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Original Research

Positive effect of fish-derived Bioactive Collagen Peptides on skin health

Abstract

The positive effect of orally administered collagen peptides on skin health has been demonstrated in several clinical trials. In this placebo-controlled study, the impact of specific fish-derived Bioactive Collagen Peptides (BCP) on skin elasticity and wrinkle reduction was investigated.

A total of 76 Asian and Caucasian women (62.2 ± 8.2 years of age) received a daily dosage of 5 g BCP or placebo. Skin elasticity and changes in eye wrinkle volume were evaluated at the beginning of the study, after 4 and 8 weeks of treatment and 4 weeks after the last intake (regression phase). In a subgroup analysis, differences between the results for Asian and Caucasian participants were investigated. The data showed a statistically significant (p<0.05) improvement in skin elasticity after only 4 weeks of BCP supplementation, compared with placebo. This positive effect persisted after 8 weeks of supplementation, and 4 weeks after BCP intake was stopped (p<0.05). Wrinkle volume was also reduced in a statistically significantly (p<0.05) manner after BCP treatment, compared to placebo. A pronounced decrease in eye wrinkle volume could be determined 4 weeks after BCP treatment commenced. After 8 weeks, a wrinkle reduction of 15% was observed and the efficacy of the treatment was confirmed at the end of the regression phase (p<0.05). The subgroup analysis revealed no statistically significant differences. The BCP treatment was effective in both Asian and Caucasian subjects. The results clearly demonstrated the efficacy of orally administered fish-derived BCP on skin health.

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Introduction

With increasing age, a progressive loss of skin elasticity and a reduction in epidermal thickness and extracellular dermal matrix content occurs. Cutaneous ageing results in an increased deepening of facial creases and wrinkles [1]. Facial skin sites, such as the canthi of the eyes in particular, are susceptible to wrinkle formation commonly known as crow's feet.

Over the last decade, the impact of collagen peptides on skin health has been investigated [2–4], and a positive effect on various clinical parameters such as skin dryness, firmness and elasticity and wrinkle formation has been demonstrated. Studies specifically investigating the effects of fish-derived collagen peptides on skin health also suggested a positive effect [5] but clear clinical evidence has so far been lacking [2–4].

The aim of the current study was to evaluate the efficacy of specific bioactive fish-derived collagen peptides on skin elasticity and eye wrinkle formation in a randomized, placebo-controlled clinical trial with healthy female subjects.

Materials and methods

Test products

The Bioactive Collagen Peptides (BCP) were provided by GELITA AG, Eberbach, Germany.

The product is commercially available under the brand name VERISOL® F. It is derived from a complex multistep procedure involving the degradation of fish skin collagen, and has a high safety profile. The placebo product containing maltodextrin is obtained by the enzymatic conversion of starch, and was provided by Cargill, Haubourdin, France.

Study design

The clinical trial was carried out as described by Proksch *et al*. in 2014 [6, 7]. In the current study, the effects of a daily dosage of 5 g of fish BCP on skin elasticity and wrinkle formation after 4 and 8 weeks of daily intake was evaluated.

The study period was extended by a 4-week wash-out phase without further product administration to investigate the ongoing efficacy of VERISOL® F treatment.

The RCT was approved by the International Ethics Committee of Freiburg, Germany, and adhered to current GCP regulations.

All test subjects received detailed information on the study and gave signed informed consent.

Subjects

A total of 76 healthy Asian and Caucasian women aged between 50 and 70 years old were enrolled in the clinical trial, and randomized to treatment with a daily dose of 5 g of fish BCP or placebo. At baseline, there were no significant differences between the treatment and the placebo groups with regard to age, eye wrinkle volume and skin elasticity (**Table 1**).

Subjects with skin ailments or other dermatological disorders, cancer or cardiac disorders, and those with food allergies to test product ingredients were excluded from the study. The use of corticoids, antihistamines and systemic medications were not permitted 4 weeks before the study commenced. Prior to the beginning of oral treatment, there was a preconditioning period of at least 7 days.

In this period, and throughout the entire duration of the study, subjects were instructed to refrain from using any leave-on products on the arms and the area around the eyes. Moreover, the use of make-up, skin cleansing tissues, wipes for make-up removal and cleansing lotion on the test sites was barred. Exposure of the test sites to intensive UV light was also prohibited (sun or solarium). The subjects were not allowed to visit saunas or swimming pools, and were to avoid intensive sporting activities on the day prior to the study visits.

They were furthermore advised not to change

their living and dietary habits or to consume any additional nutritional supplements or vitamin preparations 4 weeks prior to the start of the study and during the study.

Test areas

The test site for wrinkle volume detection was the area around the left eye (lateral canthus). The test area for skin elasticity measurement was the inner aspect of 1 volar forearm.

On every measurement day, the subjects had exposed their uncovered test areas to indoor climate conditions (50% ± 5% relative humidity and 21.5°C ± 1°C) for at least 30 min.

Measurement of eye wrinkle volume

The influence of BCP on eye wrinkle volume was measured at the outer corner of the eye (lateral canthus) using the optical 3-dimensional in vivo measuring instrument PRIMOS® Compact (GF Messtechnik GmbH).

Three measurements were conducted per test site at baseline and after 4 and 8 weeks of treatment. The final measurement was performed 4 weeks after the end of treatment. The eye wrinkle volumes were calculated and expressed in mm^3 on the basis of the images obtained.

Measurement of skin elasticity

Skin elasticity was assessed using the Cutometer® MPA 580 (Courage + Khazaka, Cologne, Germany) as described by Segger *et al*. [8, 9].

Briefly, the extension of the skin in response to a suction vacuum induced above the skin test area with a 350 mbar vacuum, consisting of a 5-sec exposure and non-exposure period, with 1 cycle per measurement, was measured. To analyze skin elasticity, the R5 value (Ur/Ue, immediate recovery/elastic deformation) was recorded. This parameter has proven to be most suitable in detecting age-related skin alterations [10, 11]. The measurement of each test area was conducted 3 times.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences software (SPSS for Windows, version 23).

The baseline values for all parameters were compared between the study groups to show the accordance between demographic and anamnestic parameters. Testing of ordinal baseline values was performed using Student's *t* test for unpaired samples.

Alterations in skin elasticity were assessed by an analysis of variance (ANOVA) over the study time frame of 8 weeks in comparison with placebo treatment. Changes in eye wrinkle volume were assessed by a repeated measurement analysis as a function of supplementation. The extension of 4 weeks without further BCP administration was also assessed in comparison with placebo *via* ANOVA. Alterations in all measurement parameters within the treatment groups and during the study period were assessed by repeated measurement analysis. In a subgroup analysis of the participants treated with BCP, the influence of a genetic difference was tested by a repeated measurement analysis with race as a covariate. All tests within the descriptive analysis were performed on a two-sided basis. The levels of significance were set at $\alpha=0.05$.

Results

Subjects and drop-outs

All 76 subjects enrolled in the study fulfilled the inclusion criteria and were randomized into groups. One participant in the treatment group was excluded because of lack of compliance.

No adverse events or unintended side effects were reported by the participants in either study group. The subjects were on average 62.2 ± 8.2 years old. There were no statistically significant differences between the treatment group and the placebo group at baseline (**Table 1**).

Skin elasticity

There was no significant difference in skin elasticity levels at the beginning of the study between the BCP group and the subjects treated with placebo (**Table 1**). The 8-week administration of BCP led to a statistically significant increase in skin elasticity (p=0.003, **Table 2**). This effect was long-lasting as shown by the increased skin elasticity seen 4 weeks after the last BCP intake (regression).

In contrast, skin elasticity decreased continuously and was statistically significant in the placebo group (p=0.031).

A comparison between the BCP and placebo groups revealed a statistically significant effect for all time points with BCP supplementation associated with superior efficacy (**Fig. 1**). On average, skin elasticity increased by 7.6% in the BCP group compared with placebo.

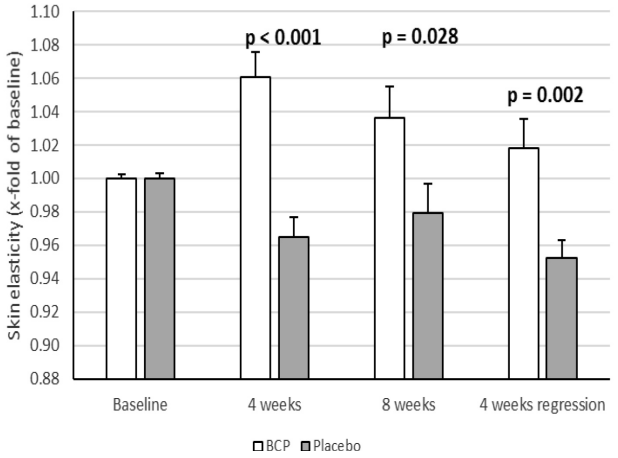

Figure 1 Changes in skin elasticity over the study duration of 12 weeks. A statistically significant increase in skin elasticity was noted after BCP treatment in comparison with the placebo control; data represented as the mean + SD

Eye wrinkle volume

At the beginning of the study, there was no statistically significant difference in eye wrinkle volume (p=0.899) between the groups (**Table 1**). During the course of treatment, eye wrinkle volume decreased in a statistically significant manner in the subjects receiving BCP (p<0.001, **Table 3**).

Although the calculation also revealed a statistically significant change in the placebo group, the effect was unclear with a positive impact after 4 weeks of treatment but with negative results after 8 weeks, compared to baseline. A comparison between the treated and untreated groups already showed a statistically significant reduction in eye wrinkle volume after BCP supplementation for 4 weeks,

	Total (n = 75)	BCP (n = 37)	Placebo (n = 38)	*p* value
Age (y)	62.2 ± 8.2	62.2 ± 8.3	62.1 ± 8.3	0.952
Eye wrinkle volume (mm^3)	1.61 ± 0.8	1.62 ± 0.8	1.64 ± 0.8	0.899
Elasticity (Ur/Ue)	0.57 ± 0.1	0.59 ± 0.1	0.56 ± 0.1	0.344

Table 1 Baseline data for the study population of the clinical trial. Ur/Ue = immediate recovery/elastic deformation; data represented as the mean ± SD

	Group	Baseline	4 weeks	8 weeks	Regression	*p* value*
Elasticity (Ur/Ue)	BCP	1.00 ± 0.01	1.06 ± 0.09	1.04 ± 0.11	1.02 ± 0.10	**0.003**
	Placebo	1.00 ± 0.02	0.97 ± 0.07	0.98 ± 0.11	0.95 ± 0.07	**0.031**

*intra-group comparison

Table 2 Overview of the mean skin elasticity (in relation to baseline) over the course of the study

	Group	Baseline	4 weeks	8 weeks	Regression	*p* value*
Eye Wrinkle Volume	BCP	1.0 ± 0.09	0.89 ± 0.18	0.86 ± 0.15	0.87 ± 0.16	**<0.001**
	Placebo	1.0 ± 0.10	0.97 ± 0.18	1.01 ± 0.16	0.97 ± 0.17	**<0.001**

* intra-group comparison

Table 3 Overview of mean eye wrinkle volume (in relation to baseline) over the course of the study

	Ethnicity	Baseline	4 weeks	8 weeks	Regression	*p* value
Elasticity (Ur/Ue)	Asian	1.0 ± 0.01	1.06 ± 0.07	1.07 ± 0.07	1.02 ± 0.08	>0.05
	Caucasian	1.0 ± 0.02	1.06 ± 0.10	1.02 ± 0.12	1.04 ± 0.11	
Eye Wrinkle Volume	Asian	1.0 ± 0.03	0.87 ± 0.15	0.83 ± 0.21	0.87 ± 0.18	>0.05
	Caucasian	1.0 ± 0.07	0.89 ± 0.17	0.87 ± 0.14	0.86 ± 0.15	

Table 4 Comparison of the efficacy of BCP with respect to different ethnicities (in relation to baseline) over the course of the study

compared to placebo (**Fig. 2**).

This positive effect was even more pronounced after an 8-week BCP intake (15%), and persisted during the 4-week regression phase. Compared to the untreated placebo group, the reduction in eye wrinkle volume was still 10% better after BCP treatment ceased. In a subgroup analysis, the efficacy of specific orally administered collagen peptides on Asian and Caucasian participants was evaluated.

Although regional and ethnic differences in the biophysical parameters of the skin exist [12], the positive effect of the BCP investigated was not significantly different in Asian and Caucasian subjects (**Table 4**).

Skin elasticity increased by up to 8% in Asian women, and by up to 6% in Caucasian women during the course of the study after BCP administration. Eye wrinkle volume furthermore decreased for both ethnicities by approximately 14% after BCP treatment.

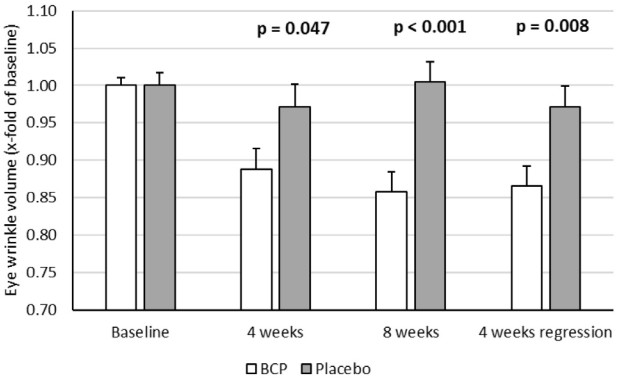

Figure 2 Eye wrinkle volume changes over the study duration of 12 weeks. A statistically significant decrease in wrinkle volume was observed after BCP treatment in comparison with the placebo control; data represented as the mean + SD

Conclusions

In this randomized, placebo-controlled trial, the oral administration of specific BCP of fish origin had a positive impact on the skin appearance of elderly women. During the treatment, a statistically significant improvement in skin elasticity and a pronounced wrinkle reduction could be observed. This decrease in eye wrinkle volume was also statistically significant compared with measured effects in the placebo group. In contrast to other investigations addressing the effects of fish-derived collagen products on skin [2, 3, 13], the data obtained from the current study demonstrated a clear clinical improvement after BCP intake.

As it is known that collagen peptides have different biological activities [14, 15], it is suggested that the specific efficacy of the tested BCP

lies in the special production process.

As a consequence, it has to be stated that the effects measured here are valid only for these specific BCP, and cannot readily be applied to other collagen products.

The current study is the first trial to compare the beneficial effects of orally administered BCP on the skin appearance of women of different ethnicities. Regional and ethnic differences in skin properties are well known [16, 17]; for example, it has been suggested that Caucasian skin is more prone to wrinkle formation whereas Asian skin tends to spotty hyperpigmentation during ageing. Nevertheless, the beneficial effects of BCP supplementation on skin appearance was clearly demonstrated in both Caucasian and Asian women. Interestingly, the improvement in skin elasticity and wrinkle reduction was very similar, independent of the participants' ethnicity. This indicates that these BCP seem to influence fundamental physiological pathways with a direct impact on fibroblast metabolism and the production of skin extracellular matrix.

In summary, it can be stated that the current study clearly demonstrated the positive effect of oral supplementation with these specific fish-derived BCP on skin health, as indicated by improved skin elasticity and pronounced wrinkle reduction. The study results also indicate a long-lasting effect of BCP intake, independent of subject ethnicity.

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