

Efficacy of a depigmenting serum containing tranexamic acid + niacinamide + 4-butylresorcinol and hydroxy acids complex compared to hydroquinone in the treatment of melasma: a randomized, double-blind, comparative clinical trial

Eficácia de um sérum despigmentante contendo ácido tranexâmico + niacinamida + 4-butilresorcinol e complexo de hidroxiácidos em comparação com hidroquinona no tratamento do melasma: ensaio clínico comparativo, randomizado e duplo-cego

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ABSTRACT

Background: Melasma is a common hyperpigmentary disorder. Hydroquinone is widely used to treat melasma, but its use may be limited by adverse effects. Topical tranexamic acid (TXA), alone or combined with other agents, is a potential alternative.

Objectives: To evaluate the noninferiority of a new quadruple combination (QC) containing 3% TXA, niacinamide, 4-butylresorcinol and a hydroxyacid complex compared with 4% hydroquinone (HQ4) in the treatment of melasma.

Methods: Eighty participants with melasma were included and randomly assigned to 2 groups: QC and HQ4. The study duration was 120 days. Efficacy criteria include mMASI, colorimetry (ITA and L*) and MELASQOL.

Results: There was a significant improvement in mMASI, ITA, L* and MELASQOL in both groups ($p < 0.05$) with no statistical difference ($p > 0.05$) between them, indicating the noninferiority of QC serum compared with HQ4. Notably, the new serum showed greater improvements in mMASI, ITA and L* at D30 compared with HQ4, suggesting a greater initial response to treatment.

Conclusion: The new QC serum demonstrated non-inferiority to HQ4 after 12 weeks of treatment. In addition, its benefits were maintained for 4 weeks after treatment discontinuation. QC serum may represent a safe and effective alternative to HQ4 in the treatment of facial melasma.

Keywords: Hyperpigmentation; Melanosis; Tranexamic Acid; Niacinamide

RESUMO

Introdução: O melasma é uma dermatose hiperpigmentária frequente. A hidroquinona é amplamente utilizada no tratamento do melasma, mas seu uso é limitado por seus efeitos adversos. O ácido tranexâmico tópico (TXA), isolado ou em combinação com outros agentes, é uma alternativa.

Objetivos: Avaliar a não inferioridade de uma nova combinação quádrupla (QC), contendo 3% de TXA, niacinamida, 4-butilresorcinol e complexo de hidroxiácidos, em comparação com 4% de hidroquinona (HQ4) no tratamento do melasma.

Métodos: Foram incluídos e randomizados 80 participantes com melasma em dois grupos: QC e HQ4. O estudo teve duração de 120 dias. Os critérios de eficácia incluíram mMASI, colorimetria (ITA e L*) e MELASQOL. Resultados: Observou-se melhora significativa dos escores de mMASI, ITA, L* e MELASQOL em ambos os grupos ($p < 0,05$), sem diferença estatística ($p > 0,05$) entre eles, indicando a não inferioridade do sérum QC em relação ao HQ4. Notavelmente, o novo sérum apresentou resultados superiores para mMASI, ITA e L* no D30 em comparação com HQ4, sugerindo uma maior resposta inicial ao tratamento.

Conclusão: O novo sérum QC demonstrou ser não inferior ao HQ4 após 12 semanas de tratamento. Além disso, seus benefícios foram mantidos 4 semanas após a interrupção do tratamento. O sérum QC representa uma alternativa segura e eficaz ao HQ4 no tratamento do melasma facial.

Palavras-chave: Hiperpigmentação; Melanose; Ácido Tranexâmico; Niacinamida

Original Article

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INTRODUCTION

Melasma is a chronic acquired hyperpigmentation disorder of the skin, clinically characterized by brownish macules, particularly on the face.¹

While it can affect both genders and various ethnicities, it is more prevalent in women of childbearing age, especially those with intermediate Fitzpatrick skin types (III to V).²

Although not fully understood, the etiology of melasma involves intrinsic factors such as familial predisposition and hormonal profile, as well as environmental factors, especially exposure to solar radiation (ultraviolet and visible light).^{2,3,4}

Due to its chronicity and tendency to relapse, the treatment of melasma remains challenging for dermatologists.

Topical hydroquinone (HQ) is considered the gold standard but may cause both transient (such as irritant contact dermatitis) or permanent (such as ochronosis) adverse effects.^{1,2} For these reasons, its use is recommended at a maximum concentration of 4% and for a limited period, usually up to 90 days.¹ This discourages doctors and patients from using it and highlights the need for safer alternatives.

Recently, new therapeutic options with fewer side-effects and comparable efficacy to HQ have been proposed for melasma.

Tranexamic acid (TXA) is emerging as an attractive alternative. TXA has been used for many years as an antifibrinolytic agent to treat heavy menstrual bleeding.^{4,5} Recent studies have shown promising results with topical TXA as an alternative treatment for melasma due to its ability to inhibit plasminogen activator (PA) and interfere with the plasminogen/plasmin pathway, thereby decreasing melanogenic factors such as prostaglandins, leukotrienes, fibroblast growth factor (FGF) and alpha-melanocyte stimulating hormone (α -MSH).^{5,6} In addition, one study found that TXA decreases the number of CD31+ blood vessels and downregulates endothelin-1, a melanogenic factor that induces pigmentation. A study in guinea pigs also found inhibition of tyrosinase activity.⁷

Based on the available literature, topical TXA at concentrations ranging from 2% to 5% has demonstrated efficacy similar to that of HQ-containing agents, with fewer adverse events.^{4,7}

TXA 2% in emulsion and lotion formulations for the treatment of melasma demonstrated a statistically significant improvement in MASI score at week 4 and 8.⁷ A double-blind, split-face trial evaluated the efficacy of liposomal TXA 5% vs. HQ 4% cream.⁷ A statistically significant reduction in MASI score was observed at week 12. Although a greater reduction in MASI score was seen with liposomal TXA 5%, no statistical difference between the 2 treatments was reported.⁷

Other effective depigmenting agents that are widely used include niacinamide and 4-n-butylresorcinol (4nBR). Niacinamide is the active form of niacin (vitamin B3) and a precursor of coenzymes such as nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate (NADPH). In vitro studies have shown that niacinamide significantly de-

creases the transfer of melanosomes to keratinocytes.⁸ It also has an anti-inflammatory effect on the skin and is considered safe for use in pregnant and breastfeeding patients.¹ In melasma, treatment with 4% niacinamide for 8 weeks resulted in a 62% reduction in MASI score.⁹

4nBR has been shown to inhibit the activity of both tyrosinase and tyrosinase-related protein-1, which catalyzes the oxidation of the melanogenic intermediate 5,6-dihydroxyindole-2-carboxylic acid. Clinical trials have shown the efficacy of 4nBR at concentrations of 0.1% and 0.3%.^{10,11}

A double-blind, randomized, split-face comparative trial compared the efficacy of twice-daily application of 0.3% 4nBR serum with vehicle in 28 women with Fitzpatrick skin types III-IV and melasma.¹² At 12 weeks, 4nBR achieved significantly lower pigmentation scores than the vehicle. Another double-blind, randomized, split-face study involving 23 Korean women with melasma found a significant decrease in the melanin index following application of liposome-encapsulated 0.1% 4nBR compared with vehicle at 8 weeks.¹³

Hydroxy acids are also reported to be beneficial in the treatment of pigmentary lesions. Hydroxy acids are a class of organic carboxylic acids with one or more hydroxyl groups attached to the alpha or beta position of the carboxyl group. They can be categorized into alpha-hydroxy acids (AHAs), beta-hydroxy acids (BHAs), and polyhydroxy acids (PHAs).¹⁴ The main activity of hydroxy acids lies in their keratolytic and keratoplastic properties, which reduce the thickness of the stratum corneum while promoting increased cell turnover, thereby enhancing the efficacy of depigmenting agents.

Furthermore, AHAs have been shown to improve skin architecture by increasing epidermal hyaluronic acid and thickening the dermis through enhanced glycosaminoglycan and collagen synthesis. Studies have demonstrated that AHAs stimulate collagen production and epidermal renewal without inducing proinflammatory cytokine production, supporting their safety profile in sensitive skin conditions like melasma.^{14,15,16} These effects contribute to the dispersion of melanin, reversal of cell atypia, and overall improvement of hyperpigmented lesions.¹⁵

Combining ingredients that target different steps of the melanogenesis pathway is a modern and efficient approach to the treatment of melasma.¹⁷ Taking this into account, a new cosmetic gel serum (QC) containing multiple effective ingredients was developed.¹⁸ This formulation contains TXA, 4nBR, niacinamide, and a combination of hydroxy acids (gluconolactone, phytic acid, mandelic acid, and salicylic acid) with exfoliating properties that promote the removal of pigmented keratinocytes from the upper layer to lighten the skin.¹⁸

The efficacy of this formulation has been previously demonstrated.¹⁸ In vitro, it reduced melanin production by 67.0% on D21 ($p < 0.001$), compared with controls. Clinical efficacy and tolerability following twice-daily applications for 3 months were demonstrated in 35 subjects with slight to moderate fa-

cial hyperpigmentation by instrumental and clinical evaluation. These results supported the efficacy and tolerability of this new formulation.

The aim of this study was to assess the noninferiority of this new formulation (QC) in the treatment of melasma compared with the gold-standard treatment, hydroquinone 4% (HQ4).

MATERIAL AND METHODS

A single-center, randomized, double-blind clinical trial was conducted in Brazil between July and December 2023.

The study was conducted in accordance with the Good Clinical Practices guidelines and received ethical approval in accordance with federal regulations issued by the Research Ethics Committee, Universidade São Francisco (USF), under CAAE number 70186923.2.0000.5514 and opinion number 6,155,206 on June 30, 2023. The volunteers signed a consent form agreeing to participate in the study and authorizing the use of the data for publication.

A total of 80 participants were included in the study. Their ages ranged from 35 to 64 years, with a mean age of 50 years.

Inclusion criteria comprised women aged between 35 and 65 years with moderate to severe melasma for at least 1 year, who received no treatment for at least 3 months. Pregnant and lactating women were excluded from the study.

Exclusion criteria included loss to follow-up, protocol deviation, or treatment compliance below 80%. Eligible participants were randomly assigned to 2 groups:

Group I – Investigational treatment – quadruple combination (QC): facial serum with TXA 3%, NIC 4.5%, 4nBR 0.3%, and a hydroxy acid complex composed of gluconolactone 5%, phytic acid 4%, and mandelic acid 1.5%, plus SPF 50+ sunscreen.

Group II – Comparative treatment – Hydroquinone 4% (HQ4) plus SPF50 + sunscreen

Participants were instructed to apply either the QC serum (group I) or HQ4 (group II) to the facial lesions, twice daily (morning and night) and to apply the sunscreen on the morning (immediately after the depigmenting treatment) and every 2 hours after. The products were used for 90 consecutive days.

Clinical evaluations, colorimetric measurements, and participant-reported quality-of-life assessments were performed at visits D0 (initial), D30 (intermediate), D90 (final product-use visit), and D120 (1-month post-treatment).

Dermatological evaluations were performed by a board-certified dermatologist and included a safety assessment and the determination of the modified Melasma Area and Severity Score (mMASI), as previously described and validated.¹⁹

Colorimetry was assessed by determining the L* parameter (luminosity) and ITA (Individual Typology Angle) in the skin affected by melasma at each visit, using the CR-400 Chroma Meter (Konica Minolta).

Colorimetry can quantify the intensity of erythema and skin pigmentation. The colorimeter makes it possible to quickly and non-invasively measure skin color, based on the L*a*b* coordinate system, established by Commission Internationale de l'Éclairage (CIE). It is determined using a polychromatic xenon arc lamp, which provides illumination to the skin, and 6 high-sensitivity silicone photocells, 3 of which monitor the light produced by the lamp, while the others measure the light reflected by the sample. A pulse of visible light is emitted from the source onto the surface of the skin, and the reflected light is analyzed by a single optical system connected to a microprocessor, which calculates the result.²⁰

The L*a*b* system is the most widely used tool to quantify the color of the skin's surface. The L* measurement runs on a scale that ranges from black to white, with values ranging from 0 to 100, respectively. The a* coordinate represents color values ranging from green (negative values) to red (positive values), and the b* coordinate represents color values ranging from blue (negative) to yellow (positive). The L* coordinate (luminosity) correlates with the melanin index.²⁰

ITA (Individual Typology Angle), determined by the equation $ITA^\circ = [\text{Arc Tangent } ((L^* - 50) / b^*)] 180 / 3.14159$ and expressed in Radians, represents the skin tone and correlates well with skin pigmentation.²⁰

At each visit, the participants were instructed to fill out the Melasma Quality of Life Scale (MELASQOL), a validated quality-of-life questionnaire.²¹

The primary outcome was to assess the noninferiority of serum QC compared to HQ4 for the treatment of facial melasma, considering the change in mMASI as the endpoint after 90 days (D90) of use and 30 days after treatment discontinuation (D120).

Secondary endpoints were the change in colorimetric parameters (ITA and L*) and quality of life as measured by the MELASQOL questionnaire.

The Shapiro-Wilk normality test was used to determine the normality of the data. If the hypothesis of normality was not rejected, Student's t-test for paired data was used to compare experimental times and Student's t-test for independent samples was used to compare treatments.

When normality is rejected, the Wilcoxon test for paired data was used to compare experimental times. Results were considered statistically significant at the 5% significance level ($P \leq 0.05$).

RESULTS

Of the 80 participants previously randomized, 58 completed the study: 30 participants in group I and 28 participants in group II.

Twenty-one participants withdrew and were excluded due to loss to follow-up. One participant withdrew from the study at visit D30 for personal reasons unrelated to the study,

and one participant was excluded from the study because her treatment compliance was below 80%, which was one of the exclusion criteria. The higher-than-expected attrition rate was mainly related to the long follow-up period and strict visit schedule, which can often limit adherence in cosmetic studies, rather than to treatment-related adverse events.

The study flowchart, according to CONSORT 2010, is presented in **Figure 1**.

Regarding safety, non-serious adverse events were observed in volunteers treated with both serum QC and HQ4. The events were considered mild, consisting primarily of burning and stinging, compatible with irritant dermatitis, and resolved despite continued treatment.

Regarding efficacy, the results of the predefined outcomes are presented below:

A – Clinical Evaluation (mMASI)

The results and the change (reduction) in mMASI from D0 to D30, D90, and D120 are presented in **table 2**.

The 2 groups showed a statistically significant reduction in mMASI at all visits compared to the initial visit. These results demonstrate the efficacy of both treatments in reducing the clinical signs of melasma during the 90-day treatment period and the 30-day post-treatment period.

Notably, at D30, the serum QC group showed a greater relative reduction in mMASI (-10.43%) compared with HQ4 (-2.65%). Although the difference was not statistically significant, there was a trend toward a faster initial response with the serum. Further investigation is needed to confirm this potential benefit.

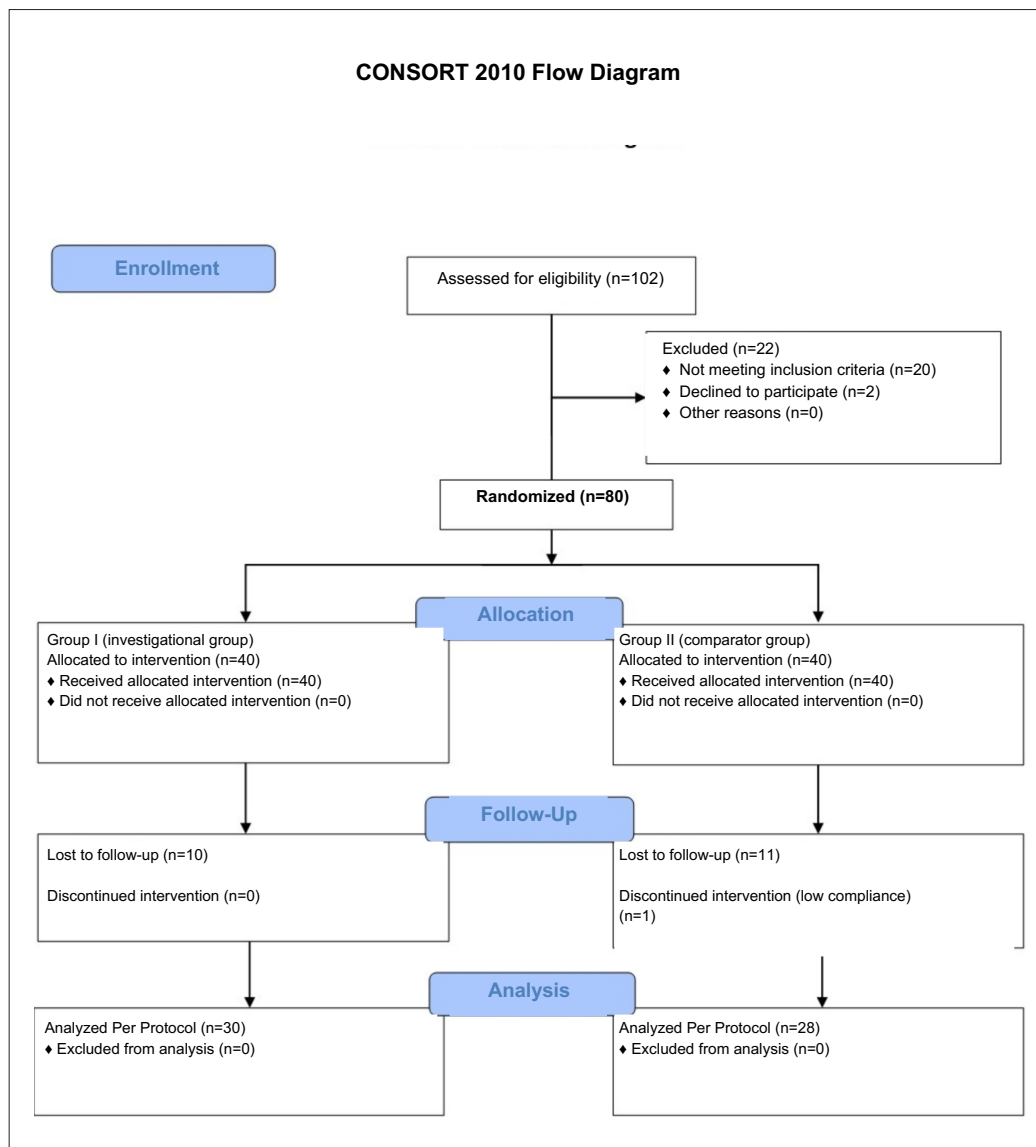


FIGURE 1: CONSORT flow diagram

The Mann-Whitney test was applied to compare changes over time between the 2 groups. Compared to D0, no statistically significant difference between serum QC and HQ4 was observed at any visit ($p > 0.05$), indicating noninferiority of serum QC compared with HQ4% for the assessment of mMASI.

Although the study was not originally powered or designed to establish a formal noninferiority margin, the absence of statistically significant differences across all endpoints suggests the comparable efficacy of both treatments.

B - Individual Typology Angle (ITA)

The results and the change (increase) in ITA from D0 to D30, D90, and D120 are presented in [table 3](#).

The results presented in table 3 showed that both treatments were effective in increasing the ITA and thereby reducing the intensity of melasma pigmentation. Both treatments showed statistically significant changes when comparing D30, D90 and D120 with the initial visit. Notably, the effect of the serum in increasing ITA was stronger at D30 (27.36%) than that of HQ4%

(20.25%), suggesting a faster initial response in line with that observed for mMASI.

Surprisingly, after treatment discontinuation, there was a continuous increase in ITA, particularly for the serum QC group (Δ ITA D120 vs D90: 0.9 for serum QC vs -0.8 for HQ4%), demonstrating a residual effect even after discontinuation. Analysis of Δ ITA between the lesion and perilesional healthy skin (data not shown) found progressive improvements in pigmentation uniformity for both treatments, with the serum QC group achieving a cumulative reduction of 56.25% at D120 compared to 50.00% for HQ4. Although the difference between groups was not statistically significant, the sustained reduction observed in the serum group suggests consistent and lasting efficacy in improving skin tone uniformity.

There was no statistically significant difference (Mann-Whitney test; $p < 0.05$) in the variation of ITA between both groups, suggesting equivalent efficacy of the treatments in reducing the intensity of pigmentation in melasma lesions.

TABLE 1: Clinical and demographic data of participants (n = 58)

Parameters	Group I (Serum QC)	Group II (HQ4%)
Age	35-39	1 (3.33%)
	40-49	12 (40.00%)
	50-59	12 (40.00%)
	60+	5 (16.67%)
Phototype	I	0 (0.00%)
	II	0 (0.00%)
	III	8 (26.67%)
	IV	18 (60.00%)
	V	4 (13.33%)
	VI	0 (0.00%)
mMASI, median (quartiles) at D0	8.15 (6.4 - 10.8)	7.55 (3.95 - 11.15)
L*, median (quartiles) at D0	51.8 (48.1; 54.3)	51.1 (47.7; 55.4)
ITA, median (quartiles) at D0	2.96 (-3.04; 4.04)	2.37 (-3.49; 3.96)
MELASQOL, median (quartiles) at D0	48.3 (13.1)	46.5 (16.6)

Table 2. Intra-group comparison of D30, D90, and D120 with D0 for groups I (Serum QC) and II (HQ4). n=58. Data presented as median and quartiles

	Group I (Serum QC)	Group II (HQ4)
mMASI	% reduction compared to D0 mMASI	% reduction compared to D0
D0	8.15 (6.4 - 10.8) -	7.55 (3.95 - 11.15) -
D30	7.30 (5.2 - 10.5) -10.43%*	7.35 (3.5 - 10.2) -2.65%*
D90	5.95 (4 - 9.6) -26.99%*	4.90 (2.8 - 6.85) -35.10%*
D120	4.95 (3.4 - 8.3) -39.26%*	3.45 (2.2 - 5.55) -54.30%*

* ($p < 0.05$) Wilcoxon test Comparison between Dx and D0

TABLE 3: Intra-group comparison of D30, D90, and D120 with D0 for groups I and II. n=58. Data presented as median and quartiles

	Group I (Serum QC)	Group II (HQ4%)
	Median ITAo (radians) % increase compared with D0 ITAo (radians)	% increase compared with D0
D0	2.96 (-3.04; 4.04) -	2.37 (-3.49; 3.96) -
D30	3.77 (-2.86; 4.23) 27.36%*	2.85 (-1.63; 4.37) 20.25%*
D90	3.56 (-0.24; 4.3) 20.27%*	3.92 (0.82; 4.27) 65.40%*
D120	3.98 (2.15; 4.45) 34.46%*	3.85 (-0.39; 4.20) 62.45%*

* (p<0.05) Wilcoxon test Comparison between Dx and D0

C – Luminosity (L*)

The results and the change (increase) in L* parameter (luminosity) from D0 to D30, D90, and D120 are presented in [table 4](#).

There was a significant increase in the luminosity of the melasma lesions during and after treatments in both groups. As observed with ITA, the increase in the L* parameter persists even after treatment discontinuation.

There was no statistically significant difference (Mann-Whitney test; p<0.05) in the variation in L* between the 2 groups, highlighting the comparable efficacy of both regimens in lightening melasma lesions.

D – MELASQOL

The results of the questionnaires completed by the volunteers to assess quality of life of patients with melasma (MELASQOL) are shown in [Table 5](#).

The results demonstrated a statistically significant reduction in the MELASQOL scores in both groups at all visits. These results reflect participant self-perception of improvement in quality of life related to melasma.

There was no statistically significant difference (Mann-Whitney test; p<0.05) in variation in MELASQOL between the 2 groups, suggesting that both treatments were well perceived by participants in terms of reducing the impact of melasma on quality of life.

DISCUSSION

The results show noninferiority in clinical, colorimetric and quality-of-life outcomes in volunteers treated with the new depigmenting combination (QC), containing 3% tranexamic acid, 4.5% niacinamide, 0.3% 4-butylresorcinol, and a hydroxy acid complex containing 5% gluconolactone, 4% phytic acid, and 1.5% mandelic acid, compared with the gold-standard treatment, 4% hydroquinone. First, mMASI was evaluated as the primary endpoint, showing a significant reduction (p < 0.05) of 10.43% after 30 days of treatment with the new combination, which continued to improve over 90 days (26.99%) and even after 30 days of treatment discontinuation (39.26%). Notably, the effect of serum QC was stronger than that of HQ4 at this point in time. The residual effect of serum QC after discontinuation is noteworthy, suggesting continued activity of the depigmenting agents in the epidermis. Compared with HQ4, there was no statistically significant difference in mMASI, indicating comparable efficacy between the investigational product and HQ4%.

As the study was not powered for a formal noninferiority design, this statement should be interpreted as comparable efficacy rather than strict statistical noninferiority. In the colorimetric evaluations, the results followed the same trend, with a significant improvement observed after 30 days of treatment and positive evolution at subsequent visits, with residual activity after discontinuation.

TABLE 4: Intra-group comparison of D30, D90, and D120 with D0 for groups I and II. n=58. Data presented as median and quartiles

	Group I (Serum QC)	Group II (HQ4)
	L* % increase compared with D0	L* % increase compared with D0
D0	51.8 (48.1; 54.3) -	51.1 (47.7; 55.4) -
D30	54.0 (48.6; 55.4) 4.25%*	51.7 (49.4; 56.1) 1.17%*
D90	53.0 (49.9; 56.9) 2.32%*	54.9 (50.3; 58.1) 7.44%*
D120	53.9 (50.8; 59.2) 4.05%*	54.1 (49.8; 56.5) 5.87%*

* (p<0.05) Wilcoxon test Comparison between Dx and D0

TABLE 5: Intra-group comparison of D30, D90, and D120 with D0 for groups I and II. n=58.
Data presented as median and quartiles

	Group I (Serum QC)	Group II (HQ4)
	MELASQOL % reduction compared with D0	MELASQOL % reduction compared with D0
D0	48.3 (13.1) -	46.5 (16.6) -
D30	38.7 (16.8) -19.88%*	34.9 (17.1) -24.95%*
D90	32.7 (17) -32.30%*	31.5 (18)-32.26%*
D120	35.1 (17.9) -27.33%*	32.8 (19.3) -29.46%*

* (p<0.05) Wilcoxon test Comparison between Dx and D0

The lack of statistically significant differences between groups supports the comparable efficacy of serum QC and HQ4. In addition, serum QC demonstrated sustained improvement, with significant residual effects in mMASI, ITA, and L* after treatment discontinuation, highlighting its potential as a long-term, well-tolerated alternative.

The MELASQOL assessment was consistent with the previous findings, with significant improvement from the initial visit through 90 days. The 2 groups evolved in a similar fashion, and no statistically significant difference was observed between them.

Mild symptoms of burning and stinging, compatible with irritant dermatitis, were reported with both serum QC and HQ4. These clinical manifestations have been widely reported in patients treated with hydroquinone. With respect to the investigational product, the symptoms may be related to the presence of the hydroxy acid complex, whose keratolytic action may affect the integrity of the skin barrier and produce the symptoms described.

Previous publications comparing products containing niacinamide and other depigmenting ingredients have found similar results, with a reduction in mMASI of around 30% at 16 weeks,¹ an improvement achieved at 12 weeks of treatment in the present study. Considering these studies, the results of the present study showed a faster activity of the QC.

Compared with the previous study conducted with the same product, some differences in the results were observed. mMASI showed a greater reduction in the previous study after 90 days of treatment (63%) compared with the results found in the present study (27%). This difference may be related to the differences in populations evaluated (Brazilians vs. Portuguese

participants) and possibly to the time of year when the studies were conducted. As is well documented, melasma tends to worsen after sun exposure, even with sunscreen use. The other parameters cannot be directly compared between the studies.

From a clinical point of view, the possibility of using a topical treatment with the efficacy comparable to that of 4% hydroquinone but with a faster onset of action is highly attractive for dermatologists and their patients alike.

This study has some limitations. It was conducted at a single center with a relatively small sample size, which may limit the generalizability of the results. The attrition rate was higher than ideal, mainly related to the long follow-up period and visit schedule rather than treatment-related events. In addition, no prespecified noninferiority margin was defined, and the study was not statistically powered for a formal noninferiority analysis. Nevertheless, the randomized, double-blind design and the consistency of results across all endpoints support the robustness of the findings. Future multicenter studies with larger and more diverse populations are warranted to confirm and expand these results.

CONCLUSION

The depigmenting serum containing tranexamic acid, niacinamide, 4-butylresorcinol, and hydroxy acids was effective in reducing clinical and colorimetric parameters and improving the quality of life in patients with melasma after 12 weeks of treatment. Its efficacy was comparable to that of 4% hydroquinone while also demonstrating a faster initial depigmenting effect and a residual benefit after treatment discontinuation. These findings support serum QC as a safe and effective alternative for the management of melasma. ●

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