

## CASE REPORT ΕΝΔΙΑΦΕΡΟΥΣΑ ΠΕΡΙΠΤΩΣΗ

### Post-treatment wound healing with gel, serum, and cream formulations

A 37-year-old woman with Fitzpatrick skin type IV presented for wound healing evaluation following a fractional CO<sub>2</sub> laser procedure. She experienced erythema, slight edema, and stinging on the face post-procedure. The patient had no history of chronic skin disease, keloids, or sensitivities to topical ingredients. Physical examination revealed mild to moderate erythema without signs of infection. The patient received wound care using topical therapy with panthenol, madecassoside, and thermal spring water in cream, gel, and serum, against a control with panthenol moisturizer. Clinical evaluation using VISIA® camera system found that the treatment side resolved erythema and edema faster than the control side. Although there were short-lived eruptions of acneiform nature, no serious side effects occurred, and there was increased patient satisfaction with the intervention products. In conclusion, topical formulation with panthenol, madecassoside, and thermal spring water was effective for wound healing after fractional CO<sub>2</sub> laser treatment and was comparable to usual moisturizers regarding increased patient satisfaction.

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Επούλωση τραυμάτων μετά τη θεραπεία με προϊόντα γέλης, ορού και κρέμας

Περίληψη στο τέλος του άρθρου

#### Key words

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Wound healing after minimally invasive dermatologic procedure is a significant clinical concern due to the likelihood of delayed erythema, edema, pain, and other issues that can impede healing.<sup>1</sup> Wound healing is a complex process with inflammation, proliferation, and tissue remodeling phases, which can be influenced by many intrinsic and extrinsic factors. The frequency of post-procedure complications, such as post-inflammatory hyperpigmentation, secondary infection, and scarring, varies depending on the type of procedure, patient skin type, and care protocols employed.<sup>2</sup> For example, Fitzpatrick skin

type IV–VI patients are at higher risk for post-inflammatory hyperpigmentation following melanocyte response to skin damage, and skin sensitivity history patients are at higher risk for irritation reactions to certain skincare products. In addition to intrinsic factors, external parameters such as ultraviolet (UV) irradiation, pollution, and air humidity also play a part in regulating wound healing speed and quality.<sup>3</sup> One of these techniques that can be regulated is the employment of topical agents for the benefit of tissue regeneration, reduction of inflammation, and hydration of the skin.<sup>4</sup> Therefore, identifying the most appropriate wound

care preparations is a significant factor in optimizing clinical outcomes following minimally invasive dermatological procedures.

One of the most frequent topical formulations in dermatology is a combination of panthenol, madecassoside, and thermal spring water, which may have the potential to improve skin regeneration and reduce inflammation.<sup>5</sup> Panthenol, a precursor to vitamin B5, possesses humectant and emollient properties that help maintain the hydration of the skin, enhance the barrier function of the skin, and enhance epithelialization of damaged tissue.<sup>6</sup> A few studies showed that panthenol may reduce erythema and inflammation in inflamed skin as well as increase skin elasticity in the healing process.<sup>5,6</sup> Madecassoside, meanwhile, is among the primary active components of *Centella asiatica* that was shown to be anti-inflammatory, antioxidant, and collagen-stimulating. It enhances type I and III collagen production, which are needed for the repair of tissue.<sup>7</sup> *In vivo* and *in vitro* studies have indicated that madecassoside is involved in wound healing by suppressing the secretion of pro-inflammatory cytokines and stimulating fibroblast proliferation.<sup>8</sup> Thermal spring water, which contains minerals such as selenium, magnesium, and calcium, is also employed for its soothing action and ability to reduce oxidative stress in inflamed skin. The combination of these ingredients in dermal products is expected to provide a synergistic effect in speeding up skin healing after dermatologic procedures.<sup>9</sup>

However, despite many studies confirming the benefits of these active ingredients,<sup>5–7</sup> there are still limitations in clinical evidence directly comparing their effectiveness across various topical products such as gels, serums, and creams. Variations in active ingredient penetration, viscosity, and physical characteristics of each product may influence their effectiveness and tolerability.<sup>10</sup> For instance, gels are often lighter in texture and get absorbed fast but may provide less long-term moisturizing than creams. Serums are likely to have higher active ingredient percentages, but since they are liquid, they may require additional moisturizing to maintain hydration of the skin. On the other hand, creams are more viscous in nature to enable them to give long-lasting hydration but might be less well tolerated in oily or acne skin patients.<sup>11</sup> Such differences in formulations also influence patients' own experience, such as comfort, ease of application, and likelihood of adverse reactions like irritation or breakouts.<sup>12</sup> Therefore, comparative investigations of the efficacy and tolerability of different topical preparations are necessary to identify the most effective preparation for the promotion of healing in wounds caused by dermatological interventions.

The aim of this case report study is to compare and assess the tolerability and efficacy of panthenol, madecassoside, and thermal spring water gel, serum, and cream preparations in promoting wound healing after fractional CO<sub>2</sub> laser treatment. We hypothesize that all preparations are different in their level of effectiveness in reducing erythema, edema, and crust formation with differences in patient comfort and satisfaction. Findings of this work may be beneficial in providing clinical guidelines for selection of post-procedure wound care products and contribute towards creating even superior dermatological products for enhanced healing of skin.

## CASE PRESENTATION

A 37-year-old Fitzpatrick skin type IV female patient presented for post-procedure wound healing assessment after undergoing a fractional CO<sub>2</sub> laser. The patient complained of redness, swelling, and low-grade burning on the face after the procedure. The patient had no chronic skin disease history, was not pregnant or breastfeeding, and did not have isotretinoin therapy in the last three months. Additionally, she had no keloid formation history or hypersensitivity to specific topical agents.

On the first day after the procedure, physical exam revealed mild to moderate erythema covering the whole face, mild edema, and no infection or major complication. Over the period between the first and fifth day, erythema and edema decreased progressively, with mild crust formation disappearing on the third day. No significant post-inflammatory hyperpigmentation was observed, but on the third day, the patient had an acneiform eruption on both sides of the face.

The patient was diagnosed with post-procedure wounds following fractional CO<sub>2</sub> laser treatment, with mild-to-moderate inflammatory reactions and no severe complications. Pre-procedure care involved instructing the patient to wash her face with a liquid facial cleanser, then applying EMLA anesthetic cream (lidocaine 2.5% and prilocaine 2.5%) (EMLA, AstraZeneca LP, Wilmington, DE, USA) for 45 minutes before the procedure. Fractional CO<sub>2</sub> laser treatment was carried out with a peak power of 40 W, pulse energy of 40 MJ, ablation depth of 0.25 mm, and density of 121 spots/cm<sup>2</sup> without an epidermal cooling device (CO<sub>2</sub> laser 10,600 nm, Bluecore Company Ltd, Korea). Post-treatment, an anti-inflammatory sheet mask was used for 15–20 minutes.

Post-procedure, the wound care agents were applied using a split-face approach. The patient received three types of treatment interventions: A gel containing 5% panthenol, 0.3% madecassoside, and thermal spring water; a serum with 10% panthenol and 5% glycerin; and a cream containing 5% panthenol, 0.3% madecassoside, and thermal spring water. A panthenol-based moisturizer was used as a control on the other side of the face. The patient was also required to use a broad-spectrum sunscreen and avoid direct sun exposure.

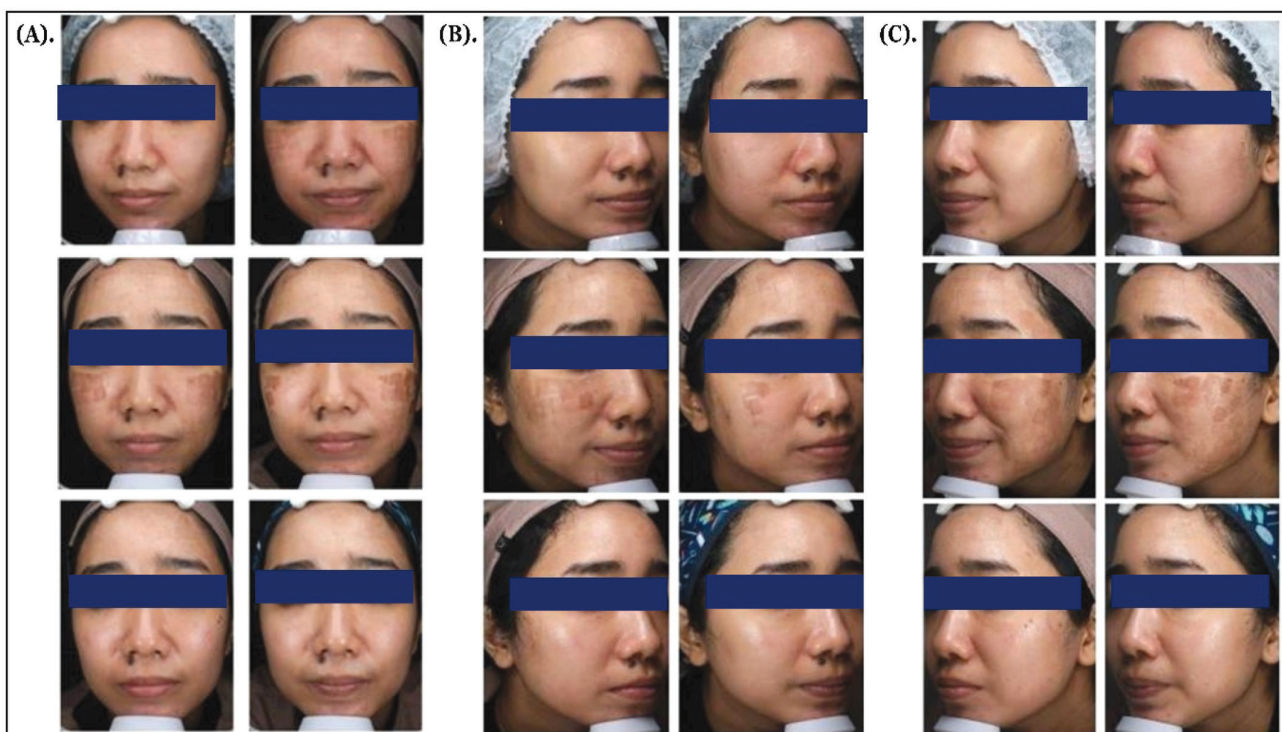
The clinical evaluation was conducted using documentation from the VISIA® camera system (CS) (Canfield Scientific, Inc; New Jersey, US) to assess changes in erythema, edema, and crust formation, as well as the subjective scale of pain and patient satisfaction. The evaluation results showed that the reduction in erythema, edema, and crust formation occurred more rapidly on the side of the face that received the intervention compared to the side that did not (fig. 1). Edema significantly decreased on the third day based on VISIA® data and direct observation. The pain scale was higher in the intervention area; however, patient satisfaction was higher compared to the non-intervention side. No serious side effects were observed, although the patient experienced a temporary acneiform eruption.

## COMMENTS

The study involved a patient who willingly participated, revealing that cream, gel, and serum were equally effective in facilitating wound healing following an esthetic procedure. Additionally, there was no significant difference in pain levels or patient satisfaction between the intervention and control areas of the face. However, a notable discrepancy was observed in wound healing improvement, with the intervention area demonstrating significantly more effective healing compared to the control area. These findings align

with previous studies. Expanding on the research conducted by Stan et al in 2021, which analyzed and compared the effectiveness of cream versus hydrogel treatments for wound healing, the results indicated that both treatment forms have promising applications in preventing infections and promoting overall healing. However, their efficacy is highly dependent on various factors, including the type, depth, and severity of the wound, as well as patient-specific characteristics.<sup>13</sup>

Wound repair was obtained in this study through the use of a combination of three active components: Thermal spring water, madecassoside, and panthenol. The active ingredients were formulated into three diverse vehicles to promote optimal action. The result showed considerable differences in the treatment area, where the right side of the face healed faster than the left, which was treated with just a moisturizer. Also noteworthy is that mineral-spring thermal water may offer wound healing benefits as well as exert antioxidant activity. A study addressed the impact on wound healing with thermal water involving twenty experimental rats. The twenty rats were divided into two equal groups: control group (10 rats) and study group (10 rats) that were equally observed simultaneously. Thermal water treatment was given to the study population with



**Figure 1.** (A) Reduction in erythema, edema, and crusting observed from immediately after treatment to day 5 on the right side of the face treated with cream, gel, and serum (intervention group) compared to the control group (left). (B) The side treated with the intervention group's cream. (C) The side treated with the control group's cream.

direct application to the wound sites and plain water to the control population. Both histological and observational findings revealed significant variations in the two populations. The findings, statistically processed, proved the reality that the healing of wounds in the study population was considerably improved.<sup>14</sup> Based on these results and observations, it can be concluded that thermal water is a good agent in wound healing.

The findings of this study can be explained by the following theoretical background. Madecassoside has been clinically well recognized in wound curing and scar therapy.<sup>15</sup> However, its hydrophilicity and poor permeability through skin tissue limit its topical application. Madecassoside, a pentacyclic triterpenoid saponin from *Centella asiatica*, exhibits diverse biological activities including anti-cancer, anti-arthritis, and neuroprotection. Its wound-healing activity has been widely targeted due to its antioxidative, antimicrobial, and anti-inflammatory activity.<sup>16,17</sup> Madecassoside plays a crucial role in stimulating cell growth and proliferation by stimulating the process of collagen synthesis, relieving oxidative stress on wounds, and causing vasodilation in experimental models of animals.<sup>18</sup> Panthenol, also known as dexpanthenol, D-panthenol, or pantothenylol, is an alcohol derivative of pantothenic acid, which is a vitamin B5 complex. It is readily absorbed from the skin and quickly metabolized to pantothenic acid, a component of coenzyme A (CoA) important for cell metabolism in the skin.<sup>6,19</sup> In addition, dexpanthenol was shown to have anti-inflammatory activity, stimulate fibroblast proliferation, and facilitate epithelialization, thereby facilitating healing processes.<sup>2</sup>

In this study, three different vehicles containing the same active ingredients were used to compare their effectiveness in promoting post-treatment wound healing. Water-in-oil emulsions (oily creams) consist of water or an aqueous solution dispersed within an oil or oleaginous continuous phase, whereas oil-in-water emulsions (aqueous creams) have the opposite composition.<sup>20</sup> The proportion of water and oil determines whether a cream is mildly greasy or non-greasy. Water-soluble drugs are typically formulated in oil-in-water emulsions, while lipid-soluble drugs are more commonly incorporated into water-in-oil emulsions.<sup>21</sup> Creams, which are opaque and viscous, either evaporate or are absorbed when applied to the skin. Unlike ointments, creams do not significantly slow heat loss as they mix with surface exudate. They are less greasy, less viscous, and more spreadable than ointments, making them more appealing to certain patients.<sup>22</sup> However, due to their lower occlusive properties, creams provide less hydration than ointments. Nevertheless, they are widely used for their moisturizing

and emollient effects, making them suitable for both dry and exudative skin conditions.<sup>22</sup> Gels, on the other hand, can be alcohol- or water-based (hydrogels) and consist of transparent lattices of organic macromolecules thickened with agents such as carboxymethylcellulose. They are typically thick but liquefy upon contact with warm skin, creating a cooling sensation. As they dry, they form a thin, non-greasy film that does not stain the skin. While gels are cosmetically favorable due to their lightweight texture and quick absorption, they are poorly occlusive and generally do not provide significant hydration.<sup>23</sup>

The clinical significance of this study revealed that panthenol, madecassoside, and thermal spring water-containing gel, serum, and cream products promoted wound healing following fractional CO<sub>2</sub> laser treatments faster than with panthenol-containing moisturizers alone. The faster reduction of erythema, edema, and crust formation in the treatment group showed the activity of such active ingredients in accelerating the process of inflammation reduction and regeneration of the skin. Moreover, the findings highlighted the significance of topical formulation selection in determining patient comfort and post-procedure downtime that impacted patient satisfaction and adherence to post-treatment procedures. The work was helpful for clinical application because it introduced a science-driven paradigm for the selection of laser procedure follow-up wound care products that guided clinicians to recommend the best treatment based on patient needs. Although mild side effects such as temporary acneiform eruptions were observed, no significant complications occurred, further confirming the very good safety profile of the formulations. Therefore, the study laid a foundation for further research into more successful and better-tolerated post-procedure care regimens.

Although this study provided valuable insights into the effectiveness of various topical formulations in wound healing following fractional CO<sub>2</sub> laser procedures, several limitations should be considered. First, this was a case report study involving only a single patient. This limitation may restrict the generalizability of the findings to a broader population, necessitating studies with a larger number of participants to ensure the validity of the results. Second, the monitoring period was limited to five days post-procedure, which may not have been sufficient to assess the long-term effects of each formulation, particularly regarding the potential for post-inflammatory hyperpigmentation or other delayed side effects. Third, while the evaluation method using the VISIA® CS provided objective data on skin changes, certain parameters, such as patient comfort and satisfaction levels, remained subjective and could be

influenced by individual factors. Additionally, this study only compared formulations based on panthenol, madecassoside, and thermal spring water, without considering other active ingredient combinations that might have synergistic effects on wound healing. Therefore, further research with a more comprehensive design, including longer observation periods and more diverse control groups, is needed to strengthen the findings and clinical recommendations of this study.

In conclusion, this study demonstrated that the use of gel, serum, and cream formulations containing panthenol, madecassoside, and thermal spring water was effective in accelerating wound healing after fractional CO<sub>2</sub> laser

procedures compared to panthenol-based moisturizers alone. Clinical evaluations indicated that these interventions significantly reduced erythema, edema, and crust formation within the first five days post-procedure, with higher patient satisfaction despite a slight increase in pain sensation. Furthermore, all three formulations exhibited good tolerability with minimal side effects. These findings lay the groundwork for clinical recommendations in selecting topical products to enhance wound healing following minimally invasive dermatological procedures. However, further research with a larger sample size and a longer observation period is needed to confirm these findings and assess the potential long-term effects of each formulation.

## ΠΕΡΙΛΗΨΗ

### Επούλωση τραυμάτων μετά τη θεραπεία με προϊόντα γέλης, ορού και κρέμας

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Μια 37χρονη γυναίκα με τύπο δέρματος Fitzpatrick IV προσήλθε για αξιολόγηση επούλωσης τραυμάτων μετά από θεραπεία με κλασματικό laser CO<sub>2</sub>. Μετά τη θεραπεία παρουσίασε ερύθημα, ήπιο οίδημα και αίσθημα καύσου στο πρόσωπο. Δεν ανέφερε ιστορικό χρόνιας δερματικής νόσου, χηλοειδών ή ευαισθησίες σε τοπικά συστατικά. Η κλινική εξέταση αποκάλυψε ήπιο έως μέτριο ερύθημα χωρίς σημεία λοίμωξης. Η ασθενής έλαβε φροντίδα τραύματος με την εφαρμογή τοπικής θεραπείας με πανθενόλη, μαντεκασοσίδη και ιαματικό νερό σε κρέμα, γέλη και ορό, έναντι μιας ομάδας ελέγχου με ενυδατική κρέμα πανθενόλης. Η κλινική αξιολόγηση χρησιμοποιώντας το σύστημα κάμερας VISIA® διαπίστωσε ότι η πλευρά της θεραπείας αντιμετώπισε το ερύθημα και το οίδημα ταχύτερα από την πλευρά ελέγχου. Αν και υπήρχαν βραχύβια εξανθήματα ακμοειδούς φύσης, δεν παρατηρήθηκαν σοβαρές ανεπιθύμητες ενέργειες και υπήρξε αυξημένη ικανοποίηση της ασθενούς με τα προϊόντα παρέμβασης. Συμπερασματικά, η τοπική σύνθεση με πανθενόλη, μαντεκασοσίδη και ιαματικό νερό ήταν αποτελεσματική για την επούλωση τραυμάτων μετά από θεραπεία με κλασματικό laser CO<sub>2</sub> και ήταν συγκρίσιμη με τις συνήθεις ενυδατικές κρέμες.

**Λέξεις ευρετηρίου:** Αποκατάσταση δέρματος και φλεγμονή, Επούλωση τραυμάτων μετά τη θεραπεία, Κλασματικό laser CO<sub>2</sub>, Πανθενόλη και μαντεκασοσίδη, Τοπικές συνθέσεις

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