Nikkei Heath

LABO REPORT

Joint pain relieving effect of Collagen TriPeptide

- Evidence Review
- Market Review
- Product Outline
Evidence Review

Collagen TriPeptide strengthens bones and joints
Clinical effect exceeding that of conventional collagen confirmed

Collagen plays an important role in bones, cartilage, and tendons

Collagen accounts for 30% of the protein that forms the body. As the main ingredient in bone, skin, and tendons etc., it plays a role in maintaining the structure and flexibility of tissues by forming a web-like fibrous structure within which the tissues can function. To consumers, it is known as the pronoun of ingredients for beautiful skin. But in fact collagen is known to play important roles in other tissues besides the skin.

For example, apart from water and calcium content (hydroxyapatite), 80-90% of bone is made up of collagen. Calcium is generally known as the strengthening ingredient of bone, however, comparing bone to a building, calcium is the concrete and collagen is the reinforcing rod. In other words, “in the absence of iron rods, the bone will never be fully strong regardless of how much calcium is ingested” (Yasuo Sakai, Jellice Central Research Center Director). In addition, collagen maintains the cushion-ness of the cartilage areas and the flexibility of the tendon areas of joints.

Because of this, administration of collagen is known to be effective in improving and preventing bone fracture and joint inflammation. Moreover, collagen tripeptide (HACP) *1, has been shown to significantly improve various symptoms such as bone fracture and osteoarthritis compared to general collagen and low-molecular weight collagen (Fig. 1).

Dual job of Collagen TriPeptide

Collagen tripeptide (1) has excellent absorbability from the small intestine, (2) is taken up selectively and effectively by tissues such as bone *2, (3) promotes collagen synthesis, and (4) is itself used as a collagen ingredient. On the other hand, “general collagen and low-molecular weight collagen are broken down by amino acid units and then absorbed. They can only be used as raw materials of collagen. Whereas, collagen tripeptide is not only used as a raw material, but also works as a functional peptide in activating the synthesis of collagen that works in osteoblasts, thus doubly promoting bone regeneration” (Director Sakai).

Collagen tripeptide has a clearly distinct functionality to conventional collagen. Apart from beauty and health, it is expected to also be useful in the anti-aging industry, sports medicine, preventive medicine etc.

Improvement effect on human osteoarthritis symptoms- Published at the 41st Meeting of the Japanese Society of Nutrition and Food Science

Jellice presented data on the symptom improving effect of collagen tripeptide in human osteoarthritis at the Meeting of the Japanese Society of Nutrition and Food Science that took place in May this year. Jellice has conducted a clinical study on 35-70 year-old subjects with comparatively mild osteoarthritis that routinely experience knee joint pain. The subjects were divided into three groups to receive a placebo (dextrin group), collagen tripeptide 2 g (the 2g HACP group) or collagen tripeptide 4 g (the 4g HACP group) for 10 weeks (double-blind study) and were evaluated by JKOM *3 and physician findings. In the evaluation by JKOM, the improvement effect in the 4g HACP group was significant as pain and stiffness in knees were significantly decreased. In the evaluation by physician findings, there was significant decrease in symptoms of hydropathy and friction sound in the 2g HACP and 4g HACP groups, and tenderness in the 4g HACP group only. To date, clinical studies that verified the effect of CP on osteoporosis have been reported, but the treatment period was generally set at about 24 weeks. Whereas, with collagen tripeptide, various osteoarthritis symptoms improve in the short period of 10 weeks. Dr. Isao Maruyama, the Director of Gate Town Hospital (Nerima-ku, Tokyo) who was in charge of the clinical studies said “I was honestly surprised that the effect was seen in such a short time of 10 weeks. Moreover, the improvement in hydropathy and friction sound could also be due to HACP enhancing hyaluronic acid synthesis in joints”.

*1 The amino acid sequence of collagen is “Gly-X-Y-Gly-X-Y-Gly-X-Y-... (X, Y are the random amino acids)”. The basic unit is a tripeptide (Gly-X-Y) consisting of an alignment of three amino acids with Gly (glycine) as the starting point. At Jellice, Collagen TriPeptide is being produced from raw ingredients of collagen by a bioreactor.

*2 Joint research between the Health Bioscience Research Clinical Nutrition Department of Tokushima Graduate University and Jellice. It was shown that, in osteoblasts, expression of the transporters called peptide transporters and intracellular uptake of collagen tripeptide take place promoting the calcification of bone.

*3 Japanese Knee Osteoarthritis Measure. Measure of the function of osteoarthritis patients based on a VAS (visual analog scale) evaluation of knee pain and an evaluation scale consisting of 25 questions on items such as pain and stiffness in knees.

[Fig. 1] Effect on osteoarthritis joint cartilage of rabbit
Rabbits with injured knee joint meniscus were divided into the following four groups: (1) no treatment, (2) porcine collagen tripeptide (80 mg/kg/day), (3) fish collagen tripeptide (same dose), and (4) general collagen peptide (same dose) group and chaps on the surface of knee cartilage were observed comparatively. After 35 days of treatment, the chaps in the collagen tripeptide groups were confirmed to be significantly mild.

(mean±SEM, n=6)

*CP: collagen peptide (conventional product)
*Data: Jellice Central Research Center
Collagen targeted for the “bone and joint” market
Evidence-rich Collagen TriPeptide

Collagen penetrates the age of quality

Collagen has been established in the market as the standard ingredient for beautiful skin. Since the 1970’s it has been used as a moisturizer in cosmetics. However, from around the mid 1990’s, its use was expanded to being added to cooking, and functional foods such as supplements. It is receiving much attention regarding beauty and anti-aging and the awareness of general consumers has expanded.

In 2001, the first case of mad cow’s disease occurred in Japan, and since then, distribution of bovine collagen has been restricted. Because of this, consumers now pay strict attention to the ingredients of foods, cosmetics etc. Ingredient makers and product makers that quickly grasped the psychology of consumers noticed the demand for higher quality, higher functionality, and safe collagen, and therefore proceeded to switch the raw materials.

Thus, presently, porcine and fish collagen are the main stream.

With such boost, the demand for collagen tripeptide is expanding. Due to the problem of mad cow’s disease, the perception on porcine and fish collagen tripeptide has improved comparatively. Furthermore, from 2000 through 2004, results of studies that support the effect of collagen tripeptide on beauty have been reported in succession mainly by Jellice for the purpose of differentiating it from conventional collagen regarding functionality.

As a result, its use in supplements and cosmetics has expanded and is being supported as a highly absorbable collagen.

Attention on the “bone and joint” area also

As such, collagen has entered the “the age where quality is being questioned”. Even in the future, the collagen market is expected to expand with it as the main ingredient in cosmetics. On the other hand, the area that is drawing attention as a new market is that centered on “bone and joints”.

With the arrival of the aging society, the needs of consumers regarding decreased bone density and so on due to dieting, and maintenance of healthy bones and joints is increasing. For example, the total number of osteoarthritis patients with pain in the knees due to abrasion of the cartilage that cushions knee joint and decreased muscle strength is estimated at 24 million.

With calcium at the top of the list, glucosamine, chondroitin sulfate etc. are the leading ingredients that are good for bones and joints, and collagen is already being used in some products. Moreover, the superior effects of collagen tripeptide in bone fracture of athletes and improving symptoms of osteoarthritis (see the enclosed text on the left page) have been verified. Much attention is being drawn to its effects on bones and joints.

Growth in the anti-aging market is Expected

The collagen tripeptide market is expected to expand particularly in the anti-aging area. The main needs of anti-aging are prevention of aging and rejuvenation of the skin, bones and joints. The main reason for this expansion is due to the attention being drawn to collagen tripeptide, which has both of these effects.

The Editorial Department of Nikkei Health has been paying attention to the skin beautifying effect of collagen for some time now and has even featured collagen tripeptide in its magazines. As such, collagen was actually evaluated by monitoring readers and the results verified. Excellent results were obtained as the elasticity of the skin of all the subjects was improved. In addition, there have also been comments such as “the pain I used to feel in the knees and joints every winter has completely disappeared since I started taking collagen tripeptide” (a male in his 40’s). As such, attention is being paid to the double effects of this product on skin and bone regarding its use as an anti-aging ingredient. The response of readers to the articles on collagen tripeptide has also been tremendous. This product is a health ingredient that can be expected to grow significantly in the anti-aging market.

### Past, Present, and Future of Collagen

<table>
<thead>
<tr>
<th>The 1970s</th>
<th>The mid 1990s</th>
<th>2000~</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen</td>
<td>Collagen</td>
<td></td>
<td>Collagen</td>
</tr>
<tr>
<td>Appeared</td>
<td>Awareness</td>
<td>Increase in consumers health consciousness</td>
<td>The age of quality-based selection</td>
</tr>
<tr>
<td>in the</td>
<td>expanded</td>
<td></td>
<td>Switch of raw materials</td>
</tr>
<tr>
<td>market</td>
<td>Use expanded to combination in cooking and supplements</td>
<td></td>
<td>Successive reporting of study results</td>
</tr>
<tr>
<td>Combined</td>
<td>Drinking and</td>
<td></td>
<td>Expansion of consumer’s support for collagen that is safe and backed by scientific evidence</td>
</tr>
<tr>
<td>in</td>
<td>eating of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cosmetics</td>
<td>collagen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(moisturizer)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The anti-aging market

- Beautiful skin
- Muscle
- Bone, joints etc.
Summary of Collagen TriPeptide Product
Excerpted from the Jellice Homepage

Product for general consumer use

Once you pass the age of 20 use “Collagen TriPeptide”

Collagen TriPeptide

Collagen is a protein that is found in high amounts in bone, the skin, tendons, and ligaments. It is an important ingredient that is indispensable to sustaining health and youthfulness. It is certainly recommended for individuals in sports and all individuals concerned about health and beauty. Collagen tripeptide, which is readily absorbed from the stomach and intestine, is optimum as a collagen supplement. It dissolves quickly even in cold liquids, so you can dissolve it in the beverage of your choice before drinking it. It can also be used in cooking.

Available as a convenient stick-type!

Jellice Collagen Petit

This is the petit type of the easy-to-use collagen tripeptide that supports beauty, health, and youthfulness by keeping the skin moist, hair shiny, gums healthy… A health supplement food that can be readily and effectively taken.

Product for professional use

HACP

“HACP” is a product that was obtained in a hydrolytic reaction using bioreactor with collagen derived from Japanese porcine or fish skin, or highly purified gelatin as the ingredient. The N-terminal is glycine and it has an amino acid chain (Glycine-X-Y) unique to collagen. HACP has a higher digestive absorbability compared to the conventional collagen and collagen peptide. It is a collagen peptide that was developed to effectively support the health and beauty of many people.

The name HACP has various meanings:
Highly Advanced Collagen Peptide
Highly Absorbable Collagen Peptide
Highly Active Collagen Peptide and so on.

Properties and effects
Contains ≥15% of the main ingredient, “Collagen TriPeptide”.

- Rapidly absorbed from the digestive system.
- Selectively and effectively absorbed by the skin/bones/cartilage/tendinous tissue.
- Improves the elasticity, moisture, and tone of the skin.
- Keeps bones, cartilage, tendons, ligaments etc. in a healthy state.

HACP specifications

<table>
<thead>
<tr>
<th>Product name</th>
<th>HACP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>0.1 (from pig skin)</td>
</tr>
<tr>
<td>Form</td>
<td>Powder</td>
</tr>
<tr>
<td>Color</td>
<td>White–opalescent</td>
</tr>
<tr>
<td>Taste</td>
<td>Natural</td>
</tr>
<tr>
<td>Spill</td>
<td>None</td>
</tr>
<tr>
<td>pH</td>
<td>5.3–8.5</td>
</tr>
<tr>
<td>Granule size</td>
<td>16 mesh pass</td>
</tr>
<tr>
<td>Heavy metals</td>
<td>≤ 20 ppm</td>
</tr>
<tr>
<td>Arsenic</td>
<td>≤ 1 ppm</td>
</tr>
<tr>
<td>Lead or Zn</td>
<td>≤ 10 ppm</td>
</tr>
<tr>
<td>Blood coagulation</td>
<td>≤ 5%</td>
</tr>
<tr>
<td>Total aerobic content</td>
<td>≤ 1000cfu</td>
</tr>
<tr>
<td>Yeast growth</td>
<td>Negative</td>
</tr>
<tr>
<td>Fungus growth</td>
<td>Negative</td>
</tr>
<tr>
<td>Foreign bodies</td>
<td>None</td>
</tr>
<tr>
<td>Nitrogen content</td>
<td>14–18%</td>
</tr>
</tbody>
</table>

Inquiries:
Jellice Co., Ltd.
4-4-1 Sakaie, Tagajo-shi, Miyagi 985-0833
TEL: 022-361-8821 FAX: 022-367-5470
Telephonic inquiries from 09:00hr to 17:00 hr (weekdays only)