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Effects of CE Ferulic[®] Combined with Microneedling in the Treatment of Pigmentary Disorders: A Monocentric, Split Face, Comparative Study

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Abstract: Pigmentary disorders of the face present a significant challenge in dermatology, impacting the confidence and well-being of affected individuals. Various approaches have been developed to address these concerns, including microneedling and topical vitamin C products. This study involved 15 participants undergoing three treatment sessions over 12 weeks, assessing the efficacy of a combined microneedling and CE Ferulic[®] serum approach. Clinical evaluation and statistical analysis were conducted before and after the intervention. Significant improvement of akin hyperpigmentation was observed, particularly on the side treated with microneedling and CE Ferulic[®] serum compared to microneedling alone. The integrated treatment protocol demonstrated a synergistic effect in improving skin texture and appearance. Integrated treatment protocols, such as combining microneedling with CE Ferulic[®] serum, show promise in managing facial hyperpigmentation disorders. Further research with larger cohorts is warranted to validate these findings and optimize treatment strategies, highlighting the potential of combined therapeutic modalities for achieving optimal clinical outcomes in pigmentary disorder management.

Keywords: microneedling; vitamin C; hyperpigmentation; aesthetic medicine



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1. Introduction

Pigmentary disorders of the face represent a significant challenge in dermatology, particularly among patients seeking facial aesthetic consultations [1]. These conditions, characterized by uneven skin tone, dark patches, and diminished skin quality, significantly impact the confidence and well-being of affected individuals [2]. Various approaches have been developed to address these concerns, including microneedling and topical vitamin C products.

Hyperpigmentation, the darkening or increase in the natural color of the skin, primarily results from increased melanin deposition in the epidermis and/or dermis. Less commonly, it may be caused by the deposition of endogenous or exogenous pigments in the dermis [3,4]. Drug-induced facial hyperpigmentation results from the use of certain medications, including antibiotics, antimalarials, antiepileptics, and chemotherapeutics. The underlying mechanism often involves stimulation of melanocytes, which produce melanin, either by the drug/metabolites or by deposition of the drug in the skin, exacerbated by sunlight. Additionally, some drugs may trigger photosensitive reactions, further contributing to pigmentation changes [5].

Acquired benign hyperpigmentary disorders encompass a wide spectrum of diseases such as lentigo, melasma, and post-inflammatory hyperpigmentation (PIH). Each disorder is heterogeneous, necessitating personalized treatment approaches tailored to individual patient needs. Additionally, patients often present with various types of pigmentary lesions in combination.

Sun exposure is a leading cause of hyperpigmentation, stimulating melanin production to protect the skin from UV damage [5]. In post-inflammatory hyperpigmentation, inflammatory mediators trigger melanocyte activity, leading to increased melanin production following skin inflammation [6]. Management strategies for hyperpigmentary disorders include topical agents, chemical peels, laser- and light-based devices, and oral agents. In case of melasma, the precise cause remains unclear, although factors such as sun exposure, hormonal fluctuations, and genetic predisposition are recognized to play contributory roles [7].

Microneedling, also known as collagen induction therapy, has emerged as a promising therapeutic option [8,9]. The SkinPen[®] is a medical-grade device equipped with fine needles that create controlled micro-injuries in the skin's surface, stimulating collagen production and promoting skin rejuvenation. It is commonly used to address various skin concerns, including fine lines, wrinkles, acne scars, enlarged pores, and uneven skin texture. Breaking down the excess of melanin deposition leads to overall improvement in skin tone and appearance [10].

The micro-injuries created during the treatment stimulate the skin's natural wound healing processes, leading to several effects in the tissue:

- Promotion of collagen (initially type I with its subsequent replacement with type III) and elastin production—essential proteins for maintaining skin structure and elasticity.
- Enhancement of the absorption of skincare products by creating temporary micro-channels in the skin, allowing for better penetration.
- Triggering the skin's natural repair mechanisms, leading to increased cell turnover, shedding old, pigmented cells with subsequent regeneration of newer, healthier cells. This process results in a more even skin tone.
- Restoration of normal pigment activity of melanocytes in hyperpigmented areas.
- Topical vitamin C products have gained attention for their potential role in managing pigmentary disorders [11,12]. Vitamin C, a potent antioxidant, is known for its skin-brightening and photoprotective properties. Among available products, CE Ferulic[®] stands out as a viable option for patients facing hyperpigmentation disorders. It contains a combination of vitamin C (ascorbic acid), vitamin E, and ferulic acid, synergistically working to neutralize free radicals, reduce oxidative damage, and improve skin texture and tone.
- Vitamin C, a powerful antioxidant, brightens the skin, promotes collagen synthesis, and protects against UV-induced photodamage.
- Vitamin E works in tandem with vitamin C to amplify its antioxidant effects, providing additional protection against environmental stressors.
- Ferulic acid, a plant-derived antioxidant, further enhances the stability and efficacy of vitamins C and E, while also exhibiting anti-inflammatory properties.
- Moreover, these ingredients, fulfill the antioxidant gold standard (Duke) criteria: presence of pure L-ascorbic acid, pH < 3.5, optimal concentration between 10 and 20%.

The literature provides evidence supporting the therapeutic potential of combined methods in treating pigmentary disorders, including the use of tranexamic acid, vitamin C, or ferulic acid in conjunction with microneedling and laser therapies. These innovative approaches offer a fresh outlook on treating patients with such conditions [12–14].

Encouraged by the promising results of studies conducted by colleagues that proved the positive impact of vitamin C and ferulic acid on skin hyperpigmentation, we decided to use a combination of both ingredients along with microneedling and investigate their effects on patients with facial pigmentation issues. The research was conducted as a single-center, prospective, quasi-experimental comparative split-face investigation from March

2023 to June 2023. Secondary objectives included assessing the treatment's impact on skin quality and long-term effectiveness. Fifteen preselected participants took part in the study. Preliminary findings showed promising results, suggesting the potential efficacy of the proposed combined treatment approach.

2. Materials and Methods

This research comprised a single-center, prospective, quasi-experimental comparative split-face investigation carried out at the Dermatological Ambulatory of Dr. Ilaria Proietti in Latina, within the province of Rome.

The study was conducted over the period spanning from March 2023 to June 2023, with patient assessments performed 12 weeks following the intervention. Our primary objective was to evaluate alterations in facial pigmentary disorders using a treatment protocol involving a microneedling treatment combined with CE Ferulic[®] serum (left, more photodamaged side of the face) compared to changes obtained by microneedling only (right side of the face). The secondary objectives included the assessment of the treatment's influence on other aspects of skin quality, such as wrinkles, skin roughness, sensitivity and hypervascularity, as well as the long-term effectiveness of this approach.

The study group comprised 15 participants, consisting of one male and 14 females aged between 18 and 72 years, with a median age of 50 years. These individuals represented a range of skin phototypes classified as falling within categories II to V according to the Fitzpatrick Skin Phototype Classification. We assessed facial wrinkles and the extent of photoaging using standardized scales (the modified Griffiths Photonumeric Scale) before and after the intervention. The assessed features comprised uneven skin texture, overall wrinkles, fine lines, excess pigmentation, diminished skin elasticity, firmness, radiance, and uneven skin tone. Each of these aspects was evaluated on a scale ranging from 1 to 10, leading to the calculation of the final Griffiths score, where a score of 10 indicated the highest degree of skin aging.

The inclusion criteria encompassed age above 18 years; expression of informed, written consent to participate in the study; participants with clinically diagnosed facial hyperpigmentation conditions, such as melasma, post-inflammatory hyperpigmentation, or solar lentigines.

Participants who met any of the following exclusion criteria were not included: presence of chronic or acute inflammation or infection in the treated area; known hypersensitivity to any of the components utilized in the study; pregnancy or lactation; tendency to keloid formation; history of severe allergies or anaphylactic reactions.

This study adhered strictly to ethical guidelines as outlined in the Declaration of Helsinki, ensuring the safety, rights, and well-being of every participant. Prior to treatment, all subjects underwent comprehensive clinical evaluations by a specialist, and written as well as verbal informed consent were obtained from each patient.

2.1. Technical Procedures

Following an initial patient evaluation and a comprehensive discussion of the potential risks associated with each procedure, the subsequent protocol was consistently implemented for all interventions. The treatment regimen commenced with the performance of microneedling on the whole face using the SkinPen[®] device (by Crown Aesthetics, Dallas, TX, USA), with simultaneous application of CE Ferulic[®] (SkinCeuticals Inc., New York, NY, USA) serum only on the left side of the face. The patients underwent three treatment sessions according to the study protocol: at baseline (time 0), after 4 weeks, and subsequently after 8 weeks. In between the sessions, patients were recommended to follow a home skin routine which consisted of daily application of 4–5 drops of CE Ferulic[®] on the left side of the face; moisturizer, and 50 + SPF sunscreen on the whole face.

Preceding each procedure, the targeted skin area underwent thorough antisepsis using 0.5% alcoholic chlorhexidine. Subsequently, a local anesthetic cream, containing 5% lidocaine, was applied to the treatment site, with a 30 min interval before the proce-

dure's initiation. This anesthetic cream was completely removed immediately prior to the commencement of the treatment.

SkinPen[®] Treatment

A meticulous clinical assessment was conducted to precisely determine the grade and extension of concerning skin problems. The dermaroller has 192 medical stainless-steel microneedles with a width of 2 cm, needle length of 1.5 mm and diameter of 0.25 mm. Full-face treatment was performed on each patient involving different depths of needle penetration, varying from 0.25 mm or 0.5 mm until desired erythema was reached, with gradual incrementation to a maximum depth of 1.5 mm, under the discretion of the experienced physician. On average, approximately 3 passages were delivered in the cheek and chin areas, and 2 passages in the frontal area in each session, following vertical, horizontal, and diagonal directions. In total, 5 drops of CE Ferulic[®] was applied on the right side of the face. CE Ferulic[®] (SkinCeuticals Inc., New York, NY, USA) is a combination serum containing 15% L-Ascorbic Acid (Vitamin C), 1% α -tocopherol (Vitamin E), and 0.5% Ferulic Acid. On the left half of the face, no product was applied.

2.2. Data Collection

In this study, a certified dermatologist was enlisted to compile data and evaluate each patient. Patients were evaluated clinically at baseline visit and after 12 weeks. During the baseline visit, the following data points were recorded:

- Patient's age
- Gender
- Phototype classification based on the Fitzpatrick scale
- At baseline visit and at the visit after 12 weeks, the following data were collected.
- Clinical evaluation of main skin problems, laxity, wrinkles on each side of the face according to the Griffiths Photonumeric Scale
- Acquisition of 3D images using the VECTRA[®] M3 system
- Acquisition of morphometric images using the OBERV 520x (Sylton, Esp 266, 5633 AC, Eindhoven, The Netherlands)

During each follow-up visit, participants were queried about any adverse events.

2.3. Statistical Analysis

Demographic and clinical characteristics were expressed as median and interquartile range (IQR) for continuous variables and as counts and percentages for categorical variables. To evaluate the effect of treatment with CE Ferulic[®] combined with microneedling, a mixed-effects ordinal logistic regression model was fitted. The model considered, as dependent variable, the Griffiths score measured for the left and the right side of the face at the baseline visit and after 12 weeks. The model included side, visit, and side-by-visit interaction as fixed effects, and subject as a random effect. All analyses were performed using R software (version 4.0.2).

3. Results

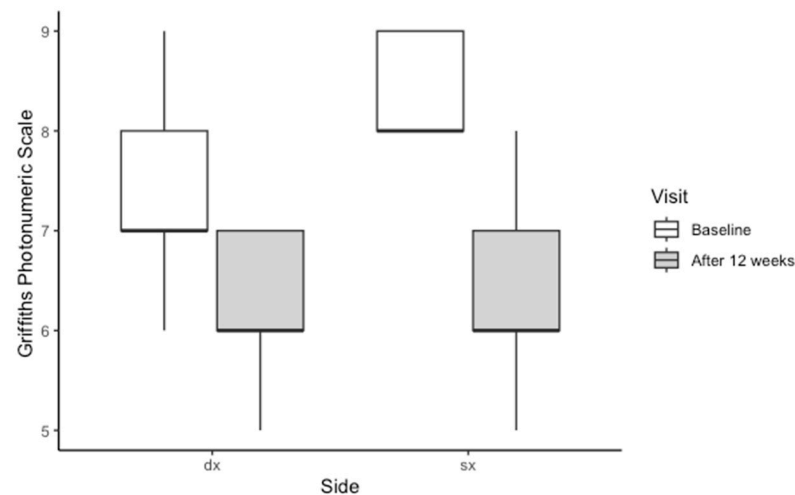
Our research involved the participation of 15 individuals (14 (93.3%) females) with ages ranging from 18 to 72 years, with a median age of 50 years (IQR: 47–57 years). None of the participants had a significant medical history of note. Subsequent review of their characteristics identified 6 menopausal patients, with half of them receiving hormone replacement therapy (HRT). Although we have noticed the trend of more severe-grade hyperpigmentation in patients with HRT, the small sample number made it difficult to evaluate its impact on treatment response.

The remaining evaluated baseline parameters are presented in Table 1.

Table 1. Baseline clinical evaluation parameters.

Age (Median [IQR])		50.00 [47.00, 57.00]
Sex (%)	Female	14 (93.30)
	Male	1 (6.7)
Phototype (%)	2	4 (26.7)
	3	5 (33.3)
	4	3 (20.0)
	5	3 (20.0)
Skin problem (%)	Photodamage	3 (20.0)
	Melasma	8 (53.3)
	Rosacea	4 (26.7)

The boxplot (Figure 1) shows that the baseline Griffiths Photonumeric Scale score was higher on the left side than on the right. At 12 weeks, the score decreased on both sides, and this decrease was greater on the left side (reaching the same Griffiths score as the right side, despite being higher before the treatment).

**Figure 1.** Boxplot containing median values (horizontal line), interquartile range (box length), highest and smallest values without outliers (whiskers) of the Griffiths Photonumeric Scale per group (Side) at each visit (baseline, after 12 weeks).

The results of the mixed-effects ordinal logistic regression model are shown in Table 2. The model shows the effect of the interaction between the visit and the side. The reference was represented by right side and baseline visit (week 0). The model shows that at the baseline visit, the left side was more likely to have a higher Griffiths score ($\beta_1 = 3.59$; 95% CI: 1.64; 6.58). At the visit after 12 weeks, the right side was more likely to have low score values ($\beta_2 = -2.18$, 95% CI: -3.79 ; -0.73).

Table 2. Mixed-effects ordinal logistic regression model.

Variable	β	95% Confidence Interval
Side sx	3.59	1.64; 6.58
At visit after 12 weeks	-2.18	-3.79; -0.73
Side sx* at visit after 12 weeks	-3.92	-7.16; -1.55

At the visit after 12 weeks, the score values for the left side had a magnitude similar to that at the baseline visit, but with the opposite sign, indicating that low score values were more likely ($\beta_3 = -3.92$; 95% CI: -7.16 ; -1.55).

Moreover, both 3D images (VECTRA® M3) and morphometric pictures (OBERV 520x) captured during the study revealed significant improvement of skin characteristics in all 15 patients; Figures 2, 3 and 4A,B illustrate representative examples.

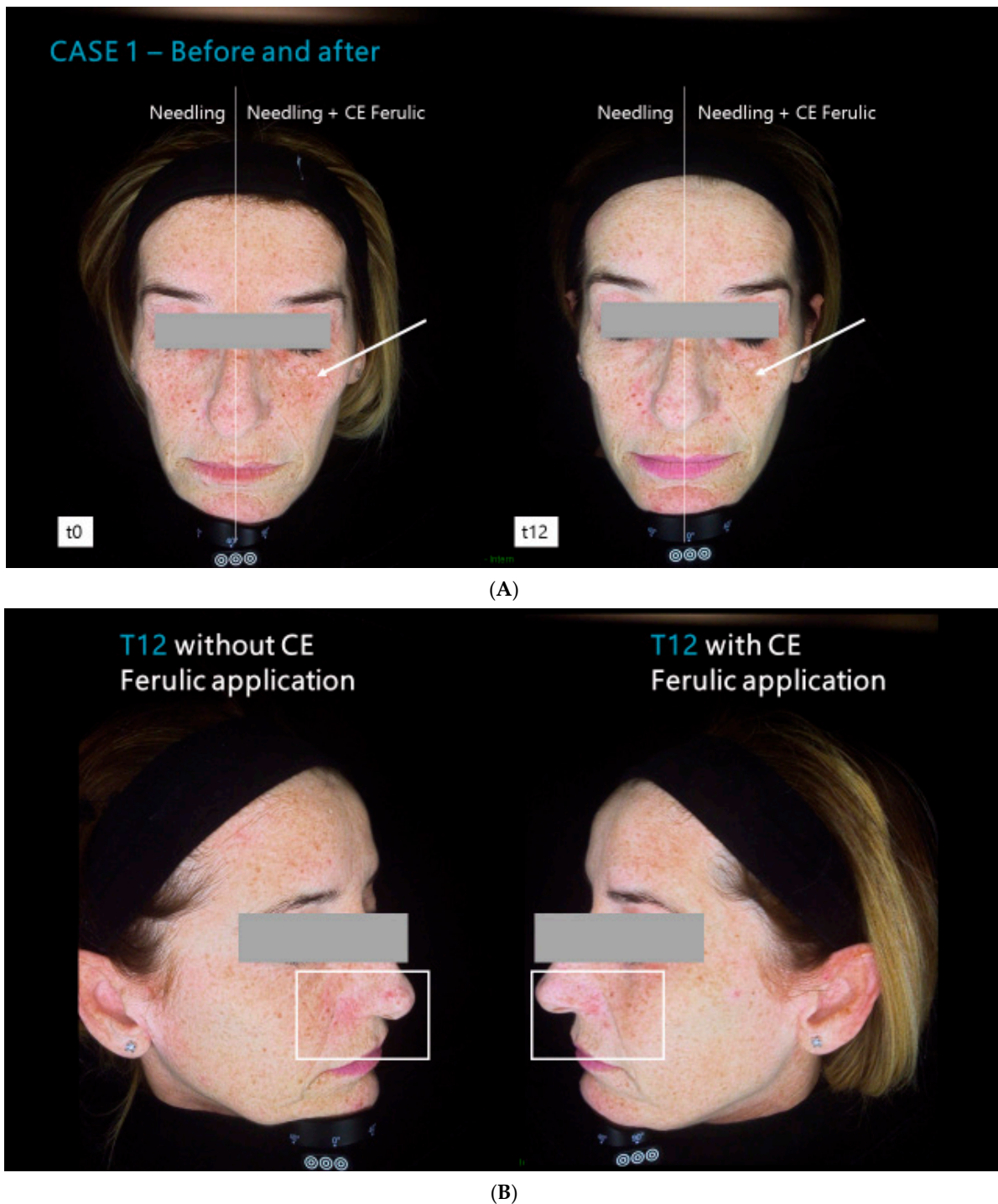
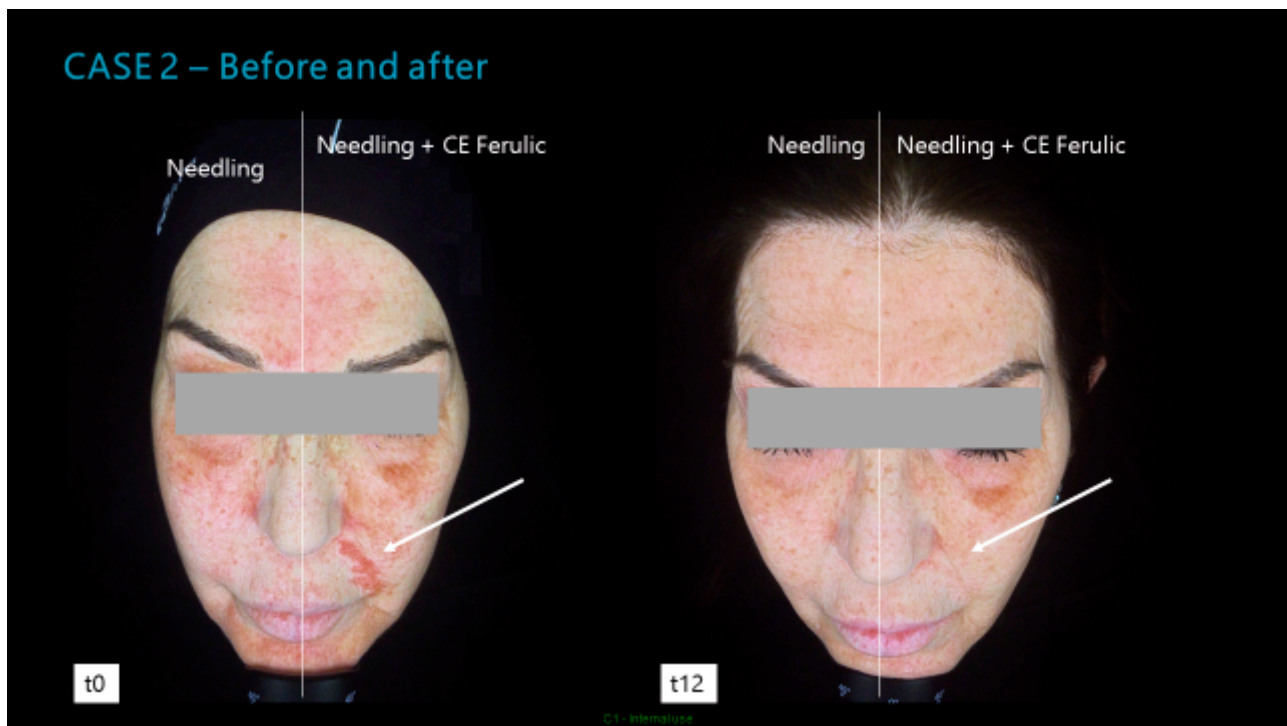
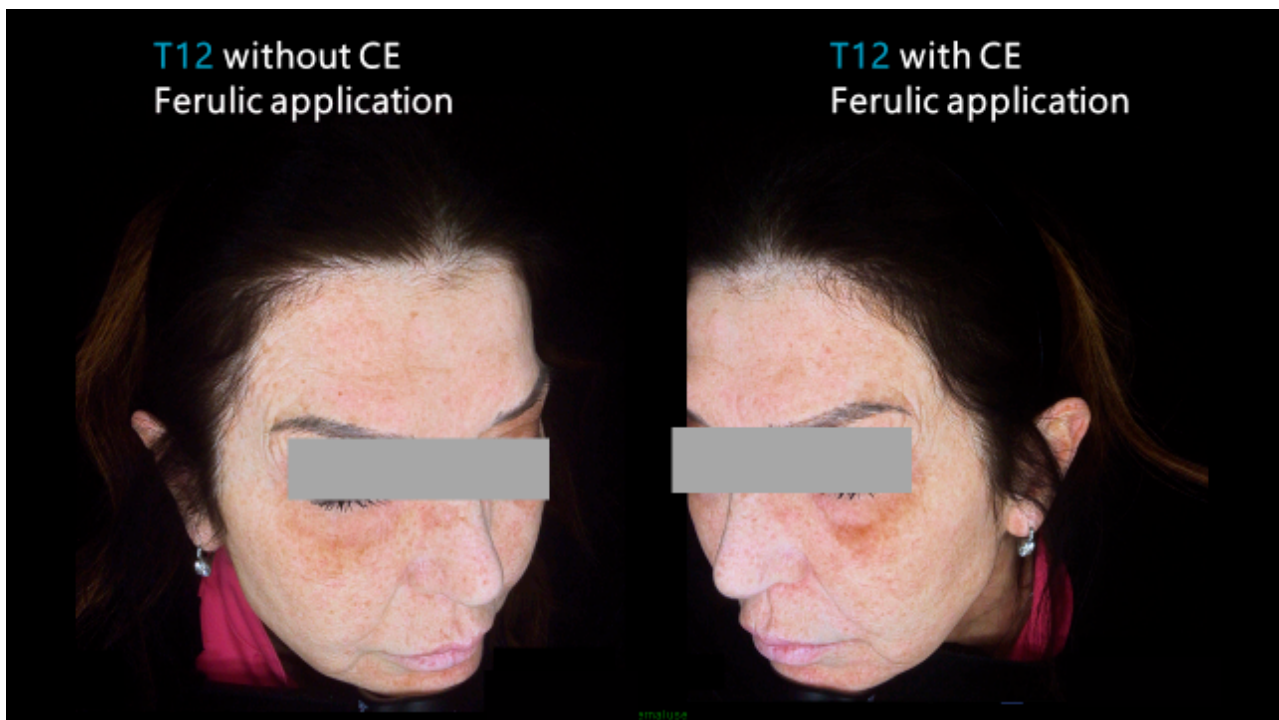


Figure 2. Case 1. Female patient, 49 years old. Morphometric pictures (OBERV 520x). (A) Pictures captured at baseline visit and after 12 weeks, showing marked improvement of hyperpigmentation and redness. (B) Pictures comparing left and right sides of patient's face, showing more improvement of skin quality on the side with microneedling and CE Ferulic application compared to the side with microneedling treatment only.

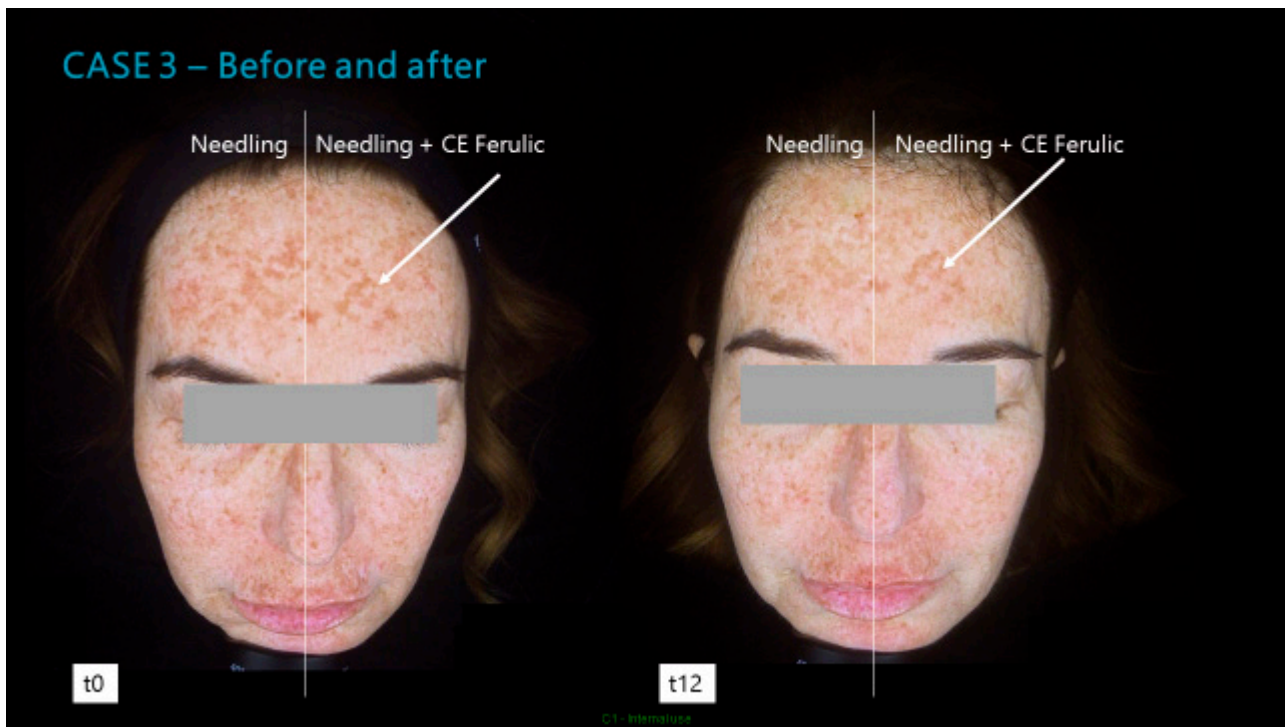


(A)

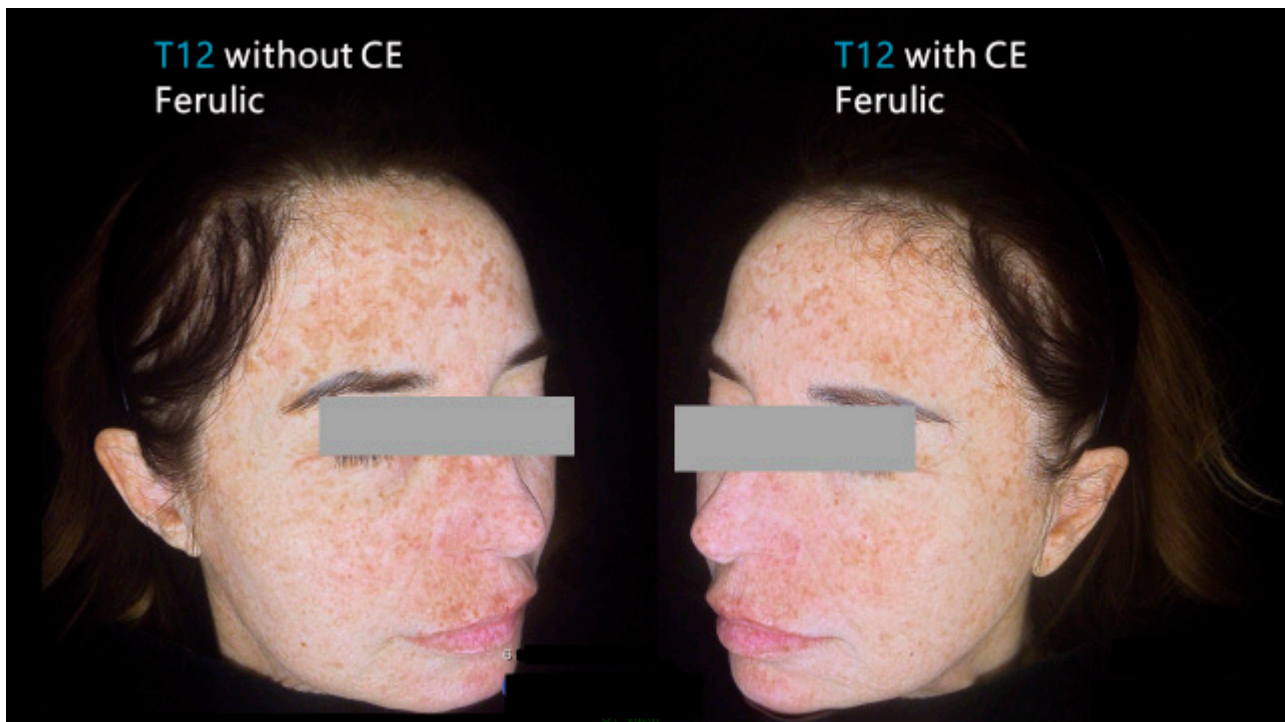


(B)

Figure 3. Case 2. Female patient, 53 years old. (A) Pictures captured at baseline visit and after 12 weeks, showing marked improvement of hyperpigmentation and redness. (B) Pictures comparing left and right sides of patient's face, showing the skin quality on the side with microneedling and CE Ferulic application compared to the side with microneedling treatment only.



(A)



(B)

Figure 4. Case 3. Female patient, 52 years old. (A) Pictures captured at baseline visit and after 12 weeks, showing marked improvement of hyperpigmentation. (B) Pictures comparing left and right sides of patient's face, showing the skin quality on the side with microneedling and CE Ferulic application compared to the side with microneedling treatment only.

4. Discussion

Pigmentary disorders of the skin present a significant concern among patients seeking consultation from dermatologists and practitioners in aesthetic medicine. Among the most prevalent types of facial hyperpigmentation are ephelis, post-inflammatory hyperpigmentation (PIH), and melasma. Melasma, characterized by acquired hyperpigmentation, typically affects regions such as the forehead, cheeks, temples, and upper lip in a symmetrical pattern. It manifests more frequently in females and is often linked to factors such as pregnancy and oral contraceptive use, with sunlight exposure exacerbating its effects. The condition commonly involves both epidermal and dermal pigmentation [15,16]. Conversely, PIH denotes a reactive hypermelanosis following inflammatory stimuli such as skin conditions (e.g., rosacea, eczema, acne) or physical/chemical trauma (e.g., burns, irritative contact dermatitis). Unlike melasma, PIH lesions are irregular, asymmetrical, and may not necessarily occur in sun-exposed areas. Individuals with a darker Fitzpatrick phototype exhibit a heightened predisposition to PIH due to increased basal epidermal melanin levels. While PIH lacks a gender predilection, melasma is notably more prevalent in females owing to hormonal influences [17–21]. Histologically, both entities exhibit similar features, necessitating clinical-anamnestic correlation [19,20].

Despite their benign nature, these lesions significantly impact patients' quality of life. Studies have demonstrated how melasma can impair work productivity, social functioning, and self-esteem, leading to heightened personal distress and fear of negative evaluation. Consequently, individuals may experience anxiety, depression, and social withdrawal. Effective management of skin hyperpigmentation disorders not only addresses their pathological aspects but also alleviates the associated emotional distress, enhancing the well-being of affected individuals [1,22,23].

Ultraviolet radiation (UVR) assumes a central role in regulating skin pigmentation. UV exposure stimulates melanin synthesis within specialized ectodermal-derived cells called melanocytes [19,24]. Melanin, synthesized within melanosomes, is subsequently transferred to surrounding keratinocytes, imparting pigmentation and providing photoprotection against DNA damage [25]. Key components in the UVR-dependent melanogenesis pathway include melanocyte-stimulating hormone (MSH) and adrenocorticotrophic hormone (ACTH), derived from pro-opiomelanocortin (POMC) cleavage, along with their G-protein-coupled receptor, melanocortin 1 receptor (MC1R). The expression of POMC is closely associated with photoexposure, with UV-induced DNA damage triggering increased POMC expression, leading to α -MSH production. Binding of α -MSH to MC1R on melanocytes elevates cyclic AMP (cAMP) levels, initiating a cascade of events involving protein kinase A (PKA) activation, phosphorylation of cAMP-responsive element-binding protein (CREB), and upregulation of microphthalmia-associated transcription factor (MITF), which governs melanocyte survival and pigment production [26–28].

Ultraviolet radiation influences melanocyte proliferation, as well as the production and secretion of melanogenesis-stimulating factors. UVR-induced release of reactive oxygen species (ROS) in the skin can trigger melanogenesis, DNA damage, melanocyte proliferation, and apoptosis [29–31]. Endogenous and exogenous antioxidant agents (REDOXs) mitigate ROS-induced oxidative damage in the skin by inhibiting melanogenesis-stimulating second messengers and interacting with copper (Cu) in the tyrosinase active site or O-quinones to prevent oxidative melanin polymerization. REDOXs include L-Ascorbic Acid (vitamin C, AsA) and its stable ester Magnesium-L-Ascorbyl-2-Phosphate (MAP), Alpha Tocopherol (vitamin E, α -Toc), and its derivative Alpha Tocopherol Ferulate (α -TF). α -Toc, a lipophilic antioxidant found in grains, vegetables, vegetable oils, and nuts, inhibits lipid peroxidation of melanocyte membranes and scavenges free radicals. α -TF, an ester compound bond-linked to ferulic acid, stabilizes α -Toc. AsA, the most abundant water-soluble antioxidant in human skin, hinders melanin synthesis by interacting with Cu and scavenging ROS [32,33]. However, its hydrophilic nature limits skin penetration, necessitating the use of its stable ester, MAP, which enhances skin permeability and undergoes hydrolysis to release AsA within the skin [34–36].

Various therapeutic modalities have been explored for melasma and PIH management, encompassing topical medications, chemical peels, laser and light therapies, and dermabrasion (microneedling) [37–39].

Microneedling has emerged as a promising therapeutic approach for addressing hyperpigmentation associated with various dermatological conditions. Numerous studies have demonstrated its efficacy in ameliorating pigmentation irregularities, especially in individuals with darker skin phenotypes. This minimally invasive technique involves the controlled creation of micro-injuries in the skin using fine needles, thereby eliciting the skin's inherent healing mechanisms [8–10,12]. Clinical evaluations of microneedling's anti-aging effects have been conducted using animal skin models, individual human skin biopsies, and human 3D skin models [40–42]. These investigations have revealed an augmentation in collagen, elastin, and other extracellular matrix components, accompanied by alterations in growth factor expression. Moreover, microneedling facilitates the transcutaneous elimination of melanin and enhances the permeation of topical agents, thereby improving the delivery of depigmenting agents to targeted hyperpigmented areas. Mechanistically, microneedling induces the release of growth factors and cytokines, activating cellular signaling pathways implicated in the regulation of melanogenesis. Consequently, this modulation mitigates melanocyte activity, thereby reducing melanin production and transfer to keratinocytes, ultimately culminating in a more uniform complexion and diminished hyperpigmentation [8–10].

Previous studies conducted by colleagues have examined various possibilities of combined treatments for facial hyperpigmentation. For example, Kamila and Helena (2020) [12] demonstrated the potential of ferulic acid and microneedling in reducing signs of photoaging, highlighting their combined efficacy in improving skin texture and appearance. Similarly, Kim et al. (2020) [13] explored the impact of a topical antioxidant serum containing vitamin C, vitamin E, and ferulic acid following Q-switched 1064-nm Nd:YAG laser treatment for environment-induced skin pigmentation, suggesting a synergistic effect in enhancing the outcomes of laser therapy for addressing skin pigmentation concerns. Additionally, Tahoun et al. (2022) [14] conducted a comparative study evaluating tranexamic acid versus vitamin C, in conjunction with microneedling, for melasma treatment, offering insights into the efficacy of these modalities and their potential role in clinical practice. It is considered that combining different procedures yields additive and synergistic effects. Motivated by the encouraging outcomes of studies by colleagues, which demonstrated the beneficial effects of vitamin C and ferulic acid on skin hyperpigmentation, we opted to combine these ingredients with microneedling to explore their impact on patients with facial hyperpigmentation.

In our comprehensive investigation, we undertook a meticulous examination of the therapeutic efficacy of a novel treatment regimen combining CE Ferulic[®] serum with microneedling, utilizing the SkinPen[®] device. This innovative approach, not studied in previous publications, aimed to address a spectrum of pigmentary skin disorders encompassing hyperpigmentation and associated dermatological concerns.

The rationale behind our choice of CE Ferulic[®] serum lies in its formulation, which integrates potent depigmenting agents, including 15% L-Ascorbic Acid (Vitamin C), 1% α -tocopherol (Vitamin E), and 0.5% Ferulic Acid. These constituents have been widely recognized for their antioxidative and skin-rejuvenating properties, making them ideal candidates for synergistic integration with microneedling therapy [43–47].

Our study design involved the application of the combined CE Ferulic[®] serum and microneedling therapy to the left side of the face, while the right side served as a control, receiving microneedling alone. Each participant underwent a total of three treatment sessions, spaced 4 weeks apart, to allow for adequate evaluation of treatment efficacy and tolerability.

Baseline assessments were conducted before the initiation of therapy, comprehensively evaluating various parameters indicative of cutaneous health, including skin texture, wrinkles, fine lines, hyperpigmentation, elasticity, firmness, radiance, and tone. These

assessments, performed using a standardized grading scale ranging from 1 to 10, facilitated the calculation of the Griffiths score, a composite measure reflecting the overall degree of skin damage [48].

Statistical analyses revealed notable disparities in baseline characteristics between the left and right facial hemispheres, with the former exhibiting a higher degree of photodamage. The left side of the face typically exhibited more severe actinic damage in patients, often due to exposure to light while driving. Furthermore, a subset of participants presented with additional dermatological concerns, such as rosacea, sensitive skin, and acne scars, necessitating careful consideration during treatment planning.

Throughout the treatment course, participants reported minimal discomfort and tolerable side effects, primarily comprising transient erythema, tenderness, and edema, which typically resolved within 24 h post-treatment. Between sessions, patients were instructed to adhere to a prescribed skincare regimen, incorporating the application of CE Ferulic[®] serum and diligent sun protection measures to optimize treatment outcomes.

Following the completion of the treatment protocol, comprehensive post-treatment evaluations were conducted after 12 weeks, revealing significant improvements in all assessed parameters on both facial sides with reduction of the Griffiths score.

Key findings from our investigation included significant enhancements in hyperpigmentation, complexion uniformity, skin elasticity, and fine wrinkles, with notable improvements observed in other dermatological concerns such as rosacea and acne scars.

Notably, the left facial hemisphere, despite its initially higher degree of damage, demonstrated improvement comparable to that of the right side, underscoring the potent augmentative effect of CE Ferulic[®] serum on microneedling efficacy. Participant satisfaction with treatment outcomes was uniformly high, underscoring the clinical relevance and patient-reported benefits of the combined CE Ferulic[®] serum and microneedling approach.

Our study introduces several novel aspects and distinguishes itself from prior research, such as those conducted by Kamila MZ and Helena R, Kim J et al., and Tahoun AI et al. [12–14], by exploring the combined effects of CE Ferulic serum and microneedling on a broader spectrum of facial hyperpigmentation, rather than focusing solely on photoaging or melasma. Unlike the split-face comparative study by Kamila MZ and Helena R [12], which concentrated specifically on photoaging, our study evaluated the comprehensive impact of the treatment on various types of pigmentary disorders, offering a more generalized understanding of its efficacy across different conditions.

Additionally, while Kim J et al.'s [13] research examined the effects of a topical antioxidant serum post Q-switched 1064-nm Nd:YAG laser treatment specifically for environmentally induced pigmentation, our study investigated a non-laser approach using microneedling combined with antioxidants for broader types of hyperpigmentation, thus expanding the scope of application and demonstrating versatility in treatment modalities that do not involve laser interventions.

Furthermore, compared to the study by Tahoun AI et al. [14], which also looked into microneedling combined with Vitamin C in treating melasma, our research added a layer of complexity by including CE Ferulic serum and assessing its synergistic effect when used in tandem with microneedling. This provided deeper insight into the potential compounded benefits of these treatments. Our study is unique in its holistic approach to patient selection and treatment protocols, addressing a diverse patient demographic with varying underlying conditions, thus enhancing the real-world applicability of our findings.

Our findings contribute significantly to the current literature by demonstrating the safety and efficacy of combining microneedling with CE Ferulic serum in treating a variety of pigmentary issues. This study paves the way for future research to explore the long-term effects of these treatments and the potential synergies with other therapeutic modalities, aiming to optimize clinical outcomes and patient satisfaction. Through this comprehensive approach, we aim to establish a more robust foundation for the integrated treatment of pigmentary disorders, potentially setting a new standard for therapeutic strategies in dermatology.

Although our study showed promising outcomes, it was constrained by its small sample size, highlighting the need for further studies with larger cohorts to confirm these results and improve treatment approaches. The small sample size did not allow us to evaluate other important factors possibly influencing the response to treatment, such as menopause or HRT. These factors should be examined in a larger cohort of patients. Moreover, the patients had various conditions that responded positively to the treatment. The diversity of the sample and the lack of randomization in choosing the treatment side (microneedling and CE Ferulic[®] serum) were additional limitations. Despite these issues, our research contributes to the existing evidence of the effectiveness and safety of combining CE Ferulic[®] serum with microneedling therapy as an effective treatment for various pigmented skin conditions. Future research should investigate the long-term effectiveness of these treatments and the potential benefits of combining them with other therapies to maximize clinical outcomes and patient satisfaction.

5. Conclusions

In conclusion, skin pigmented disorders such as melasma and post-inflammatory hyperpigmentation (PIH) pose substantial challenges to patients and clinicians alike, impacting both physical appearance and psychological well-being, thereby affecting self-esteem and quality of life. Our study highlights the necessity of management approaches that tackle both the clinical and emotional aspects of these conditions.

The role of ultraviolet radiation (UVR) in melanogenesis is critical, as UV exposure initiates melanin production and melanocyte activity, emphasizing the need for sun protection to manage and prevent hyperpigmentation. Additionally, the role of oxidative stress suggests that antioxidants might help mitigate these disorders.

Microneedling has proven effective in improving skin texture, tone, and elasticity by promoting natural healing and collagen production, which helps remove melanin through the skin. Our research shows enhanced outcomes when microneedling is combined with CE Ferulic[®] serum and the SkinPen[®] device.

The results support the effectiveness and safety of combined treatments for hyperpigmentation, although more extensive research is necessary to refine these protocols and explore long-term effects and potential synergies with other therapies.

Ultimately, adopting innovative treatments based on a deep understanding of the pathophysiology of these disorders promises to improve patient outcomes and quality of life by providing comprehensive care that addresses both the physical and emotional impacts of hyperpigmentation.

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