Prospective single-center clinical study of GelcoPEP, a new multifunctional hydrolyzed collagen type I

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ABSTRACT

Introduction: *The present prospective single-center clinical study investigated the safety and efficacy of GelcoPEP, a new multifunctional hydrolyzed collagen type I.*

Methods and materials: *Safety and clinical efficacy of the new multifunctional hydrolyzed collagen type I were determined. A total of eight parameters were investigated at the beginning (D0) and after 30 ± 2, 60 ± 4 and 90 ± 4 days by a questionnaire. Firmness and elasticity were assessed by cutometry, and wrinkles, by Reveal Imager.*

Results: *The results indicated that administration of 10 g/day of GelcoPEP for 90 days improved important essential symptoms in individuals, considering skin and joint. No adverse effects were detected during the observation period.*

Conclusion: *The obtained data support the view that GelcoPEP, a new multifunctional hydrolyzed collagen type I, is safe and efficacious and may be ingested worldwide as a nutritional supplement by healthy people.*

Keywords: *Collagen, GelcoPEP, joint, skin, type I.*

Introduction

GelcoPEP, a new multifunctional hydrolyzed collagen type I, is a dietary supplement that may be beneficial for the improvement of skin and cartilage tissues. Its use in the supplementation has increasingly gained support in the medical and nutraceutical community, and among consumers[1].

It has been verified, in preclinical studies, that orally administered hydrolyzed collagen type I is thoroughly absorbed by the intestine and circulated in the blood stream in peptides form[2], accumulating in skin for up to 96h[3]. It was also revealed that collagen bioactive peptides have the ability of exerting remarkable antioxidant effects in different biological systems[4].

Hydrolyzed collagen type I is one of the main structural element that confers resistance to skin and cartilage tissues. It is known that, in addition to the support function, it participates in cell differentiation, adhesion, migration and proliferation [5,6].

The composition and complex structural organization between collagen and proteoglycans ensures the inherent tissue properties, such as strength, elasticity and compressibility, necessary to dissipate and cushion the forces, as well as reduce friction, without much energy expenditure. Therefore, the integrity of the components is essential to ensure normal tissues function[6].

Additionally, hydrolyzed collagen type I has been reported to have beneficial therapeutically functions in skin. Studies have shown that collagen peptides stimulate the growth of mouse skin fibroblasts[7] and are chemotactic attracted for human skin fibroblasts[8]. The effects of hydrolyzed collagen ingestion on fibroblast and collagen densities were also investigated and the results showed that density and diameter of fibroblasts and density of collagen fibrils were significantly larger in the collagen group than in the control group[9].

Although, from the preclinical perspective, there is convincing evidence that collagen ingestion may improve skin conditions, and, based on the findings that collagen is absorbed in its molecular form, accumulating in skin, it might be reasonable to investigate a new multifunctional hydrolyzed collagen type I as a nutritional supplement. Thus, the aim of this single-center investigation is to extend these earlier findings with GelcoPEP.

Methods and materials

Participants' selection

In accordance with the ethical standards of the Ethics Committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 and 2008, this prospective single-center clinical observational study was approved by its responsible committee and managed in its Department of Clinical Medicine.

According to study schedule, the consent form was discussed, signed, and a complete physical examination was executed at screening. Activity level, diet history, medication/supplement use and medical history were recorded. A total of 68 subjects were recruited using the inclusion and exclusion criteria outlined in Table 1.

Table 1. Inclusion and non-inclusion/exclusion criteria

Inclusion criteria
Age: 40 to 65 years old
Gender: female
Healthy participants (assessed by the dermatologist)
Phototypes: I to IV (according to Fitzpatrick classification);
Intact skin in the study region (face, eyes, cheeks, wrinkles);
Having been clarified and signed the Informed Consent Term (ICT);
Participants that want to participate in the study without financial profit. They will only be reimbursed for expenses such as transportation and food;
Participants that accept not using products from the same category on the test region during the research;
Participants that have not taken part of similar studies at least 2 months before the research;
Occasional user of cosmetic products similar to the investigational product;
Participants that declare not to expose to pregnancy risk during the research.
Non-inclusion/exclusion criteria
Allergy to the test product category;
Pregnant or lactating women;
Immunodeficiency;
Active atopic dermatitis;
Participants that had their kidney, heart or liver transplanted;
Use of the following the drugs: immunosuppressive, antihistamines, non-hormonal anti-inflammatories and steroids;
Any condition not mentioned above that, in the opinion of the investigator, might compromise the assessment of the study;
History of noncompliance or unwillingness to adhere to study protocol.

Test product application

The participants used the products during 90 ± 4 days in their residence and in accordance with the instructions supplied. The participants were divided in two study groups: one group used the control product (placebo group) and the other used the collagen (treated group). The participants' distribution among the groups was randomized and performed in accordance with Table 2 below. The study was simple-blind, which means that the participants were unaware of the product they received (collagen or placebo) during the whole study.

Table 2. Participants randomization in the clinical study.

Participant #	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
Treatment	P	T	T	P	P	P	T	P	T	T	P	T	P	P	P	T	T
Participant #	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**
Treatment	T	P	T	P	T	P	P	P	T	T	P	T	T	T	P	T	P
Participant #	**35**	**36**	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**45**	**46**	**47**	**48**	**49**	**50**	**51**
Treatment	T	P	P	T	T	P	P	P	T	P	T	T	P	T	P	P	P
Participant #	**52**	**53**	**54**	**55**	**56**	**57**	**58**	**59**	**60**	**61**	**62**	**63**	**64**	**65**	**66**	**67**	**68**
Treatment	T	T	T	P	P	P	T	P	P	P	T	T	P	T	T	T	P

P = placebo (no active); T = treated (with hydrolyzed collagen).

Medical assessment of the clinical signs and discomfort sensations

The initial medical assessment was performed in the participants' moment of inclusion to verify the absence of clinical signs incompatible with the inclusion criteria. After 30 ± 2, 60 ± 4, 90 ± 4 days of product use, the participants returned to the Institution for the final medical assessment of the clinical signs presented and questioning of the discomfort sensations felt.

The data of the medical assessment were registered in the investigation brochure. The dermatologist was available during the whole study in case of adverse reactions.

The results were evaluated as follows:

- Discomfort sensations: the participants were questioned about the discomfort sensations felt during the clinical exam. The reported discomfort

sensations were described (example: blazing, stinging, pruritus, cooling, burning, etc.) and were classified according to: intensity (slight, moderate or intense); localization and duration.

- Clinical signs: if applicable, the signs were evaluated as erythema, soap effect, edema, papules, coloring (hyperchromia), pustules, bulla, nodules, desquamation/dryness, crust or vesicle and were classified according to: intensity (slight, moderate or intense); appearance and number. The attributability of the reactions to the test product was investigated.

Anti-wrinkle subjective efficacy assessment

In order to determine the clinical efficacy of this product, the dermatologist assessed the following parameters at the beginning (D0) and after 30 ± 2, 60 ± 4 and 90 ± 4 days of product use:

Table 3. Parameters for anti-wrinkle subjective efficacy assessment

Eye wrinkles	Determined in accordance with the atlas[10].
Nasolabial folds	
Forehead wrinkles	Determined in accordance with the photographic scale for the assessment of human facial wrinkles[11].
Elasticity	Determined as: 1 = very hydrated/firm/elastic; 2 = hydrated/firm/elastic; 3 = little hydrated/firm/elastic; 4 = very little hydrated/firm/elastic.
Firmness	
Hydration	

Cosmetic appreciability assessment (participants' opinion)

The participants were instructed to answer a questionnaire containing the questions and possible answers described below after 30 ± 2, 60 ± 4 and 90 ± 4 days of investigational product use.

Table 4. Cosmetic appreciability assessment questionnaire.

After ingesting the product, did you think that:
1. Was the product effective to reduce wrinkles?
2. Did the product improve skin hydration?
3. Did the product improve skin elasticity?
4. Did you notice improvement considering skin general aspect?
5. Did the product reduce joint pain?
6. Did the product improve nail hardness?
7. Did the product reduce “hunger” sensation?
8. Did the product improve the general aspect of hair (volume and strength)?

At the first visit, selected subjects, properly informed by the Consent Term approved by the Scientific Committee of the Institute, were assigned to receive 10 g of GelcoPEP (Gelco International, Inc., Pedreira, SP) daily. At the second and the final visit, subjects were required to come to the clinical division for clinical assessment. A subject treatment diary was completed by each patient throughout the study period to determine product compliance, side effects, and supplementation use.

Firmness and elasticity assessment by cutometry

The participants were instructed to interrupt the use of products (creams, oils, lotions and similar) on the face 24 hours before the beginning of the study.

The participants came to the Institution for the initial medical assessment and verification of the accomplishment of the inclusion and non-inclusion criteria. Then, they were submitted to an acclimatization period of 30 minutes at 20 ± 2°C and 50 ± 5% relative humidity before the beginning of the measurements.

After this time, the baseline cutometry measurements (D0) were performed to assess skin firmness and elasticity using the Cutometer® MPA 580 probe coupled to the equipment *Multi Probe Adapter*, MPA 580, (CK eletronics, Germany). The measurements were performed on the face (malar region).

Then, the participants used the product at home according to the how to use instructions supplied by the Sponsor during 90 ± 4 days. On D30, D60 and

D90 (respectively after 30, 60 and 90 days of product use), the participants returned to the Institution for another cutometry reading after performed after a 30 min acclimatization period at 20 ± 2°C and 50 ± 5% relative humidity.

Firmness and elasticity[12]:

- Firmness assessment:

R0 (Uf): total skin deformation after suction, encompassing elastic and plastic deformation. The lower the R0 value, bigger the firmness (less extensible skin and therefore firmer).

- Elasticity assessment:

R5 (Ur/Ue): corresponds to the ratio of the "immediate retraction" to the "immediate distention". This parameter refers to the elastic part of the skin, disregarding viscous deformation. The higher the value, bigger the skin elasticity.

R7 (Ur/Uf): corresponds to the biologic elasticity. The higher the R7 value, bigger the skin elasticity.

The following softwares were applied to analyze the data:

- Software for measurement acquisition - *MPA for Windows® NT/XP.*
- Software for data analysis - *Microsoft® Office Excel 2007*
- Software for statistical analysis - *SPSS Statistics 22.0.*

Instrumental efficacy assessment (wrinkles)

The equipment Reveal Imager® (Canfield) was used to capture images from the face of the participants to quantitatively determine wrinkle improvement. Therefore, the following capture positions were used: front, right side and left side.

The images were captured at the following experimental times: D0 (baseline) and D90 (after 90 days of product use).

Results and discussion

Dermatological acceptability

No participant referred discomfort sensations and no clinical signs were detected after 90 ± 4 days of product use.

Subjective dermatological efficacy (wrinkle)

The subjective dermatological efficacy results are summarized in figures below:

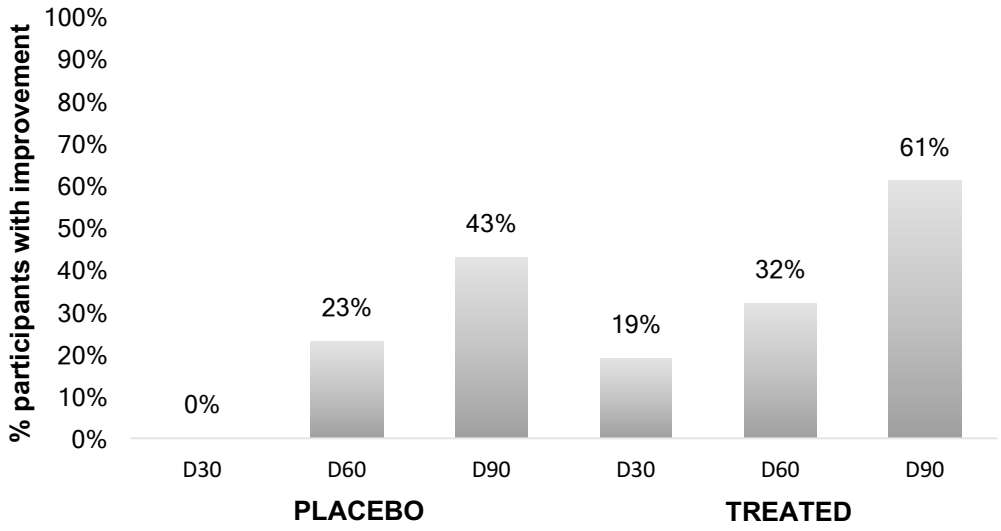

Figure 1. Eye wrinkles efficacy results.

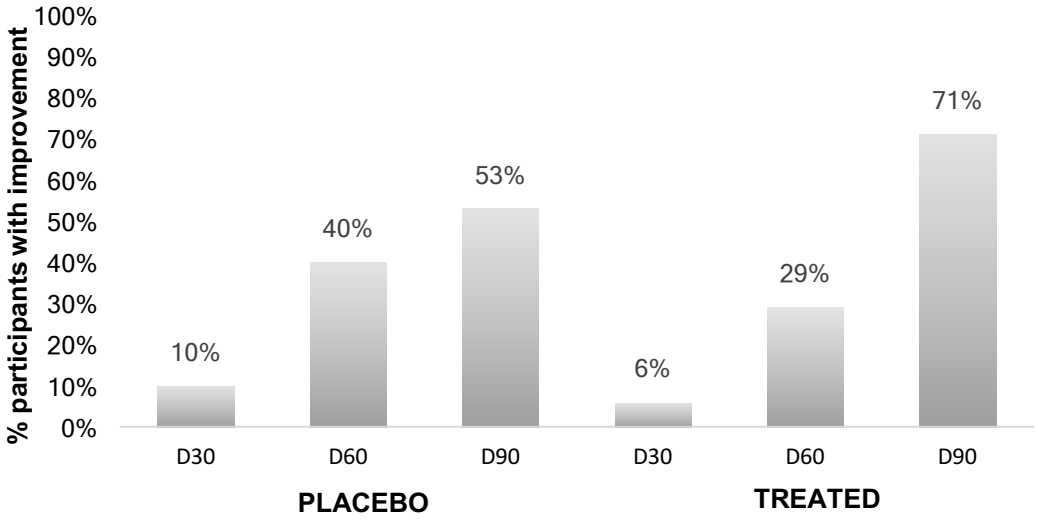

Figure 2. Forehead wrinkles efficacy results.

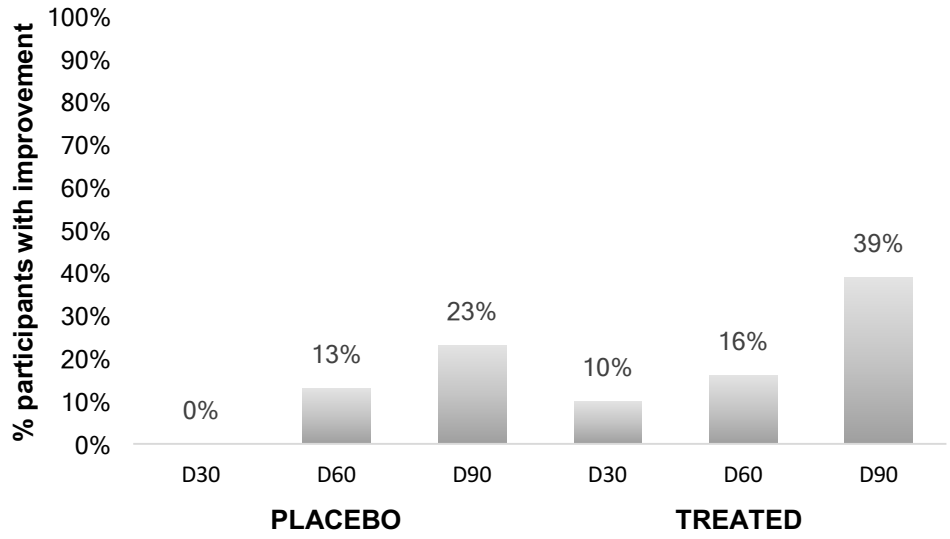

Figure 3. Elasticity efficacy results.

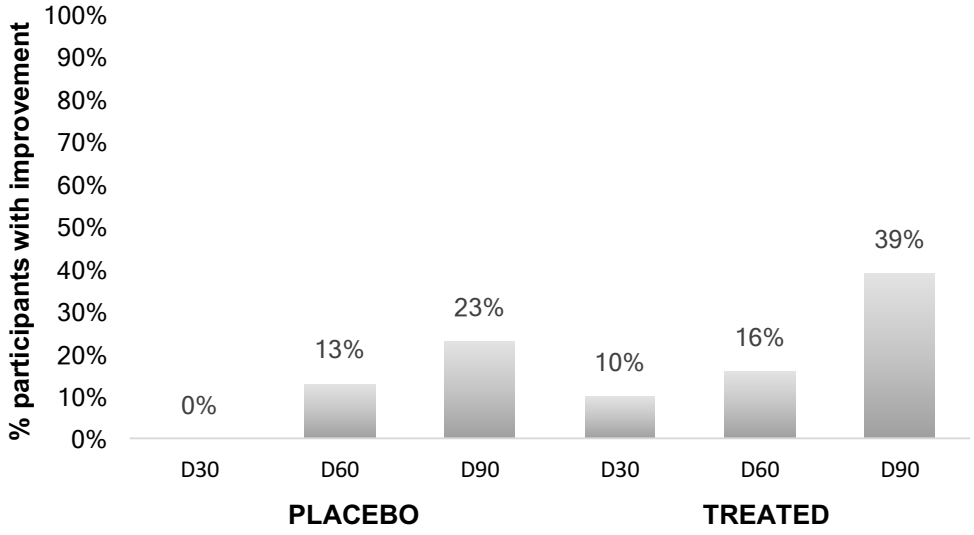

Figure 4. Firmness efficacy results.

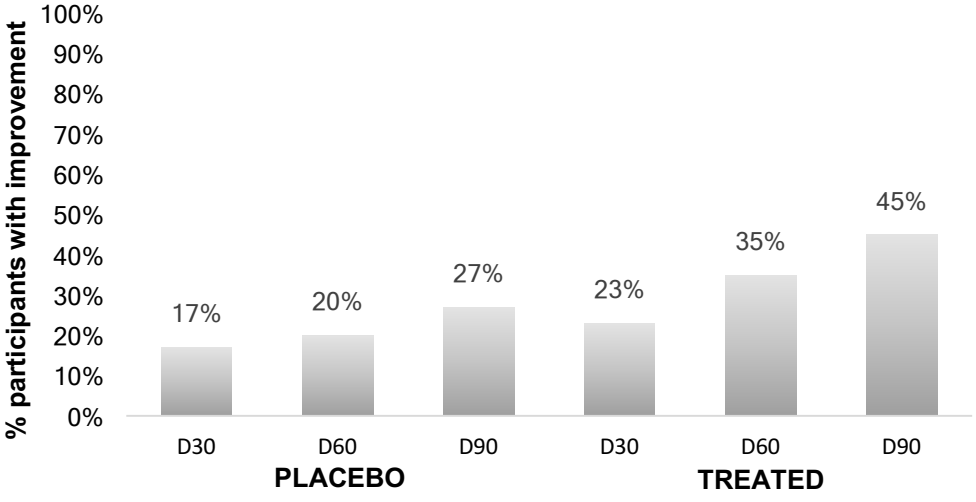

Figure 5. Hydration efficacy results.

Among the parameters assessed by the dermatologist, those, where the investigational product presented a better performance compared to placebo, were eye wrinkles (on D30, D60 and D90); forehead wrinkles (on D90); elasticity (on D30, D60 and D90); firmness (on D30, D60 and D90); and hydration (on D30, D60 and D90).

Cosmetic appreciability assessment (participants' opinion)

In the cosmetic appreciability assessment (participants' opinion), the investigational product presented a better performance compared to the placebo for the following parameters:

- Efficacy in wrinkle reduction on D30, D60 and D90;
- Efficacy in articulation pain reduction on D30, D60 and D90;
- Efficacy in nail hardness improvement on D30, D60 e D90;
- Hunger sensation reduction on D30, D60 and D90.

Firmness and elasticity assessment by cutometry

The firmness (R0) and elasticity data (R5 and7) obtained with the Cutometer® probe were statistically analyzed by variance analysis (ANOVA) comparing the baseline condition with the other experimental times per treatment. Besides, the cutometry data were also compared between treatments for each experimental time by variance analysis (ANOVA) with Dunnett post-test. These analysis were performed with the software SPSS Statistics 22.0.

According to the obtained results, there was no statistically significant difference in the firmness (R0) and elasticity values (R5 and R7), neither between experimental times, nor between treatments for each time.

However, the investigational product presented a tendency to promote improvement in skin firmness (R0) of 11% after 60 days of use (D60) and of 10% after 90 days of use (D90). The placebo did not present any tendency to improve firmness. Table 5 and Figure 6 contain the means of the firmness and elasticity values obtained per treatment per experimental time.

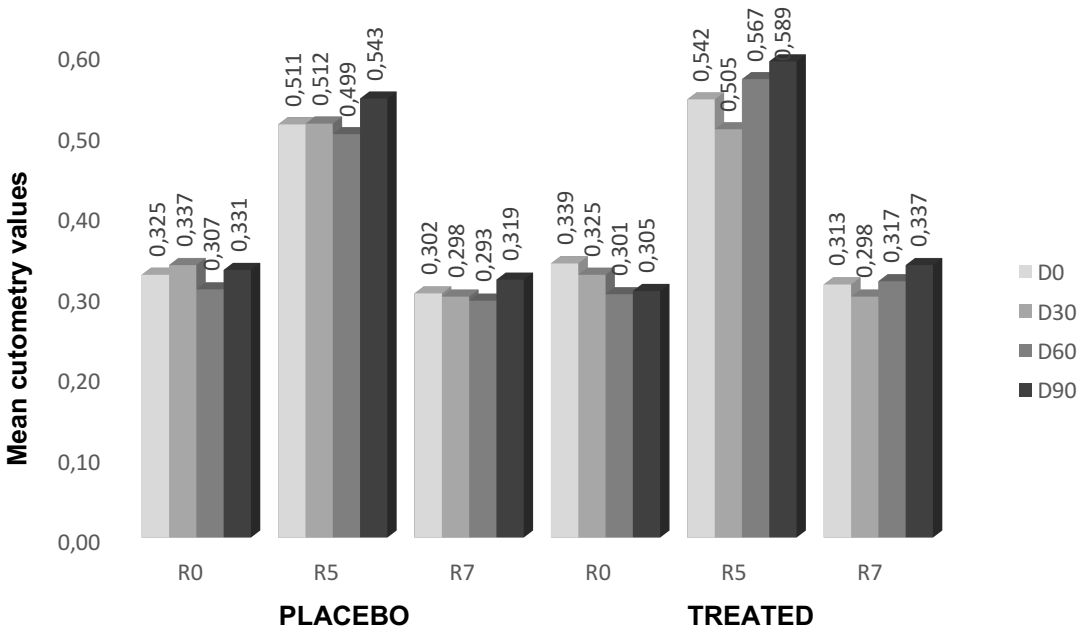

Figure 6. Mean cutometry values per time and treatment.

Instrumental efficacy assessment

The mean wrinkle data obtained (mean of participants) per treatment (treated and placebo) per angle of capture (right, left and front) per time (D0 and D90) for the quantitative analysis with the equipment Reveal® Imager (Canfield) are summarized in Figure 7 below.

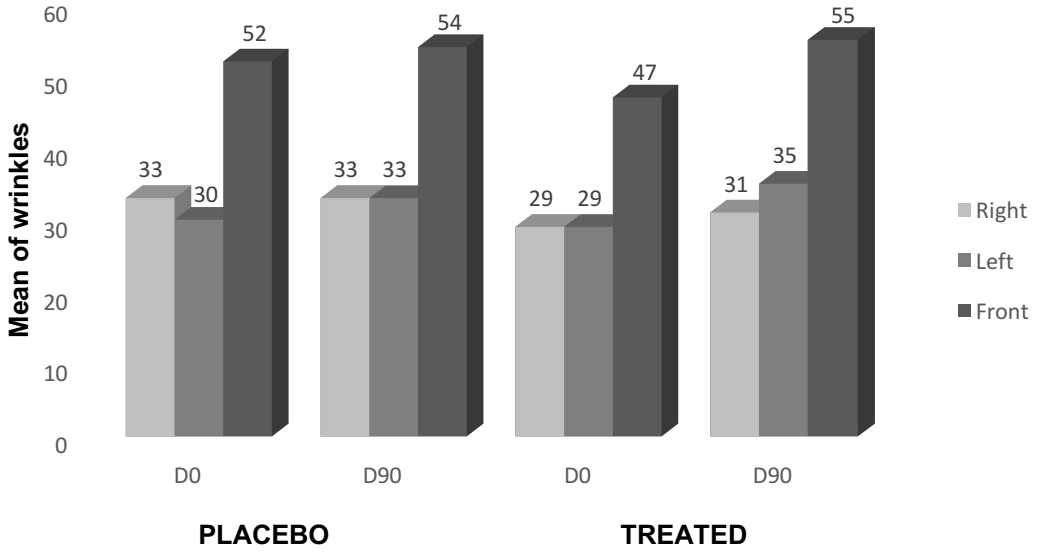

Figure 7. Mean of data obtained with the equipment Reveal Imager (Canfied).

According to the obtained results, there was no statistically significant difference in the wrinkle values by Reveal (right, left and front) between the experimental times, nor between treatments for each time ($p > 0.05$);

However, the investigational product (hydrolyzed collagen type I) presented a higher tendency to improve wrinkles when compared with the placebo. After 90 days of use, the collagen product promoted an improvement of the wrinkles of 7% for the right side; of 20% for the left side; and of 16% for the frontal angle.

Conclusion

The purpose of this study was to define whether administration of 10 g of GelcoPEP daily would improve skin and cartilage tissues in healthy volunteers. The design of the observational study was appropriate to reveal that hydrolyzed collagen type I as a nutritional supplement ingested over 90 days was safe and efficacious in improving skin and cartilage tissues. The results of the study provide data supporting the view that GelcoPEP may be administered to healthy patients as a potential. Further research will elucidate additional benefits from this multifunctional source.

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