

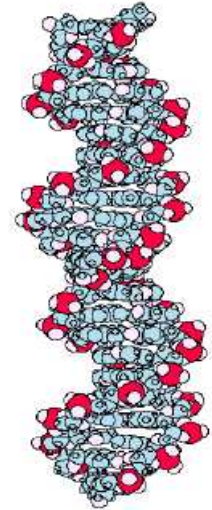


## Physiological function of DNA-Na

### \*What's DNA-Na?

DNA (Deoxyribonucleic acid) plays a role of genetic information in our life. It is also a source of important nutrients along with sugar, protein, vitamins and minerals for our body, and it is recognized as “the 7th essential nutrient”. Nucleic acid is biosynthesized by *de novo* pathways in our body, but this ability is reduced by aging. Therefore it is important to take DNA as a food ingredient or a supplement for providing a source of salvaged biosynthesis of DNA.

Our DNA-Na and NUCLEOPROTEIN (mixture of DNA and gene protein) is purified from high quality natural salmon milt. It is safe and available for dietary supplements. This report demonstrates the results of our study of DNA-Na.



Model of double stranded DNA

From PDB

### \*The Effect of taking DNA-Na on Alcohol Metabolism.

It is thought that DNA-Na is able to improve the hepatic function of consuming alcohol. We studied the effect of taking DNA-Na on alcohol metabolism. And we also tested turmeric extract, which is expected the same effect on alcohol.

In this study, healthy volunteers (men, n=11, Age: 30y. -50y.) took DNA-Na (2 g) tablets, or turmeric extract (1.5g : granulated powder containing 30mg of curucumin) 30 min before drinking beer (633 mL, alcoholicity: 5.5%). Their blood was tested at regular intervals (0,1,2,4hr). At these points, their blood alcohol level, blood acetaldehyde level, and blood acetic acid level were checked.

As a result of alcohol level, neither the test groups who consumed the DNA-Na supplement nor who consumed the turmeric extract supplement showed significant difference compared with the control group.

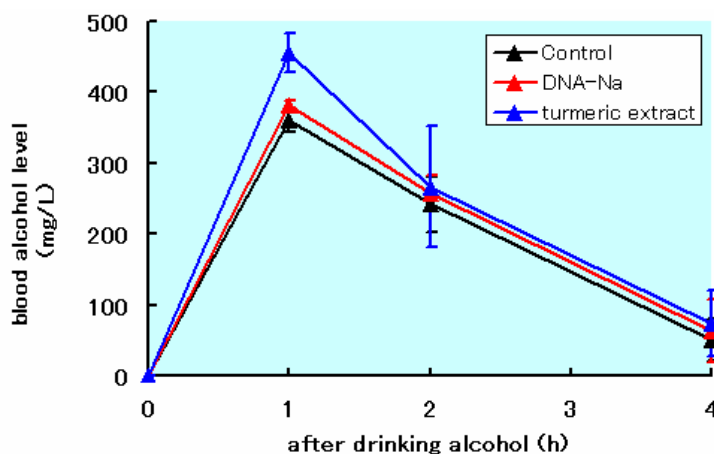


Fig.1  
Change of blood alcohol level  
after drinking alcohol

On the other hand, the results of their blood acetaldehyde level and acetic acid level showed a significant difference between the test groups who consumed the DNA-Na (not only 2000mg taken group but also 500mg taken group) and the control group. Therefore, DNA-Na suppressed the elevation of blood acetaldehyde level and accelerated up-tendency of blood acetic acid level.

These results suggested that DNA-Na activated acetaldehydedehydrogenase (ALDH) activity and it had an improvement effect against bad-feeling of alcohol more than the turmeric extract.

These blood kinetics data were supported by volunteer's comments "DNA-Na didn't make them sick after drinking."

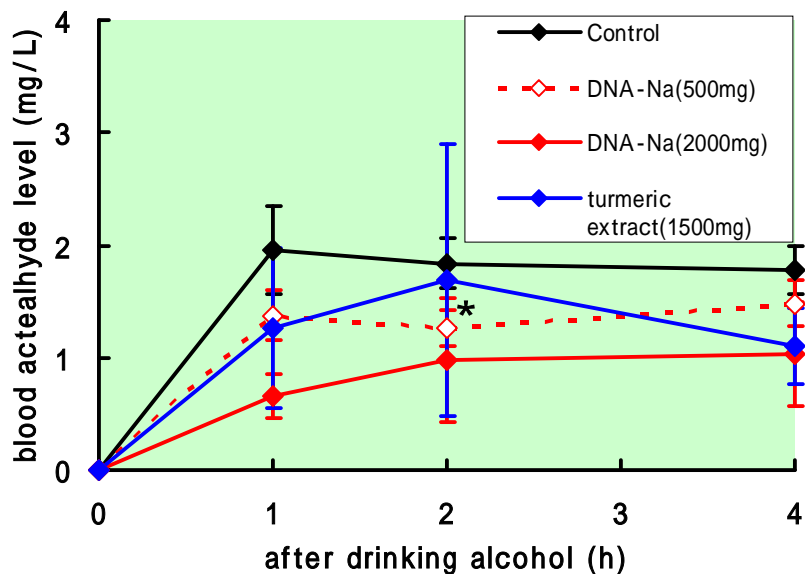


Fig2. Change of blood acetaldehyde level after drinking alcohol (\* : p<0.005)

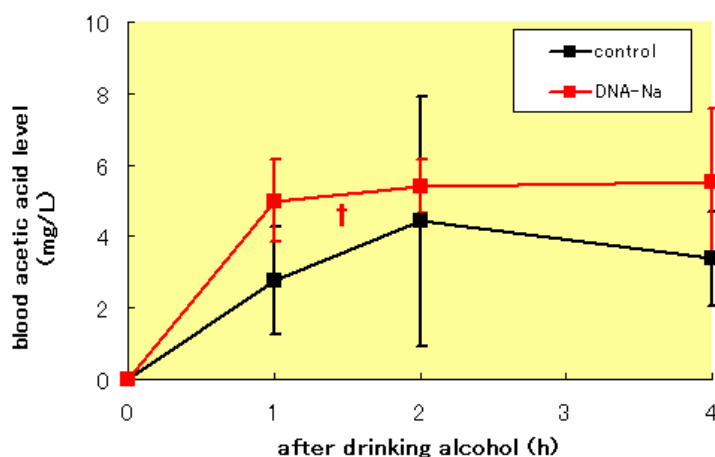
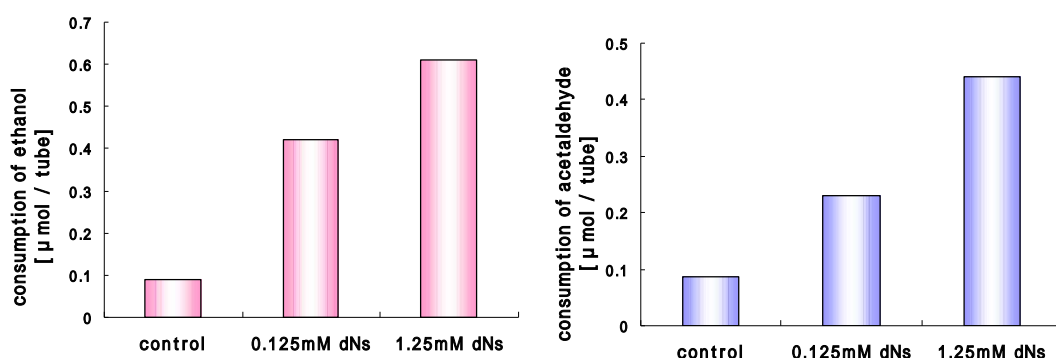


Fig3. Change of blood acetic acid level after drinking alcohol († : p<0.1)

We tried to clarify the mechanism of alcohol metabolism *in vitro* on taking DNA-Na. So, ethanol and the digestive of DNA -Na (deoxyadenosine ; dA, thymine ; dT, deoxyguanosine ; dG, deoxycytidine ; dC) was added to the homogenate of rat liver, and the mixture was incubated at 37 °C for 1.5 h. Then the concentration of alcohol and acetaldehyde in the mixture was measured. The result showed that the homogenate including the digestive DNA-Na promoted the consumption of ethanol and acetaldehyde compared with control. Furthermore, interestingly, dA and dG had stronger effect than dT or dC.

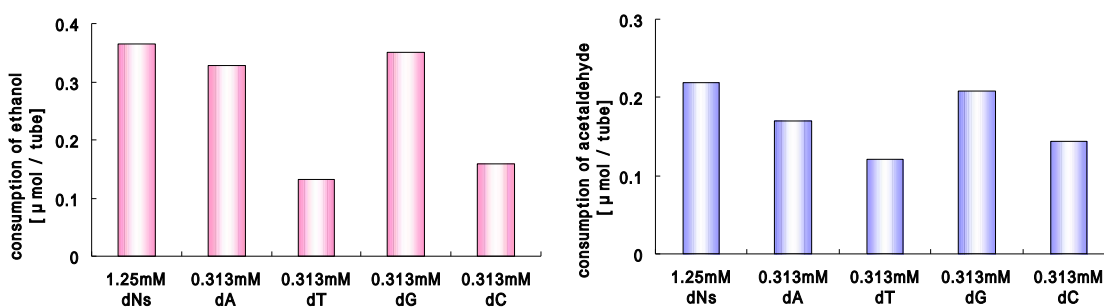
Ethanol is converted into acetaldehyde by alcohol dehydrogenase (ADH) and the acetaldehyde is changed into aldehyde dehydrogenase (ALDH). These alcohol metabolizing enzyme reactions are conjugated with the cycle of coenzyme (NAD<sup>+</sup>/NADH).

According to the promotion effect on both ethanol and acetaldehyde, digestive DNA-Na might be involved in the cycle of NAD<sup>+</sup>/NADH.



**Fig.4 The effect of deoxyribonucleosides on ethanol metabolism**  
(*in vitro* test, liver homogenate of rat)

(a) consumption of ethanol, (b) consumption of acetaldehyde

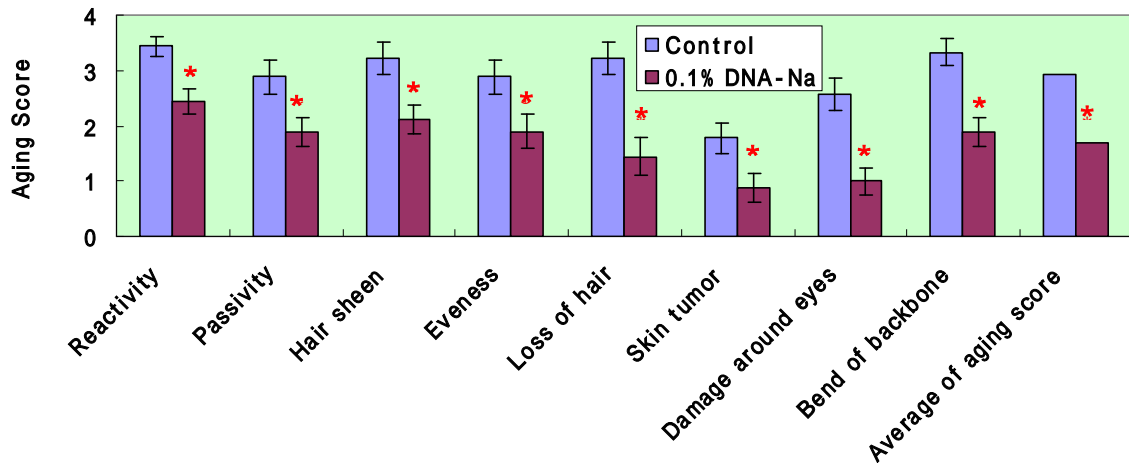


**Fig.5 The effect of each deoxyribonucleoside on ethanol metabolism**  
(*in vitro* test, liver homogenate of rat)

(a) consumption of ethanol, (b) consumption of acetaldehyde

**\*The Effect of taking DNA-Na on inhibition of aging.**

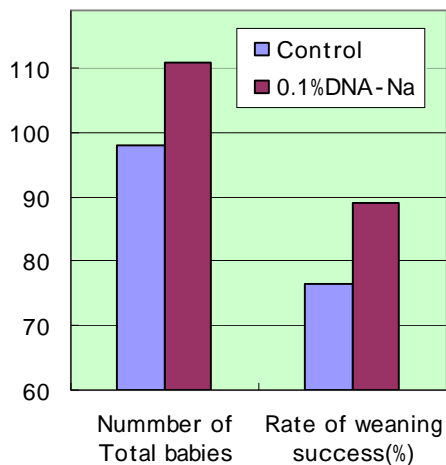
The shortage of nucleic acids in our body may be contributed to the aging process. Taking high nucleic acid containing supplements may prevent the aging process. We have studied the anti-aging function on DNA-Na. In this study, 0.1% of DNA-Na was administrated to senescence-accelerated mice (SAMP male and female n= 7 respectively) with their feed for 11 months. The results showed that the mice administrated DNA-Na received better aging scores compared with the control mice.



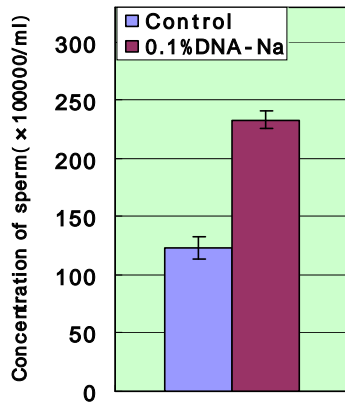
**Fig.6 Improvement of aging score (\* p<0.05)**

In the same experiment, it was found that the abilities of breeding (number of total babies) and weaning were improved. The rate of weaning success was defined as a number of babies that were alive for 3 weeks against the number of total babies. Improving of the rate of weaning success means that parents' physical strength and their brain function were in a good condition. Besides the concentration and the activity of sperm were improved.

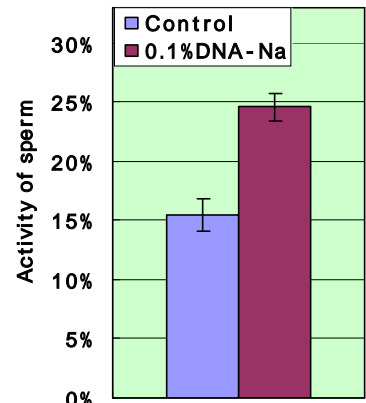
[Collaboration with Prof. S.Yamamoto (Ochanomizu women's University) and Providence University in Taiwan]



**Fig.7 Improvement of breeding and weaning success**



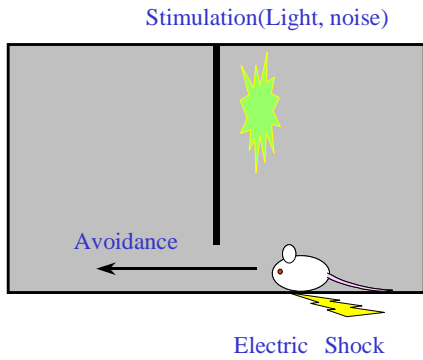
**Fig.8 Concentration of sperm**



**Fig.9 Activity of sperm**

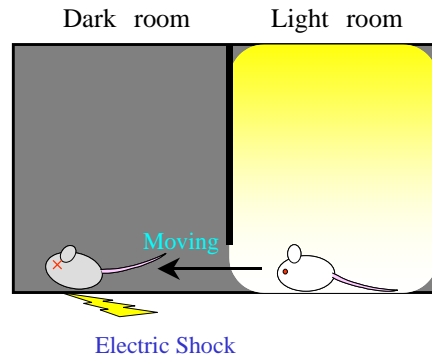
**\*The Effect of taking DNA-Na on brain function.**

We have studied the effect of taking DNA-Na on brain function. The diet containing 0.1% of DNA-Na was administrated to senescence-accelerated mice (male and female n= 7 respectively) for 11 months.



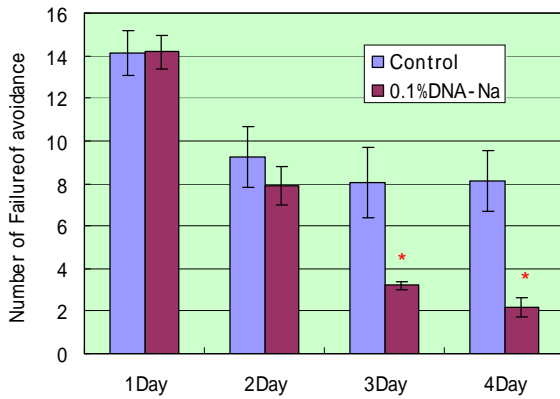
**Active Avoidance Test**

If mice didn't move to next room after receiving the stimulation, they were punished by electric shock.



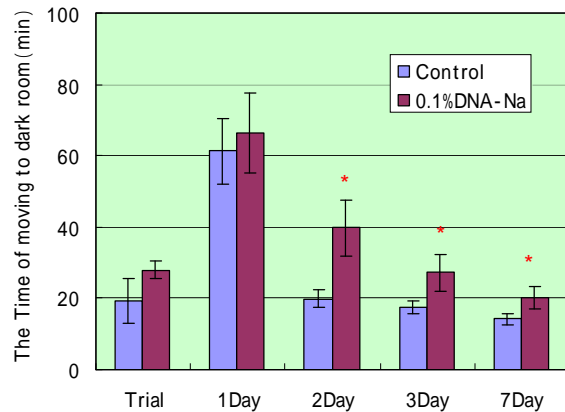
**Passive Avoidance Test**

Mice favor dark atmosphere. If they moved to the dark room, they were punished by electric shock. In this study, the tendency staying in bright room was measured.



**Fig.10 Number of failure of avoidance**

After 3 days, the number of avoiding failure was decreased on administrating DNA-Na for control.



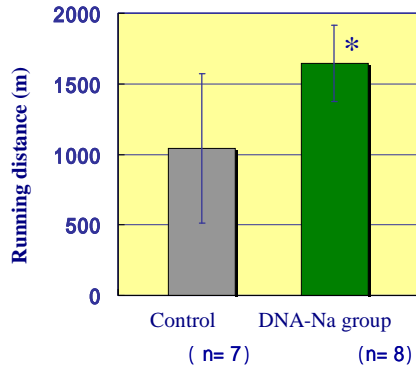
**Fig.11 Time of moving to dark room**

After 2 days, the staying time in the bright room was tend to extend against control significantly ( $p < 0.05$ ). Therefore the abilities of learning and memorizing were improved.

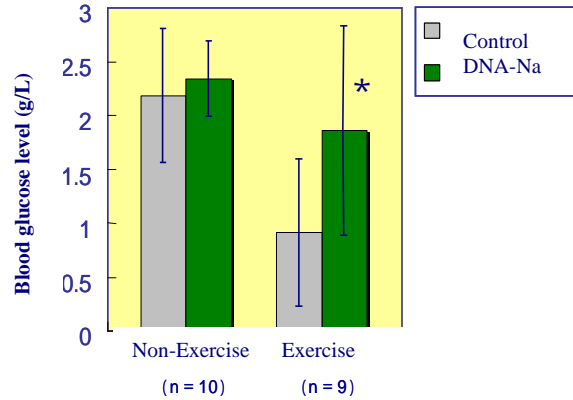
These results suggested that supplementation of DNA-Na may reduce the age-induced deterioration of certain memory tasks in senescence-accelerated mice.

**\*The Effect of taking DNA-Na on endurance running capacity.**

We researched the effect of taking DNA-Na on endurance running capacity. In this study, 0.1% of DNA-Na containing diet was administrated to mice (5 week-age, n=7- 10) for 12 weeks, and their endurance running capacity was measured with treadmill. As the results, mice ran a significant longer distance in the DNA group than the control group ( $p<0.05$ ). After the running exercise, their blood sugar level was measured. The blood glucose level was significantly higher in the DNA group ( $p<0.05$ ). These results suggested that dietary DNA activated the glucose metabolism and consequently enhances the running capacity in mice. [Collaboration with Kagawa Nutrition University]



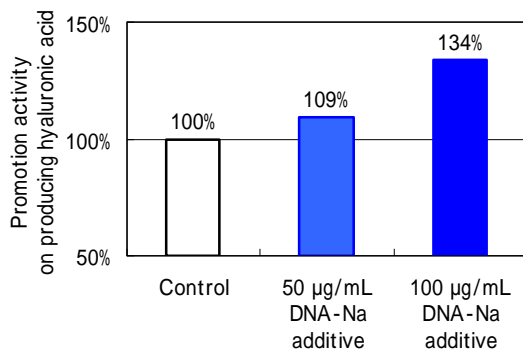
**Fig.12 Running distance (\* $p<0.05$ )**



**Fig.13 Blood glucose level**

**\*The effect of DNA-Na on the production of hyaluronic acid using human cell.**

Hyaluronic acid, which is a content of extracellular matrix, is able to hold a lot of moisture and it contributes to our skin moisture. Therefore promoting the produce of hyaluronic acid is expected to improve our skin conditions (moisture, elasticity, tension and sleek etc). We evaluated the promoting effect of DNA-Na on the production of hyaluronic acid using human normal dermal fibroblast (SF-TY cell). The results showed that DNA-Na has the promoting effect of hyaluronic acid production on the fibroblast (Fig.14). This data suggested that DNA-Na would improve skin conditions.



**Fig.14 Promotion activity of DNA-Na on producing hyaluronic acid**

**< Improving effect of DNA-Na on skin care >**

We investigated the effect of rubbing and taking the DNA-Na from salmon milt on human skin.

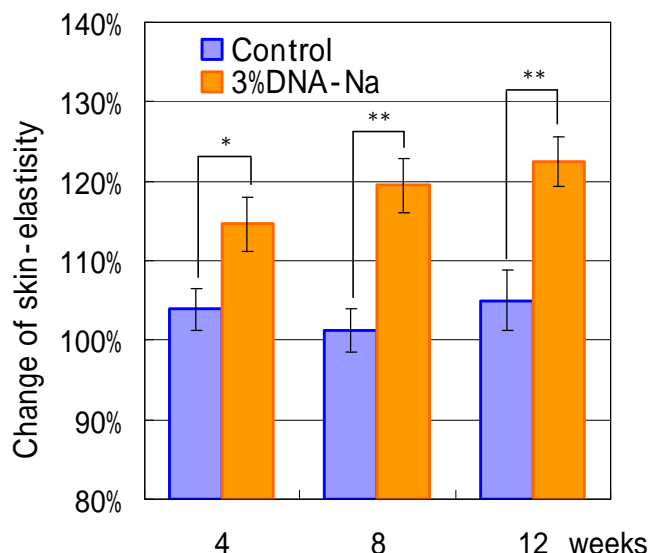
**\*Effect of the DNA-Na cream on skin (human study)**

At first, we investigated the effect of the DNA-Na on skin. The cream containing DNA-Na (3%) or the control cream was rubbed to the male subjects (n=10 each group) for 12 weeks. The result showed that the DNA cream improved the skin-elasticity more than the control after the fourth week. The change of skin-elasticity was improved significantly (Fig.15). Rubbing of the DNA cream tended to decrease transepithelial water loss (TEWL) and to increase water content in the face skin at 12th week. (Fig.16, 17).

**< Summary of the protocol >**  
 Subjects :  
 healthy adult men(Age:30 ~ 59)  
 Ten people / each group

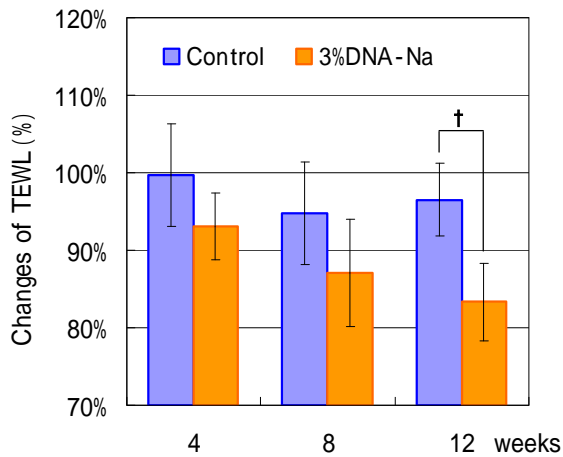
Test method:  
 Each cream was rubbed to the subject's face.  
 Skin-Elasticity was measured by Cutometer.

Measurement method and Definition of Skin-Elasticity  
 Put the probe of Cutometer on the skin and pull it by constant negative pressure.  
 We measured the height (Uf) that skin was drawn into the probe.  
 Releasing the constant negative pressure, we measured the restored height (Ur).  
 Skin-Elasticity was defined in Ur/Uf.

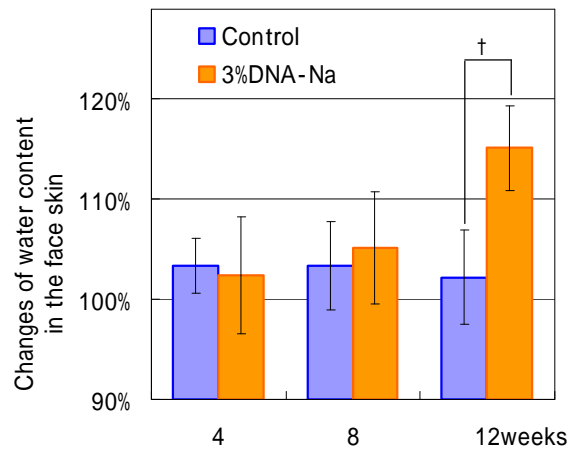


**Fig.15 Effect of rubbing DNA-Na Cream on Skin-Elasticity.**

(n = 10, means±S.E., Student's t-test \* p < 0.05, \*\* < 0.01 )



**Fig.16 Effect of rubbing DNA-Na Cream on TEWL.**



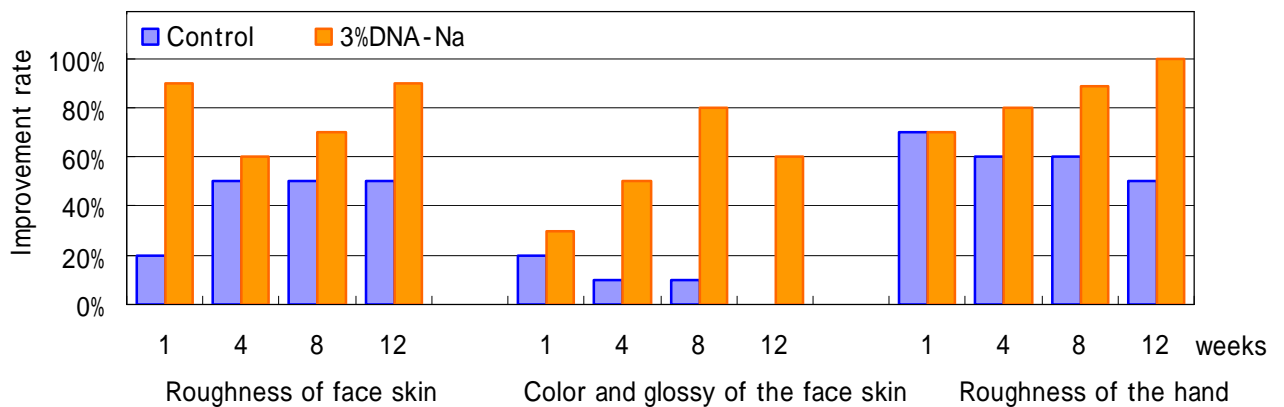
**Fig.17 Changes of water content in the face skin.**

( $n = 10$ , means  $\pm$  S.E., Student's  $t$ -test †  $p < 0.10$ )

( $n = 10$ , means  $\pm$  S.E., Student's  $t$ -test †  $p < 0.10$ )

In addition, according to the answer of questionnaire, more than 90 percent of the subjects who used DNA cream felt improving roughness of the skin (Fig.18). Furthermore, the subjects using the DNA cream had a good impression. The DNA Cream could be expected an improvement effect on the tension of the skin.

( Collaboration with Ochanomizu University, Professor Shigeru Yamamoto and Providence University (Taiwan) )



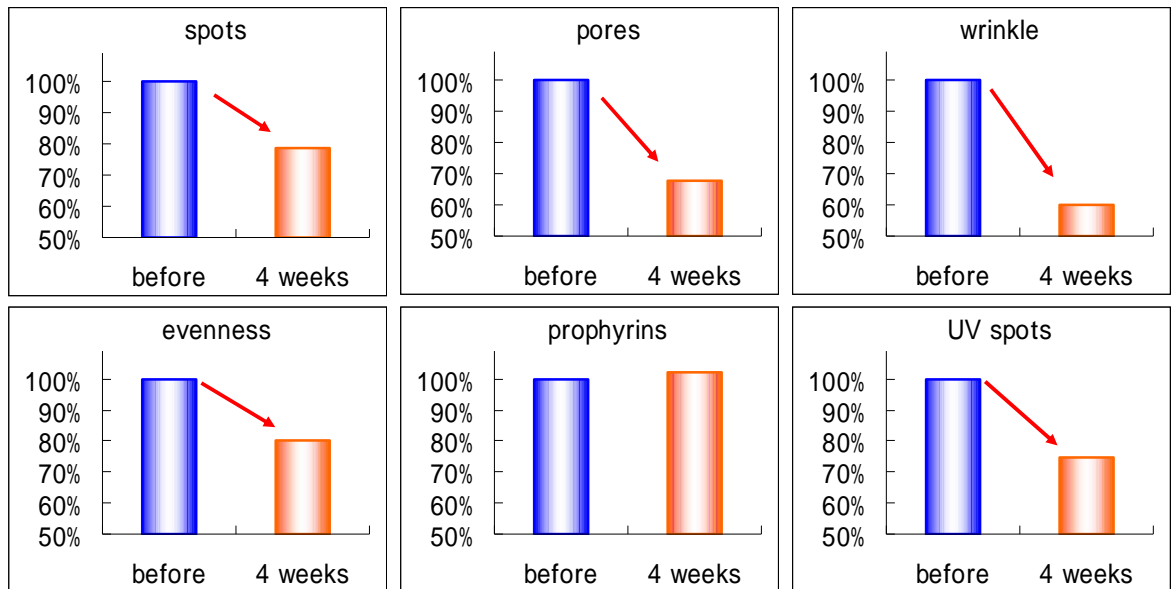
**Fig.18 Result of questionnaire (n = 10).**

**Impression when the subjects used DNA-Na 3% cream**  
 Suppressing the drying of the skin. Cream was immediately absorbed into the skin.



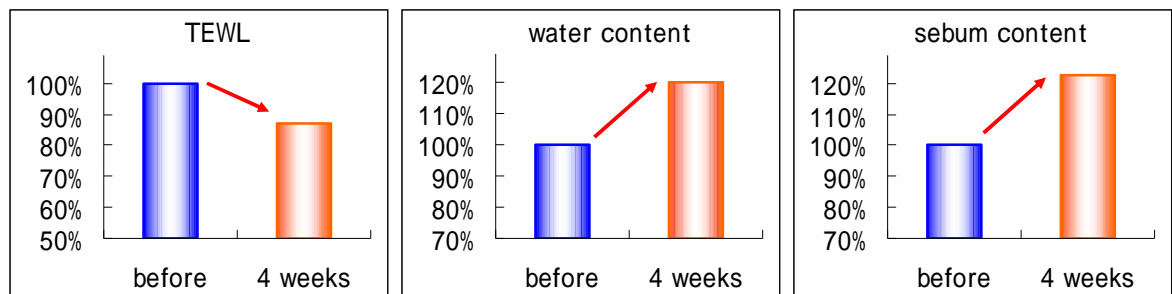
**\*Effect of taking DNA-Na on human skin conditions.**

We investigated the effect of taking DNA-Na on human skin conditions. In this study, the male subjects ( $n = 7$ , Age:40-60 years) took DNA-Na (1 g/day) for 4 weeks and their skin conditions were inspected. After 4 weeks, taking DNA-Na tended to improve the face skin conditions (spots, pores, wrinkle, evenness), and to increase water content in the face skin (Fig.19, 20). In conclusion, these results showed that their skin conditions were improved by taking DNA-Na.  
[Collaboration with Providence University in Taiwan]



**Fig.19 Improvement of skin conditions. ( $n = 7$ , means  $\pm$  S.E. )**

Measurement equipment : VISIA II Complexion Analysis



**Fig.20 Effect of taking DNA-Na on TEWL, water content and sebum content**

( $n = 7$ , means  $\pm$  S.E. )

Measurement equipment

( All of the equipment are manufactured by Courage + Khazaka electronic GmbH, Germany )

TEWL : Tewameter ( TM300 )

Water content : Corneometer ( CM825 )

Sebum content : Sebumeter ( SM815 )

It was shown the images which measured the same part of subject's face with VISIA II. The original image for VISIA II analysis data was shown in Fig.21, and high-contrast image of pores and spots in face was shown in Fig.22. Taking DNA-Na for 4 weeks (1g / day), pores and spots were decreased. These results suggested that taking DNA-Na improved complexion and skin-condition.

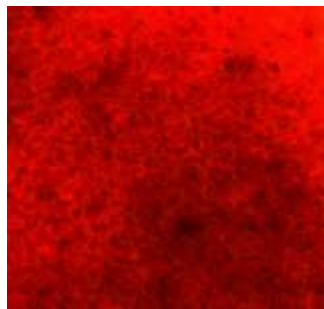


**Before taking**

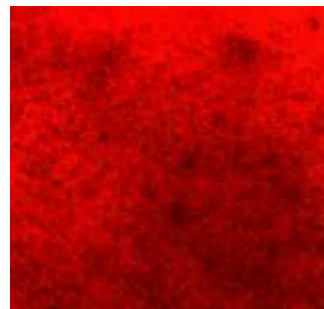


**After 4 weeks**

**Fig.21 Original image of VISIA II data analysis**



**Before taking**

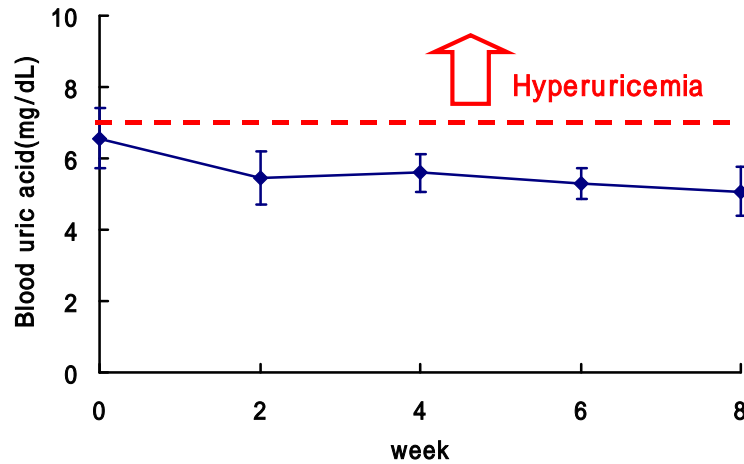


**After 4 weeks**

**Fig.22 High-contrast image of pores and spots (Color revision image )**  
**Software : Zoom Browser EX (Canon)**

**\*The effect of blood uric acid level by taking DNA-Na.**

Gout (*metabolic arthritis*) is a disease due to a congenital disorder of the uric acid metabolism. In this condition monosodium urate crystals are deposited on the articular cartilage of joints and in particular tissues like tendons. Previously it was thought that the uric acid in our body is generated from nucleic acids which have purine base structures. However, recent study revealed that drinking alcohol and obesity have a negative effect on our uric metabolism.



**Fig.23 Change of blood uric acid level (n=7, mean ± SE)**

We researched the effect of blood uric acid level by taking DNA-Na for healthy 9 volunteers (men, n=9, Age: 40y. -60y.). They took DNA-Na (2g) wrapped with cachet everyday for 8 weeks. The result showed that their uric acid level didn't increase. Therefore, taking DNA-Na is not related to rising uric acid levels. It is important that we take care to ingest purine base and have a good eating habit.

**Reference**

(1)T.Takeda *et al.*, *Mechanisms of Aging and development*, **17**,183-194, (1981).

