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Kaneka

Natural N-Acetyl Glucosamine

Beauty within
Global Company established in southern Japan

For 40 years in Europe and over 60 in Japan and USA

Involved in High Technology

More than 800 people dedicated to R&D (over 10% staff)

Social responsibility

*Science FOR the People*

Quality Of Life Division is developing and producing INNOVATIVE and NATURAL ACTIVE ingredients, in southern Japan and in the USA, to answer your needs
Nature offers N-acetylglucosamine and naturally human body uses it everywhere
KANEKA offers the unique manufacturing method of Natural N-Acetylglucosamine through Enzymatic Hydrolysis

Structure of skin

- Epidermis
- Dermis
- Subcutaneous tissue

Hyaluronic acid = Extracellular matrix

Collagen

Glucuronic acid

N-acetylglucosamin
EINECS/ELINCS n°: 233-115-1
Natural N-acetylglucosamine
GRAS status
White crystalline powder
High purity >95%
Sweet taste (half of sucrose)
High water-soluble
(21.8% w/w at Room Temp.)
More Stable than glucosamine
• Against pH change
• Against heating

Efficacy on the improvement of skin condition
Better bioavailability about 3 times of glucosamine
Effective dose 500 mg/day vs 1 500 mg glucosamine/day)
Stability of Kaneka NAG™ vs. glucosamine against heating (Maillard reaction) and pH (5% solution)

Before Heating

100°C, 1 hr

121°C, 15 min
Bioavailability of N-Acetyl Glucosamine

Blood Concentration of Radioactivity after a Single Oral Administration of N-Acetyl-D-[1-14C] Glucosamine to Rats. (Dose: 250 mg/kg)

- **Bioavailability of NAG is about 3 times of glucosamine sulfate**
- **Moreover Glucosamine has to be converted to NAG: the key source of polyglycans**

Skin Conditioning functions of

- **Enhance of production of hyaluronic acid**
  
  

- **Improvement of skin condition**
  
  
Hyaluronic acid in the skin decreases with aging.

It is important to maintain HA content highly in skin in order to keep youth of the skin.

Bioavailability - KanekaNAV vs hyaluronic acid

Intestine

Concentrations of KanekaNAV/HA in the fluid

(Everted sac method (Internal data))
Kaneka NAG increases the content of hyaluronic acid in skin

The content of hyaluronic acid in skin of hairless rats fed with NAG for a month.

<table>
<thead>
<tr>
<th></th>
<th>Epidermis</th>
<th>Dermis</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAG, 0 mg/kg B.W</td>
<td>32 µg/dry tissue</td>
<td>400 µg/dry tissue</td>
</tr>
<tr>
<td>NAG, 20 mg/kg B.W</td>
<td>34 µg/dry tissue</td>
<td>540 µg/dry tissue</td>
</tr>
<tr>
<td>NAG, 200 mg/kg B.W</td>
<td>35 µg/dry tissue</td>
<td>560 µg/dry tissue</td>
</tr>
</tbody>
</table>

(Internal data)
Clinical study of NAG on the improvement of skin condition

<Method>
Subjects: Women with dry/rough skin, 22 people (Average age 25.5 ± 10.7 years old)
Test product: NAG 1 g/day or placebo 1 g/day, 8 weeks (As food supplement)
Measurements: Before, 4 weeks, 8 weeks
Statistical analysis: non-parametric analysis

(Randomized, double-blind study)

<Results>
(1) Skin observation (Diagnostic score)
   NAG showed statistically significant improvement of dry level at Week 4 and Week 8.
(2) Moisture
   Moisture content: Statistical increase of the moisture content was observed in the NAG group at Week 4 week and Week 8.
(3) Analysis by microscopic observation
   NAG showed the improvement of the skin condition by microscopical analysis.

Kikuchi, et al., J. Appl. Cosmetol. 20, 143-152, 2002
Results of the face skin condition

Observation of skin condition

Moisture of skin

Confidential

Mean±SD / Wilcoxon test: *(p<0.05), **(p<0.01)
Microscopic inspection

VISIOSCAN (Courage+Khazaka Electronic GmbH): Analytical system of the condition of the skin with UV.

Calculated from the depth and width of wrinkle

![Graph showing changes in SE sm over weeks for NAG and placebo treatments.](image-url)

Mean±S.D. / Wilcoxon test: *(p<0.05)*

**Before**

8 weeks

NAG 8 weeks

**SE sm**
<Methods>

Subjects: Women with dry skin, 39 people (Average age, 37.7 years old)

Test design: Placebo-controlled, double-blind trial

Test Product: Milk beverage (250 mL)
- 500 mg NAG (NAG group)
- 50 mg Hyaluronic acid (HA group)
- Nothing (Placebo group)

Dosing: Once a day for 8 weeks

Measurement: Moisture content (Instrumental analysis by Corneometer) at Before and 4 weeks and 8 weeks after dosing

<Result>

(1) Ingestion of 500 mg NAG succeeded in increasing skin moisture
(2) Ingestion of 50 mg hyaluronic acid didn’t increase skin moisture
   (50 mg hyaluronic acid is a typical dose in Japanese beauty supplements.)

Shibata K. et al, Aesthetic Dermatology, 18, 91-99 2008
Result of Skin moisture

Region below left eye

Left cheek

Change of moisture content (%)

Improve

Before 4 weeks 8 weeks

500mg Kaneka group

50 mg HA group

Placebo group

*: p<0.05 (vs. before treatment)
#: p<0.05 (vs. placebo)
### Summary of Safety Data of natural Kaneka NAG

<table>
<thead>
<tr>
<th>Study type</th>
<th>Species/Test system</th>
<th>Conclusion</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-clinical study</strong></td>
<td></td>
<td></td>
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<tr>
<td>Acute toxicity</td>
<td>Rat</td>
<td>The median lethal dose (LD$_{50}$) : $&gt; 5,000$ mg/kg.</td>
<td>Report of Biosafety research center, food, drug and pesticides. March, 6, 1991.</td>
</tr>
<tr>
<td></td>
<td>Single oral administration</td>
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<tr>
<td>90-day subchronic toxicity</td>
<td>Rat</td>
<td>no-observed-adverse-effect level (NOAEL) : 2,476mg/kg/day (male) 2,834mg/kg/day (female)</td>
<td>Food Chem Toxicol. 42(4), 687-695, 2004.</td>
</tr>
<tr>
<td></td>
<td>90 days repeated dose study</td>
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<tr>
<td><strong>Clinical studies</strong></td>
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<tr>
<td>8-weeks repeated dose study</td>
<td>Human (aged subject with osteoarthritis (average age: 74.4 years old)) 500, 1000 mg/man Oral administration</td>
<td>No side effect was observed</td>
<td>J New Rem &amp; Clin, 52, 301-312, 2003.</td>
</tr>
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