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**(Preliminary Report)**  
**Clinical Effects of Fish Type I Collagen Hydrolysate on Skin Properties**

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**ABSTRACT**

The effects of the daily ingestion of a collagen hydrolysate mixture (including 5 g of fish type I collagen hydrolysate) on the skin properties of 25 Japanese women volunteers who usually tend to have dry and rough skin were examined. The women's skin properties were observed before and after the six weeks of ingestion. The moisture content of their face cheeks generally increased. Moreover, the moisture content of their forearms and the backs of their necks showed a significant increase after the ingestion. The viscoelastic properties (pliability and elasticity), and properties evaluated by a microscopic skin surface analysis (skin smoothness, skin wrinkles and skin roughness values) of their face cheeks significantly improved, whereas the sebum content of the cheeks decreased. Although a placebo effect cannot be discounted, the oral administration of the fish type I collagen hydrolysate mixture induced improvement in 60-100% of the subjects' symptoms. Since this trial was pilot study, the further evaluation in a placebo double-blind controlled studies was needed to assess the long-term efficacy of this treatment approach.

**KEYWORDS:** Collagen hydrolysate; Skin properties; Moisture; Viscoelasticity.

**INTRODUCTION**

A skin condition is generally defined by the surface texture, color, and physiological properties such as hydration, sebum content, and surface acidity [1]. The skin of patients with atopic dermatitis tends to be drier than usual [2]. Even in ordinary persons, the skin properties are important factors in the quality of life. Many skin problems originate from endogenous sources and may have underlying dietary causes [3]. Dietary supplementation of the deficient vitamins, minerals, or essential fatty acids has been reported to improve skin conditions [4]. There is a wide variety of foods available on the market to maintain and

improve the skin condition. However, scientific justifications of these remedies are scarce.

Collagen is a major constituent of the connective tissues of animals, birds, fish and so on. Gelatin, a denatured form of collagen, has been prepared on an industrial scale from these materials [5]. Gelatin has also been used as a folk medicine in Asia to improve blood circulation and arrest bleeding [6]. In Western countries, the first known description of the beneficial effect of gelatin ingestion can be found in 1175. St Hildegard wrote that eating gelatin improved joint condition by reducing pain [7].

Some animal experiments and preclinical human trials have also suggested that the oral ingestion of collagen hydrolysate might have beneficial effects similar to those of gelatin [8]. Recently, Wu et al. demonstrated the safety of orally ingesting a high dose

(1.66 g/kg body weight) of collagen hydrolysate in an animal model [9]. Type II collagen is the major protein in articular cartilage. Supplementation of type II collagen was found to the alleviate symptoms of rheumatoid arthritis [10].

Typically, collagen and gelatin used in foods and pharmaceuticals are derived from bovine or porcine sources. The use of bovine collagen may be problematic because there is a risk of exposure to bovine spongiform encephalitis, whereas collagen from other warm-blooded animals may carry risks of other infectious diseases, e.g. foot and mouth disease in porcine, scrapie in sheep and avian influenza in chicken. Therefore, fish collagen, which is obtained by processing the skin or scales of edible fish, is quite suitable as a health food. In this study, a collagen hydrolysate mixture was prepared by hydrolysis of the fish type I collagen, which is the major structural component of fish skin. We surmised that the supplementation of the fish type I collagen hydrolysate mixture might improve skin properties. Since this study was designed as a pilot study, we evaluate the possibility how a fish collagen peptide mixture improved the skin properties and dermatological symptoms in humans. After this study, we will have a plan of placebo controlled double-blind study to demonstrate this material as a new food supplement that may be taken to obtain an optimal skin condition.

## EXPERIMENTAL

### Test sample

A commercially available fish type I collagen hydrolysate mixture was used (Amino collagen, Meiji Seika, Tokyo, Japan). A test sample (7 g) contained 5 g fish type I collagen hydrolysate, 50 mg vitamin C, and 60mg glucosamine.

### Study design

This study was performed according to the Helsinki Declaration and was approved by the local Ethical Committee. The possible risks of the experiments were explained to all subjects and informed consent was obtained prior to entry in the study. This study was performed using 25 Japanese women volunteers (35.1±5.4 years old) who usually tend to have dry and rough skin. Seven grams of the test sample (5 g of fish type I collagen hydrolysate) were ingested once daily for six weeks, and the subjects' skin conditions were measured before and after this period. Prior to making each measurement, the volunteers were placed in a room with a controlled temperature of 23±1°C and 40±2% relative humidity for at least 60 min.

### Measurement of skin properties

The moisture contents of the stratum corneum of the face cheeks, forearms, and the back of necks were

measured using a Corneometer CM (Courage+Khazaka, Cologne, Germany) [11]. All measurements were performed in triplicate. Data are reported as the mean value ±SD for each site. The casual sebum content was evaluated using a Sebmeter SM810 (Courage+Khazaka), which is based on the principle of photometry of a special quilted plastic strip becoming transparent after fat absorption [11]. The skin surface pH of the face cheeks was determined using a skin pH meter PH900 (Courage+Khazaka). An electrode was placed onto the face cheek with a slight pressure for 3 s [12]. The viscoelastic properties of the skin were evaluated using a Cutometer SEM575 (Courage+Khazaka) with a 2-mm probe [13] at three points on the face cheek. The operating conditions used for the measurements were as follows: the strain time was 2 s, the relaxation time was 2 s, and the pressure was 400 hPa. Pliability was defined as the maximal deformation (mm), and elasticity was defined as the difference between the maximum deformation and restoration to normal.

The skin surface analysis of the face cheeks was carried out using a video camera equipped with an internal ultraviolet-emitting unit: Visioscan (Courage+Khazaka) [14]. All parameters of the skin surface analysis were calculated by the methods of Tronnier et al. [15,16]. Briefly, the indicator of the skin smoothness (SEsm) was calculated from the mean width and depth of the wrinkles. The indicators of the number of the skin wrinkles (SEw) were calculated from the fineness of skin texture in both the vertical and horizontal directions, and the number and width of the wrinkles. The indicator of skin roughness (SEr) was obtained by calculating the percentage of areas darker than the designated points from the entire area on the screen. The indicator of skin scaliness and keratin dryness (SEsc) was calculated as the percentage of the area with skin exfoliation. The overall smoothness of the skin (K) indicates the quality of the histogram of the skin color point. The subjective symptoms for skin improvement were assessed by a questionnaire.

### Statistics

Statistical analyses were conducted using SPSS version 10.02 for Windows with the data expressed as mean ± SE. The Student's paired t-test was used to determine whether there were any differences between before and after six weeks of ingestion. The statistical significance was set at  $P < 0.05$ .

## RESULTS AND DISCUSSION

In the present study, we designed as a pilot study, whether the ingestion of the fish type I collagen hydrolysate mixture affects skin properties.

Table 1. The moisture content in the stratum corneum

	face cheek	forearm	back of the neck
Before	65.75±10.75	46.99±7.17	64.51±10.90
6 weeks	68.84±10.43†	52.21±9.38 *	68.92±9.56 *

Data expressed as mean ± SD. \*: Significant difference at 6 weeks, p<0.05.  
†: Tended to increase by 6 weeks, p<0.1.

The moisture content of the face cheek tended to increase and the moisture contents of the forearm and back of the neck showed a significant increase after ingestion of the hydrolysate (Table 1).

Conversely, the sebum content values significantly decreased during the period of ingestion (Table 2). Generally, moisture is inversely proportional to the sebum, so these data indicate a shift in this balance [17]. The present study was conducted in the winter (from the beginning in November to the end of December in the Northern Hemisphere); therefore, environmental factors accompanying an alteration in the climate might influence the results of our study. Regardless of the cold climate and drier air of the winter environment, these results indicate that the fish collagen peptide mixture was a participating factor in the increase of the moisture content and the decrease in the sebum content.

The skin surface pH was pH 5.9 at both the outset and at the 6-week time point (Table 2). The pH of healthy skin is weakly acidic [18]. Therefore, a good condition was maintained during the study period.

The viscoelastic properties (pliability and elasticity) showed a significant improvement (Table 2). The presence of an adequate amount of water in the stratum corneum is important for the general appearance of soft and smooth skin [1].

The improvement of the viscoelasticity may therefore be related to the moisture content. On the other hand, the skin pliability and elasticity are related to the formation of the epidermis, i.e., dermal fibroblasts [13]. The frame of the fibroblasts primarily consists of the type I collagen fiber.

Oesser et al. determined the bioavailability of collagen using the <sup>14</sup>C labeled collagen hydrolysate after oral administration in mice [19]. The distribution of the labeled amino acid in skin was confirmed and remained at 58% of the peak value 192 h after administration. On the other hand, Iwai et al. identified a small peptide (Pro-Hyp) in the serum and plasma of healthy human volunteers who ingested the porcine skin collagen hydrolysates [20]. An in vitro study using a cell culture system showed that some collagen hydrolysate peptides (Pro-Hyp-Gly, Pro-Hyp) have a chemotactic activity for fibroblasts, peripheral blood neutrophils [21,22] and monocytes [23]. These facts suggest that the oral intake of collagen hydrolysate, which is also possibly generated by degradation of the extracellular matrix, might be associated with wound healing and inflammatory processes.

Some parameters measured by the skin surface analysis also improved (Table 3).

Table 2. pH, lipid and viscoelastic properties of face cheek before and after hydrolysate intake

	sebum content	skin surface pH	pliability	elasticity
Before	25.8±18.8	5.9±0.5	0.662±0.068	0.151±0.051
6 weeks	14.2±10.6 *	5.9±0.5	0.698±0.073 *	0.253±0.137 *

Data expressed as mean ± SD. \*: Significant difference between before and 6week, p<0.05.

Table 3. Skin surface pattern determined by VISIOSCAN on face cheek before and after intake

	SEsm	SEw	SEr	SEsc	K
Before	25.79±3.45	34.96±3.72	0.796±0.648	0.440±0.171	3.20±0.04
6 weeks	24.40±2.86*	33.95±2.34	0.635±0.409*	0.411±0.152	3.19±0.02

Data expressed as mean ± SD. \*: Significant difference between before study and at 6 weeks, p<0.05.

Table 4. Improvement of symptoms after intake

Symptom	Number of subjects with symptom	Degree of improvement		Improvement rate
		Improved	Unchanged Exacerbated	
Face dryness	25	23	2	92.0%
Hardness to apply make-up	22	21	1	95.5%
Rash caused by make-up	5	5	0	100%
Flush	13	10	3	76.9%
Pimple	15	13	2	86.7%
Wrinkle	25	15	9	60.0%
Speckle	25	18	7	72.0%
Undereye dirk circle	20	19	1	95.0%
Dropsy	15	10	4	66.7%
Body itchiness	21	15	6	71.4%
Dryness	25	20	4	80.0%
Flush	11	9	2	81.8%
Exfoliation	19	14	4	73.7%
Vesicle	6	5	0	83.3%
Total	247	197	45	79.8%

Although we did not conduct placebo-controlled studies, the oral administration of the fish type I collagen hydrolysate mixture induced an improvement in 60-100% of the subjects' symptoms (Table 4). These data shows the possibility which a fish collagen peptide mixture improved the skin properties and dermatological symptoms in humans. After this study, we will have a plan of placebo controlled double-blind study to demonstrate the intake of collagen hydrolyzate as a new food supplement that may be taken to obtain an optimal skin condition.

Type II collagen is the major protein in articular cartilage. Supplementation with type II collagen has been used to treat rheumatoid arthritis [5]. On the other hand, the dermis predominantly contains type I collagen (85-90%), which contains lesser amounts of type III collagen (10-15%). Therefore, it has been hypothesized that supplementation with type I collagen, the major structural component of skin, may promote collagen synthesis in the skin. However, it is difficult to grasp how collagen, with an average molecular weight of about 300,000, could be absorbed and transported to the dermis. Further experiments are also necessary to obtain more detailed information the about mechanisms behind the effects seen in this study.

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