

Nutritional approach to skin aging: Correlation between the effects on fibroblasts and clinical results

Abordagem nutricional do envelhecimento cutâneo: correlação entre os efeitos em fibroblastos e os resultados clínicos

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ABSTRACT

Introduction: Some foods can have therapeutic value in the treatment of photoaging.

Objective: To clinically evaluate the efficacy of a nutritional supplement in the improvement of photoaging signs and correlate with an in vitro study.

Methods: A nutritional supplement was evaluated clinically and in vitro, with a culture of fibroblasts. Patients with clinical signs of photoaging (n = 48) were studied while using a nutritional supplement, with clinical and instrumental (cutometry) evaluations at 56, 84 and 112 days.

Results: There was progressive and significant improvement (p < 0.05) in the elasticity, firmness, fine lines and general appearance of the skin. The fibroblast cultures indicated a significant rate of collagen synthesis when compared to the control culture after 48 hours of incubation.

Discussion: The oral use of some vitamins and natural compounds has a therapeutic effect on the signs of photoaging. This study has demonstrated that a combination of linseed oil, lycopene, carotenoids, vitamin E, zinc and selenium possibly improve the signs of aging not only through antioxidant and anti-inflammatory mechanisms, but also by increasing collagen production.

Conclusions: Nutritional supplements are useful in the care of photoaged skin.

Keywords: fibroblasts; skin aging; antioxidants.

RESUMO

Introdução: Alguns alimentos podem ter valor terapêutico na abordagem do fotoenvelhecimento.

Objetivo: Avaliar clinicamente a eficácia de um suplemento nutricional na melhora de sinais de fotoenvelhecimento e correlacionar com estudo in vitro.

Métodos: Foram avaliadas 48 pacientes com clínica de fotoenvelhecimento em uso de um suplemento nutricional (com cultura para fibroblastos) com observações em 56, 84 e 112 dias. As avaliações foram clínicas e instrumentais (por cutometria).

Resultados: Houve melhora progressiva e significativa (p < 0,05) da elasticidade, firmeza, linhas finas e aparência geral da pele. A cultura de fibroblastos demonstrou significativa taxa de síntese de colágeno com relação à cultura-controle, após 48 horas de incubação.

Discussão: Algumas vitaminas e compostos naturais possuem, em uso oral, propriedades terapêuticas sobre os sinais de fotoenvelhecimento. Este estudo demonstrou que a associação de óleo de linhaça, licopeno, carotenoides, vitamina E, zinco e selênio possivelmente melhoram os sinais de envelhecimento não somente por mecanismos antioxidantes e anti-inflamatórios, mas também por aumento da colagênese.

Conclusões: Os suplementos alimentares são aliados no cuidado com a pele fotoenvelhecida.

Palavras-chave: fibroblastos; envelhecimento da pele; antioxidantes.

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INTRODUCTION

With longer life expectancies, people are increasingly taking steps earlier and earlier to thwart the signs of aging and improve their quality of life as they grow older. Cutaneous aging is characterized by a decline in cellular functions, with structural modifications and clinical repercussions.¹ Its main cause is sun exposure, which can be largely prevented by protecting the skin from the sun.

Likewise, the intrinsic mechanisms of aging, such as cellular oxidation, and the decline of cellular functions – including immunity, cutaneous barrier and collagen production, among others – can be stimulated by some topical or oral substances.

A great amount of research has been conducted on the nutritional impact of foods containing antioxidants – part of a group of foods with therapeutic properties known as “functional foods” – on the skin.³ Research on the substances themselves and on associations has also been performed extensively. For instance, ascorbic acid and zinc have a synergic action in the preservation and stimulation of the cutaneous immune function, which declines with age and stress level – thus increasing the skin’s susceptibility to UV damage.²

The use of dietary supplements should ideally take into account medical advice and follow up, given the need to educate patients on the selection of appropriate nutrients and the use of safe doses.⁴ The present study demonstrates the clinical effects of a combination of nutrients in the treatment of signs related to cutaneous aging. It also demonstrates the cellular mechanism related to those clinical effects in an in vitro model.

OBJECTIVE

To evaluate the effects of a dietary supplement in the clinical improvement of cutaneous aging related parameters.

METHODS

The study lasted 112 days and involved female volunteers (n = 60) aged 30-60 with clinically observed cutaneous aging who had not undergone cosmetic procedures within the last month. This was a prospective, open and blind study, carried out at a private laboratory after the approval of the Ethics Committee. Of the 60 patients who started the study, 10 dropped out and 2 were excluded for not fulfilling the inclusion criteria.

The patients were clinically assessed by a dermatologist regarding the firmness, elasticity, thin lines, and general appearance of the skin at 4 time periods: baseline, 56 days, 84 days, and 112 days. In addition, they underwent photographic documentation (Visia CR Canfield®) and cutaneous micro-relief measurement through the micro measurement and quantitative analysis of silicone molds using SkinVisiometer® (model SV500, Courage&Kazhaka). The silicone replica placed in a specific support in the equipment, which beams parallel light rays that penetrate the silicone replica of the skin. The visualization is provided by a digitization unit and a graphic board connected to a computer.^{5,6}

All women ingested the supplement daily until the end of the study. Each capsule contained: linseed oil (266.2 mg), lutein (4 mg), lycopene (5.1 mg), beta-carotene (600 mcg), ascorbic acid (45 mg), vitamin E acetate (10 mg), zinc (7 mg), and selenium (34 mcg). The capsules are commercially available as Eximia Temporize® (Herbarium Laboratorio Botanico Ltda, Brazil)

The statistical evaluation was carried out by adjusting the linear models (McCulloch & Searle, 2002) in which the effect of time is analyzed. The SAS software’s MIXED procedure was used, within the LINUX operating system.

RESULTS

From the 48 patients who began the study, one was excluded after reporting pruritus over her whole body, therefore requiring medication. There has not been confirmation of the cause and effect.

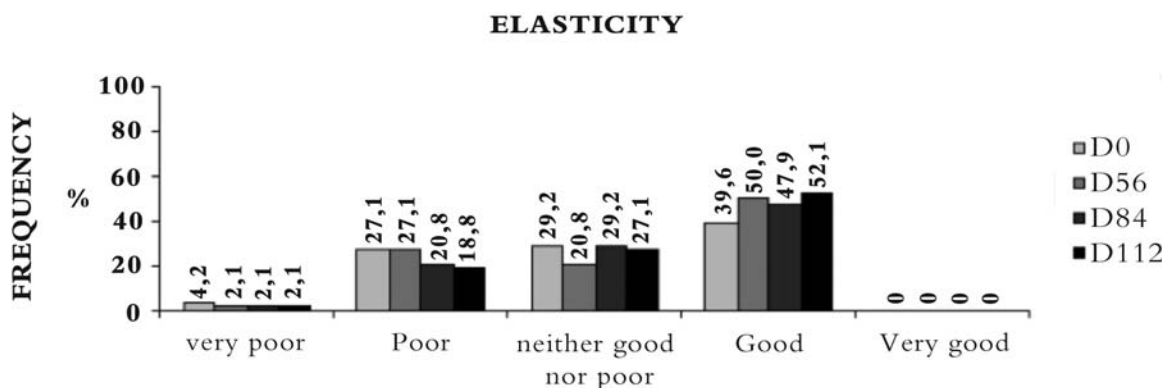
Regarding the clinical effects, all items demonstrated progressive improvement from baseline (D0). The following graphs demonstrate the percentage of improvement of each.

Figure 1 shows the percentages of improvement over time for the criterion “elasticity.”

Figure 2 depicts the change in firmness/elasticity over time.

Results for the criterion “thin lines” are summarized in Figure 3.

The results for general appearance over time are shown in Figure 4.



Graph 1: Elasticity improved significantly (p < 0.05) from baseline to days 56, 84 and 112.

The results for rugosity, quantitatively evaluated by Skin Visiometer®, demonstrated a statistically significant reduction from day 56. As shown in Figure 5, the quantitative evaluation of the average rugosity using Skin Visiometer® verified statistically significant improvement ($p < 0.05$) between days 56/84, and 56/112.

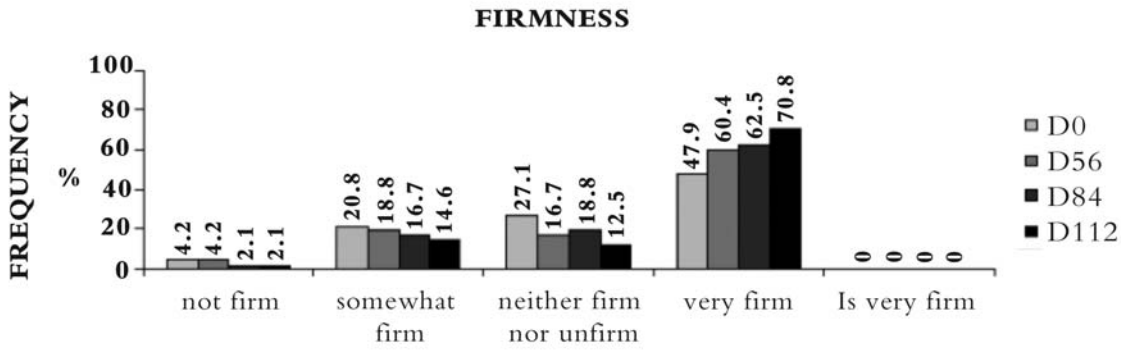
IN VITRO EVALUATION: ACTIVITY IN THE FIBROBLASTS

An in vitro complementary study was carried out in a culture of fibroblasts to evaluate the action of the nutrients on the cutaneous tissue. Collagen synthesis was compared to a negative control after 48 hours of incubation.

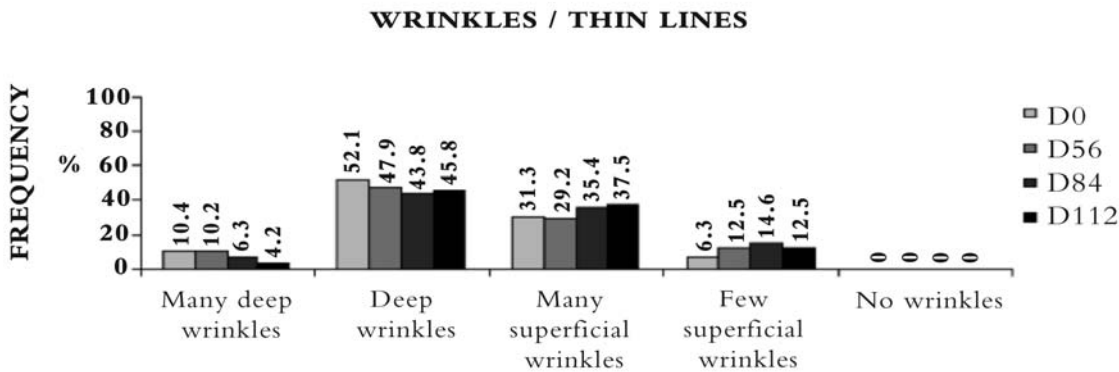
Figure 6: Collagen synthesis*: $p < 0.05$ and #: $p < 0.001$
 Figure 6 shows 22% and 29% increases in collagen synthesis for 0.006% and 0.012% concentrations, respectively, after 48 hours. Both presented statistical significance ($p < 0.05$ and $p < 0.001$, respectively).

DISCUSSION

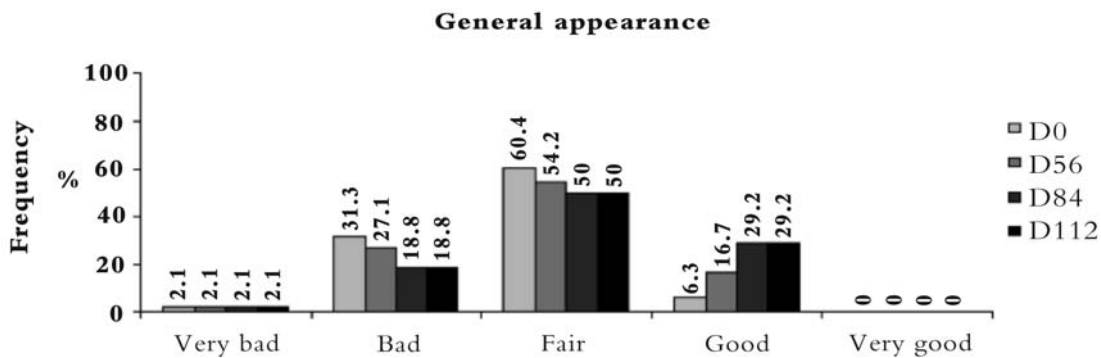
Due to their composition, some foods present therapeutic properties in addition to vitamins and oligoelements. A well-documented example is linseed oil. Linseed oil is composed of a combination of several molecules such as alpha-linolenic, oleic and linoleic acids, in addition to Omega-6 acids, which provide



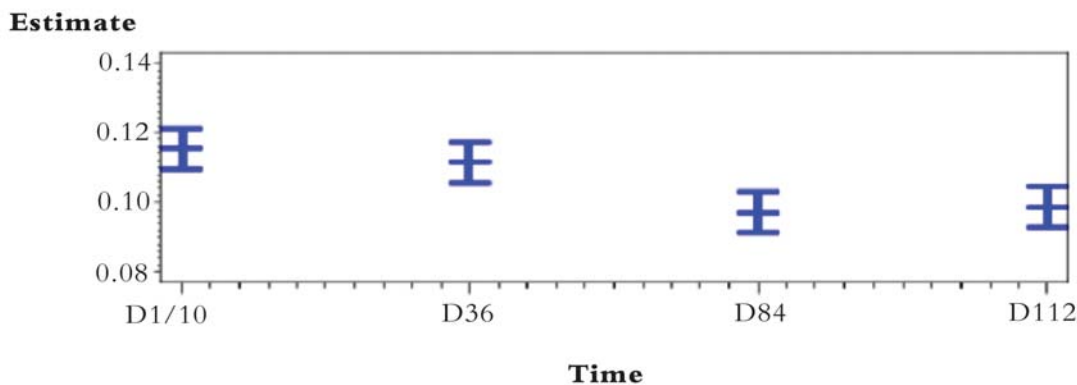
Graph 2: Significant improvement ($p < 0.05$) from baseline to days 56, 84 and 112



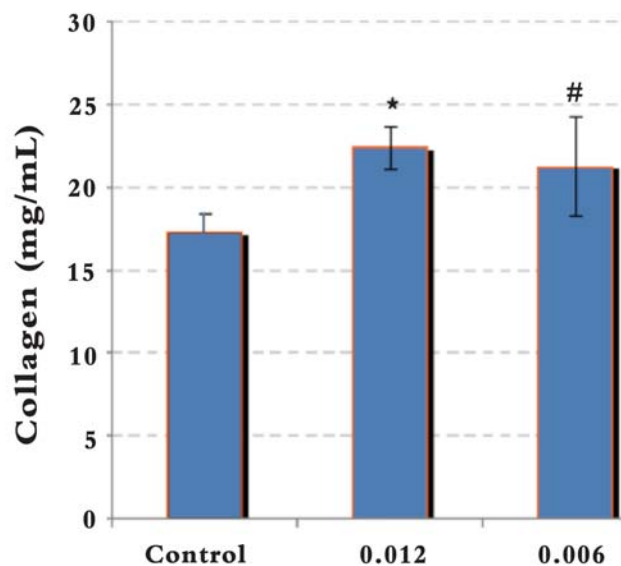
Graph 3: Significant improvement ($p < 0.05$) from baseline to days 56, 84 and 112



Graph 4: General appearance over time. Significant improvement ($p < 0.05$) from baseline to days 56, 84 and 112



Graph 5: Quantitative evaluation of average rugosity using Skin Visiometer®



Graph 6: Synthesis of collagen in fibroblast culture

this substance with modulatory properties of the inflammation and cutaneous barrier formation that are also being studied in cardiology.^{7,8,9} Alpha-linolenic acid is an Omega-3 acid that, together with Omega-6 acid, acts decisively in the maintenance of the cutaneous barrier and in the differentiation of the stratum corneum.^{10,11} In fact there is some evidence that its use would interfere in the expression of the protein p53, which would help prevent photocarcinogenesis.¹²

Although the skin has its own antioxidant enzymatic system, it progressively loses its effectiveness with age.¹³ Supplementation with lutein – a carotenoid – was proved to reduce UV-mediated inflammation mediated in laboratory animals.¹⁴ Likewise, tocopherol – a powerful antioxidant – can mediate inflammation by inhibiting the Cyclooxygenase 2 (COX 2), an important mediator of UV-induced inflammation.¹⁵ In doses of up to 30 mg/day, oral carotene can also increase the expression of procollagen.¹⁶

The association among antioxidants such as tocopherol, beta-carotene, carotenoids and linseed oil was studied in human skin, and demonstrated significant improvement in rugosity compared to controls.¹⁷

The literature offers plenty of evidence for lycopene and lutein as antioxidants. In Brazil, both are approved as functional foods for their antioxidant properties when ingested orally. The use of these compounds as systemic photoprotectors, to reduce UV-induced oxidative damage, is referenced several times in the literature.¹⁸

CONCLUSION

According to the dose and proposed association, dietary supplements are currently seen as contributing to the care of photoaged skin. Substances with antioxidant or anti-inflammatory properties help prevent or even reduce UV damage. Substances with regenerating actions are capable of increasing the expression of some enzymes and proteins involved in metabolism and tissular structures, and can help reconstitute elements of the cutaneous barrier, such as fatty acids. ●

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