

## Case Report

### **Case Study: Optimizing Skin Regeneration After Aesthetic Procedures with Dermocosmetic Skin-Healing Care**

Studi Kasus: Optimalisasi Regenerasi Kulit Paska Prosedur Estetika dengan Perawatan Penyembuhan Kulit Dermokosmetik

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#### **Abstract**

The use of ecobiology-based dermocosmetics containing Antalgicine™ can expedite the optimization of skin regeneration post-aesthetic procedures. The aim of this case study assess the clinical benefit of Antalgicine™ post-aesthetic procedures. Six patients were recruited into this case study which utilizes subjective and objective measurements. Antalgicine™ was applied using a split-face study method. Subjective evaluation is graded by patients using a 1-5 Likert scale, along with objective evaluation, was performed by a blinded dermatologist. Results showed an objective reduction in post-aesthetic procedure on day 7, namely 40% for microneedling, 32% for fractional radiofrequency, and 29% for picosecond laser, as well as subjective reductions in every post-aesthetic procedure sensation, specifically pain, pruritus, tightness, and burning sensation at 67%, 75%, 67%, 33% for microneedling, 71%, 67%, 67%, 50% for fractional radiofrequency, and 67%, 75%, 78%, 60% for picosecond laser, respectively. As a conclusion, Antalgicine™ can reduce post-aesthetic procedure effects for optimizing skin regeneration.

**Keywords:** antalgicine; ecobiology-based dermocosmetics; skin regeneration

#### **How to Cite:**

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### Abstrak

Penggunaan dermocosmetik berbasis ekobiologi yang mengandung Antalgicine™ dapat mempercepat optimalisasi regenerasi kulit pasca prosedur estetika. Tujuan penulisan studi kasus ini adalah menilai manfaat klinis Antalgicine™ pasca prosedur estetika. Sejumlah enam pasien dilibatkan pada studi kasus dengan menggunakan pengukuran subjektif dan objektif. Antalgicine™ dioleskan menggunakan metode *split-face study*. Evaluasi subjektif diukur oleh pasien dengan skala 1-5 Likert dan evaluasi objektif dilakukan dokter spesialis kulit-kelamin-estetika secara *blinded*. Hasil menunjukkan pengurangan objektif pasca prosedur estetika pada hari ketujuh, yakni 40% untuk *microneedling*, 32% untuk *fractional radiofrequency*, dan 29% untuk *picosecond laser*, diikuti pengurangan subjektif setiap sensasi pasca prosedur estetika, yakni nyeri, gatal, tertarik, and terbakar di 67%, 75%, 67%, 33% untuk *microneedling*, 71%, 67%, 67%, 50% untuk *fractional radiofrequency*, dan 67%, 75%, 78%, 60% untuk *picosecond laser*, secara berurutan. Sebagai simpulan, Antalgicine™ menurunkan efek pasca prosedur estetika untuk optimalisasi regenerasi kulit.

**Kata kunci:** antalgicine; *ecobiology-based dermocosmetics*; *skin regeneration*

### Introduction

Skin healing is a systematic process, traditionally including four overlapping classic phases: vascular, inflammation, proliferation, and remodeling that involves interaction between resident cells, infiltrating cell subtypes, extracellular matrix molecules, and cytokines for skin regeneration after trauma, e.g., post-aesthetic procedure.<sup>1-4</sup> Skin regeneration is defined as a substitution of the superficial dermis that is particularly complete replacement of damaged tissue with new tissue after passing the skin healing process.<sup>5,6</sup> Post-aesthetic procedures such as microneedling, fractional radiofrequency, and picosecond laser will produce cutaneous microwounds invasively and proinflammatory mediators (neuromediator).<sup>7-9</sup> So, utilizing dermocosmetics can reduce proinflammatory mediators by managing skin inflammation and improving collagen synthesis in the remodeling phase, resulting in optimal skin regeneration due to its active substance.<sup>6,10,11</sup> Dermocosmetic is a branch of dermatology using cosmetics that is defined as a skincare solution comprising a dermatologically active substance to maintain a variety of skin disorders and nowadays for maintaining aesthetic appearance, such as post-aesthetic procedures can induce healing process and accelerate skin regeneration.<sup>12-17</sup>

Ecobiology is a new scientific approach that is based on the principle that the skin is an ever-evolving ecosystem composed of cutaneous cells and a complex microbiome that constitute a real ecosystem in which the various components interact with each other and adapt to their environment.<sup>18,19</sup> Ecobiology skincare products use the principle of biomimicry to give the skin molecules that are naturally found in its biological composition therefore, it both supports and respects the skin's natural metabolism.<sup>20</sup> Skincare and cosmetic development can take these principles into account, possibly leading to better-adapted dermocosmetic.<sup>19,21</sup>

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The ecobiology-based dermocosmetic in question is Antalgicine™, a dipeptide (tyrosine and arginine) with a structure similar to kyotorphin.<sup>22,23</sup> Kyotorphin has an analgesic effect by inhibiting the release of the neuromodulators in nerve cells.<sup>24</sup> Antalgicine™ is used in this case study because it is an ecobiology-based dermocosmetic using either the principles of biomimicry that are naturally found in its biological composition of the skin or maintaining skin regeneration during the process of skin healing by inhibiting neuromodulators.<sup>19–24</sup>

Two different single-center open-label uncontrolled clinical trials enrolling dialysis patients and diabetic patients presented with skin dryness and pruritus, applied with dermocosmetic product formulated with Antalgicine™ suggested that after 28 days of application, the product significantly reduced the Scaling Roughness Redness and Cracks (SRRC) global score of 83% and 66%, as well as pruritus intensity of 76% and 78% in dialysis and diabetic patients, respectively.<sup>22</sup> Another study investigating the effects of a dermocosmetic product formulated with Antalgicine™ in tattoo aftercare also suggested that redness was absent for 100% and 96% of subjects, and edema had completely disappeared. Most subjects rated the skin quality repair and the aesthetic outcomes as very good to excellent after 14 days of application. Soothing and moisturizing effects were observed as early as the first day. The effects were maintained over 14 days. Discomfort sensations were judged absent to slight in 96%–100% of cases after 7 days. They were assessed as absent to slight in all cases for pain, pruritus, and tingling, and 96% for burning sensations after 14 days.<sup>24</sup>

The purpose of this case study is to assess the clinical benefit of Antalgicine™ in addressing post-aesthetic procedure issues due to its targeted function in the analgesic and wound healing process. Clinical benefit was defined by the FDA (Food and Drug Administration) as a favorable effect on a meaningful aspect of how a patient feels, e.g., symptom relief, functions, e.g., improved mobility, or survival as a result of treatment.<sup>25</sup>

### Methods

Subjects were selected from patients who underwent aesthetic procedures. The aesthetic procedures used in this case study were microneedling, fractional radiofrequency, and picosecond laser. These aesthetic procedures were chosen due to their mechanism for invasively producing cutaneous microwounds.<sup>7–9</sup> Two patients were selected from each aesthetic procedure using nonsimple random sampling, making a total of six subjects with ages ranging from 35 to 40. This age range is considered to be in the “aging occurrence period” where skin begins to develop aging features such as freckles, rough skin textures, wrinkles, and darkening skin tone.<sup>26</sup>

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All subjects had signed informed consent, indicating their willingness to participate in this case study. After an aesthetic procedure, Antalgicine™ was applied by a dermatologist on the right side of the face, while the left side was applied with petroleum jelly as a control. This procedure uses a split-face study method, assessing clinical benefit in dermocosmetic.<sup>27</sup> Petroleum jelly was chosen as a control due to its inert nature by having no active chemical properties. Its inert nature as a physical barrier also allowed petroleum jelly to be a positive control.<sup>28</sup> Antalgicine™ and petroleum jelly were then continued to be applied twice a day for seven days in each designated area.

Both subjective and objective measurements were evaluated in this case study. Subjective evaluation was assessed twice (immediately and 7 days post-treatment), and objective evaluation was assessed five times (immediately, one hour, 24 hours, 72 hours, and 7 days post-treatment). Most post-aesthetic procedures have a downtime ranging from 3 to 7 days. Hence, we've decided on day 7 as the end point of our evaluation.<sup>29-31</sup>

Subjective evaluations were assessed by asking patients about the sensations they experienced, including pain, pruritus, tightness, and burning sensation. Patients then were asked to rate the intensity using a 1-5 Likert scale. They could assign the lowest score of 1 if they did not experience pain, pruritus, tightness, and burning sensation, up to the highest score of 5, indicating a very high intensity. Objectively, evaluation was documented using a skin analysis tool that captures facial photos on standardized settings, including lighting, position, distance, camera settings, and background. Patient facial images were taken from the front view and left and right oblique angles at 45°. The photos were then assessed blindly by a dermatologist's colleague who later joined this case study but wasn't notified which side of the face had been applied with Antalgicine™. The dermatologist's colleague would assess:

1. The degree of redness and improvement in skin quality (smoothness, reduced pore size, moisture, and brightness level) and
2. The extent of redness and improvements in skin quality (smoothness, reduced pore size, moisture, and brightness level)

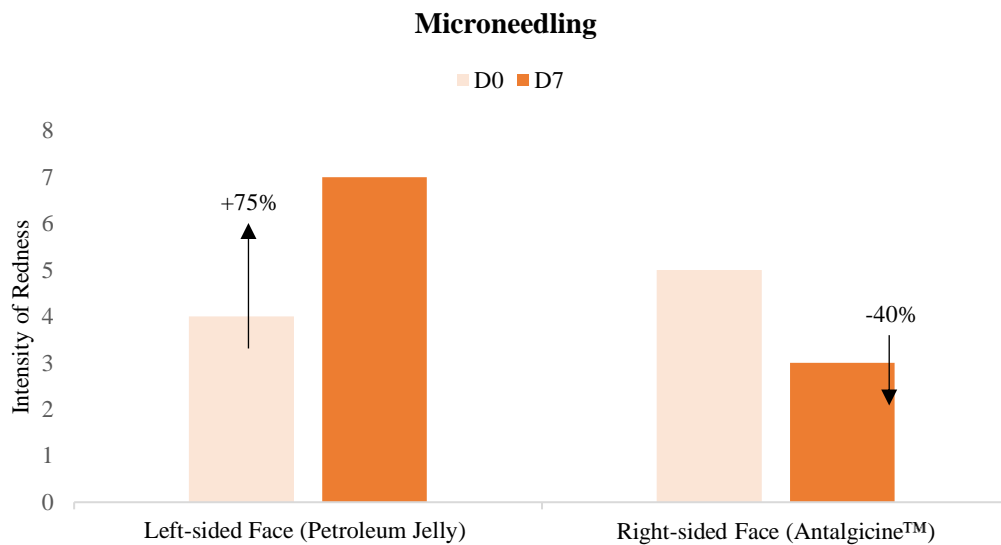
This study was conducted in Skinsation, Dermatology and Aesthetic Center, Jakarta, that was supervised by a dermatologist and six patients agreed to participate in this study by taking a signature in informed consent.

### Results

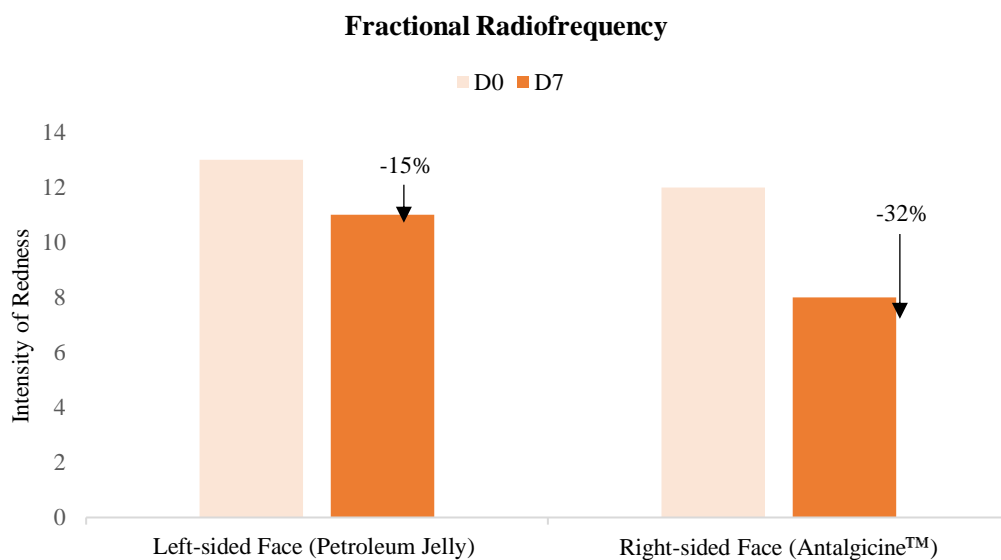
A total of six subjects were recruited into this case study which utilizes both objective and subjective measurements. Results of objective therapy evaluation (redness) at immediate (D0)

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and day 7 (D7) post-microneedling, showed an increase of redness intensity by 75% at the petroleum jelly applied area (control) and a decrease of redness intensity by 40% at Antalgicine™ applied area (Figure 1), for post-fractional radiofrequency both showing a decrease of redness intensity by 15% and 32% at petroleum jelly (control) and Antalgicine™ applied area respectively (Figure 2), and for post-picosecond laser showing an increase of redness intensity by 15% at petroleum jelly applied area (control) and a decrease of redness intensity by 29% at Antalgicine™ applied area (Figure 3).

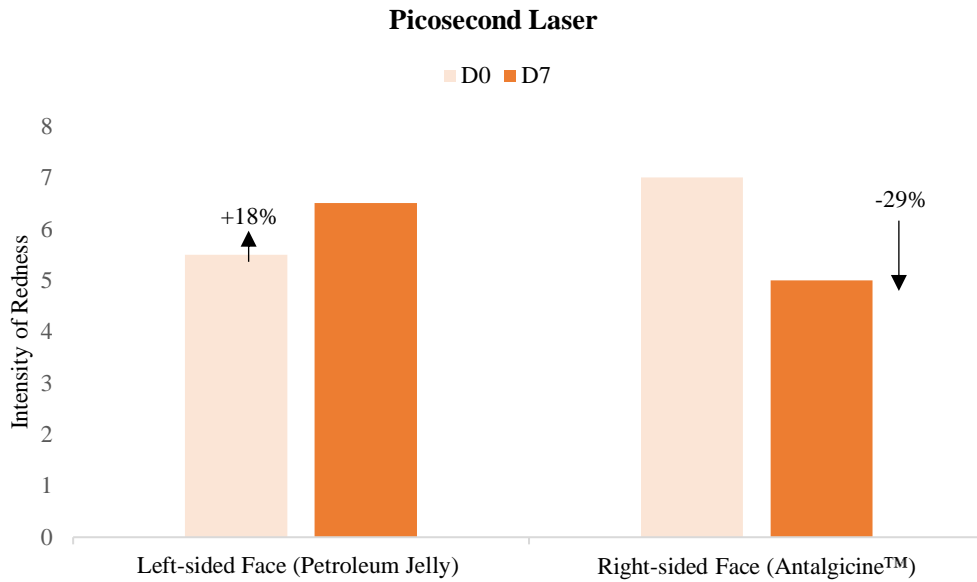


**Figure 1 Results of Objective Therapy Evaluation (Redness) at Immediate (D0) and Day 7 (D7) in Post-microneedling.**



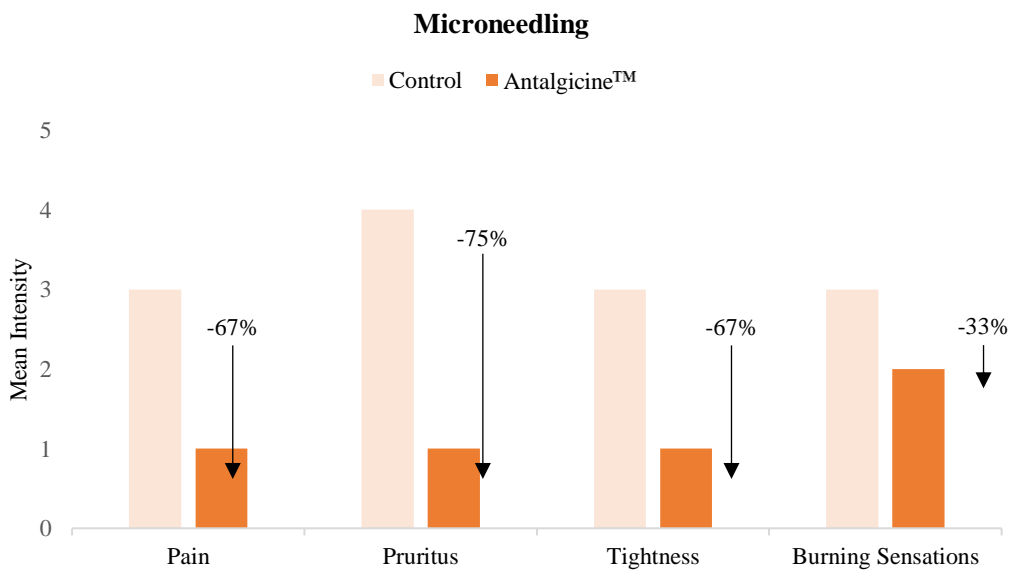
**Figure 2 Results of Objective Therapy Evaluation (Redness) at Immediate (D0) and Day 7 (D7) in Post-fractional Radiofrequency**

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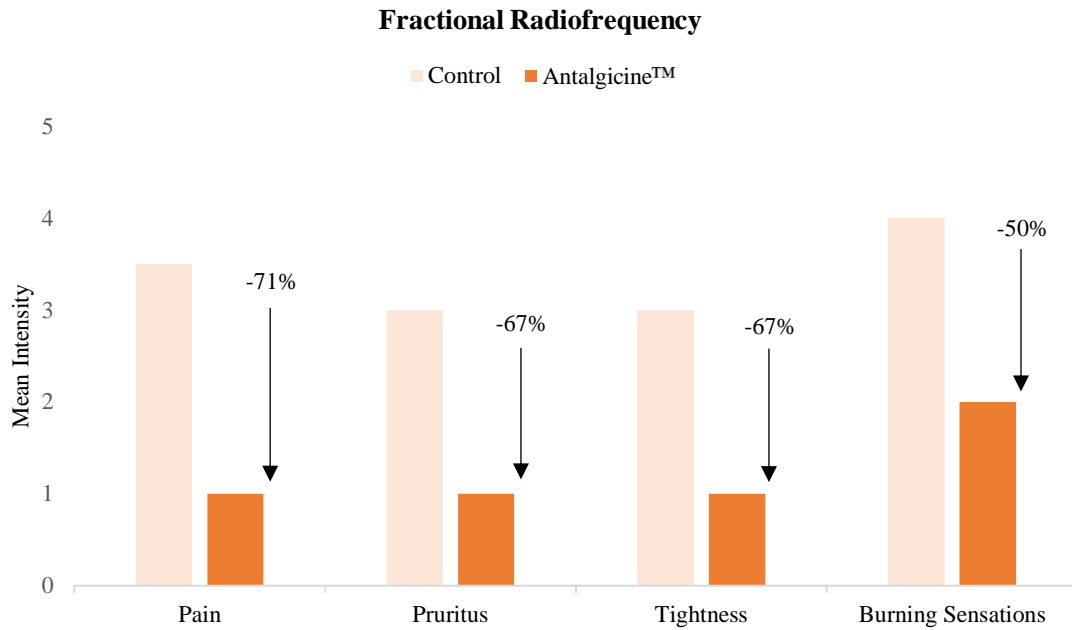
**Figure 3 Results of Objective Therapy Evaluation (Redness) at Immediate (D0) and Day 7 (D7) in Post-picosecond Laser**

Subjectively, on 7th-day post-aesthetic procedures, there was a decrease of average intensity in pain, pruritus, tightness, and burning sensations for microneedling by 67%, 75%, 67%, 33% (figure 4), for fractional radiofrequency by 71%, 67%, 67%, 50% (figure 5), and for picosecond laser by 67%, 75%, 78%, 60% (figure 6) respectively at the area applied with Antalgicine™.

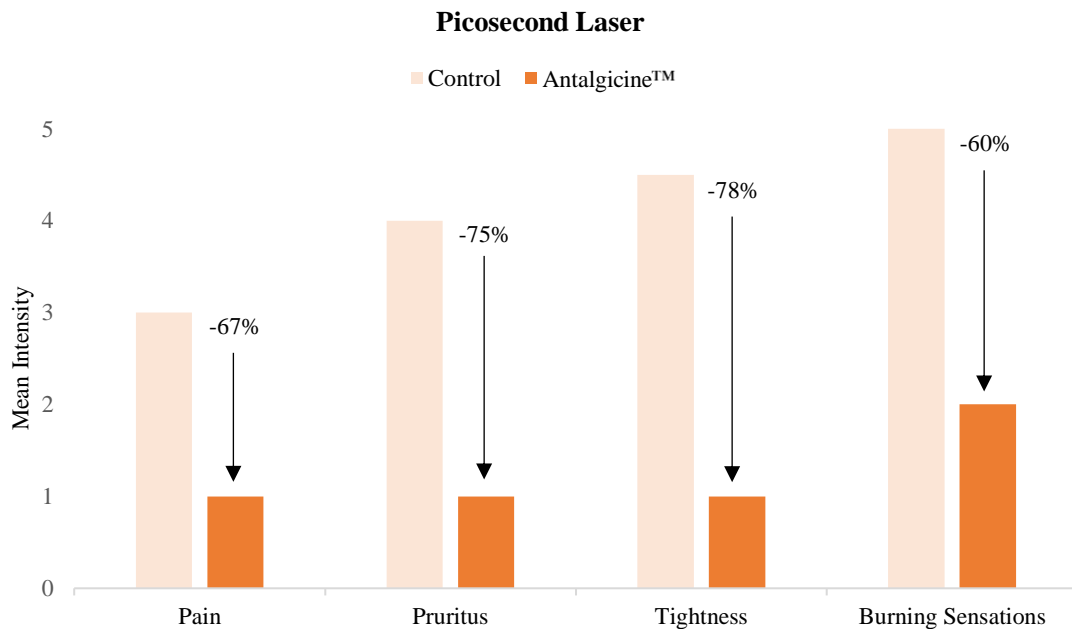


**Figure 4 Results of Subjective Therapy Evaluation on 7th Day in Post-microneedling**

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**Figure 5 Results of Subjective Therapy Evaluation on 7th Day in Post-fractional Radiofrequency**

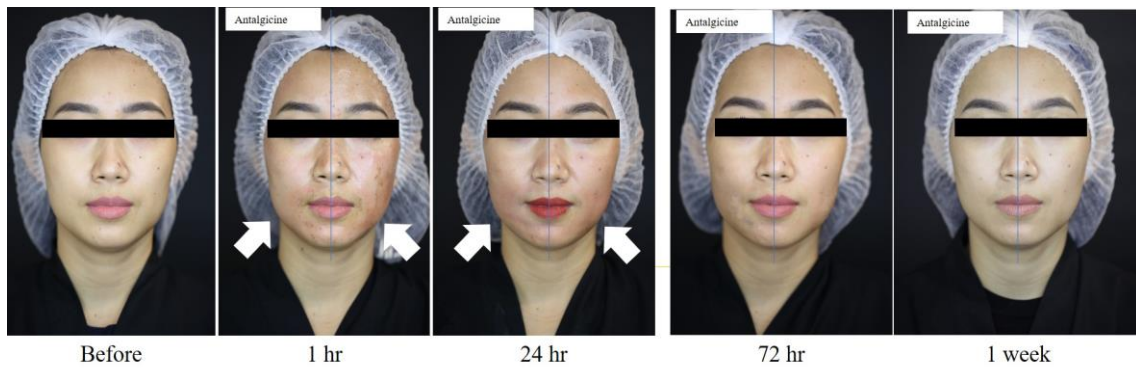


**Figure 6 Results of Subjective Therapy Evaluation on 7th Day in Post- picosecond Laser**

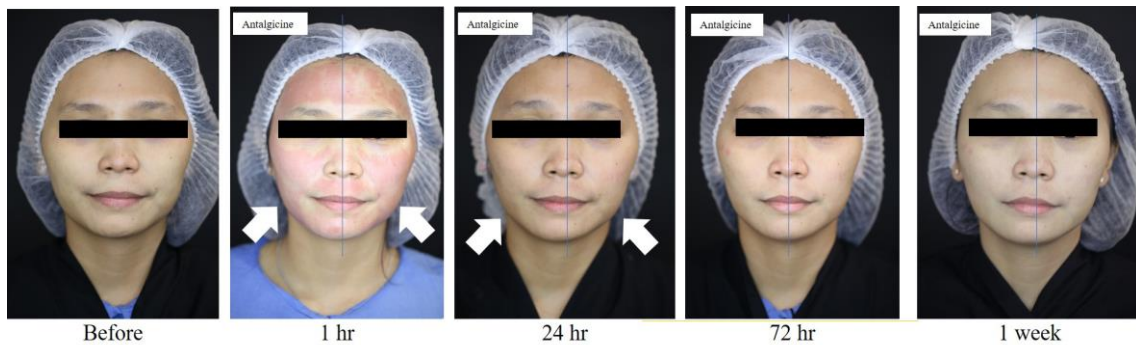
Figures 7, 8, and 9 show split facial photos captured by a skin analysis tool comparing the right side of the face applied with Antalgicine™ and the left side of the face applied with petroleum jelly as a control. Figure 1 shows a significantly improved skin quality post-microneedling procedure on the Antalgicine™ applied side compared to the control side. By

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comparing both cheek areas on the first and 24-hour post-microneedling treatment, the amount and intensity of redness on Antalgicine™ applied side are significantly reduced compared to the control side (Figure 7). Figure 2 overall shows a significantly improved skin quality post-fractional radiofrequency procedure on the Antalgicine™ applied side. On the first hour post-fractional radiofrequency, the redness intensity was much reduced at the Antalgicine™ applied side compared to the controlled side. It is also noted on 24-hour post-fractional radiofrequency, as there was still some redness visible at the maxillae region of the controlled area (Figure 8). Figure 3 shows a significantly improved skin quality post-picosecond laser procedure on the Antalgicine™ applied side. This could be seen on especially 24-hour post-picosecond laser, as there is still much visible redness and enhanced skin texture on the forehead and cheek region in controlled area compared to the Antalgicine™ applied area (Figure 9).



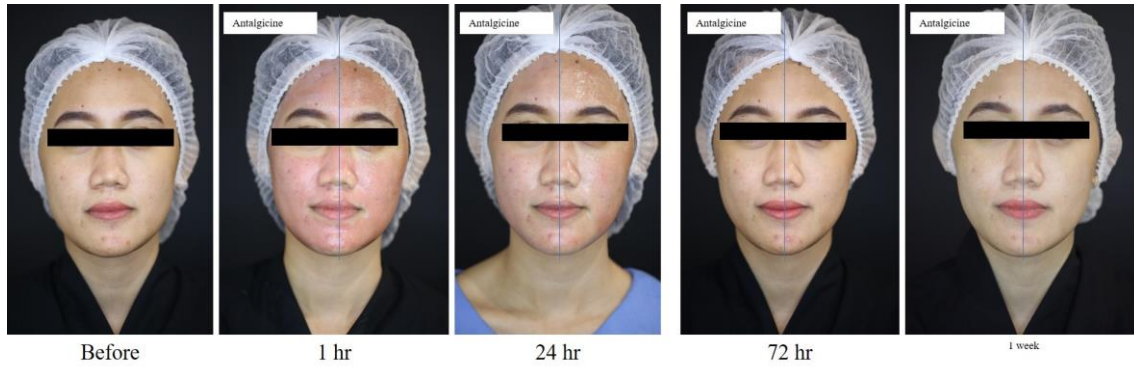
**Figure 7 The application of Antalgicine™ on The Right Side of The Face Significantly Improves Skin Quality Post-microneedling Procedure, as Evidenced by The Reduction in Redness**



**Figure 8 The Application of Antalgicine™ on The Right Side of The Face Significantly Improved Skin Quality Post-fractional Radiofrequency Procedure, as Evidenced by The Reduction in Redness**



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**Figure 9 The Application of Antalgicine™ on The Right Side of The Face Significantly Improved Skin Quality Post-Picosecond Laser Procedure, as Evidenced by Reduced Redness**

### Discussion

The skin healing process is a complex and multifactorial biological process aimed at restoring the integrity of damaged tissues through a coordinated cascade of interrelated events, such as inflammation, proliferation, and remodeling, which are in coordination, releasing cytokines, growth factors, and collagen produced by keratinocytes, fibroblasts, and endothelial cells during the skin healing process.<sup>1,32</sup>

Dermatologists, particularly those performing aesthetic energy-based therapy procedures such as microneedling, fractional radio frequency, and picosecond laser, primarily aim for a rapid skin healing process, minimal pain, and reduced sensations of redness and swelling after aesthetic procedures. Hence, the result is optimal skin regeneration.<sup>14,15</sup> The process can involve the use of ecobiology-based dermocosmetics, which represent an innovative approach in the field of skincare that follows the principles of the skin ecosystem. The skin ecosystem comprises normal flora and skin cells to maintain skin integrity.<sup>21</sup> In the modern era, ecobiology-based dermocosmetics are gaining popularity in the dermatocosmetic and aesthetic fields because they can expedite the healing process post-aesthetic procedures.<sup>33</sup>

The ecobiology-based dermocosmetic in this case study is Antalgicine™, a dipeptide with a structure similar to kyotorphin, which exhibits analgetic effects.<sup>22</sup> Kyotorphin was discovered in 1979 as a result of research conducted by scientists at the University of Aberdeen in Scotland, resulting in the discovery of an opioid-like receptor fractionated through chromatography, namely a dipeptide chain (tyrosine and arginine).<sup>23</sup> Kyotorphin works by inhibiting the neuromediators in nerve cells.<sup>24</sup> During aesthetic procedures involving energy-based therapies, the skin undergoes damage which either modulating neuromediators such as substance P, calcitonin gene-related peptide (CGRP), and bradykinin or neurohormones, such as

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melanocyte-stimulating hormone (MSH), adrenocorticotrophic hormone (ACTH), catecholamines, enkephalin, endorphins, and acetylcholine including skin cells involved in this process, such as keratinocytes, Langerhans cells, melanocytes, endothelial cells, and fibroblasts.<sup>10</sup>

The initial phase is hemostasis or vascular, in which endothelial cells are involved in activating a cascade to form fibrin; the subsequent phase is inflammation, the Langerhans cells play a role following neutrophils and inflammatory cell chemotaxis activated to release pro-inflammatory cytokines such as TNF- $\alpha$ , IL-6, IL-1 $\beta$ , IL-8, and IL-12, leading to modulate nerve cells in the skin releasing neuromediators and neurohormones, resulting in pain, redness, and swelling sensation.<sup>3,4</sup> During the proliferation phase, keratinocytes, fibroblasts, and endothelial cells increase in number and migrate to the wound, replacing fibrin formed during the hemostasis phase. Fibroblasts from the reticular dermis migrate to the inflamed area to produce collagen and extracellular matrix, then fill the wound, blocking it. Finally, the remodeling phase involves the skin returning to its initial structure (skin regeneration).<sup>2,10,34</sup>

The ecobiology-based dermocosmetics with an active substance, specifically Antalgicine™, then applied to one side of the face (right-sided face) which undergoes aesthetic procedure in this case study because refer to study by Fauger, shows Antalgicine™ reduced skin discomfort (pain, pruritus, a burning sensation, and tingling) after seven days of application while providing efficient soothing and a moisturizing effect for 14 days after laser tattoo procedure while protecting skin ecosystem and maintaining skin regeneration during the process of skin healing.<sup>19,24</sup>

The study showed that Antalgicine™ treated in the right-sided face showed reduced redness, pain, burning sensation, tightness, and itching post-aesthetic procedures on day 7 compared to the left side of the face, which was only treated with petroleum jelly.

### Conclusion

Aesthetic procedures performed by a dermatologist, such as microneedling, fractional radio frequency, and picosecond laser, can induce skin stress, leading to the release of neuromediators. Antalgicine™ is an ecobiology-based dermocosmetic with a dipeptide chain found in one of its products, which can be utilized by dermatologists post-aesthetic procedures. Antalgicine™ can expedite the skin healing process post-aesthetic procedures, resulting in reduced pain, redness, burning sensation, tightness, and pruritus for optimizing skin regeneration.

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### Disclosure

This case study was sponsored by Bioderma®, but they had no participation in the study proceedings, data analysis, or the process of manuscript preparation and submission. The authors report no conflicts of interest in this work.

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