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Dermatology Research

Melanyc: Powerful Depigmenting Agent With Action on the Epigenetics of Melasma

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Keywords

Pigmentary disorder, Pro-melanotic genes, Keratinocyte interactions.

Introduction

Melasma is a common acquired pigmentary disorder characterized by chronic and recurrent hypermelanosis in sun-exposed areas, associated with emotional and psychological stress [1]. The pathogenesis of melasma is highly complex and, although initially believed to be solely related to melanocytes, it is now understood that the disorder extends far beyond the pigmentary cells of the skin. It involves keratinocyte interactions, abnormal activation of melanocytes, accumulation of melanin and melanosomes in the epidermis, increased mast cell count, enhanced vascularization, damage to the basement membrane, alterations in the extracellular matrix, and photoaging [2].

Patients present with complex clinical and histological characteristics, suggesting the involvement of multiple pathogenic pathways. Transcriptional analysis of melasma-related skin lesions has shown that approximately 300 genes are differentially expressed in the affected skin and surrounding areas, highlighting the complexity of its etiopathogenesis [3,4].

Thus, treating melasma is extremely challenging due to its complexity and diverse etiology, often showing resistance and high recurrence rates. The essential factor in melasma treatment is photoprotection and the use of a multifactorial approach with appropriate maintenance therapy. The main objectives of melasma lightening treatment include inhibiting melanin production pathways, reducing melanosome transfer from melanocytes to keratinocytes, and promoting melanin removal pathways. An ideal approach should address various pathogenic mechanisms to achieve the best possible results [5]. Current treatments include topical application of various depigmenting agents, chemical peels, laser treatments, mesotherapy, microneedling, and the combination with systemic medications [6].

In recent decades, medications that act on epigenetics have been gaining ground in medicine—these are known as epigenetic drugs (epidrugs) [7]. Epigenetics is the study of chemical modifications to the genome that do not affect the DNA sequence. These modifications can be activated by environmental factors (e.g., sunlight) on the skin, causing cellular adaptations to long-term physiological changes. Increasingly, studies show that epigenetic mechanisms are involved in the regulation and aspects of epidermal growth and differentiation [8]. The primary epigenetic mechanism is DNA methylation, which involves transferring a methyl donor group to cytosine residues [9]. Dermatological disease studies show that epigenetic alterations in the epidermis contribute to their pathogenesis. Unlike genetic mutations, which are irreversible, epigenetic tools can be used for prevention, diagnosis, and therapy [10].

Although epigenetic alterations in melasma are not yet fully documented, changes have been observed in the micromorphology of basal keratinocytes (increased diameter, perimeter, and chromatin texture), likely associated with high DNA methylation levels that induce pro-inflammatory activity of pro-melanotic genes [11-13]. Thus, in this study, we evaluated the use of a new depigmenting agent that acts through an epigenetic mechanism to control the skin's response to environmental triggers of melasma.

Materials and Methods

We selected 30 female patients clinically diagnosed with treatment-resistant facial melasma for treatment with Melanyc. All patients had been without specific melasma treatment for at least 30 days, using only sunscreen. The treatment protocol consisted of four sessions of topical application of Melanyc MD (medical doctor)

cream (at 30-day intervals) and daily nighttime use of Melanyc HC (home care) topical cream for four months.

Evaluation was conducted using digital photography taken before the first session and thirty days after the last session. Photo comparisons were performed by two dermatologists blinded to the study to classify the treatment as showing improvement, no improvement, or worsening. The Melasma Area and Severity Index (MASI) was calculated before and after treatment. Additionally, patient satisfaction was assessed (satisfied/unsatisfied). Patients were instructed not to undergo any other topical or oral treatments for melasma at home, maintaining only sunscreen use. They were also advised to avoid sun exposure during treatment. All patients were followed up for 30 days after the last session.

Melanyc HC topical cream consists of: water, propylene glycol, liquid paraffin, cetearyl alcohol, pyruvic acid, Phyllantus emblica plant extract, arbutin, Vitis vinifera seed oil, glycyrrhetinic acid, phytic acid, ceteareth-12, butylene glycol, Arnica montana plant extract, Cupressus sempervirens seed extract, Polygonatum multiflorum extract, glycerin, hydrogenated lecithin, soybean oil glycine, oligopeptide-68, sodium oleate, disodium EDTA, phenoxyethanol, benzyl alcohol, sodium lauryl sulfate, sodium cetearyl sulfate, retinol, polysorbate 20, ethylenoxy glycerin, potassium sorbate, sodium hydroxide, sodium metabisulfite, sodium ascorbate, and tocopherol. It also contains SMART GPS delivery system and a blend of epigenetic active ingredients.

Melanyc MD topical cream consists of: water, mandelic acid, propylene glycol, liquid paraffin, niacinamide, cetearyl alcohol, sodium cetearyl sulfate, kojic acid, salicylic acid, retinol, polysorbate 20, cetearyl alcohol, titanium dioxide, ceteareth-12, phenoxyethanol, benzyl alcohol, Arnica montana flower extract, Cupressus sempervirens seed extract, Polygonatum multiflorum extract, lactobionic acid, sodium metabisulfite, sodium ascorbate, alumina, silica, sodium polyacrylate, potassium sorbate, ethylhexyl glycerin, tocopherol, SMART GPS system, and a blend of epigenetic active ingredients.

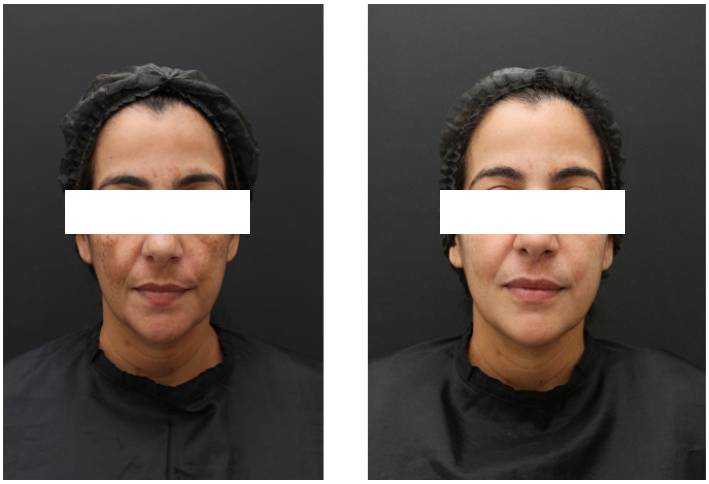
Results

Based on the digital photography analysis conducted by dermatologists, all patients were classified as having shown improvement in melasma after treatment (Images 1, 2, 3, and 4). There was an average reduction of 64% in the MASI (Melasma Area and Severity Index) following the treatment. Regarding patient satisfaction, all reported being satisfied with the treatment. No significant side effects were observed during the one-month follow-up after the final session. A few patients experienced erythema and mild desquamation after applying Melanyc MD.

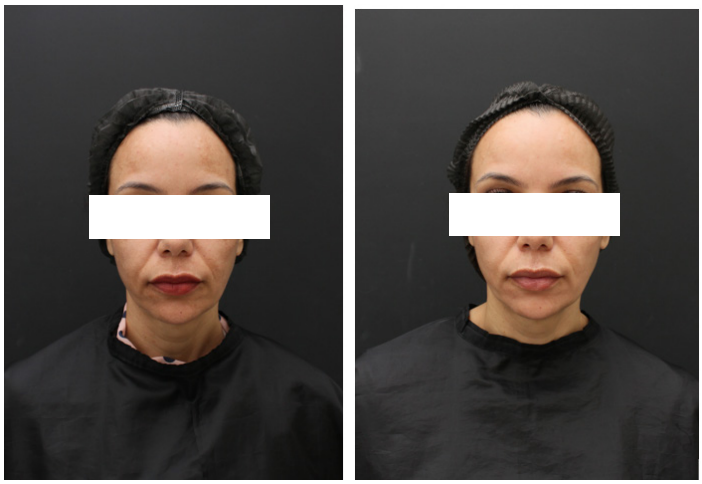
Discussion

We know that the differentiation process of epidermal cells occurs through progenitor cells in the basal layer by a process of specialized programming and proliferation, leading to the formation of a cornified envelope composed of terminally differentiated and enucleated keratinocytes [13]. Epidermal growth and differentiation are driven by the expression of multiple genes regulated by transcriptional and post-transcriptional mechanisms. This control is often altered by external biological and environmental factors (such as UV light) and modulated by physiological factors (e.g., aging) [7,14,15].

As a result, genomic changes lead to widespread dysregulation of gene expression and dysfunction of transcription signaling pathways that control cell proliferation and multiple functions. In addition to changes in DNA structure and sequence, it is increasingly evident that all cellular processes can be profoundly orchestrated by epigenetic mechanisms [16]. Epigenetic changes are reversible modifications in gene expression that do not alter the DNA sequence and may occur at different stages of development or in response to environmental factors. Therefore, epigenetics plays a crucial role in regulating cellular functions and may help explain the relationships between genetic background and environmental effects on susceptibility to various diseases, including skin disorders [17,18].



Patient Before Treatment on the Left and Patient 30 Days After the Last Application of Melanyc HD.



Patient Before Treatment on the Left and Patient 30 Days After the Last Application of Melanyc HD.

Melanyc is composed of a blend of epigenetic active ingredients that act on the epigenome without altering DNA sequences. They influence gene expression in dermal cells involved in cellular regeneration. The lightening agents in its formulation are well combined with complementary mechanisms of action:

- **Alpha-lipoic acid**: Renews skin surface, increases elasticity, tone, and texture; reduces fine lines, enlarged pores, and scars.
- **Azelaic acid**: Potently inhibits tyrosinase, reducing melanin synthesis.
- **Kojic acid**: Chelates iron and peroxidase.
- **Lactobionic acid**: Strong antioxidant, moisturizing, and rejuvenating action.
- **Lactic acid**: Moisturizing and humectant properties used for lightening and rejuvenation.
- **Tranexamic acid**: Iron chelator in hemosiderin that reduces tyrosinase activity.
- **Acnebiol**: A complex of salicylic acid, oligozinc, organic silicon, and botanical extract that normalizes keratinization, refines skin texture, and stimulates healing.
- **Alpha-bisabolol**: Strong anti-inflammatory, healing, and mild antiseptic.
- **Niacinamide**: Multifunctional agent that inhibits melanosome transfer from melanocytes to keratinocytes.
- **Urucum oil**: Acts as a UV filter during prolonged sun exposure.
- **Zinc oxide**: Physical sunscreen capable of absorbing UV light.
- **Papain**: Healing accelerator extracted from papaya.
- **Resorcinol**: Antiseptic, exfoliant, and keratolytic properties.
- **Skin whitening complex**: A balanced phytocomplex that acts at different stages of the pigmentation process, targeting melanin synthesis and breaking down existing pigment.
- **Vitamin C (Thalapheras)**: Anti-inflammatory and anti-aging, stimulates collagen and elastin production, reducing fine lines and dark spots.
- **Ubiquinone**: Acts on prostaglandin 2 with potent antioxidant action, protects ischemic tissue and reduces cellular damage [19-21].

In the study by Campuzano-García et al., 2019, the authors evaluated the role of epigenetics in melasma by analyzing DNA methylation in 30 patients. They found increased DNA methylation in skin affected by melasma compared to unaffected areas, demonstrating that environmental factors trigger cellular changes that activate hyperpigmentation via epigenetic pathways. Furthermore, the study showed that after treatment with sunscreen, niacinamide, and retinoic acid, DNA methylation decreased, indicating a reduction in epigenetic alterations [22]. This was the first study to provide evidence of epigenetic changes in melasma via DNA methylation.

Therefore, acting on the epigenome becomes fundamental for optimizing melasma treatment outcomes. Additionally, Melanyc incorporates an ingredient delivery technology called the **SMART GPS SYSTEM**. This patented system enables uniform penetration and distribution of active ingredients, ensuring they remain within the epidermis, controlling their concentration and preventing release beyond the target area. The system delivers ingredients to specific cell groups for maximum therapeutic effect, promoting cell stability, protection against degradation, preserving skin integrity, and supporting tissue renewal. Thus, it enhances the effectiveness of the powerful depigmenting agents in its formula.

Conclusion

This study demonstrated significant improvement in melasma and high patient satisfaction among individuals with treatment-resistant cases who were treated with Melanyc. In addition to combining powerful depigmenting agents that act on the various pathways involved in melasma pathogenesis, Melanyc includes two revolutionary components for melasma treatment: **epigenetic active ingredients** and the **SMART GPS SYSTEM**.

The epigenetic actives enhance results by modulating gene expression in the basal dermal cells without altering DNA sequences. The SMART GPS system ensures the precise delivery of depigm enting agents to specific cellular targets in the skin, optimizing therapeutic outcomes. Therefore, we conclude that this new therapy for melasma is both effective and safe. It represents an evolution in the treatment of this condition, which remains a therapeutic challenge in dermatology.

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