

Ácido chiquímico para esfoliação cutânea

Shikimic acid: a potential active principle for skin exfoliation

RESUMO

Introdução: Ácidos orgânicos são amplamente utilizados na área dermocosmética, pois apresentam efeitos relacionados à esfoliação e à renovação celular. Deles, pode-se citar o derivado do anis-estrelado, conhecido como ácido chiquímico.

Objetivos: Avaliar a atividade antioxidante do ácido chiquímico e a eficácia clínica de preparações dermocosméticas acrescidas de 3% desse ativo.

Métodos: A atividade antioxidante foi avaliada por um método *in vitro*. Sequencialmente, foram elaboradas preparações de gel, gel creme e solução a 3% do ácido, as quais foram submetidas a estudos preliminares de estabilidade e análise sensorial. O estudo clínico foi realizado por técnicas não invasivas de biofísica e imagem da pele.

Resultados: O ácido chiquímico apresentou potencial antioxidante. Todas as preparações foram consideradas estáveis, e a adição do ácido chiquímico melhorou o sensorial do gel e do gel creme. No estudo clínico, o gel e a solução mostraram alterações significativas no microrrelevo e nos parâmetros relacionados à esfoliação da pele. Entretanto, a formulação gel creme não proporcionou tal efeito, mostrando a importância do veículo para a eficácia de cosméticos.

Conclusões: O ácido chiquímico pode ser considerado potencial ativo para aplicação em formulações dermocosméticas para esfoliação e melhora do microrrelevo da pele.

Palavras-chave: abrasão química; antioxidantes; cosméticos; eficácia; ácido chiquímico.

ABSTRACT

Introduction: Organic acids are widely used in cosmeceutic-based skincare due to their exfoliation and cell renewal related effects. A star anise derivative known as shikimic acid is an example.

Objectives: To evaluate the antioxidant activity of shikimic acid and the clinical efficacy of dermocosmetic preparations containing 3% of this active principle.

Methods: The antioxidant activity was assessed through an *in vitro* method. Formulations of gel, gel cream, and a 3% solution of the acid were sequentially dispensed and preliminarily subjected to stability and sensory analysis. The clinical study was performed through non-invasive biophysical and skin imaging techniques.

Results: The shikimic acid showed antioxidant potential. All formulations were found to be stable and the addition of shikimic acid improved the sensory analysis of the gel and gel cream. In the clinical assessment, the gel and the solution showed significant alterations in microrelief and in the parameters linked to skin exfoliation. However, the gel cream formulation did not show such an effect, suggesting the importance of the vehicle for the effectiveness of the cosmeceutics.

Conclusions: Shikimic acid can be considered an active principle with good potential for application in dermocosmetic formulations aimed at exfoliation and improvement of the skin's microrelief.

Keywords: chemexfoliation; antioxidants; cosmetics; efficacy; shikimic acid.

Original Articles

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INTRODUCTION

The dermo-cosmetics industry has turned its focus to the use of plant-based compounds, resulting in a significant level of acceptance by consumers, who have taken into account the pleasant fragrances, beneficial properties, and the understanding that these formulations are safer than their synthetic derivatives-based analogues.^{1,2}

Among natural compounds, organic acids – which are commonly found in many types of fruits and have been widely used for many decades – stand out. Their effects on the skin are mainly linked to cellular exfoliation and renewal, and are thus indicated for the treatment of photoaging, acne, and cutaneous hyperpigmentation.^{3,4}

As chemical exfoliating agents, organic acids have been employed over time for the treatment of various skin diseases, as well as for aesthetic purposes. The depth in the skin's layers at which the action of acids occurs may result in cell renewal, skin whitening, collagen synthesis, and epidermal thickening, among other effects.

The choice of the acid depends on the desired results, i.e., it depends on the depth of the action required.^{5,6}

The chemical exfoliation process based on an organic acid can result from the reduction of the cohesion force between the cells of the stratum corneum, promoting desquamation and, therefore, a more flexible and compact layer.⁷ In addition to these benefits, deodorant, antimicrobial, and antioxidant actions are also among the properties of an organic acid obtained from star anise (*Illicium verum*): the shikimic acid. This active principle is a multifunctional component capable of protecting the skin and helping it maintain its essential functionality. Recent studies report that shikimic acid can inhibit the activity of the lipase enzyme, blocking the production of fatty acids, thus also acting as an odor control agent. Moreover, it has an inhibitory effect on the microbial growth of a causative agent of seborrheic dermatitis of the scalp.^{8,9}

When developing cosmetic formulations with organic acids, the concentration of the acid, the pH of the formulation, the amount of free acid present, the acid type, the vehicle, the duration of exposure, and the consumer's skin type among other factors, should be taken into account.⁴ Interference in these conditions can lead to the ineffectiveness of the final product.

Next to development, a primary stability assessment is crucial for predicting the behavior of the active principle – as well as that of the formulation – as compared to the actual use and storage conditions. To this end, the organoleptic characteristics, pH behavior, and phase separation are analyzed.

In addition, *in vitro* methods for assessing the antioxidant action have been widely used as they provide valuable information on the potential of the substance to be used in the cosmetic product. Among them, the HRP-luminol-H₂O₂ based chemiluminescence method has currently been one of the most used because it is fast, reliable, and effective in determining the ability of some antioxidants to neutralize free radicals.¹⁰

Regarding the antioxidant effects of polyphenols, the

characterization of shikimic acid's antioxidant activity is very important since it has a chemical structure capable of neutralizing free radicals and becoming stable, avoiding uncontrolled reactions with the skin's biomolecules.

Before having its clinical efficacy checked, the finished cosmetic product should be assessed for its sensory characteristics, which can decisively influence the consumers' choice for the product, and cause the user to change the form of application, frequency of use, and amount of product applied, depending on the greater or lesser acceptance of its sensory properties, which influences its effectiveness.¹¹

Whereas the sensory evaluation – as well as clinical observations – are strictly qualitative, the quantitative assessment of the formulation's efficacy under actual conditions of use (i.e. in human skin through biophysical and image analysis techniques, which have been the choice in studies of safety and efficacy and have been recommended by regulatory agencies such as ANVISA, FDA and Colipa), is also crucial.

The biophysical and imaging techniques for analyzing the skin comprise the study of some variables such as the water content of the stratum corneum, transepidermal water loss (TEWL), and the skin's microrelief, among others.¹²

The measurement of the water content of the stratum corneum has been largely carried out using the capacitance method, with the assistance of a corneometer device.¹²

The *tewameter* measures the TEWL by analyzing the water pressure gradient adjacent to the skin's surface. Thus, the lower the gauged value, the better the skin barrier's function.¹²

For investigating the skin's surface Visioscan® VC 98 equipment (Courage & Kazaka Electronic GmbH, Cologne, Germany) can be used. This device allows qualitative and quantitative assessment of the skin's surface under physiological conditions through the optical profilometry technique.¹³

Finally, based on the properties of shikimic acid described above, it was introduced as an active ingredient for use in cosmetic formulations, which lent it great importance in studies aimed at proving the proposed benefits.

OBJECTIVES

The present study was aimed at evaluating the *in vitro* antioxidant activity of star anise derived shikimic acid, as well as the development and the clinical efficacy of dermo-cosmetic preparations containing this natural origin component.

METHODS

Research and development of cosmetic preparations

The pH stability, the concentration, sensory characteristics, and the interaction between the raw materials used were considered in the preparation of the formulations.

Three vehicles were developed: a gel cream, a gel, and an aqueous solution, to which shikimic acid was added (Table 1).

The developed gel, gel cream, and solution underwent centrifugation-assisted preliminary stability studies and pH

determination 24 hours after preparation, as well as weekly assessments (for 30 days) of their organoleptic properties, being kept in the environment and subjected to thermal stress (37°C and 45°C) in thermostated greenhouses (Eletrolab, model 111FC), with controlled humidity and photoperiod.

Preliminary stability studies

For the centrifugation test, a 3 g sample of each was centrifuged in Falcon plastic tubes for three 30-minute cycles at 3,000 rpm in an Excelsa Baby II centrifuge (model R-206, 0.0440 potency, Fanem). The measurement of pH was carried out with a DM 20 pH meter (Digimed), using aqueous solutions of the formulations at a concentration of 10%.¹⁴

Changes in color, phase separation and homogeneity were considered in the organoleptic evaluation.

Sensory evaluation

This evaluation was conducted as one of the stages of the development of the studied gel and gel cream formulations; 12 female volunteers applied a standardized amount (50ml) of the formulations in different regions of the lower middle portion of the forearms.

The analysis was carried out by comparing the formulations of the original vehicles with analogues, which were added to the active principle studied.

Finally, the volunteers received a sensory evaluation questionnaire and were asked to assign grades according to the quality parameters provided,¹⁵ as shown in Chart 1.

The sensory evaluation was carried out in two steps, with the results being presented in a box type plot graph.

This graph type has a central box representing 50% of the core values of the scores assigned by the volunteers; a horizontal line inside the box represents the median of the scores, while the maximum and minimum scores are represented by lines running from the central box's upper and lower ends, respectively.

Antioxidant activity evaluation

The luminol-dependent chemiluminescence method was chosen to assess the studied compound's antioxidant potential. The method's principle is based on the detection of photons emitted by the luminol when it is oxidized by hydrogen perox-

ide in the presence of a catalyst, the HRP enzyme (horseradish peroxidase). As a result, an intermediate reactive is formed (free radical), and when this agitated product returns to the fundamental state it emits photons, which are captured by the device.¹⁶

Therefore, the stronger the signal captured by the device, the greater the production of free radicals. When an antioxidant substance is added, a partial neutralization of the free radicals takes place, leading to a lower emission of photons and hence, a weaker signal is detected by the device.¹⁰

Various dilutions of the active principle were prepared in a 0.1M (pH 7.4) phosphate buffer. Subsequently, 10µl aliquots of these solutions and of a control solution containing only the buffer, were added with 400µl of 0.1M (pH 7.4) phosphate buffer, 100µl H₂O₂, and 10µl luminol solution (5mg/ml). The reaction was then initiated by the addition of 500µl HRP solution (0.2UI/ml), with the chemiluminescence being quantified using a luminometer (Autolumat, LB953, EG&G Berthold).^{10,17,18}

Three measurements were carried out for each sample and the results were expressed as a geometric area below the curve (AUC), which corresponds to the total amount of free radicals produced in 10 minutes at 30°C. In this manner, it was possible to calculate the inhibition percentage for each concentration of the compound according to the following equation:

$$\text{Inhibition rate (\%)} = 100 - (100 \times \text{AUC}_{\text{sample}} / \text{AUC}_{\text{control}}) \text{ where:}$$

$$\text{AUC}_{\text{sample}} = \text{area below the sample's curve}$$

$$\text{AUC}_{\text{control}} = \text{area under the control's curve}^{19}$$

Clinical efficacy evaluation

Case series

This phase of the study was carried out after approval by the Research Involving Humans Ethics Committee of the Faculdade de Ciências Farmacêuticas de Ribeirão Preto (Universidade de São Paulo – USP), Ribeirão Preto, São Paulo, Brazil, under the protocol N. 143 – CEP/FCFRP.

The volunteers were then informed and instructed about the objectives and methods of the research, having signed a free and informed term of consent, prepared according to the Declaration of Helsinki and approved by the Research Ethics Committee.

TABLE 1: Composition of the cosmetic preparations

Raw materials (% per part)	F1	F2	F3
Modified starch polymer	3	7	-
Non-ionic self-emulsifying cetostearyl alcohol wax and cetostearyl alcohol 20 EO	3	-	-
Methyldibromo glutaronitrile	0.2	0.2	0.2
Propylene glycol	2.5	2.5	-
Glycerin	2.5	2.5	-
Amino nitropropanol 95% (10%)	1	-	-
Water qs	100	100	100
Shikimic acid	3	3	3

CHART 1: Sensory evaluation form

Raw materials (% per part)	F1	F2	F3
Modified starch polymer	3	7	-
Non-ionic self-emulsifying cetostearyl alcohol wax and cetostearyl alcohol 20 EO	3	-	-
Methyldibromo glutaronitrile	0,2	0,2	0,2
Propylene glycol	2,5	2,5	-
Glycerin	2,5	2,5	-
Amino nitropropanol 95% (10%)	1	-	-
Water qs	100	100	100
Shikimic acid	3	3	3

Ten volunteers were selected (skin phototypes II and III, aged between 20 and 35 years). The following exclusion criteria were considered in this selection: pregnancy or lactation, previous history of adverse reactions with the use of cosmetic products, use of drugs likely to produce abnormal cutaneous response, localized or generalized skin conditions, and excessive hair growth in the areas of study.

Analysis of clinical efficacy through biophysical and skin imaging analysis techniques

Prior to the measurements, the volunteers were acclimatized for 10 minutes at room temperature (20°C to 22°C) and at a controlled relative humidity (45% to 55%) level.

The cosmetic preparations underwent the clinical study with the aim of comparing the used vehicles regarding the effectiveness of the shikimic acid.

The solutions, along with the other formulations considered stable in the preliminary stability studies, underwent the clinical study with a view to having their effectiveness determined.

The clinical study was carried out in two steps: firstly, the F1 preparation was evaluated, with analysis of the F2 and F3 preparations. Ten selected volunteers had the lower middle region of their forearms divided into 2 squares, each with 25cm². These regions were randomized and one of them was designated as a control-region. In the second step, the lower middle region of the forearm was divided into 3 squares, each with 25cm². These regions were randomized and one was designated as a control-region. Once acclimatized, the volunteers underwent baseline measurements for the assessment of the skin's microrelief, the water content of the stratum corneum, and the TEWL.

The application of the gel cream (F1) and gel (F2) was made with the help of an automatic pipette for viscous samples, while the application of the solution (F3) was carried out with an automatic pipette for fluid samples. Similar volumes of each formulation (50 ml or 2ml/cm²) were applied in the delimited regions.

Two hours after the application of the cosmetic preparations, the volunteers returned and underwent another round of

acclimatization, followed by a second round of measurements to evaluate the immediate effects being performed.

Determination of the water content of the stratum corneum

The water content measurements of the stratum corneum were taken using a CM 825 Corneometer device (Courage & Kazaka Electronic GmbH, Cologne, Germany), which indirectly measured the hydration level of the stratum corneum by gauging the skin's electrical capacitance.

The results were quantified in arbitrary units (AU) –the device determines that 1AU corresponds to a range of 0.2mg to 0.9mg of water per gram of stratum corneum.^{12,20}

The determination of the TEWL aimed at evaluating the barrier function of the skin was carried out with the TM 210 Tewameter device (Courage & Kazaka, Electronic GmbH, Cologne, Germany). The device measures the evaporation of water from the skin's surface, based on the Fick's laws of diffusion.^{20,21}

Determination of skin microrelief

The Visioscan® VC 98 device was used for the assessment of the skin's surface, providing a qualitative and quantitative assessment of the cutaneous surface under physiological conditions through the optical profilometry technique.

The software provides a histogram showing the distribution of different hues of gray, quantifying the dark spots – which correspond to the roughness –and light spots – which correspond to plateaus in the skin's microrelief. The parameters related to the skin's surface were evaluated through this method (Chart 2).¹³

The experimental data obtained in the evaluation of clinical efficacy were subjected to statistical analysis, in which preliminary tests of distribution normality and homogeneity of variances involved in the experiment were performed.

Statistical analysis

The above statistical tests were performed using the GMC statistical software, developed by Maia Campos (1999),²² and the Minitab statistical software.¹⁶

CHART 2: SKIN SURFACE RELATED PARAMETERS MEASURED WITH THE VISIOSCAN® VC 98 DEVICE.

Parameters	Definitions
SeR Aspereza	Roughness
SeW Rugas	Wrinkles
SeSM Suavidade	Smoothness
SeSC Descamação	Scaling
RT Rugosidade	Rugosity

RESULTS

Development of formulations

Preliminary stability analysis

The cosmetic preparations remained stable during the 30 days of the study

Sensory evaluation

The sensory evaluation results for formulation F1 as compared to its vehicle are in Graph 1. The results for F2 and its respective vehicle are in Graph 2.

Antioxidant activity evaluation

Graph 3 shows the results of the antioxidant activity evaluation through the percentage of inhibition of free radicals formed as a function of the concentration of the shikimic acid.

Clinical efficacy evaluation

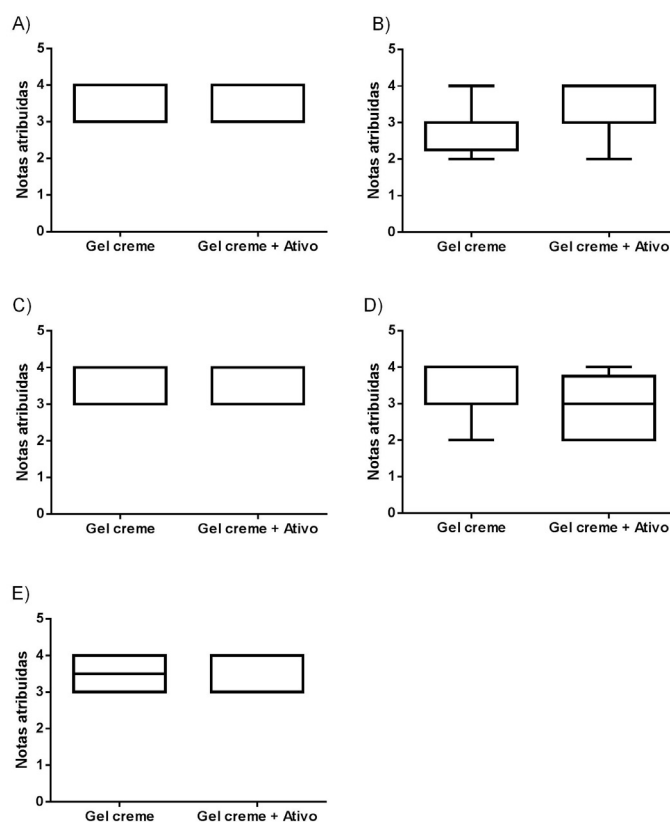
In this clinical study, measurements of the water content of the stratum corneum (Graph 4), TEWL (Graph 5), and cutaneous microrelief (Graph 6) were performed at baseline and 2 hours after the single application of the studied formulations in the volunteers' forearms. The values obtained were subjected to statistical analysis.

Statistical analysis of the results obtained

The experimental results of the assessment of the immediate effects of the preparation F1 after a single application in the forearms consisted of 40 numeric values corresponding to the factors *variation*, *time*, and *studied formulation*. These values are the result of the crossing of two areas of application of the formulation F1 and the control, at two different time points (before and 2 hours after the application of the formulations) x 10 repetitions, yielding the factorial product $2 \times 2 \times 10 = 40$.

The experimental results of the assessment of preparations F2 and F3's immediate effects after a single application in the forearms consisted of 60 numeric values, corresponding to the factors *variation*, *time*, and *studied formulations*. These values are the result of the intersection of three areas of application of the preparations that are the object of study (F2 and F3) and the control at two different times (before and two hours after application of the formulations) x 10 reps, giving the product $3 \text{ factorial} \times 2 \times 10 = 60$.

The preliminary tests were performed in order to verify the normality and homogeneity of the sample's distribution, allowing for the decision as to whether to use parametric or nonparametric tests.



GRAPH 1: Sensory evaluation. Gel cream (F1) combined with or not (vehicle) with shikimic acid (active principle), regarding the parameters: **A)** feeling to the touch; **B)** spreadability; **C)** hydration; **D)** smoothness; **E)** skin feel after 5 minutes

The results of these preliminary tests indicated that the tested samples were homogeneous and the distribution of frequencies was close to that of the mathematically normal curve.

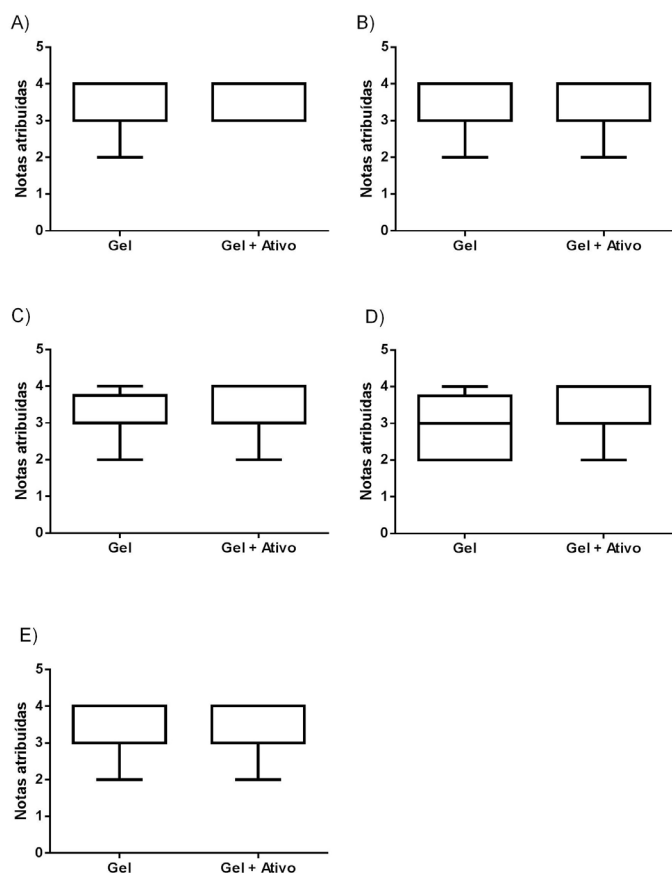
As a result, the parametric test that best fitted the experimental model was the variance analysis, followed by the Tukey's test for comparison of mean values.

DISCUSSION

Based on the preliminary stability analysis, the cosmetic preparations were evaluated. It was possible to verify that during the 30-day storage period, it remained stable. Regarding the visual assessment, it was possible to verify the absence of phase separation and changes in color and consistency.

All formulations remained at the initial pH range and when subjected to physical centrifugation stress, they remained homogeneous – i.e. without separation of phases.

According to the described protocol, formulations F1 and F2 underwent sensory evaluation. Initially, formulation F1 (gel cream) was evaluated as compared to its vehicle. As a result, both formulations showed adequate sensory characteristics, with the formulation containing the active principle deemed better in the following parameters: *sensation to the touch*, with varying



GRAPH 2: Sensory evaluation. Gel cream (F1) combined with or not (vehicle) with shikimic acid (active principle), regarding the parameters: **A)** feeling to the touch; **B)** spreadability; **C)** hydration; **D)** smoothness; **E)** skin feel after 5 minutes

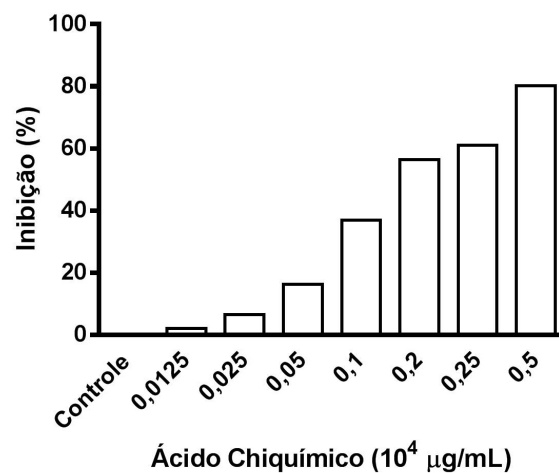
ratings ranging from 3 to 4; *spreadability*, with ratings from 2 to 4; *skin feel five minutes after application*, with ratings ranging from 3 to 4.

The two formulations were considered similar regarding the parameter *hydration capacity*, with ratings mainly falling between 3 and 4. For the parameter *smoothness*, the vehicle obtained more homogeneous ratings, which mainly fell between 3 and 4, with a median of 3.

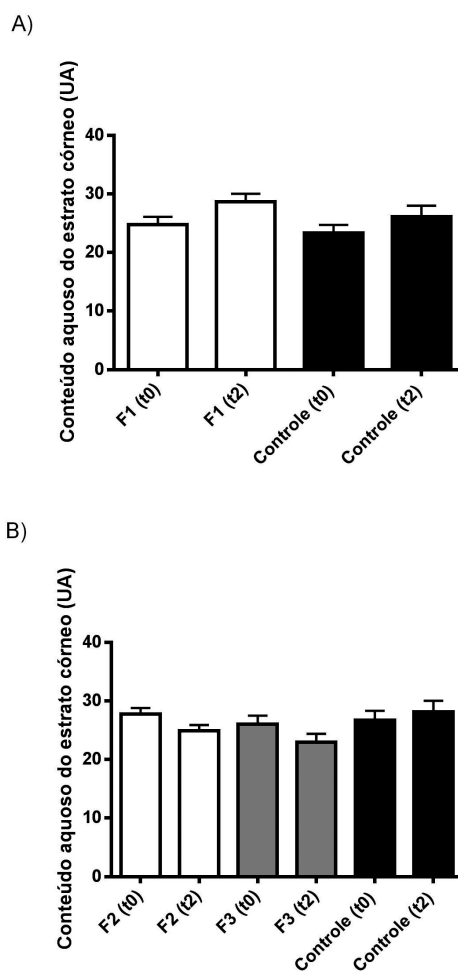
The second step occurred with the evaluation of formulation F2 (gel), and its respective vehicle. As a result, the formulations were deemed equal regarding the parameters: *spreadability* and *skin feel five minutes after application*, with ratings ranging from 2 to 4, with a median of 3.

The addition of the active principle earned formulation F2 a better final score than that of its vehicle regarding the other parameters: *sensation to the touch*, *hydration capacity*, and *smoothness*, with ratings falling mainly between 3 and 4.

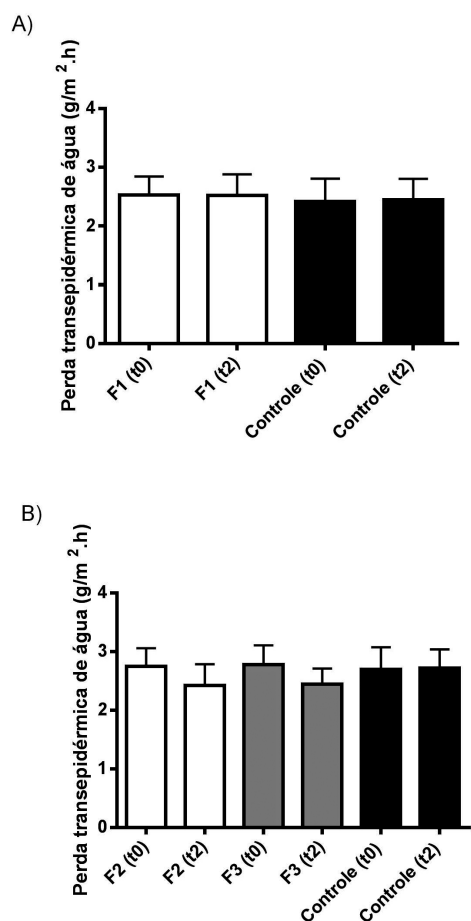
Analyzing the set of outcomes, it was possible to state that the formulation F1 (gel cream plus active principle) was deemed the best regarding the sensory parameters analyzed in the present study.



GRAPH 3: Inhibition of free radicals by shikimic acid through dependent HRP-luminol-H₂O₂ chemiluminescence trial.



GRAPH 4: **A AND B)** Water content of stratum corneum with the application of preparations F1 (cream gel), F2 (gel), and F3 (solution), at the baseline (t0) and after 2 hours (t2).



GRAPH 5: A AND B) TEWL with the application of preparations F1 (cream gel), F2 (gel) and F3 (solution), at the baseline (t0) and after 2 hours (t2).

Once the sensory evaluation was complete, the active principle underwent evaluation for its antioxidant activity. With those results, it was possible to draw a graph for the inhibition percentage of free radicals formed due to the shikimic acid concentration.

The control was prepared in the absence of the active principle, thus representing 100% of the production of free radicals. It was possible to observe that an increase in the concentration of the active principle led to a reduction in the production of photons (i.e. increased neutralization of free radicals produced).

This inhibition of the radicals produced takes place as a result of the chemical structure of shikimic acid, which has a polyphenolic ring (Figure 1). According to past studies, the components that are mainly responsible for the antioxidant activity are the polyphenols.^{18,22} This acid can thus stabilize the free radicals by donating electrons, therefore providing stability via an internal rearrangement. As a result, the stabilized free radicals become less reactive to biomolecules –the reaction of these free radicals with the skin's biomolecules (oxidative stress) contributes to aging.

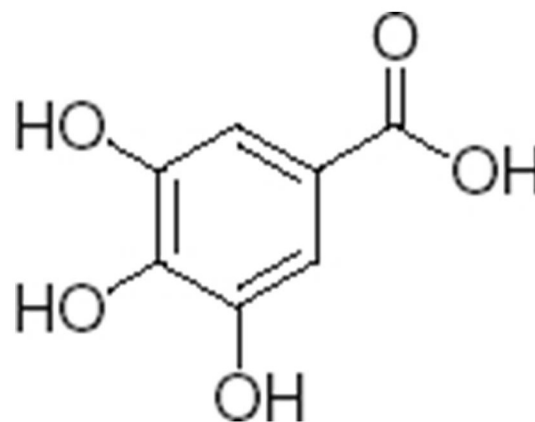


Figura 1: Ácido chiquímico

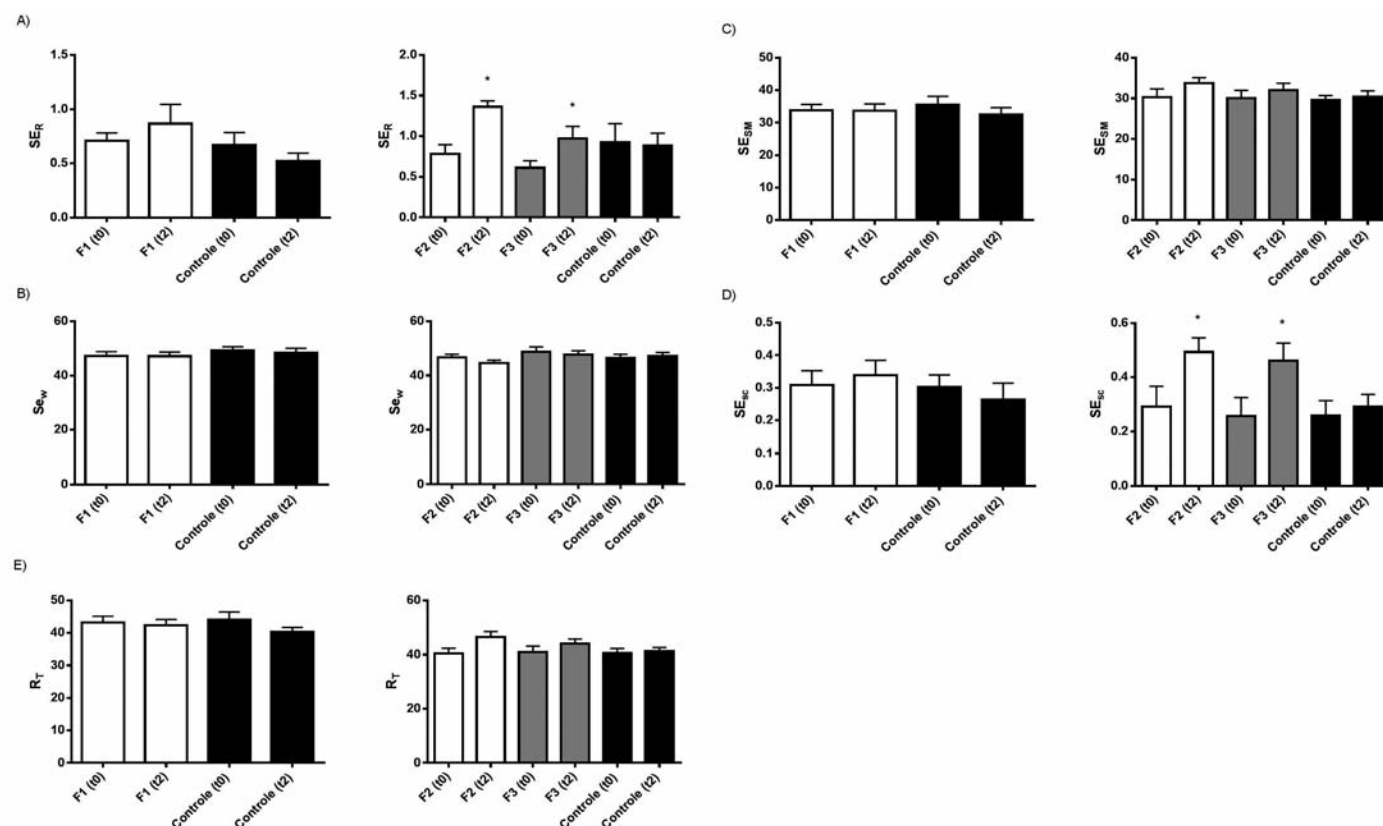
The chosen *in vitro* trial method (HRP-luminol-H₂O₂ dependent chemiluminescence) has been widely used because it is highly sensitive, practical, and reproducible, thus allowing the analysis of many samples in a short period of time.²³

Finally, the preparations underwent evaluation of their clinical efficacy. Based on the analysis of the present study's graphs, it was possible to verify that the preparations of gel cream (F1), gel (F2), and solution (F3), when combined with the studied compound did not result in statistically significant differences ($p > 0.05$) for the water content of the stratum corneum (Graph 4) and TEWL (Graph 5), when compared with the baseline and control values. This outcome is very important in exfoliating products, for it can demonstrate that its mechanism of exfoliating action does not cause negative effects on the skin's hydration and barrier function (i.e. it does not affect the skin barrier, as some peeling agents do).^{7,24}

For instance, an important feature for therapeutic applications in skin disorders such as atopic dermatitis is that they not disrupt the skin barrier, as the skin barrier's structure is chronically affected with these disorders.^{7,24-26}

Regarding the microrelief of the skin, preparation F1 did not yield statistically significant differences ($p > 0.05$). On the other hand, preparations F2 and F3 led to an increase in the SE_R parameter 2 hours after the application of the formulation, with a statistical significance of ($p < 0.05$). However, this effect was more pronounced for preparation F2. The SE_{SC} parameter also increased 2 hours after the application of the two preparations, with a statistical significance of ($p < 0.05$). The increase in the values of the roughness related parameter (SE_{SC}) is consistent with the properties of shikimic acid, since it can be related with the onset of the exfoliation process. In the long run, continuous treatment with shikimic acid could result in the cell renewal process, which makes it of interest as an application in dermo-cosmetic preparations with anti-aging properties.

According to the results obtained, the vehicle is of crucial importance in the development of a dermo-cosmetic prod-



GRAPH 6: Skin's microrelief with the application of preparations F1 (cream gel), F2 (gel), and F3 (solution), at the baseline (t0) and after 2 hours (t2). Parameters: roughness (A), texture (B), smoothness (C), scaling (D), and rugosity (E).

uct²⁷ since improper selection of the preparation's components may be related to the absence of significant outcomes regarding the expected effectiveness of the final product, rather than that of the active principle used. The vehicle should allow the incorporation of the active principle without destabilizing the formula, while being simultaneously capable of releasing it when applied on the skin in order for it to achieve its potential effect. In this manner, for the active principle in question, the best vehicles used in the present study were the gel and the solution, which probably allowed the release of the active principle and strengthened the effects in the improvement of the skin's microrelief.

CONCLUSION

Under the present study's experimental conditions, it was possible to conclude that:

The formulations assessed (gel, gel cream, and solution) were compatible with the active principle shikimic acid (i.e. they were stable in the preliminary stability studies);

The addition of shikimic acid to the gel cream and to the gel vehicles resulted in improved sensory parameters;

Shikimic acid is a compound with antioxidant activity and is therefore indicated for use in cosmetic preparations with protective and anti-aging properties for the skin;

The immediate effects, two hours after the application of the preparations studied, were correlated to the alterations in the skin's microrelief parameters related to the roughness and squamation of the skin, which, taken together, suggest the onset of the exfoliation process;

In the present study, the gel and the solution were the most efficient cosmetic preparations in achieving the exfoliating effects attributed to the shikimic acid;

Regarding the sensory and clinical effectiveness evaluations through objective methods, the gel preparation showed the most satisfactory results for the studied parameters;

According to the clinical efficacy evaluation results, shikimic acid can be considered an active principle with potential for use in cosmetics for exfoliation with an aim at improving the skin's microrelief. ●

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