



Q. P. Corporation

No. 4-13, 1-CHOME SHIBUYA SHIBUYA-KU, TOKYO, JAPAN

Hyalo-Oligo[®]

~Hyaluronic Acid with low molecular weight of average less than 10,000~

Hyalo-Oligo penetrates through horney layer of skin

Q.P. Corporation has verified that Hyaluronic Acid of average molecular weight less than 10,000 (product name : Hyalo-Oligo) penetrates through the horney layer of skin.

Make Hyalo-Oligo your favourite and let its moisture retaining capacity activate from inside of your skin.

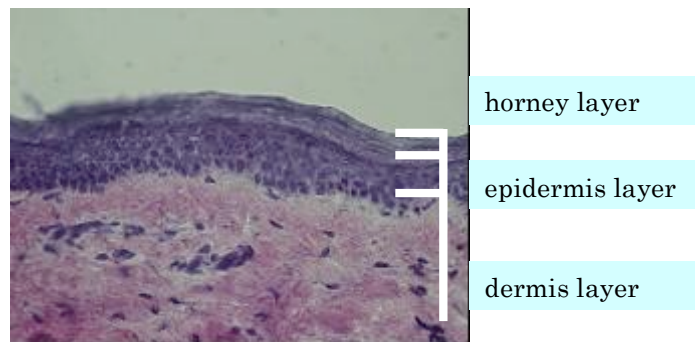


Fig.1 Hemato-xylin/eosin dying of skin

Fluorescent colouring is seen in the horney layer of skin where Hyalo-Oligo

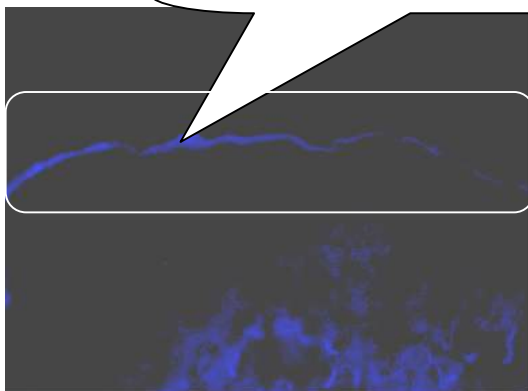


Fig.2 Penetration of Hyalo-Oligo through the horney layer of skin (fluorescent picture).

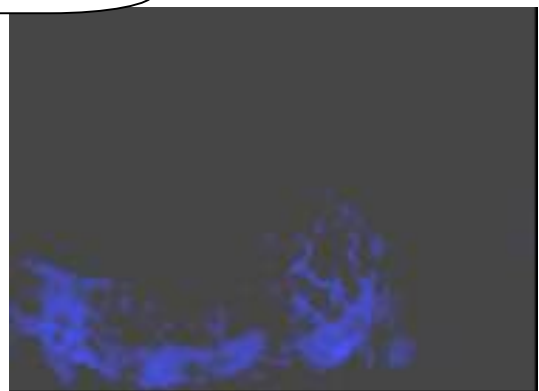


Fig.3 Reference –no Hyalo-Oligo is applied(fluorescent picture).



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Note) Fluorescent colouring at the lower part of the Fig.2 is of **elastinic protein** which by nature exists in the skin cell.

As the result of trans-humandermal absorption test, a characteristic fluorescent colour to Hyalo-Oligo has been detected in the horny layer, which is a layer above the purple colour of haematoxylin dyeing. By this test it is verified that Hyalo-Oligo with average molecular weight less than 10,000 penetrates through the horny layer of skin and exercises its moisture retaining capacity for long period.



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【Trans-humandermal absorption test】

Preparation of Hyalo-Oligo

Reagent was prepared by resolving high purity Hyaluronic Acid (made by Q.P. Corp.) with acid to make Hyalo-Oligo of average molecular weight of 6,000 (made by Q.P. Corp.).

Preparation of Hyalo-Oligo

In order to detect Hyalo-Oligo being penetrating through the skin, reagent Hyalo-Oligo was labeled with **fluorescent dye agent** 6,7-dimethoxy-1-methyl-2(H)-quinox-alinone-3-propionohydrazide (hereafter "DMEQ-hydrazide).

transdermal absorption test

A test piece of skin which had been surgically cut out from abdomen was fixed on **Franz diffusion cell for transdermal absorption test** with its horny layer upper side. In order to keep the temperature of test skin at 32 ± 1 °C, **thermal liquid** was being circulated in the diffusion cell jacket.

Then 1% aqueous solution of Hyalo-Oligo labeled with fluorescent dye was applied to the surface of the test skin. Application of Hyalo-Oligo to the test skin was continued for one hour and **such application was made in three parts**

Observation by fluorescent microscope

After washing the test skin was cut out to the size of $10 \mu\text{m}$ and observed by a fluorescent microscope.(magnified by 40, excitation wavelength : 340~380nm, fluorescent wavelength 435~485nm)

Tissue dyeing

The test skin was dyed with **haematoxylin/eosin**. Then washed and was observed by a microscope. The purple parts of the skin are horny layer and epidermis, pinkish part is dermis.

Conclusion (summary)

As the result of trans-humandermal absorption test, a characteristic fluorescent colour to Hyalo-Oligo has been detected in the horny layer, which is a layer above the purple colour of **haematoxylin/eosin** dyeing. By this test it is verified that Hyalo-Oligo with average molecular weight less than 10,000 penetrates through the horny layer of



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skin and exercises its moisture retaining capacity for many hours.

【Control】 Hyaluronic Acid

Hyaluronic Acid mainly exists in the skin, joint serous, eyes and umbilical cord.

It has high water-binding capacity and has many uses like producing eyewash for dry-eyes and other medicines and cosmetics as well as for food use.

For cosmetics use average molecular weight 500~2,000 thousand of Hyaluronic Acid is commonly being used.

advancement of osteoarthritis (see-**Exhibit5 6**).