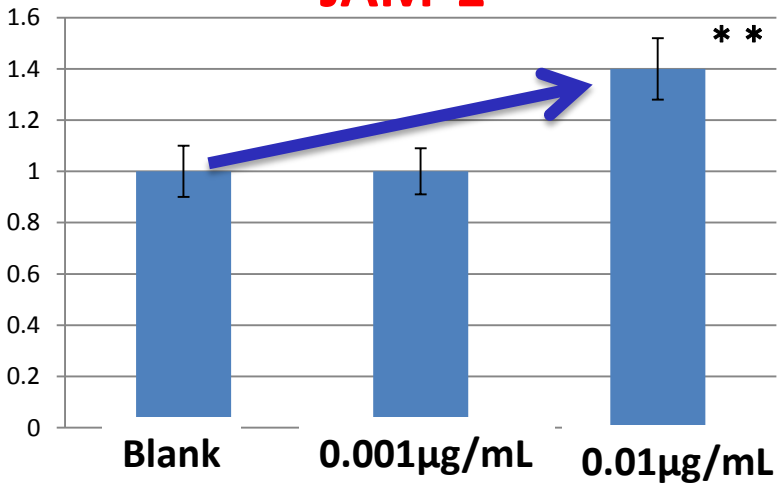
Occludin



claudin1



JAM-1



Significance: *, $p<0.1$; **,