Original Article

Treating cutaneous photoaging in women with an oral supplement based on marine protein, concentrated acerola, grape seed extract and tomato extract, for 360 days

Resultado de 360 dias de uso de suplemento oral à base de proteína marinha, acerola concentrada, extrato de semente de uva e extrato de tomate em mulheres portadoras de envelhecimento cutâneo

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ABSTRACT

Introduction: *Cutaneous aging affects (or will affect) all people at some point in their life, and its treatment represents a clinical challenge.*

Objective: *To evaluate the cutaneous effects of an oral supplement based on marine protein, concentrated acerola and extracts of grape seed and tomato in women with cutaneous aging.*

Methods: *Forty-five volunteers used 2 daily tablets of the supplement for 360 consecutive days. Clinical evaluations (carried out by both the investigator physicians and by the volunteers), ultrasonographic and photographic examinations were carried out every 30 days.*

Results: *Thirty-three volunteers (73.3%) completed the study. Clinically significant improvement was verified by the investigator physicians and the volunteers after 30 days of using the oral supplement ($p < 0.05$). The results were maintained after 330 days ($p \geq 0.05$). The ultrasonographic analysis demonstrated increases in the dermal density of the photoexposed (132.3%; $p < 0.001$) and photoprotected areas (51.9%; p " 0.001). Through medical analysis, statistically significant improvements were found in the following criteria: wrinkles, fine lines, solar melanoses, other hyperchromias, erythema, hydration, radiance , sebum, smoothness and overall appearance of the skin. Through the volunteers' self-evaluation, improvements in the wrinkles' pattern, fine lines, solar melanoses, other hyperchromias, erythema, hydration, radiance, sebum, smoothness and overall appearance of the skin were reported.*

Conclusion: *The long-term use (360 days) of an oral supplement based on marine protein, concentrated acerola and extracts of grape seed and tomato was proven to be a good adjuvant systemic approach for treating cutaneous aging.*

Keywords: *skin aging; dietary supplements; vitamin C; grape seed extract*

RESUMO

Introdução: *O envelhecimento cutâneo atinge ou atingirá todas as pessoas, e seu tratamento representa um desafio clínico.*

Objetivo: *Avaliar efeitos cutâneos do uso de um suplemento oral a base de proteína marinha, acerola concentrada e extratos de semente de uva e tomate por 360 dias em portadoras de fotoenvelhecimento cutâneo.*

Métodos: *Quarenta e cinco voluntárias usaram dois comprimidos diários do referido suplemento por 360 dias consecutivos. Avaliações clínicas (por parte dos investigadores e das voluntárias), ultrassonográficas e fotográficas foram realizadas a cada 30 dias.*

Resultados: *Trinta e três voluntárias (73,3%) concluíram o estudo. A melhora clínica foi evidenciada pelos investigadores e voluntárias após 30 dias de uso do suplemento oral, o que resultou em ganho estatístico ao longo do tempo ($p<0,05$). Após 330 dias, constatou-se a tendência à estabilização dos resultados ($p\geq0,05$). Pela análise ultrassonográfica, percebeu-se aumento na densidade dérmica das áreas fotoexpostas (132,3%; $p<0,001$) e das fotoprotegidas (51,9%; p"0,001). Encontraram-se melhorias estatisticamente significativas nos quesitos rugas, linhas finas, melanoses solares, outras hipercromias, eritema, hidratação, viço, oleosidade, suavidade ao toque e aparência geral da pele através da análise médica; segundo a autoavaliação das voluntárias, obteve-se melhoria no padrão das rugas, linhas finas, melanoses solares, outras hipercromias, eritema, hidratação, viço, oleosidade, suavidade ao toque e aparência geral da pele.*

Conclusão: *O uso de suplementação oral à base de proteína marinha, acerola concentrada e extratos de semente de uva e tomate por longo prazo (360 dias) mostra-se boa abordagem sistêmica adjuvante para o fotoenvelhecimento cutâneo.*

Palavras-chave: *envelhecimento da pele; suplementos dietéticos; vitamina C; extrato de semente de uva.*

INTRODUCTION

The skin aging process in humans is complex and driven by multiple causes including environmental and genetic factors.[1-4] Exposure to UV radiation, which is the main environmental factor, results in morphological alterations, mainly in the dermis. In areas protected from the sun, the deepest morphologic alterations occur in the epidermis.3 Photoprotected skin presents thin and delicate wrinkles (intrinsic aging). In contrast, skin that is frequently exposed to the sun is characterized by deep and well-marked wrinkles, a rough appearance and mottled pigmentation (photoaged skin). [1-4]

Intrinsic skin aging is determined by genetic and hormonal factors. The physiological hormone decrease resulting from the aging process seems to be one of the most important factors for the aging of the skin and other organs.[4, 5]

UV radiation damages human skin – affecting its color, tone and resistance – and causes premature aging.[3,6,7] Photoaged skin presents prominent alterations in the connective tissue's cellular component and extracellular matrix, with an accumulation of disorganized elastin in the deep dermis and a severe loss of collagen. 6 This process is a result of the activation of matrix metalloproteinases, which are responsible for the changes in the extracellular matrix of the connective tissue's collagen. [6] UV rays also attack keratinocytes and fibroblasts. 3 These alterations cause a number of molecular changes that lead to the destruction of extracellular collagen and halt collagen synthesis.[3]

According to a theory developed by Denham Harman in 1956,[8,9] free radicals also have an important role in the aging process. Oxidative stress is caused by an imbalance between the formation of oxidants and the activity of antioxidant defense systems; free radicals are formed by the metabolism of oxygen. 9 Free radicals damage important skin structures such as cell membranes, DNA segments, collagen and elastic fibers, causing the clinically recognizable signs of skin aging. [8] The degradation of oxidized products is carried out by the proteasome, a multicatalytic protease whose activity seems to decrease over an individual's lifetime, causing the incomplete degradation of oxidized proteins, an increase in protein aggregates and the acceleration of cellular dysfunction.[8-10]

Oxidative reactions occur physiologically in the human body, but are nevertheless counterbalanced by the action of endogenous antioxidants in an individual's diet. When there is an imbalance in the oxidation-reduction state in favor of pro-oxidative reactions, cell damage takes place. This process is called oxidative stress.[11]

Antioxidant defense mechanisms prevent or limit the effects of oxidative stress, with the participation of endogenous enzymes such as the superoxide dismutase, catalase, glutathione peroxidase and other substances present in the diet, such as carotenoids, phenolic compounds, tocopherols and ascorbic acid.[11, 12]

Carotenoids are naturally present in human skin; lycopene, a substance belonging into this group, is found in fruits and vegetables – especially in reddish ones such as tomatoes. [10, 12] When exposed to excessive UVB radiation, the skin protects itself forming erythema; nonetheless, this defense mechanism causes oxidative stress, interfering with the regulation of the genetic expression and damaging the DNA. [12] Oral supplementation of lycopene – which has great antioxidant potential – seems able to provide protection against the erythema caused by UV radiation, with a subsequent reduction in oxidative stress.[12]

Flavonoids, found in grapes, are polyphenolic compounds.[13, 14] In 1936, Rusznyák and Szent-György [13] showed that the flavonoids contained in citrus fruits decreased capillary permeability and fragility in humans due to their antioxidant action.[13]

Ascorbic acid (vitamin C) is essential for the synthesis of collagen and participates in the regeneration system of tocopherols (vitamin E), maintaining the plasmatic antioxidant potential.11 Vitamin E is found in serum and in LDL particles, protecting lipids from oxidation. Studies have shown its ability to reduce oxidative stress' biomarkers.[11, 14] An important source of ascorbic acid is acerola extract. The Biomarine Complex is rich in proteins and polysaccharides, and when present in oral supplements has been shown to improve the skin's structure.[15-17]

In this manner, both clinical research on the use of oral supplements and the encouragement of their use are a growing practice in modern dermatology. This study evaluated, through subjective and objective assessments, the efficacy, safety and tolerability of an oral supplement based on marine protein, concentrated acerola and grape seed and tomato extracts, used for 360 days by 45 volunteers affected by photoaging.

METHODS

A monocentric, phase IV, prospective, non-comparative, open clinical study was designed and approved by the Human Research Ethics Committee. It consisted of the use of Imedeen® Time Perfection (102.5 mg of Biomarine Complex® – composed of marine proteins and polysaccharides –14.8 mg of Lycophence® GS – composed of lycopene and grape seed extract, and 30 mg of acerola extract (Ferrosan Laboratories S/A, Copenhagen, Denmark)), taken in the form of two daily tablets, ingested together, combined with the use of SPF 15 Episol® sunscreen (Mantecorp Indústria Química e Farmacêutica Ltda., Rio de Janeiro, Brazil) on the face twice a day. The volunteers were instructed to use only the study sunscreen for 30 days prior to taking the oral supplement. The treatment lasted 360 days, and volunteers attended the research center monthly.

The clinical trial included 45 female volunteers, who signed a term of free and informed consent. Study participants had a general dermatologic evaluation in order to verify that they met the inclusion criteria (aged 35-60; habitual users of SPF 15 facial sunscreen for at least 30 days prior to the beginning of treatment; Fitzpatrick phototype I to III; absence of known history of allergic reaction to test products and seafood; absence of systemic and/or skin conditions that might interfere in the evaluation of skin aging). The exclusion criteria included the presence of other dermatoses, systemic conditions or use of medications and/or products that interfered with the clinical evalua-

tion of the study treatment; use of cosmetics in the area of the body being analyzed; use of oral supplement for photoaging; smoking; use of illicit drugs; intense sun exposure during the course of the study or in the 60 days prior to the study; pregnancy or breastfeeding. Participants were excluded from the study if they failed to use any of the products in their full daily dose or less than 50% of the daily dose for more than seven consecutive days or 15 non-consecutive days.

The volunteers underwent monthly skin ultrasound with 22 MHz probe (DUB®-USB, SkinScanner, Luneburg, Germany) on the face (left zygomatic region) and in the superomedial face of the left arm (4 cm below the lower limit of the axillary hair implantation line), and answered questionnaires regarding the evaluator physician's and volunteers' perceptions of the treatment's clinical efficacy and safety. The criteria evaluated by the subjective questionnaires were: wrinkles, fine lines, solar melanoses, other hyperchromias, erythema, hydration, radiance, sebum, smoothness, and overall appearance of the skin. Possible standardized answers were: total improvement, marked improvement, moderate improvement, slight improvement, unchanged, discreet worsening, moderate worsening, marked worsening and total worsening. The volunteers were also photographed (Canon® PowerShot G10, Oita, Japan) in their clinical evaluation.

Since the variables did not present a standard normal distribution (Gauss curve) according to the Anderson-Darling test, non-parametric statistical tests were used. A significance level of $p < 0.05$, with 95% confidence intervals, was used. We used the test for equality of two proportions to analyze the questionnaire responses, and Wilcoxon and Friedman tests to evaluate ultrasound results.

RESULTS

Of the 45 volunteers, 33 (73.3%) completed the study. Seven dropped out for personal reasons, and five were removed due to the study's exclusion criteria (one pregnancy, one lumbar spine surgery, one dengue fever case and two cases of antibiotic use). There were no exclusions linked to the use of the study product.

Several changes considered statistically significant in all aspects ($p < 0.05$) were found in the efficacy questionnaire answered by the evaluator physician (clinical assessment). According to the questionnaire's answers, in 360 days of use of the product, 6.1% of the volunteers showed improvement of wrinkles. Of these, 9.1% in fine lines, 12.1% in melanoses, 12.1% in other hyperchromias, 9.1% in erythema, 84.9% in hydration, 63.7% in radiance , 12.1% in sebum, 84.8% in smoothness , and 45.4% in the overall appearance of the skin. A significant improvement of the parameters was demonstrated after 30 days of product use, and the results were maintained after 330 days (Table 1, Graph 1 and Figure 1).

Patient reported results were similar to those of the clinical evaluation. The results after 330 days suggested improvement: 27.3% in wrinkles, 30.3% in fine lines, 21.2% in melanoses, 21.2% in other hyperchromias, 12.1% in erythema, 45.5 % in hydration, 42.4% in radiance; 18.2% in sebum , 42.5% in smoothness , and 48.6% in overall appearance (Table 2, Graph 2 and Figure 1).

In the ultrasound examination – the results of which were easily observed – it was concluded that there was a progressive increase in the values of dermal density in almost all visits, with improvements in the collagen and elastic fibers' pattern. Compared to the beginning of the study, at Day 360 was a statistically significant increase in dermal density in both the face (132.3%, $p < 0.001$) and the left arm (51.9%, $p < 0.001$) – areas exposed to the sun and photoprotected (Tables 3 and 4, Graph 3, and Figure 2).

DISCUSSION

Skin aging is caused by solar radiation and endogenous factors.4 With the advancement of age, there is an increase in free radicals and a decrease in the skin's defense mechanisms, which accelerates skin aging. [3] Nevertheless, antioxidant products can attenuate that process.18 The availability of treatments that can stabilize or reverse the changes caused by aging is relevant to improving the population's quality of life and health. In this effort, nutraceuticals have arisen as a feasible option for systemically treating photoaging.

Based on both the physician's and the volunteers' clinical assessments carried out in this study, oral supplementation containing marine protein and acerola, grape seed and tomato extracts was demonstrated to improve Fine lines, melanoses, other hyperchromias, erythema, radiance, sebum, smoothness, and the overall appearance of photoaged skin. A significant improvement in these characteristics was observed early in the treatment and was maintained throughout the study.

In 1998 Kieffer and colleagues 15 randomized two groups of volunteers to receive either placebo or the oral supplied used in this article for 12 months. Similarly to the findings of the present study, the authors observed improvement in a number of features of the skin (fine lines, global aging, hyperpigmentation and telangiectasia) through photographic assessment. Likewise, there was improvement in the self-assessment analysis and in skin density, which was measured by ultrasound (an increase in papillary and reticular dermis thickness was observed); there were no significant side effects.[15]

The successful use of products enriched with Biomarine Complex in their formulation to treat the signs of skin aging was also described by Heule in 1992. He knew that improving photoaged skin required more than topical cosmetic action, so he conducted a pilot study with the Biomarine Complex. Objective and subjective improvements of the symptoms of aging skin were observed, including the attenuation of fine lines and skin pigmentation. The 90-day study included ultrasound examinations of the periocular region, which showed increased thickness of the epidermis and dermis (8.3% and 83.3%, respectively).[19]

In 2011, Costa and colleagues 16 showed that the use of the product from the present study for 120 days was effective in improving aged skin features; statistically significant values were

Table 1: P-values of clinical parameters, based on the analysis of medical efficacy during 360 days of nutriconcentrate use

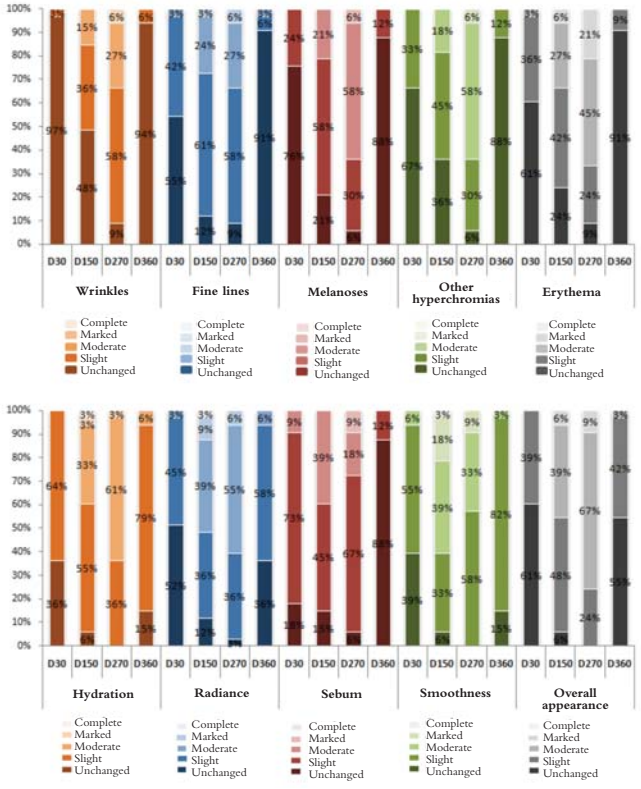
Statistical significance of the physician-evaluated parameters			D30	D150	D270
Wrinkles	Unchanged	D150	<0,001		
		D270	<0,001	<0,001	
		D360	-	<0,001	<0,001
	Slight	D150	0,001		
		D270	<0,001	0,084	
		D360	-	0,003	<0,001
	Moderate	D150	0,02		
		D270	0,001	-	
		D360	-	0,02	0,001
	Marked	D330	0,039	-	-
		D270	-	-	
		D360	-	-	-
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Fine lines	Unchanged	D150	<0,001		
		D270	<0,001	-	
		D360	0,001	<0,001	<0,001
	Slight	D150	-		
		D270	-	-	
		D360	0,001	<0,001	<0,001
	Moderate	D150	0,012		
		D270	0,006	-	
		D360	-	0,012	0,006
	Marked	D150	-		
		D270	-	-	
		D360	-	-	-
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Melanoses	Unchanged	D150	<0,001		
		D270	<0,001	0,073	
		D360	-	<0,001	<0,001
	Slight	D150	0,006		
		D270	-	-	
		D360	-	<0,001	0,071
	Moderate	D150	0,005		
		D270	<0,001	0,003	
		D360	-	0,005	<0,001
	Marked	D150	-		
		D270	-	-	
		D360	-	-	-
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Other hyperchromias	Marked	D150	0,014		
		D270	<0,001	0,003	
		D360	0,04	<0,001	<0,001
	Slight	D150	-		
		D270	-	-	
		D360	0,04	0,003	0,071
	Moderate	D150	0,010		
		D270	<0,001	0,001	
		D360	-	0,010	<0,001
	Marked	D150	-		
		D270	-	-	
		D360	-	-	-
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Erythema	Unchanged	D150	0,003		
		D270	<0,001	0,099	
		D360	0,004	<0,001	<0,001
	Slight	D150	-		
		D270	-	-	
		D360	0,008	0,002	0,099
	Moderate	D150	0,006		
		D270	<0,001	-	
		D360	-	0,001	<0,001
	Marked	D150	-		
		D270	0,005	-	
		D360	-	-	0,005
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Hydration	Unchanged	D150	0,003		
		D270	<0,001	-	
		D360	0,049	-	0,02
	Slight	D150	-		
		D270	0,027	-	
		D360	-	0,037	<0,001
	Moderate	D150	<0,001		
		D270	<0,001	0,026	
		D360	-	0,005	<0,001
	Marked	D150	-		
		D270	-	-	
		D360	-	-	-
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Radiance	Unchanged	D150	0,001		
		D270	<0,001	-	
		D360	-	0,022	0,001
	Slight	D150	-		
		D270	-	-	
		D360	-	0,084	0,084
	Moderate	D120	<0,001		
		D270	<0,001	-	
		D360	-	0,001	<0,001
	Marked	D150	0,076		
		D270	-	-	
		D360	-	0,076	-

Continuação...

Table 1: P-values of clinical parameters, based on the analysis of medical efficacy during 360 days of nutriconcentrate use

Statistical significance of the physician-evaluated parameters			D30	D150	D270
Sebum	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
	Unchanged	D150	-		
		D270	-	-	
		D360	<0,001	<0,001	<0,001
	Slight	D150	0,024		
		D270	-	0,083	
		D360	<0,001	0,003	<0,001
	Moderate	D150	0,004		
		D270	-	0,057	
		D360	0,076	<0,001	0,01
	Marked	D150	-		
		D270	0,076	0,076	
		D360	-	-	0,076
Smoothness	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
	Unchanged	D150	0,001		
		D270	<0,001	-	
		D360	0,027	-	0,02
	Slight	D150	0,083		
		D270	-	0,048	
		D360	0,017	<0,001	0,032

Statistical significance of the physician-evaluated parameters			D30	D150	D270
	Moderate	D150	0,001		
		D270	0,005	-	
		D360	-	<0,001	0,001
	Marked	D150	0,01		
		D270	0,076	0,282	
		D360	-	0,01	0,076
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Overall appearance	Moderate	D150	<0,001		
		D270	<0,001	-	
		D360	-	<0,001	<0,001
	Slight	D150	-		
		D270	-	0,041	
		D360	-	-	-
	Moderate	D150	<0,001		
		D270	<0,001	0,026	
		D360	-	<0,001	<0,001
	Marked	D150	-		
		D270	0,076	-	
		D360	-	-	0,076
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-



Graph 1: Development of clinical parameters according to the medical efficacy evaluation during the 360 days of nutraceutical use

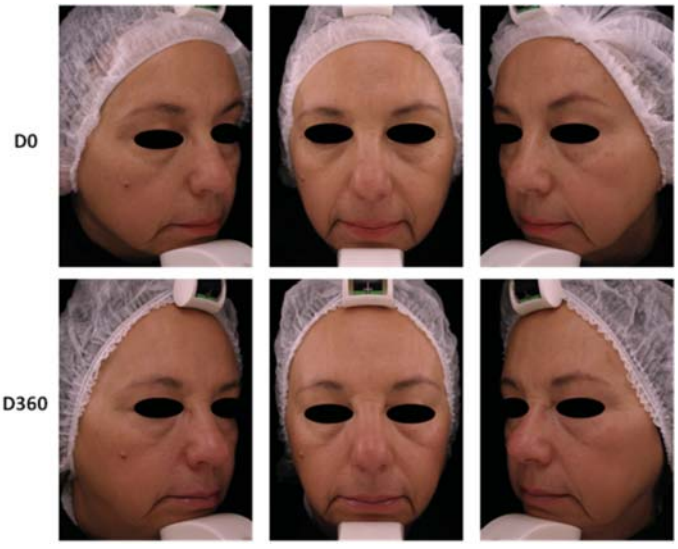


Figure 1- Picture of volunteer who used the nutraceutical for 360 days: improvement in the overall appearance of the face can be observed, due to the improvement in periocular Fine lines, nasolabial folds' depth, and radiance

Table 2: P-values of clinical parameters, based on the volunteers' analysis of efficacy during 360 days of nutriconcentrate use

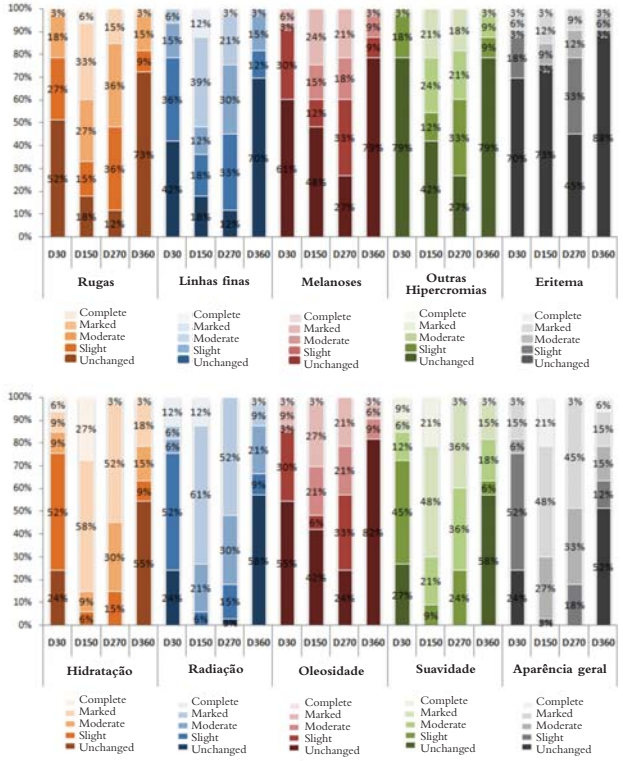
Statistical significance of the physician-evaluated parameters			D30	D150	D270
Wrinkles	Unchanged	D150	0,004		
		D270	0,001	-	
		D360	0,076	<0,001	<0,001
	Slight	D150	-		
		D270	-	0,049	
		D360	0,056	0,099	0,008
	Moderate	D150	-		
		D270	0,097	-	
		D360	-	-	0,049
	Marked	D150	0,001		
		D270	0,087	0,085	
		D360	-	0,001	0,087
	Complete	D150	-		
		D270	-		
		D360	-	-	-
Fine lines	Unchanged	D150	0,032		
		D270	0,006	-	
		D360	0,026	<0,001	<0,001
	Slight	D150	0,097		
		D270	-	-	
		D360	0,022	-	0,040
	Moderate	D150	-		
		D270	-	0,071	
		D360	-	-	-
	Marked	D150	0,001		
		D270	0,073	-	
		D360	-	<0,001	0,024
	Complete	D150	0,039		
		D270	-	-	
		D360	-	0,039	-
Melanoses	Unchanged	D150	-		
		D270	0,006	0,076	
		D360	-	0,011	<0,001
	Slight	D150	0,071		
		D270	-	0,040	
		D360	0,030	-	0,016
	Moderate	D150	0,087		
		D270	0,046	-	
		D360	-	-	-
	Marked	D150	0,039		
		D270	0,073	-	
		D360	-	0,012	0,024
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Other hyperchromias	Moderate	D150	0,003		
		D270	<0,001	-	
		D360	-	0,003	<0,001
	Slight	D150	-		
		D270	-	-	
		D360	-	-	0,016
	Moderate	D150	0,012		
		D270	0,024	-	
		D360	-	0,099	-
	Marked	D150	0,005		
		D270	0,010	-	
		D360	-	0,024	0,046
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Erythema	Unchanged	D150	-		
		D270	0,046	0,024	
		D360	0,071	-	<0,001
	Slight	D150	0,046		
		D270	-	0,001	
		D360	0,046	-	0,001
	Moderada	D150	-		
		D270	-	-	
		D360	-	-	-
	Marked	D150	-		
		D270	-	-	
		D360	-	-	-
	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
Hydration	Unchanged	D150	0,003		
		D270	0,003	-	
		D360	0,012	<0,001	<0,001
	Slight	D150	<0,001		
		D270	0,002	-	
		D360	<0,001	-	-
	Moderate	D150	-		
		D270	0,030	0,030	
		D360	-	-	-
	Marked	D150	<0,001		
		D270	<0,001	-	
		D360	-	0,001	0,004
	Complete	D150	0,021		
		D270	-	0,006	
		D360	-	0,006	-
Radiance	Unchanged	D150	0,003		
		D270	0,012	-	
		D360	0,006	<0,001	<0,001
	Slight	D150	<0,001		
		D270	0,002	-	
		D360	<0,001	-	-
	Moderate	D150	0,073		
		D270	0,011	-	
		D360	0,073	-	-
	Marked	D150	<0,001		
		D270	<0,001	-	
		D360	-	<0,001	<0,001

Continued ...

Table 2: P-values of clinical parameters, based on the volunteers' analysis of efficacy during 360 days of nutriconcentrate use

Statistical significance of the physician-evaluated parameters			D30	D150	D270
Sebum	Complete	D150	-		
		D270	0,039	0,039	
		D360	-	-	-
	Unchanged	D150	-		
		D270	0,012	-	
		D360	0,017	0,001	<0,001
	Slight	D150	0,011		
		D270	-	-	
		D360	0,001	-	<0,001
	Moderate	D150	0,024		
		D270	0,024	-	
		D360	-	-	-
	Marked	D150	0,056		
		D270	-	-	
		D360	-	0,021	0,073
Smoothness	Complete	D150	-		
		D270	-	-	
		D360	-	-	-
	Unchanged	D150	0,001		
		D270	0,001	-	
		D360	0,013	<0,001	<0,001
	Slight	D150	0,001		
		D270	0,071	0,099	
		D360	<0,001	-	0,039

Statistical significance of the physician-evaluated parameters			D30	D150	D270
Overall appearance	Moderate	D150	-		
		D270	0,022	-	
		D360	-	-	0,097
	Marked	D150	<0,001		
		D270	0,003	-	
		D360	-	-	0,049
	Complete	D150	-		
		D270	-	0,024	
		D360	-	0,024	-
	Unchanged	D150	0,003		
		D270	0,003	-	
		D360	0,022	<0,001	<0,001
	Slight	D150	<0,001		
		D270	0,004	0,046	
		D360	0,001	-	-
	Moderate	D150	0,021		
		D270	0,005	-	
		D360	-	-	-
	Marked	D150	0,004		
		D270	0,007	-	
		D360	-	0,004	0,007
	Complete	D150	0,024		
		D270	-	0,024	
		D360	-	0,073	-



Graph 2 - Development of clinical parameters according to the volunteers' efficacy evaluation during the 360 days of nutraceutical use

found in objective and subjective analyses. Through both the physician's and the volunteer's evaluations, the authors observed clinical improvement in wrinkles, fine lines, other hyperchromias, hydration, radiance, smoothness and overall appearance. In the corneometry examination, there were increases of 25.41% in the face and of 35.17% in the arm. In the pH test, there was a reduction of 10.37% and 10.10% in the face and arm, respectively. As a result, an improvement in the skin's hydration and a reduction (acidification) in the skin's pH (an ideal marker for hydrated skin) were observed. There was a significant reduction in seborrhoea, demonstrated by a 29.26% decrease in sebumetry measurements. According to the ultrasound examination, there was a gradual increase in measurements for the skin on the face and arm to 49.94% and 13.90%, respectively. All numerical parameters mentioned were statistically significant.

The skin's acidity is of crucial importance to its hydration; it controls the integrity and cohesion of the epidermis' stratum corneum. Acidity is of paramount importance for the epidermal antimicrobial barrier and in establishing the epidermic barrier's permeability. 17 The epidermal permeability function is explained by the capacity of the billamelar lipid barrier's lipid secretor enzymes to be activated in acid pH, enhancing the integrity and cohesion of the stratum corneum and increasing the skin's hydration capacity. 17,20 In our clinical findings, we

Table 3: Ultrasound results visit-by-visit during 360 days of nutraceutical use

Density	Face						Arm					
	D0	D30	D120	D180	D210	D360	D0	D30	D120	D180	D210	D360
Mean	25,9	32,3	39,3	50,3	55,8	57,6	61,2	66,4	69,4	81,9	86,5	89,1
Median	25	32	39	51	54	55	63	66	69	83	87	88
Standard deviation	6,2	6,8	7,6	6,6	7,8	8,4	12,3	12,4	8,8	11,7	12,4	12,8
Q1	22	28	33	48	51	52	56	61	65	73	76	79
Q3	29	35	44	54	63	63	67	74	78	91	96	99
N	33	33	33	33	33	33	33	33	33	33	33	33
IC	2,1	2,3	2,6	2,3	2,6	2,9	4,2	4,2	3	4	4,2	4,4

Table 4: P-values of the ultrasound analysis obtained during 360 days of nutraceutical use

	D0	D30	D90	D180	D210	
Face	D30	<0,001				
	D120	<0,001	<0,001			
	D180	<0,001	<0,001	<0,001		
	D210	<0,001	<0,001	<0,001	<0,001	
	D360	<0,001	<0,001	<0,001	<0,001	0,003
Arm	D30	0,012				
	D120	0,001				
	D180	<0,001	<0,001	<0,001		
	D210	<0,001	<0,001	<0,001	<0,001	
	D360	<0,001	<0,001	<0,001	<0,001	0,001

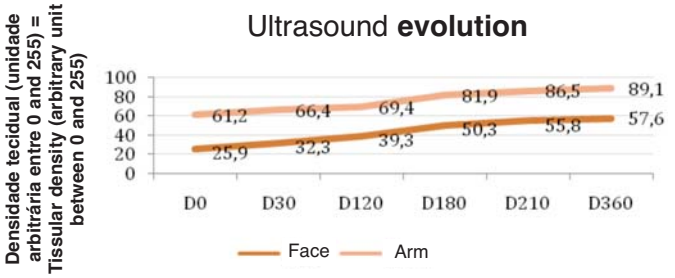


Chart 3 - Evolution of the analysis of ultrasound data during 360 days of nutraceutical use

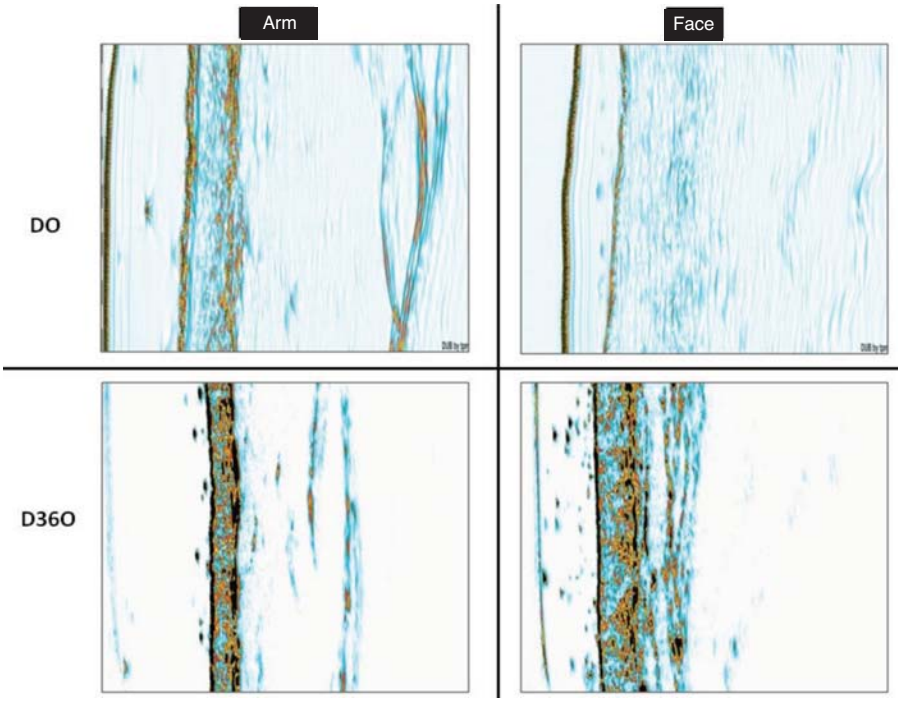


Figure 2 - Comparative ultrasound

found improvement in the overall appearance of the volunteers' skin, a fact that was corroborated by the hydration capacity attributed to this nutraceutical combination, as described in previous studies.[16]

Vitamin C also has the ability to stabilize and reduce collagen's thermal sensitivity, stimulating collagen production in vitro and in vivo, and protect skin from photodamage. [21] These benefits can sustain a steady increase in dermal density obtained using

the supplement, which is important for the repair of aged skin.

There are reduced amounts of lycopene in dry skin, which is the most important sign of dehydration of the skin and of the early stages of wrinkle formation. [20,22,23] Combined lycopene and vitamin C has the ability to sequester free radicals and defend the skin against damage caused by exposure to radiation.[24-26] The presence of lycopene in the nutraceutical is able to improve hydration, which was verified in our results and in the above-mentioned findings of Costa and colleagues.[16]

Oral ingestion of polyphenols prevents alterations in the epidermal barrier and improves the skin's protection against UVB; the grape seed extract contained in the study product helped improve skin hydration, since it is rich in polyphenols. [22] High concentrations of flavonoids were found in these polyphenols that, in in vitro studies, show higher antioxidant activity than that of vitamins E and C. [27] In the present study, the results demonstrated by the objective and subjective analyses reinforce our inference of how a product based on polyphenols has the ability to improve the appearance of aged skin, restoring hydration and generating a greater tolerance to UVB rays.[22]

The relevance and credibility of the present study are based not only on the long-term use of the compound, but also on the quality and reliability of the analysis of the results, which were substantiated in the volunteers' subjective analysis and the physician's clinical analysis, and were assisted by the high standard of the tools used, such as digital photographic records and skin ultrasonography.

CONCLUSION

This study verified the high quality of an alternative treatment for photoaged skin, leading to the conclusion that the long-term use of the nutraceutical based on marine protein, acerola concentrate, and grape seed and tomato extracts is reliably effective and safe in improving aspects of cutaneous photoaging. The results were documented by photographic records, ultrasonography, and clinical and subjective evaluations. ●

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