Proposal for products using

「Hyalorepair®」

【Patent】international publication number:WO 2011/102462 A1

＜Brand new hyaluronic acid featuring barrier function recovery＞

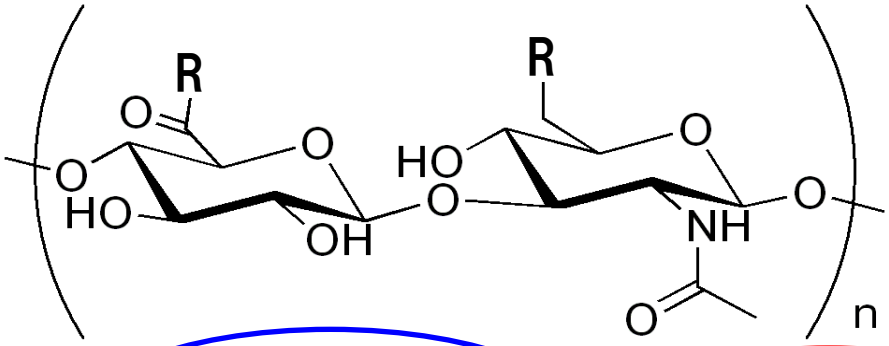
Kewpie Corporation
Fine Chemical Div.

2012.7.30

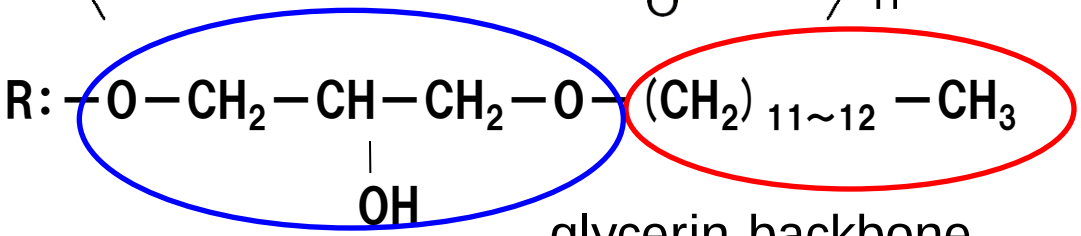
Structure of Hyalorepair®

Adjoined hydrophobic group to hydrophilic HA (hyaluronic acid)

This unique HA features barrier function recovery in the skin



Hydrophobic group introduction by chemical modification through glycerin backbone



glycerin backbone

hydrophobic group

INCI name: C12-13 Alkyl Glyceryl Hydrolyzed Hyaluronate

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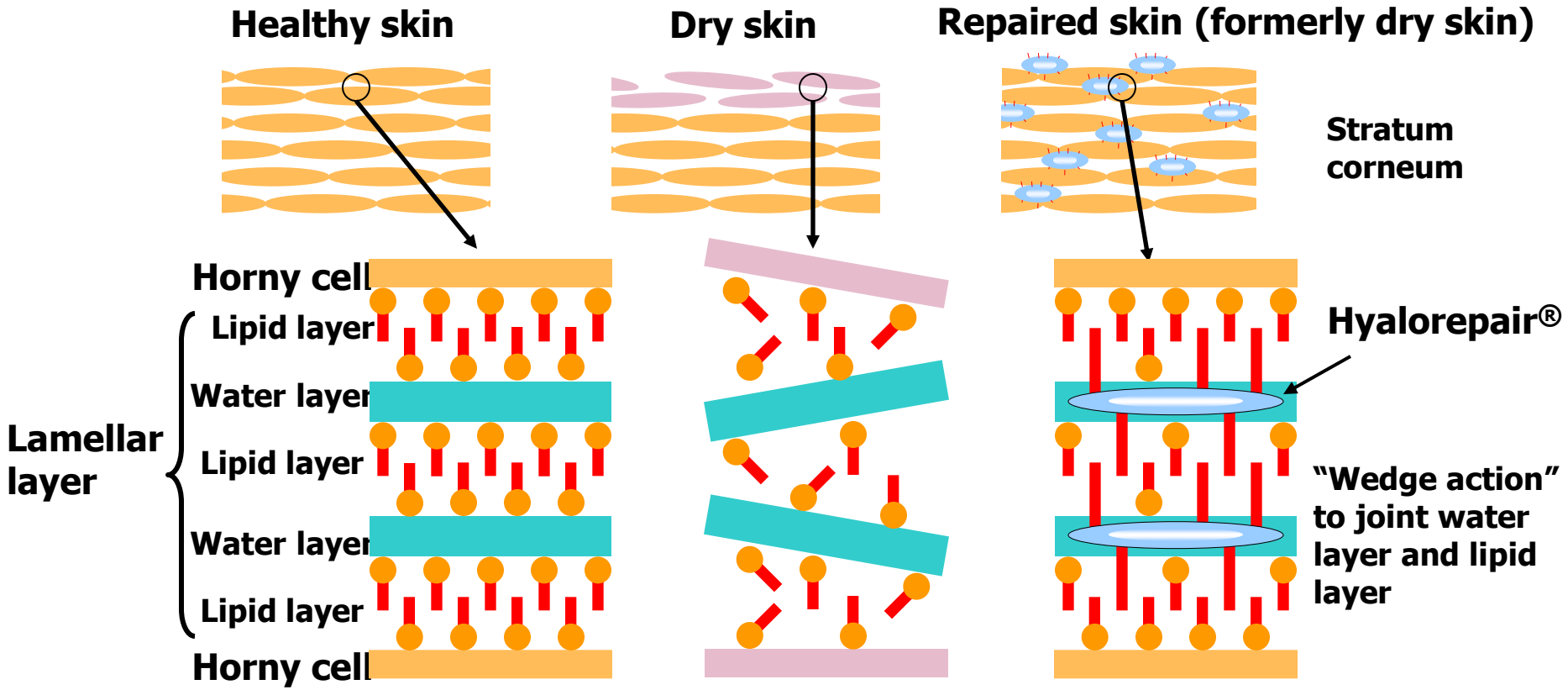
Approach to Barrier function recovery
~Mechanism (including hypothesis)~



Healthy skin: Lamellar layer acts as barrier to prevent skin from water evaporation

Dry skin: Out-balanced lamellar layer causes disorder of barrier function, resulting in dry skin from water evaporation.

Repaired skin: Hyalorepair® repairs out-balanced lamellar layer. When it's repaired, the barrier function gets recovered, which helps skin to retain moisture.

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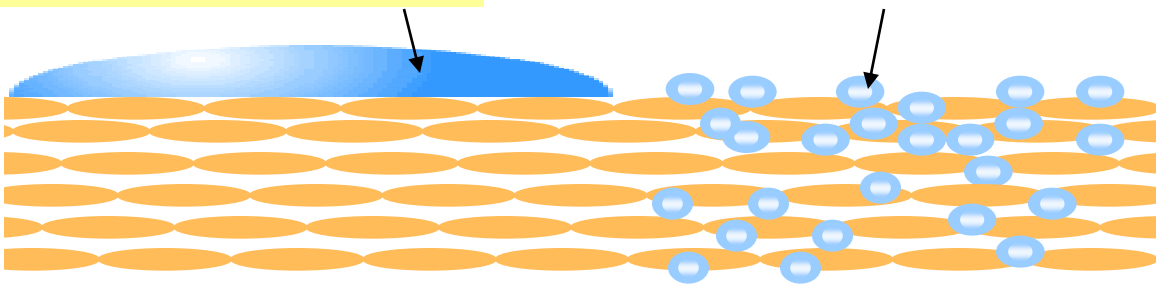
Variety of HA and its function

Hyaluronsan HA-LQ
Hyaloveil® -P

Hyalo-Oligo®

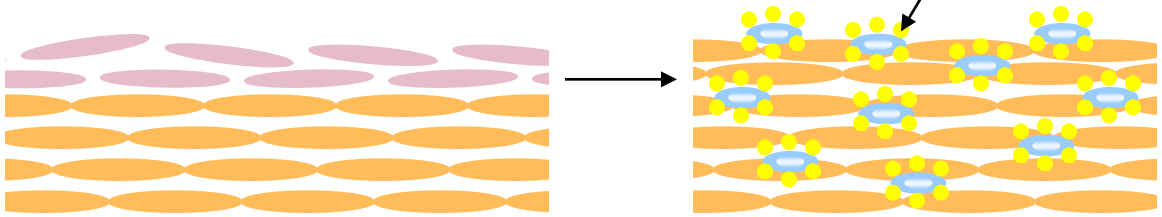


Stratum corneum

Retaining moisture by covering the surface of the skin

Moisturization by penetrating into the skin

Hyalorepair®



Stratum corneum

Dry skin, chapped skin

Repairing the skin to normal condition

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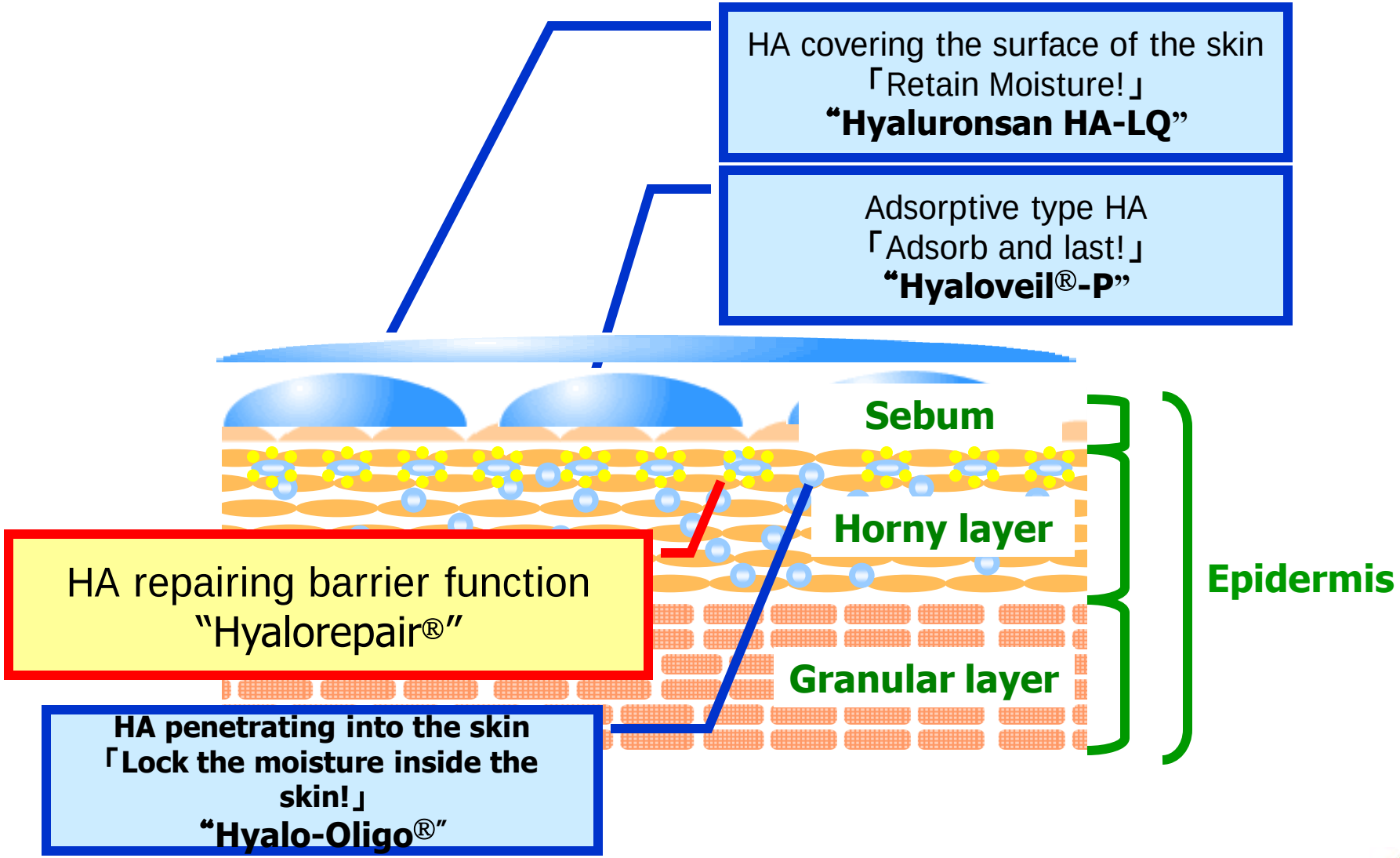
【Proposal】Triple moisturing effects +1



Four types of HA achieve triple moisturing effects +1

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Functionality test result of Skin Care

「Hyalorepair®」

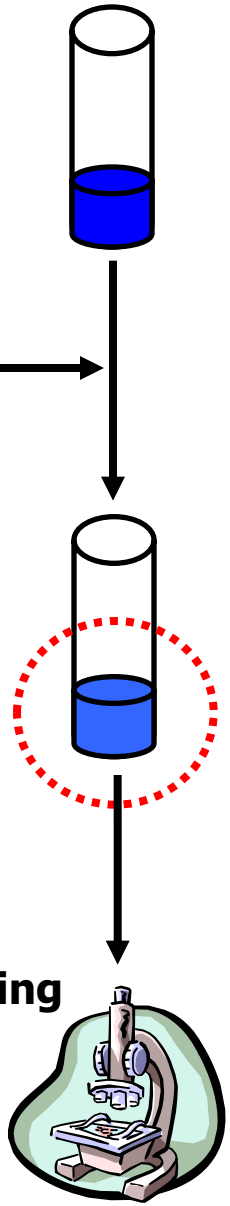
＜Brand new hyaluronic acid featuring barrier function recovery＞

In Vitro test confirmation of lamella structure formation

① Replicate intercellular condition of dry skin

② add Hyalorepair®

③ Microscope photographing



Number of Maltese Cross =1 (Average)

【water only added】

Number of Maltese Cross =10 (Average)

【Hyalorepair® added】

Lamella structure being confirmed
(Circled in red)

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In vivo test ~ confirmation of effectiveness on damaged skin

Sample

①Water

②1% solution of Hyalorepair®

③1% solution of Sodium Hyaluronate

Test method

【Subject】

16 females (aged 20's～50's with healthy skin）

【Test method】

Damage the forearm skin with mixed solution of acetone and ether.

Apply the sample everyday to the damaged skin before bedtime for 5 days.

【Test items】

Observation by a doctor, Microscope photographing

Measurement of water content in stratum corneum, measurement of transepidermal water loss（TEWL）

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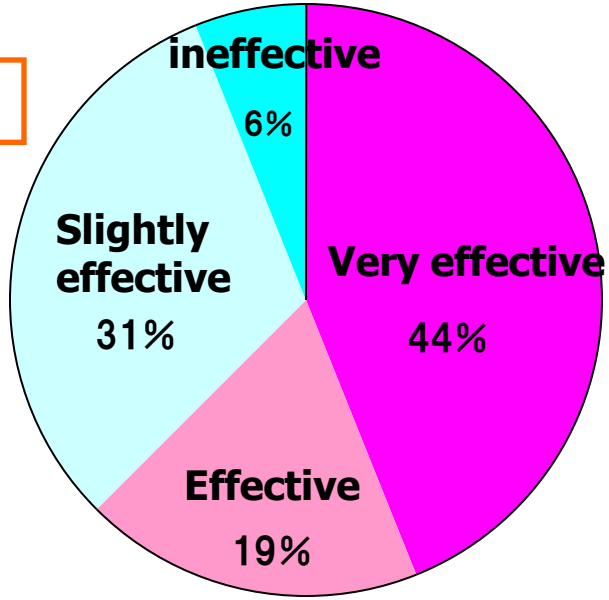
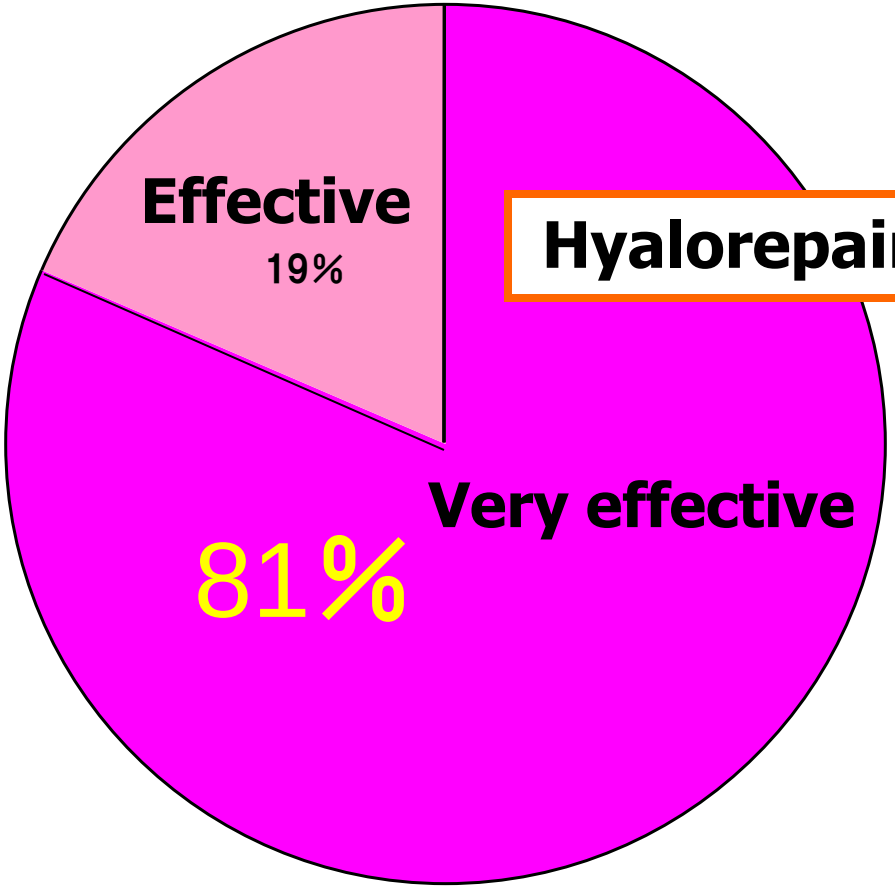
【Result】~ Observation by a doctor

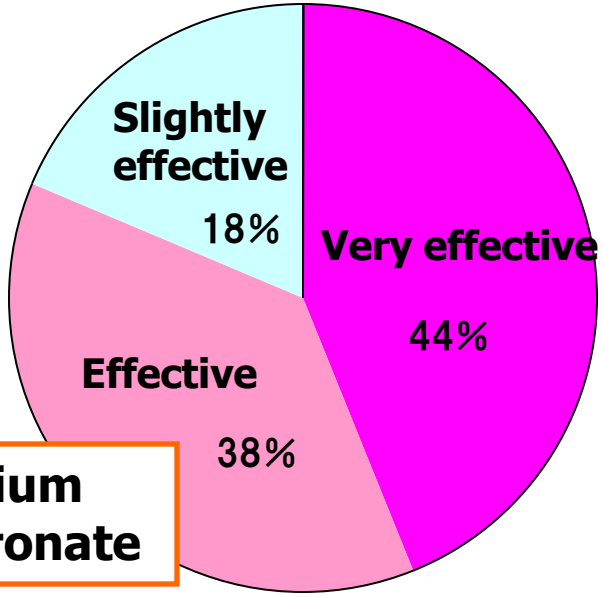
Water



Hyalorepair®



Sodium Hyaluronate



Applying Hyalorepair® improves damaged skin

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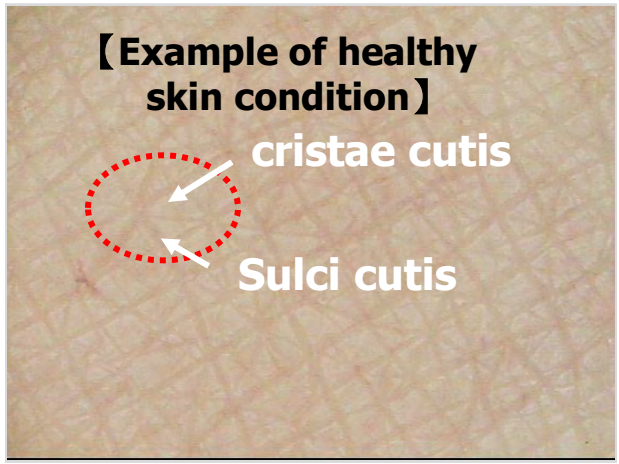
【Observation of skin condition】 ~ microscope photographing

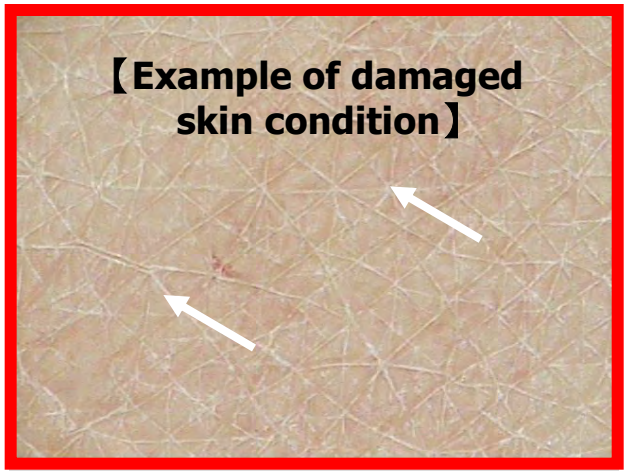
	After damage processing	5 days later (applying everyday)
Water		
Hyalorepair®		
Sodium Hyaluronate		

Improved!

【 Observation of skin condition】 ~ microscope photographing



Before damage processing



After damage processing

Interpretation of the image

*Sulci cutis looks powdered because of dryness

*No prominence of cristae cutis confirmed

*Stratum corneum is peeling and damaged

Subject sample: water

1 day later

3 days later

5 days later

Subject: female in 30's

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Microscope photographing【Hyalorepair®】

Before damage processing

After damage processing

1 day later

3 days later

5 days later

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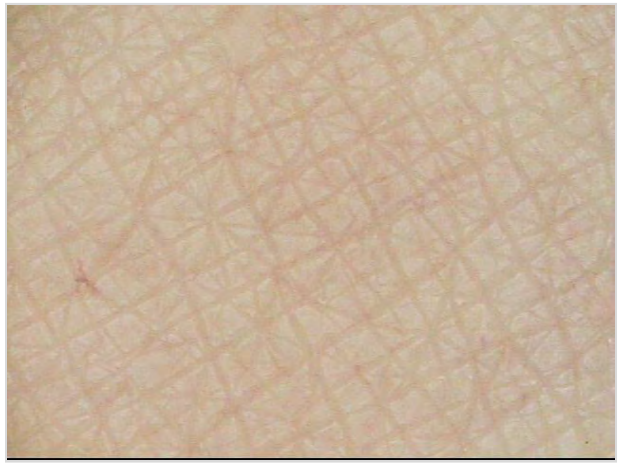
Microscope photographing【Water】



Before damage processing

After damage processing

1 day later

3 days later

5 days later

Subject: female in 30's

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Microscope photographing【Sodium Hyaluronate】

Before damage processing

After damage processing

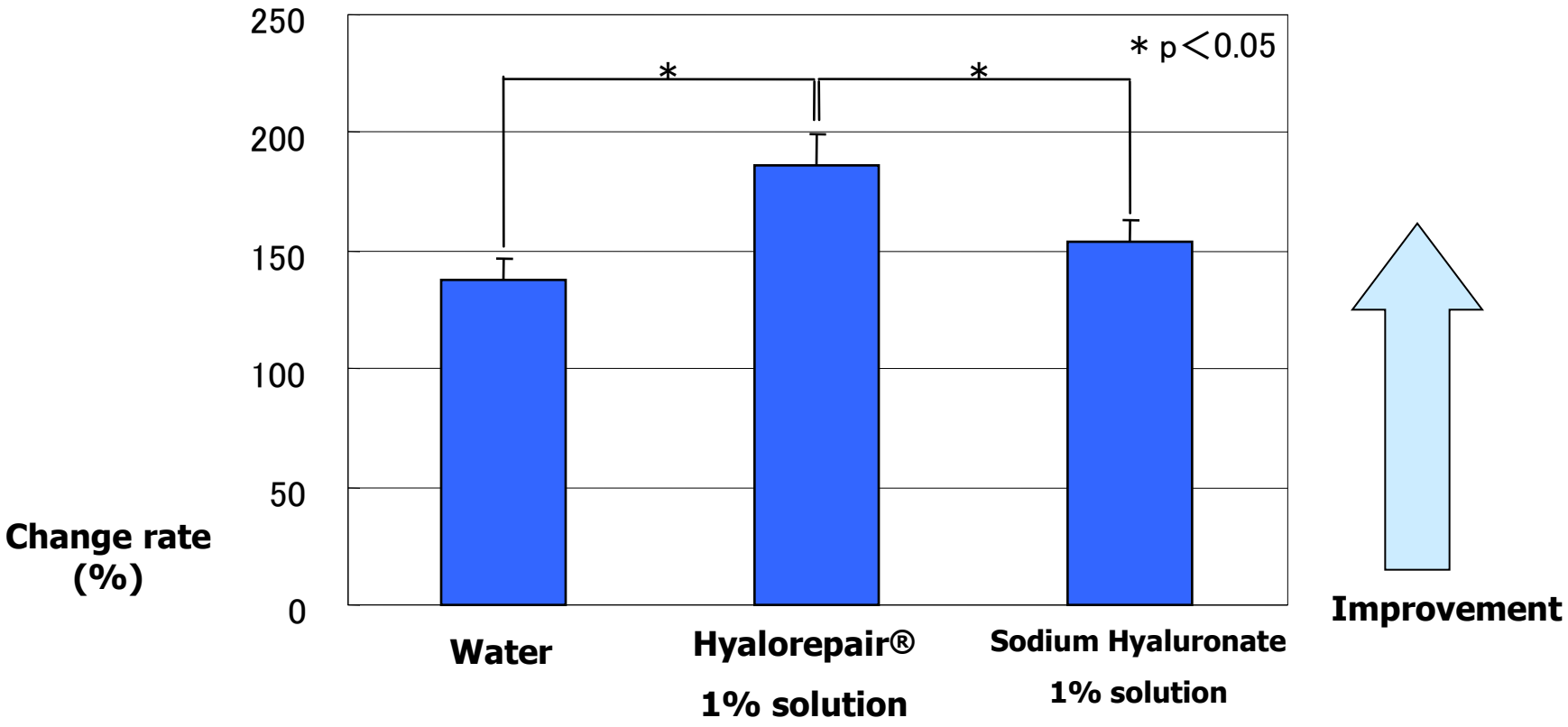
1 day later

3 days later

5 days later

【Test result】*Water content in stratum corneum*

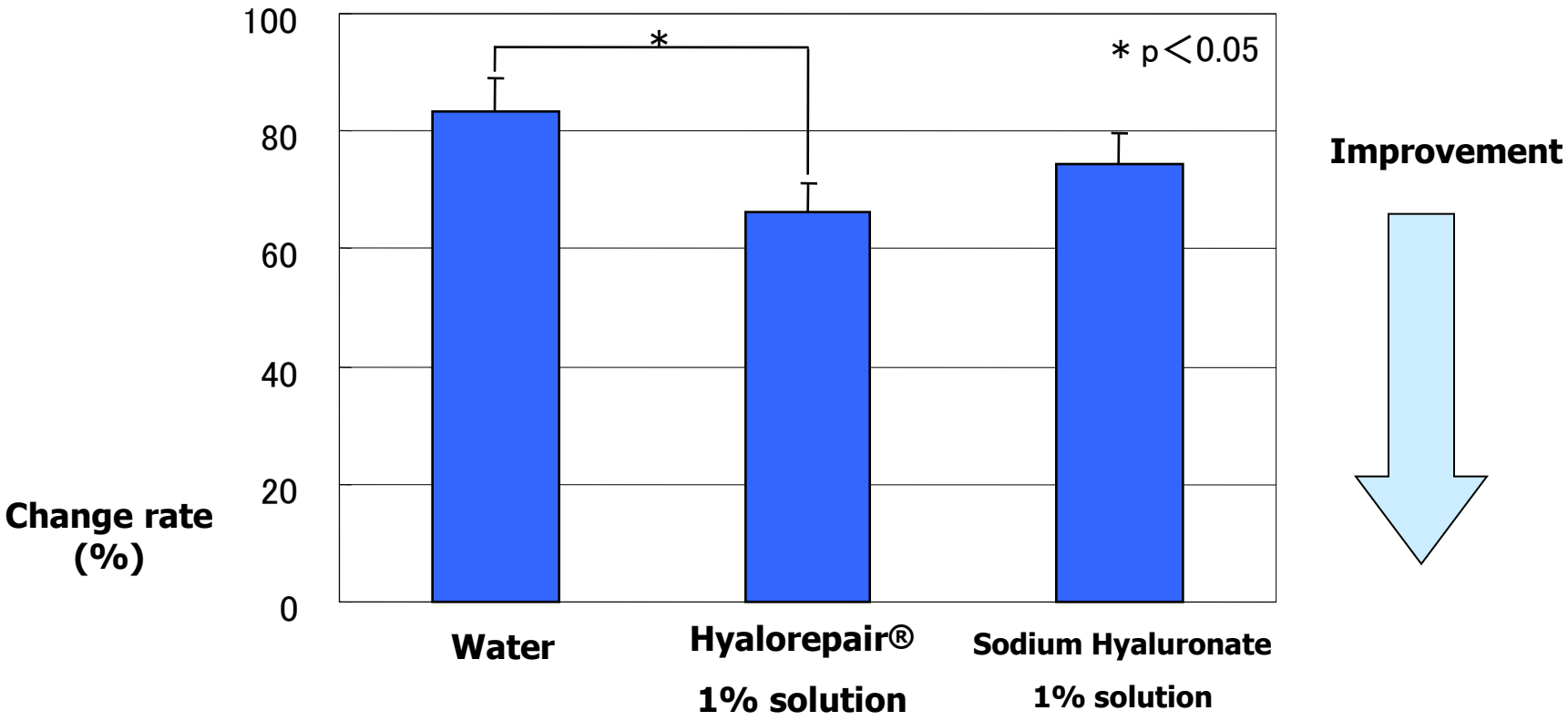
Change rate of water content in stratum corneum 3 days later



Hyalorepair® improves the moisturization of the skin

【Test result】*Measurement of transepidermal water loss (TEWL)*

Change rate of transepidermal water loss 3 days later



Hyalorepair® prevents skin moisture from evaporation

In vivo test

~ confirmation of effectiveness on damaged skin (0.05% Solution)

Sample

①Water

②0.05% solution of Hyalorepair®

Test method

【Subject】

6 females (aged 20's～50's with healthy skin）

【Test method】

Damage the forearm skin with mixed solution of acetone and ether.

Apply the sample everyday to the damaged skin before bedtime for 5 days.

【Test items】

measurement of transepidermal water loss（TEWL）

Testing facility: Inforward, inc., Ebisu skin research center

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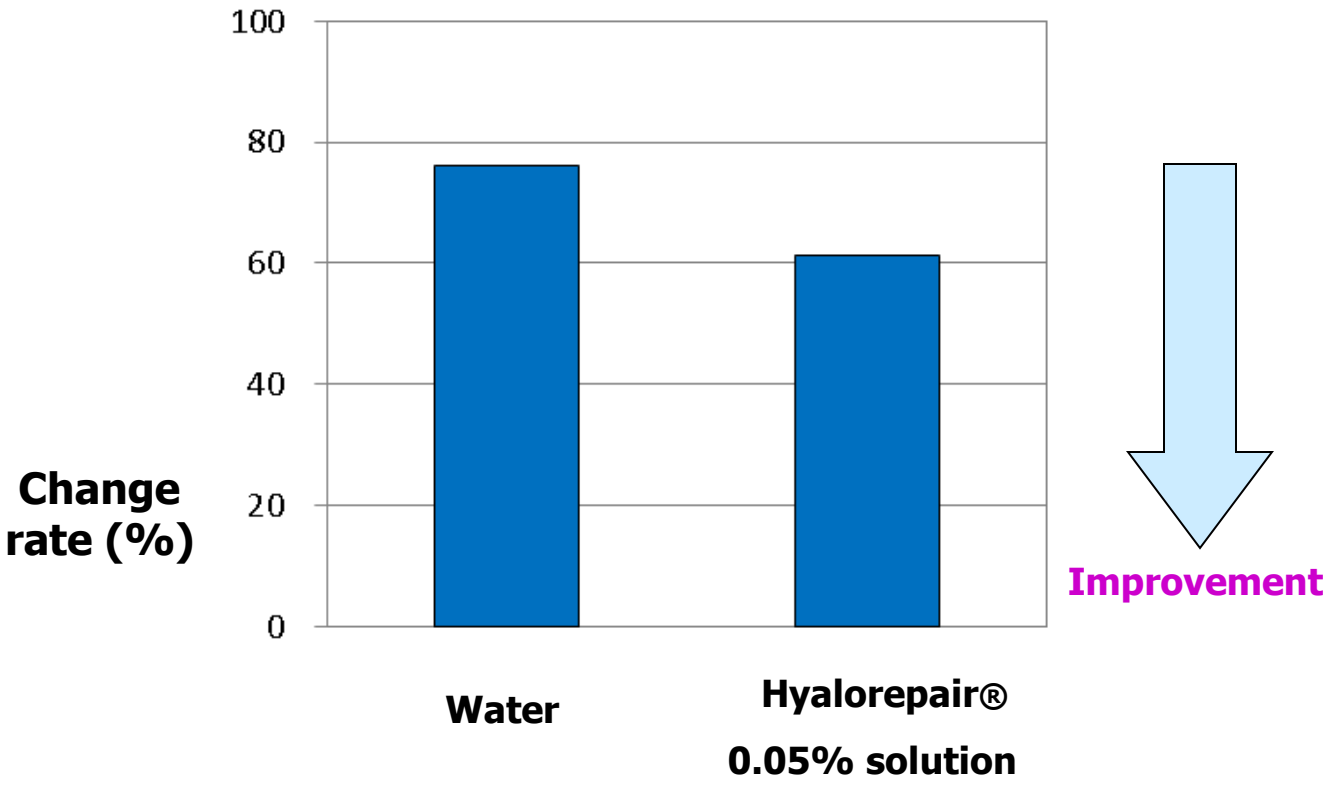
【Test result】*Measurement of transepidermal water loss（TEWL）*

Change rate of transepidermal water loss 3 days later



Hyalorepair® 0.05% solution prevents skin moisture from evaporation

In vivo test

~ confirmation of effectiveness on damaged skin (Comparison with Ceramide)

Sample

①Cosmetic product containing 1 % Ceramide

②Cosmetic product containing 1 % Hyalorepair®

Test method

【Subject】

9 females (aged 20's～50's with healthy skin）

【Test method】

Damage the forearm skin with mixed solution of acetone and ether.

Apply the sample everyday to the damaged skin before bedtime for 5 days.

【Test items】

measurement of transepidermal water loss（TEWL）

Testing facility: Inforward, inc., Ebisu skin research center

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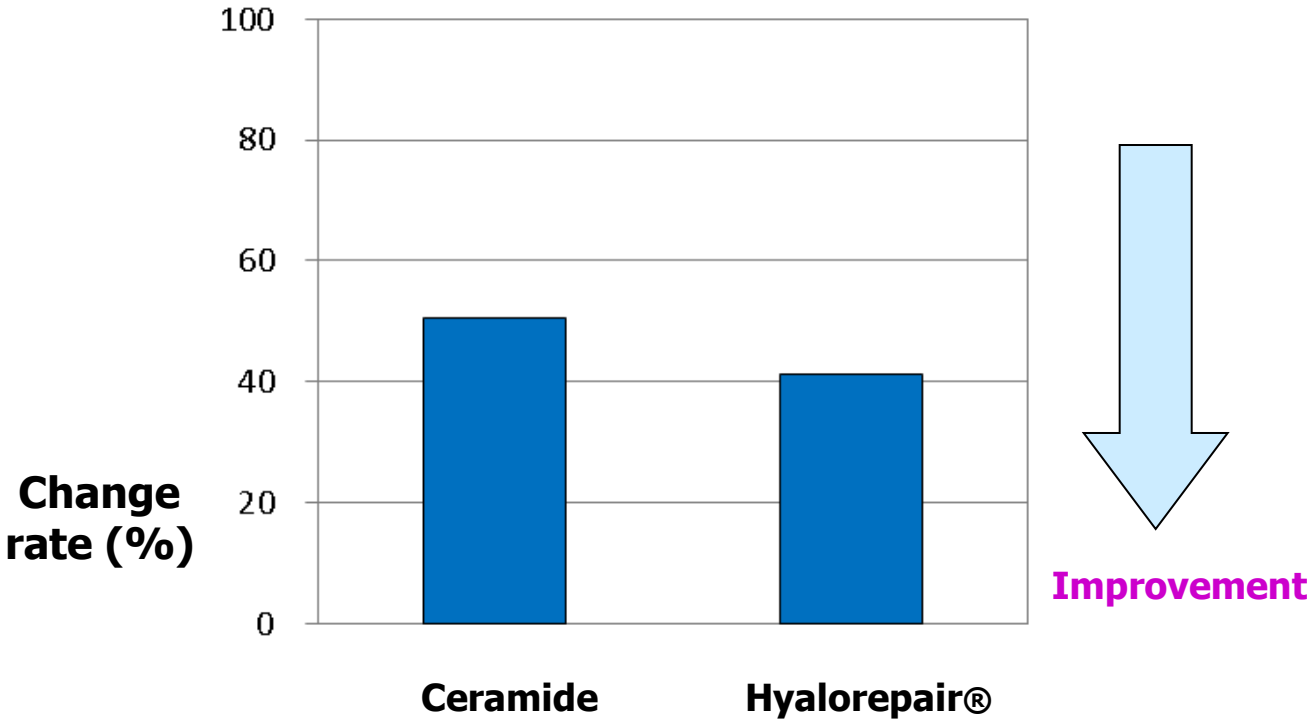
【Test result】*Measurement of transepidermal water loss（TEWL）*

Change rate of transepidermal water loss 3 days later



Hyalorepair® is more effective than Ceramide.

In vivo test

~ confirmation of effectiveness on damaged skin (Combined with Ceramide)

Sample

①Cosmetic product containing 1 % Ceramide

②Cosmetic product containing 1 % Hyalorepair®

③Cosmetic product containing 0.5% Hyalorepair® and 0.5 % Ceramide

Test method

【Subject】

9 females (aged 20's～50's with healthy skin）

【Test method】

Damage the forearm skin with mixed solution of acetone and ether.

Apply the sample everyday to the damaged skin before bedtime for 5 days.

【Test items】

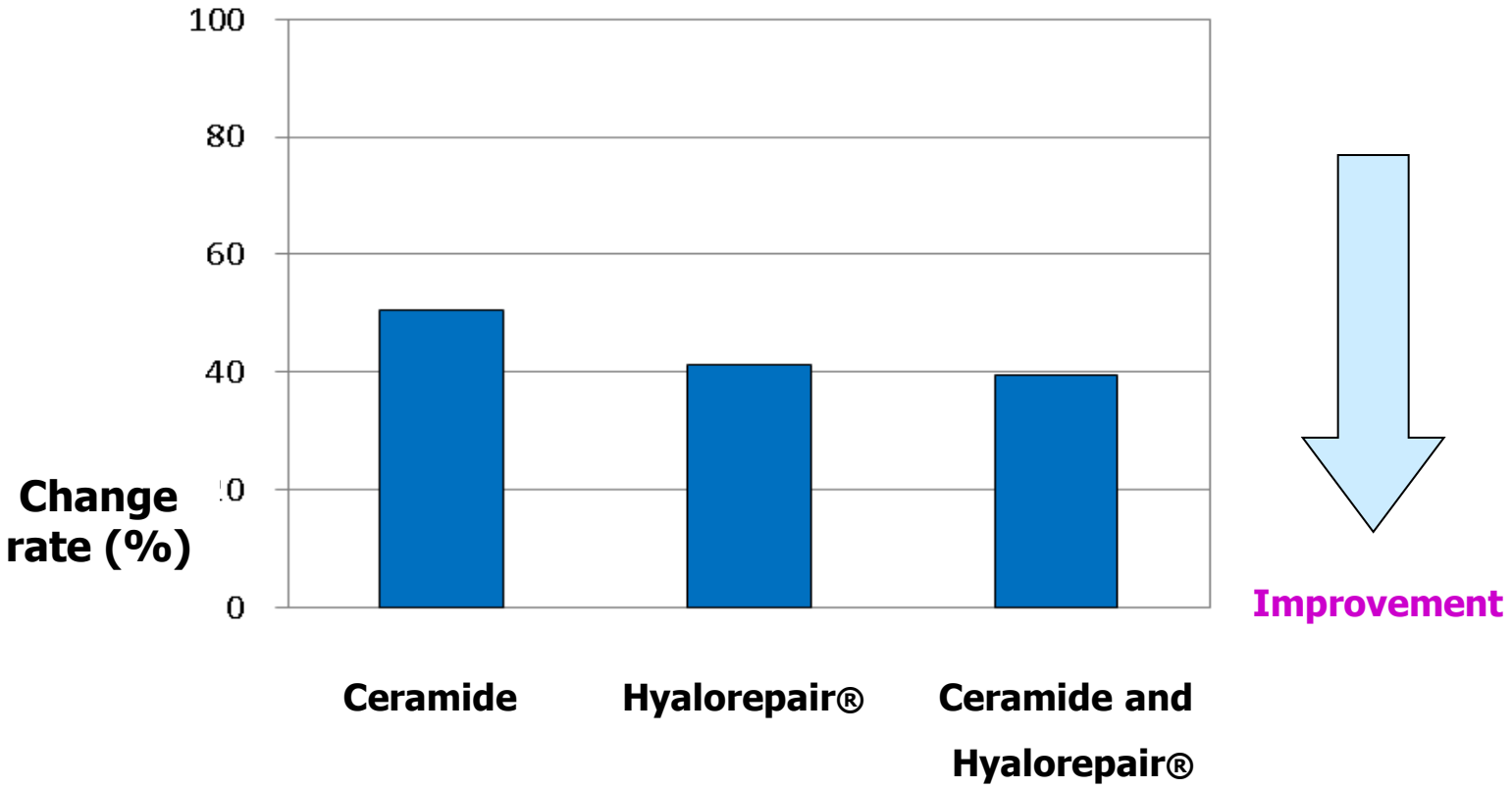
measurement of transepidermal water loss（TEWL）

Testing facility: Inforward, inc., Ebisu skin research center

QPFC ® ®

【Test result】*Measurement of transepidermal water loss（TEWL）*

Change rate of transepidermal water loss 3 days later



Combination of Hyalorepair® & Ceramide is more effective than Ceramide alone.

＜Brand new hyaluronic acid featuring barrier function recovery＞

「Hyalorepair®」

Sample formulation
（Toner・Emulsion・Gel cream）

【Precaution】

◆ We do not guarantee the stability, safety, or effectiveness and industrial property right of the finished product formulated with this sample formulation.

◆ All this information shall not relieve the User from undertaking its own investigations and tests of stability, safety or effectiveness and industrial property right.

◆ Copy, use of this information without notifying us are strictly prohibited.

◆ We do request that you notify us of any use of this information, whether in part or in its entirety, for commercial or personal use.

◆ The presentation and information of this document are subject to change without notice.

Kewpie Corporation Fine Chemical Division 2011.09.27

Sample Formulation【Toner】

	Ingredient (INCI Name) ＊:Product name	Proportion (Wt. %)
1	WATER	87.55
2	Ethyl Alcohol (ALCOHOL)	4.50
3	GLYCERIN	3.00
4	PEG-30 LANOLIN	2.00
5	BG (BUTYLENE GLYCOL)	2.00
6	HYALOVEIL®-P＊ (HYDROXYPROPYLTRIMONIUM HYALURONATE)	0.30
7	PHENOXYETHANOL	0.20
8	METHYL PERFLUOROBUTYL ETHER	0.10
9	EDTA-2Na (DISODIUM EDTA)	0.10
10	SODIUM CITRATE	0.09
11	HYALO-OLIGO®＊ (HYDROLYZED HYALURONIC ACID)	0.05
12	CITRIC ACID	0.01
13	HYALOREPAIR®	0.10
TOTAL		100.00

Sample Formulation【Emulsion】

	Ingredient（INCI Name） ＊:Product name	Proportion (Wt. %)
1	WATER	80.48
2	BG (BUTYLENE GLYCOL)	6.00
3	SQUALANE	3.00
4	GLYCERIN	2.50
5	TRIETHYLHEXANOIN	2.00
6	PHYTOSTERYL/OCTYLDODECYL LAUROYL GLUTAMATE	1.60
7	MACADAMIA TERNIFOLIA SEED OIL	1.50
8	POLYGLYCERYL-10 STEARATE	1.20
9	CARBOMER	0.40
10	HYALOVEIL-P®＊ (HYDROXYPROPYLTRIMONIUM HYALURONATE)	0.30
11	HYDROGENATED LECITHIN	0.30
12	POLYSORBATE 60	0.20
13	SODIUM HYDROXIDE	0.11
14	METHYL PERFLUOROBUTYL ETHER	0.10
15	PHYTOSTEROLS	0.05
16	TOCOPHEROL	0.05
17	PROPYLPARABEN	0.05
18	EDTA-2Na (DISODIUM EDTA)	0.05
19	SIMETHICONE	0.01
20	HYALOREPAIR®	0.10
TOTAL		100.00

Sample Formulation【Gel cream】

	Ingredient (INCI Name) * : Product name	Proportion (Wt. %)
1	WATER	83.14
2	GLYCERIN	5.00
3	BG (BUTYLENE GLYCOL)	5.00
4	SQUALANE	5.00
5	CARBOMER	0.60
6	LUBRAJEL OIL* (PROPYLENE GLYCOL, CARBOMER, GLYCERIN, SODIUM POLYACRYLATE)	0.50
7	HYALOVEIL®P* (HYDROXYPROPYLTRIMONIUM HYALURONATE)	0.20
8	SODIUM HYDROXIDE	0.20
9	METHYL PERFLUOROBUTYL ETHER	0.15
10	HYALOREPAIR®	0.10
11	HYALURONSAN HA-LQH* (SODIUM HYALURONATE)	0.05
12	HYALO-OLIGO®* (HYDROLYZED HYALURONIC ACID)	0.05
13	EDTA-4Na (TETRASODIUM EDTA)	0.01
	TOTAL	100.00

＜Brand new hyaluronic acid featuring barrier function recovery＞

「Hyalorepair®」

～Proposal for lipstick (lip balm, lip gloss)～

【Patent】international publication number：WO 2011/102462 A1

*This documentation is to explain the materials and does not guarantee effectiveness or efficacy of any product into which the said materials are formulated.

Kewpie Corporation Fine Chemical Div.

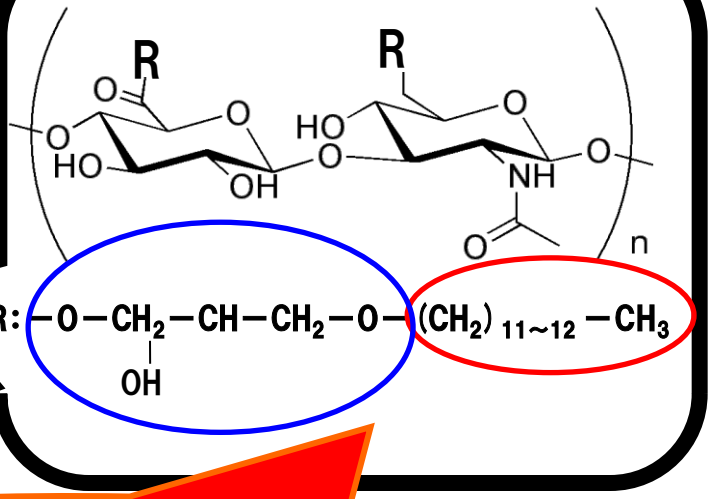
New proposal of formulation using Hyalorepair®

Common Hyaluronic Acid

→ “aqueous” (water-soluble)

Not suitable for lipstick

For “non-aqueous” Formulation…



Hyalorepair®

Hyalorepair®

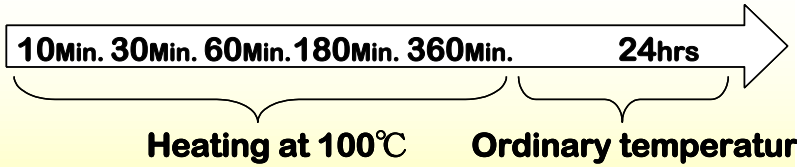
Hydrophobic group introduction by chemical modification through glycerin backbone

Solubility test on oil-based material

＜Test sample＞
①oil-based materials
②Hyalorepair®／ Hyaluronic acid with low molecular weight

＜Test method＞
1) Blend ② to each oil-based materials and adjust HA concentration to be 0.05% and 0.1%.
2) Heat each samples for 6 hours at 100℃
3) Leave the samples for 24 hours at ordinary temperature
4) Test the solubility of each samples

＜Evaluation method＞
Check the solubility at following measurement points:



○：Totally swollen △Partially swollen

＊Swollen means no grainy HA (lumps) is seen in the test sample.

Material Name	Time (Min.)	Conc. Of Hyalorepair® 0.05%	Conc. Of Hyalorepair® 0.10%
Parleam® 18	10	△	△
	30	○	○
	60		
	180		
	360		
Parleam® 24	10	△	△
	30		
	60	○	○
	180		
	360		
T. I. O	10	△	△
	30		
	60		
	180	○	
	360		○
Eldew® CL-301	10	△	△
	30		
	60		
	180	○	
	360		○
Cosmol® 42V	10	△	△
	30		
	60		
	180	○	
	360		○

＊Hyaluronic acid with low molecular weight was insoluble in all oil-based materials.
＊Hyalorepair® transparently dissolved after 10 Min. with Glycerin and remained the same after 24 hrs.

Conclusion

＜Solubility test result of Hyalorepair®＞

- Keeping stirring the solution while heating reduces time to dissolve and swell.
- Transparently dissolved after 10 Min. with Glycerin
- Swollen after 30 Min. at 100℃ with Hydrogenated Polyisobutene (Parleam® 18)
- With all oil-based materials;
  Hyalorepair® 0.05% swelled after 3 hrs at 100℃
  Hyalorepair® 0.1% swelled after 6 hrs at 100℃

No grainy HA (lumps) is seen in the test samples.

New formulation proposal !

Hyalorepair® can be formulated in lipstick (lip balm, lip gloss)!

Sample formulatioin【Lip balm】

INCI NAME	With Glycerin		With Hydrogenated Polyisobutene	
	(%)	Quantity (g)	(%)	Quantity (g)
PEG-9 POLYDIMETHYLSILOXYETHYL DIMETHICONE	10	10	10	10
NEOPENTYL GLYCOL DICAPRATE	2.13	2.13	2.13	2.13
TOCOPHEROL	0.02	0.02	0.02	0.02
TRIMETHYLSILOXYSILICATE、CYCLOPENTASILOXANE	3	3	3	3
HYDROGENATED POLYISOBUTENE	10	10	10	10
CHOLESTERYL HYDROXYSTEARATE	5	5	5	5
DIISOSTEARYL MALATE	10	10	10	10
CHOLESTERYL/BEHENYL/OCTYLDODECYL LAUROYL GLUTAMATE	2	2	2	2
PROPYLENE GLYCOL	0.2	0.2	0.2	0.2
CERESINE	1.8	1.8	1.8	1.8
CANDELILLA WAX	3	3	3	3
MICRO CRYSTALLINE WAXES	7.5	7.5	7.5	7.5
PARAFFIN	6	6	6	6
PROPYLPARABEN	0.05	0.05	0.05	0.05
TRIETHYLHEXANOIN	30.25	30.25	30.25	30.25
STEAROYL INULIN	2	2	2	2
SILICA	2.5	2.5	2.5	2.5
MICA	2	2	2	2
MICA, POLYQUATERNIUM-61	1	1	1	1
NYLON	0.5	0.5	0.5	0.5
GLYCERIN	1	1		
HYDROGENATED POLYISOBUTENE			1	1
C12-13 ALKYL GLYCERYL HYDROLYZED HYALURONATE	**0.05**			
TOTAL	100	100	100	100

～Proposal for Hair Care Products using～

「Hyalorepair®」

【Patent】international publication number：WO 2011/102462 A1

<Barrier Function Recovery HA>

【Patent】
International Publication Number：WO 2011/102462 A1

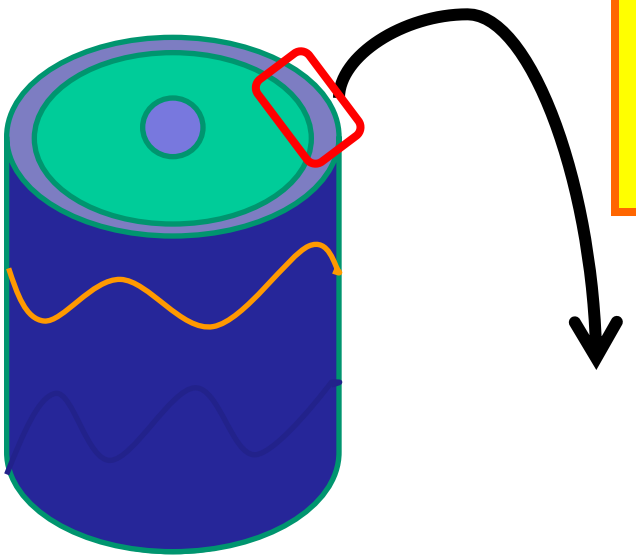
Kewpie Corporation Fine Chemical Div.

Possible Approach to the Intercelluar Lipid of Hair

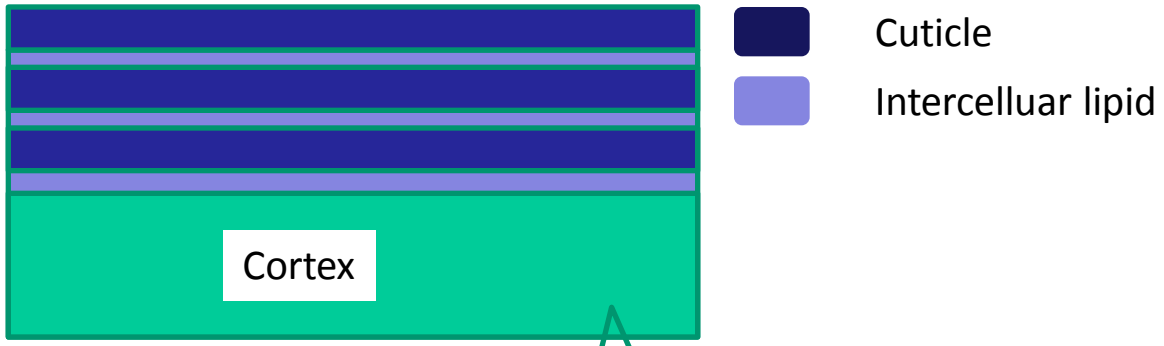
Intercellular Lipid is…

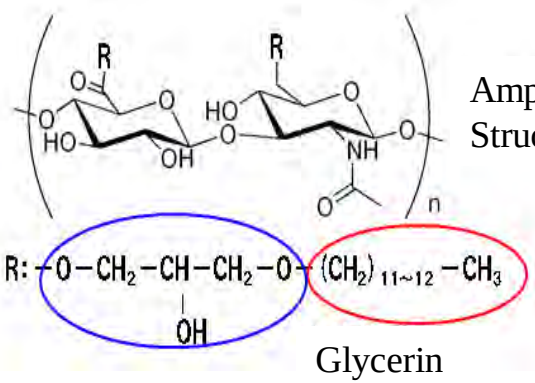
associated with healthy cuticles and cortex.

It is important for maintaining the structure of surface and inside of the hair. It gives softness and pliancy to the hair.



【Cross-section diagram of the Hair】

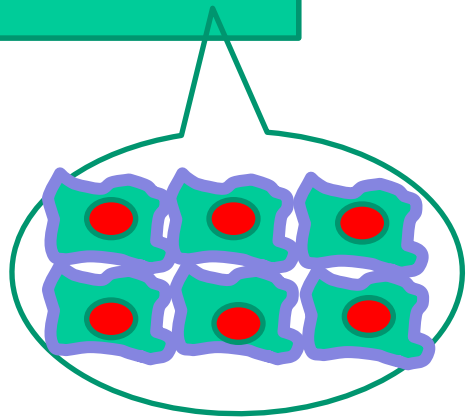




Amphophilic Structure

Glycerin backbone

"Hyalorepair®" interacts with Intercelluar Lipid.



Functionally Test Result of Hair Care

「Hyalorepair® 」

【Patent】international publication number：WO 2011/102462 A1

＜Brand new hyaluronic acid featuring barrier function recovery ＞

The Result of Sensory Rating

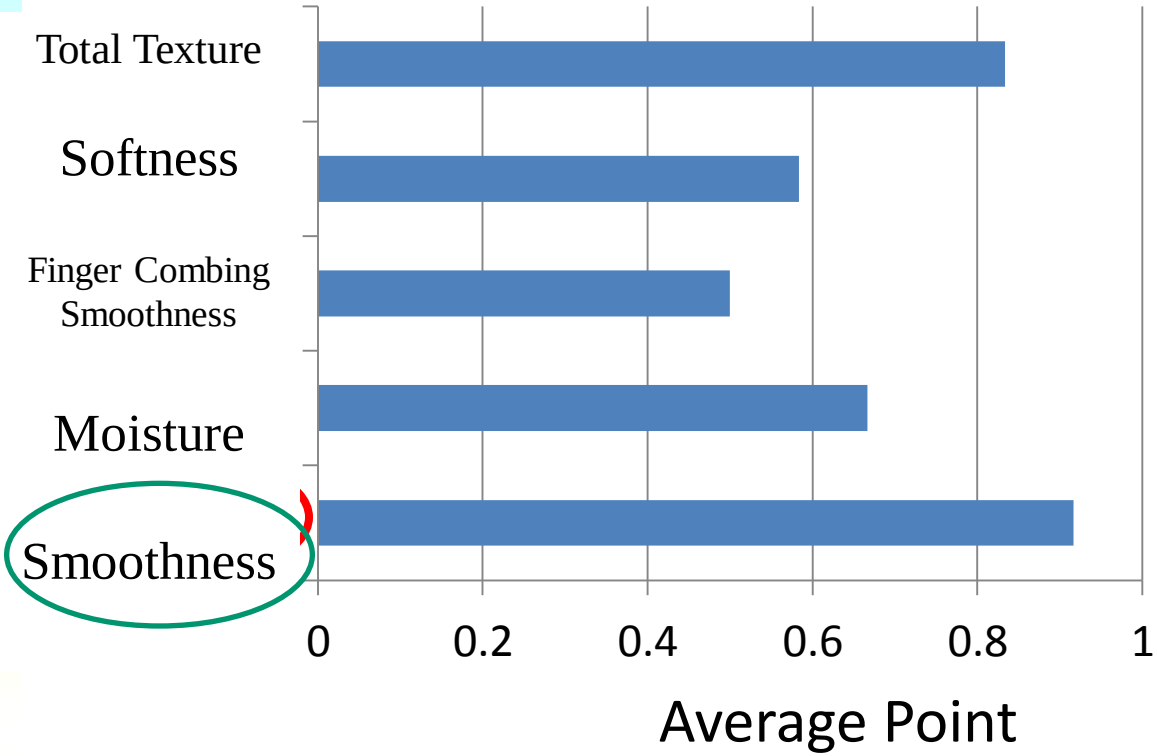
<Sample>

①Hyalorepair® 1% Solution

②Water

<Test Method>

Sample Solution
↓← Damaged Hair (Bleached)
Soaking (40℃ x 20min)
↓
Rinse with Water
↓
Drying (Drier+Leave for 12hours)
↓
Sensory Rating



Hyalorepair® brings smoothness and moisture into the hair.

*The sensory rating score is based on the comparison with water:
The scores are evaluated as Very Good:2pt, Good:1pt, No Difference:0pt, Bad:-1pt, Very Bad: 2pt

The Result of Friction Sensitivity Test

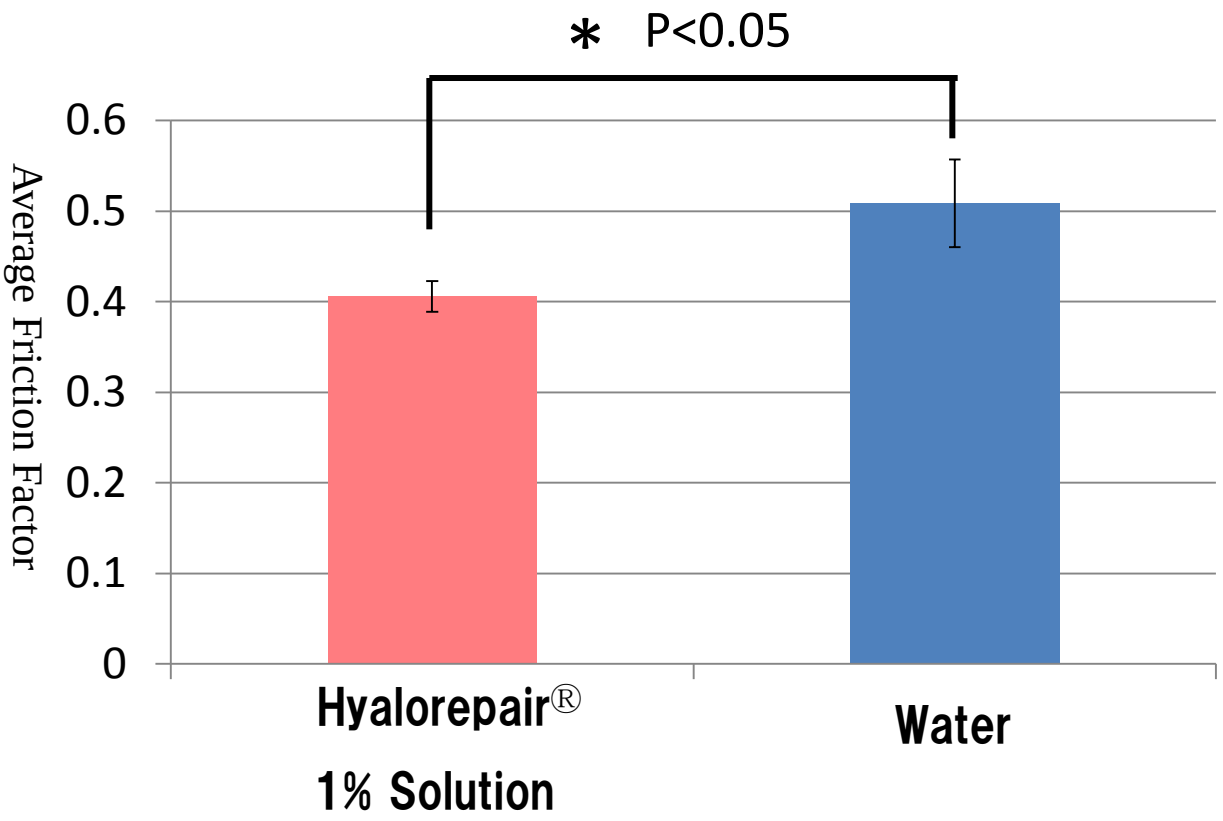
<Sample>

①Hyalorepair® 1% Solution

②Water

<Test Method>

Sample Solution
↓←Damaged Hair (Bleached)
Soaking (40℃ x 20min)
↓
Rinse with Water
↓
Drying (Drier+Leave for 4 hours)
↓
Friction Sensitivity Tester



Hyalorepair® makes hair surface smooth.

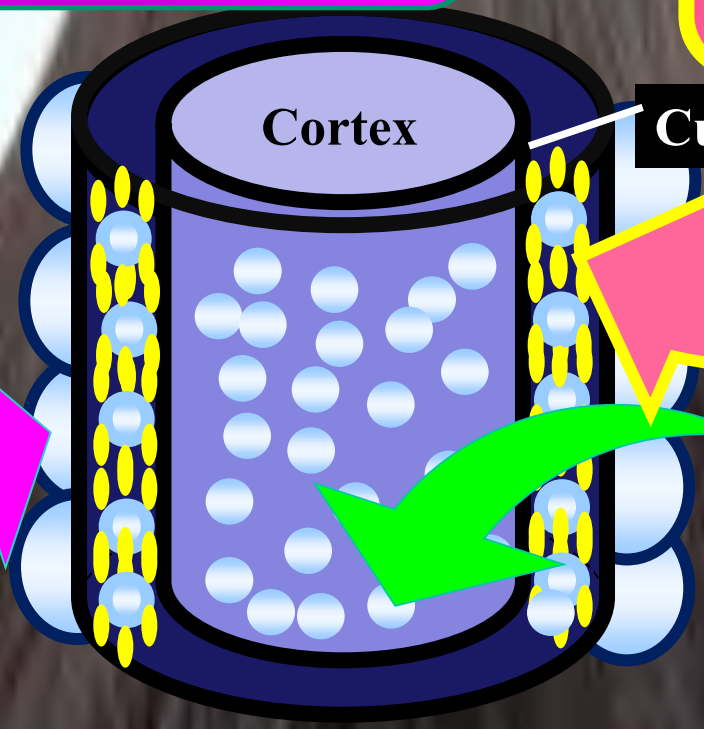
【Proposal】Not only “Maintain the Hair” but Also “Improve the Hair”

Hyaloveil-P®

Adhesive type of HA
“Not easily washed off and protects the hair by keeping moisture”

Hyalorepair®

Recovery type of HA
“Improves the hair to nice silky texture by approaching to Cuticle and Cortex”



The Image of Hair

Hyalo-Oligo®

Penetration type of HA
“Keeps the moisture in Cortex”

Formulate our Innovative HA depending on your needs

(Reference)

Application of Hyalorepair® for Scalp care

~Scalp Care & Barrier Function~

Almost every Atopic Dermatitis Patients has Inflammation and Scaling in their Scalp.
A contributory factor is decrease of ceramide.

The less Lipid in Scalp Horny Layer (ceramide etc.)
was found in the scalps of scaling patients compared to healthy scalps.
The scaling was improved by increasing Lipid in Scalp Horny Layer（maintained moisture）

<Scalp Condition>

・Many people are worried about their itch, dandruff, and damage of their hair, caused by decrease of barrier function, since scalp gets easily dry, compared to skin.

・Healthy Scalp helps grow healthy hair.

“Introduction of Hyalorepair® for Skin care” presentation sheet shows Improvement in Skin Barrier Function.

Summary of Hyalorepair ® Characteristics

①Interacts with Intercelluar Lipid of Hair and improves Cortex and Cuticle.

→**Brings you Smooth and Moist hair**

② Improves Horny Layer of Scalp and Normalize Scalp Condition.

→Promotes the **Increase in Elasticity of the Scalp and Growth of the Healthy Hair**

⇒ ***Please consider our Hyalorepair® as one of the best ingredients for Aging Care products***