

The 730 nm Picosecond Titanium Sapphire Laser for Treatment of Kratom-Induced Hyperpigmentation

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Received: 18 January 2025 | **Revised:** 22 March 2025 | **Accepted:** 16 April 2025

Funding: The authors received no specific funding for this work.

Keywords: 730 nm | cosmetic | kratom | laser | picosecond

ABSTRACT

Objectives: This case series reports the use of the 730-nm picosecond titanium-sapphire laser in the treatment of kratom-induced hyperpigmentation, a dermatological side effect associated with the use of *Mitragyna speciosa*, which remains poorly understood.

Methods: A series of patients with kratom-induced hyperpigmentation were treated using the 730-nm picosecond titanium-sapphire laser. Treatment outcomes were documented by assessing the degree of pigmentation improvement and noting the occurrence of any adverse effects or recurrence of hyperpigmentation.

Results: All patients showed significant improvement in the appearance of hyperpigmentation following treatment. No adverse effects or recurrence of hyperpigmentation were observed during the follow-up period.

Conclusions: This case series represents the first documented use of the 730-nm picosecond titanium-sapphire laser for treating kratom-induced hyperpigmentation. The laser's precision and minimal tissue disruption suggest it as a promising treatment option for this challenging dermatological side effect.

1 | Introduction

Kratom, scientifically known as *Mitragyna speciosa*, is a plant indigenous to Southeast Asia, where it has been utilized for centuries in traditional herbal medicine. Historically, it has been employed to manage pain and enhance endurance for agricultural and manual labor. In recent years, kratom has gained popularity in the United States, where it is marketed as a "natural" herbal supplement, often touted as a legal alternative to recreational drugs or as a remedy for pain, anxiety, depression, and opioid withdrawal. However, despite its widespread use, the US Food and Drug Administration (FDA) issued a warning in 2019 regarding the potential risks of kratom, including its addictive properties, abuse potential, and lack of conclusive evidence supporting its therapeutic

efficacy. Nevertheless, kratom remains widely accessible and continues to be used by many individuals seeking relief from chronic pain, mental health issues, and opioid dependence [1].

As concerns about the safety of kratom have grown, several regions, including six US states, have enacted bans on its sale and use, while other countries have similarly restricted its availability. Literature reports have highlighted a range of adverse effects associated with kratom, including significant elevation in blood pressure, central nervous system disturbances, and potential hepatotoxicity and nephrotoxicity. In some extreme cases, kratom use has been linked to fatalities [2]. Despite these serious risks, one of the more puzzling and underreported side effects is the development of

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hyperpigmentation, a condition that is often difficult to treat and has garnered limited attention in the medical literature [3–5].

Anecdotal evidence suggests that kratom-induced hyperpigmentation may be more common than previously recognized, yet there is a lack of established treatment protocols or effective solutions.

In this context, we present the first case series documenting the use of the 730-nm picosecond titanium-sapphire laser in the treatment of kratom-induced hyperpigmentation. Picosecond laser technology is known for its short pulse width, precision, and ability to target pigment with minimal collateral damage to surrounding tissue. It offers a promising and effective approach for addressing this challenging dermatological condition. In the following case series, we discuss treatment parameters, clinical outcomes, and the potential role of picosecond laser therapy as a safe and efficacious option for patients suffering from this difficult-to-treat side effect of kratom use.

2 | Case Report

2.1 | Case 1

A 32-year-old Caucasian male presented with a gradually progressive, asymptomatic hyperpigmentation that had developed over the course of 1 year. On examination, the patient exhibited diffuse, photo-distributed, confluent brown to gray hyperpigmented patches affecting the face, neck (Figures 1 and 2) and bilateral hands. Notably, the discoloration spared the submental region and knuckles. The patient's medical history included the use of Escitalopram for anxiety and Sumatriptan as needed for migraines. In an effort to better manage his migraine symptoms, the patient had been using over-the-counter kratom tablets as a supplement. There was no other significant medical history.

A punch biopsy from the left lateral neck revealed scattered deposits of clustered, refractile, interstitial red-brown pigment, ranging in size from 1 to 12 μm (Figures 3 and 4). Besides the presence of pigment-laden histiocytes, no significant inflammation was noted. Based on the photo-distributed pattern of pigmentation, the histopathological findings, and the temporal relationship between the onset of hyperpigmentation and the initiation of kratom use, the diagnosis of kratom-induced photo-distributed hyperpigmentation was made. The patient was advised to taper off kratom to minimize further exacerbation of the condition.

For treatment of the hyperpigmentation, two test spots were initially performed using Q-switched 1064 nm, picosecond 1064 nm, and picosecond 730 nm laser (PicoWay laser, Candela Medical Corporation, Wayland, MA, USA). The picosecond 730 nm laser demonstrated the most favorable response. The patient underwent a series of three treatments, spaced 4–6 weeks apart, using the picosecond 730 nm laser (spot size: 3 mm, fluence: 1.0–1.8 J/cm², frequency: 4–5 Hz). Immediate light to moderate pigment whitening of the treated areas, with or without edema, was observed during treatments, and this was used as an endpoint to assess treatment efficacy.



FIGURE 1 | Kratom hyperpigmentation involving the face and neck.



FIGURE 2 | Left profile of patient showing kratom hyperpigmentation using polarizing camera filter.

Following the treatment regimen, the patient showed significant improvement in the hyperpigmentation, with no reported side effects or complications (Figures 5 and 6).

2.2 | Case 2

A 42-year-old Caucasian female, with no significant past medical history, presented with gradually progressive, asymptomatic hyperpigmentation over a span of 6–9 months. On examination, she was found to have confluent, photo-distributed brown to gray hyperpigmented patches involving the face (Figure 7), chest, and bilateral

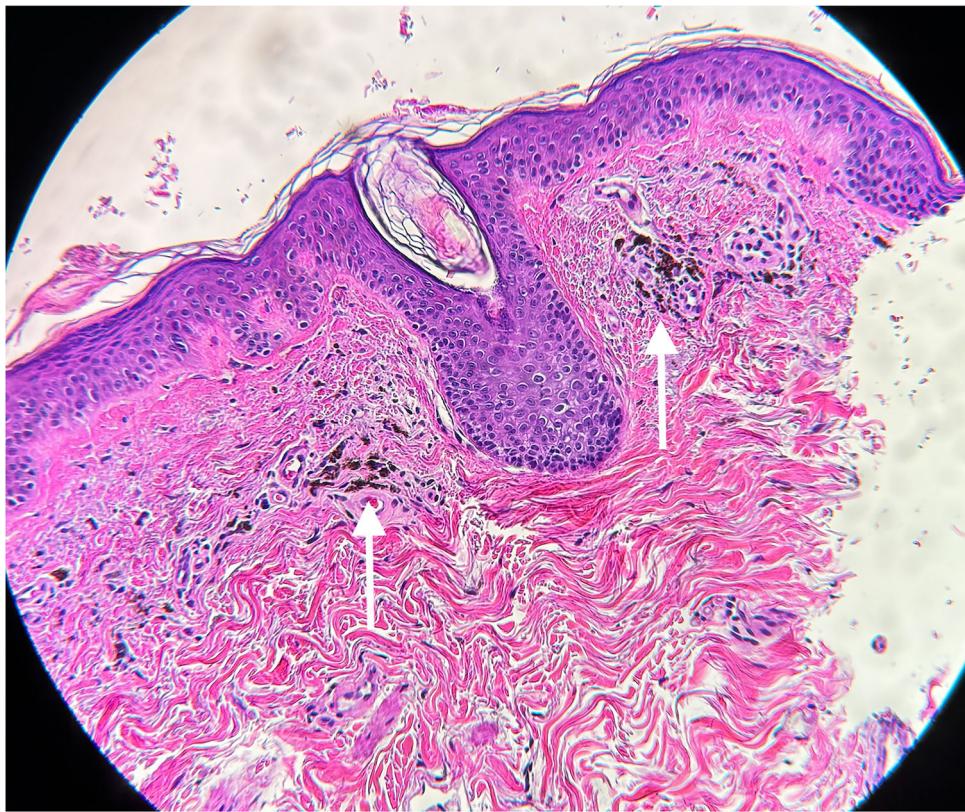


FIGURE 3 | Pigment deposition in upper dermis (arrows) (hematoxylin-eosin stain; original magnification: $\times 200$).

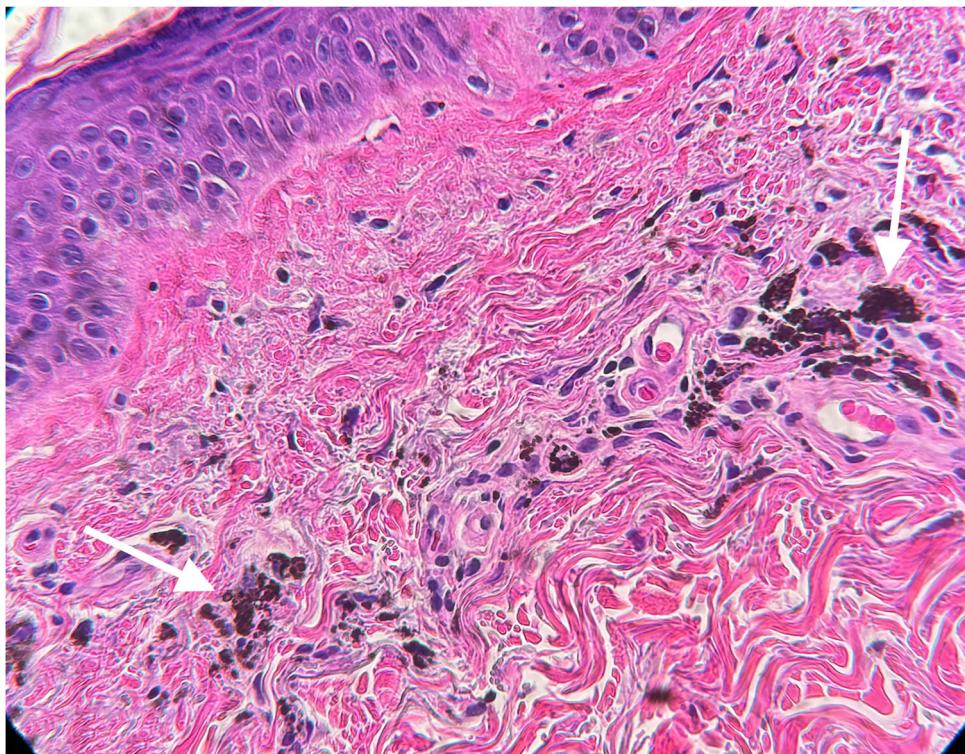


FIGURE 4 | Pigment deposition within macrophages (arrows) (hematoxylin-eosin stain; original magnification: $\times 400$).

hands. Notably, sparing knuckles and jewelry areas (Figure 8). The patient reported initiating the use of kratom tea approximately 3–4 years prior, primarily to manage insomnia.

Given the temporal association between the onset of the hyperpigmentation and kratom use, as well as the clinical presentation, the patient was diagnosed with kratom-induced hyperpigmentation. She was subsequently tapered off kratom to



FIGURE 5 | (A) kratom hyperpigmentation pretreatment and (B) kratom hyperpigmentation posttreatment with picosecond 730-nm laser.

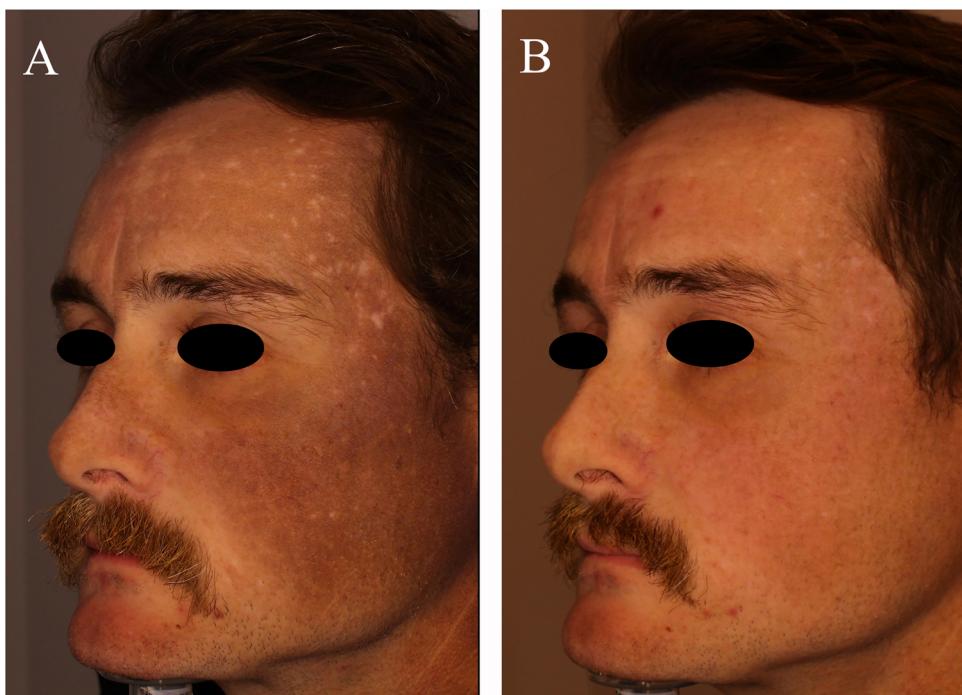


FIGURE 6 | (A) kratom hyperpigmentation pretreatment and (B) kratom hyperpigmentation posttreatment with picosecond 730-nm laser (polarizing camera filter used).

prevent further exacerbation of the condition. A punch biopsy from the dorsal right hand revealed scattered melanin deposits in the superficial dermis, with a background of solar elastosis (Figures 9 and 10). In addition to the presence of pigment-laden histiocytes, no significant inflammation was observed. Scant extravasated erythrocytes were noted; however, a Perls stain was negative for hemosiderin (Figure 11). The pigment was positive for Fontana-Masson stain (Figure 12), further supporting the diagnosis.

Similar to the first case, two test spots were conducted using picosecond 1064 nm and picosecond 730 nm lasers. The picosecond 730 nm laser showed a significant response (Figure 13), and the patient underwent a series of treatments with this modality. Immediate light to moderate pigment whitening of the treated

areas, with or without edema, was observed during treatments and used as an endpoint to assess treatment efficacy (Figure 14). Treatments were spaced 4–6 weeks apart, using the picosecond 730 nm laser (spot size: 3 mm, fluence: 1.5–1.8 J/cm², frequency: 3–4 Hz). Notably, the patient has experienced 98% clearance in the appearance of the hyperpigmentation, with no significant side effects (Figures 15 and 16).

3 | Discussion

The use of dietary supplements has surged in developed nations over the past decade, driven by growing consumer demand for natural or alternative health remedies. While many supplements, including herbal products, are marketed as safe and effective

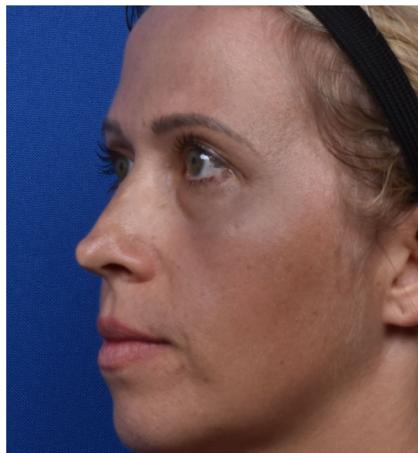


FIGURE 7 | Kratom hyperpigmentation involving the face.

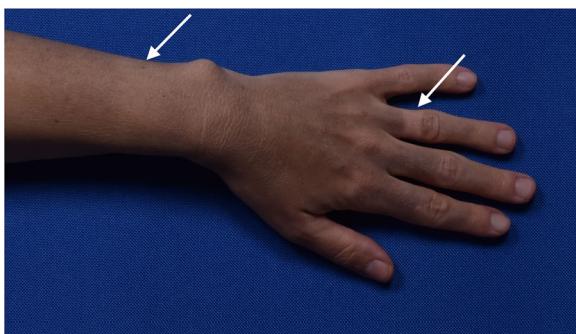


FIGURE 8 | Kratom hyperpigmentation involving the hands sparing knuckles and jewelry areas.

alternatives to prescription medications, the safety, efficacy, and potential side effects of many have not been thoroughly studied. As a result, patients often remain unaware of the possible adverse effects these supplements may cause, leading to unintended health risks.

One such supplement that has gained significant traction in the United States is kratom (*Mitragyna speciosa*), a plant native to Southeast Asia. The traditional use of kratom dates back over 150 years in Southeast Asia, where fresh leaves are chewed for stimulant effects or brewed into a tea for their analgesic properties. Beyond its use as a pain reliever, kratom has historically been employed as a substitute for opium, as an antispasmodic, muscle relaxant, and even an antidiarrheal agent [2, 6]. In Western countries, kratom is primarily sought after for its analgesic properties, as a substitute for opiates or a “legal high,” and for alleviating symptoms of opioid withdrawal and mood disorders.

While kratom’s widespread use is increasingly reported in online forums and anecdotal sources, it is notably under-represented in the formal medical literature, particularly regarding its potential side effects. One such adverse effect that has emerged in anecdotal reports is kratom-induced hyperpigmentation [3–5]. This condition typically manifests as photo-distributed, hyperpigmented patches that are resistant to topical treatments. The pigmentation is deposited in a scattered fashion in the upper dermis, making it particularly challenging to treat using conventional methods. Notably, kratom-induced hyperpigmentation often appears in areas of the skin most exposed to sunlight, such as the face, hands, and neck, although the mechanism behind this phenomenon remains poorly understood.

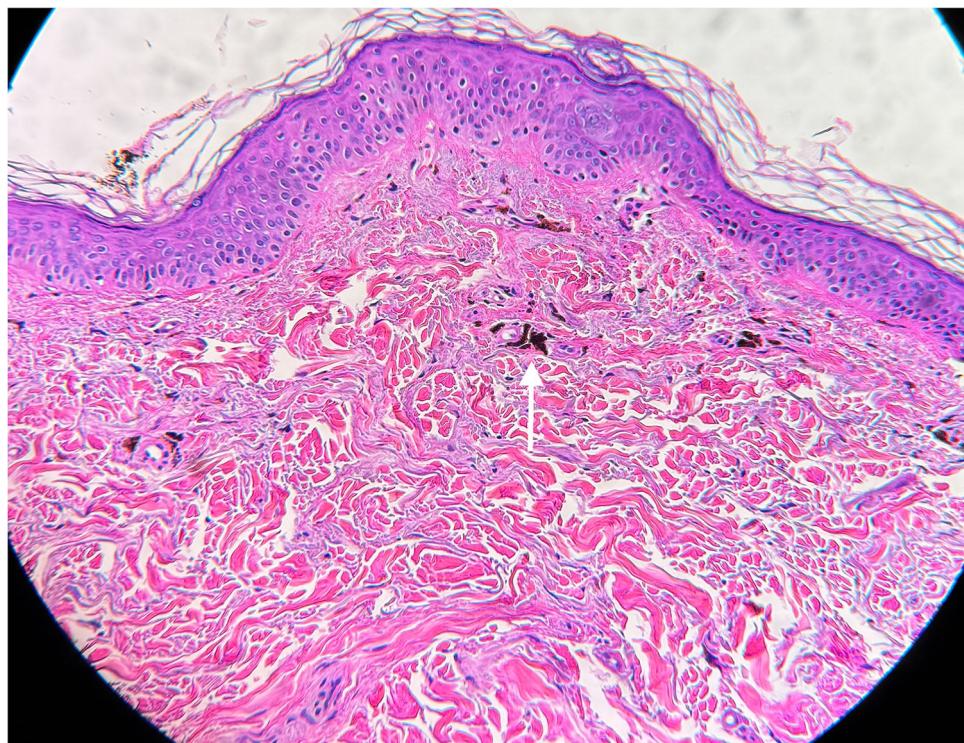


FIGURE 9 | Melanin deposits in the superficial dermis (arrows) with a background of solar elastosis (hematoxylin-eosin stain; original magnification: $\times 200$).

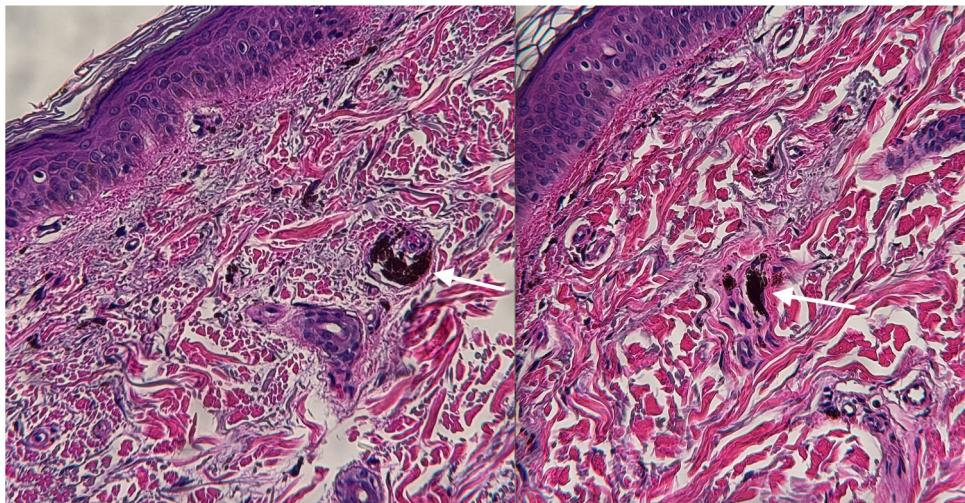


FIGURE 10 | Pigment deposition within macrophages (arrows) (hematoxylin-eosin stain; original magnification: $\times 400$).

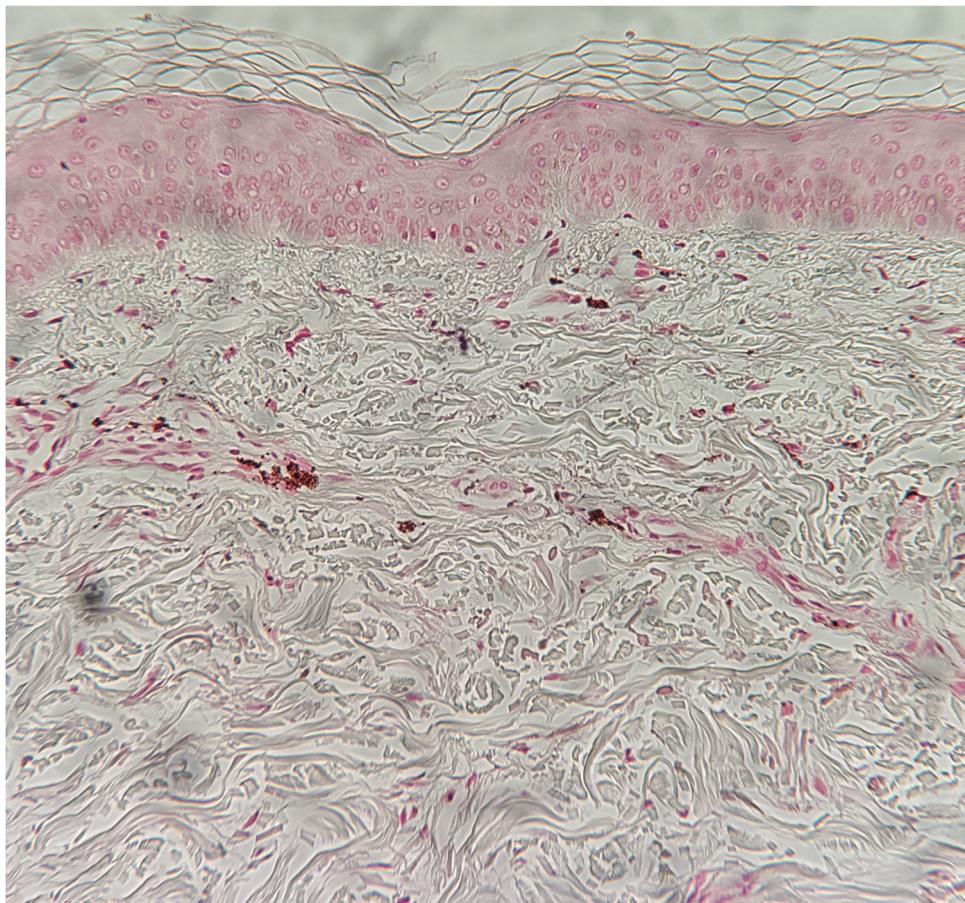


FIGURE 11 | Pigment deposits staining negative for hemosiderin (perls stain; original magnification: $\times 400$).

Several hypotheses have been proposed to explain the pathophysiology of kratom-induced hyperpigmentation. Powell et al. suggest that the active alkaloid mitragynine may trigger increased melanocyte-stimulating peptides through its dopaminergic activity. Alternatively, the pigmentation could result from the deposition of melanin-drug complexes, where kratom metabolites interact directly with melanin in the dermis [3]. Further research is needed to

definitively elucidate the precise biological mechanisms underlying this pigmentation disorder.

Histopathologically, the few reported cases of kratom-induced hyperpigmentation have demonstrated nonspecific findings. Most biopsies show a sparse superficial perivascular lymphocytic infiltrate, accompanied by a significant presence of melanophages in the dermis. The pigment stains

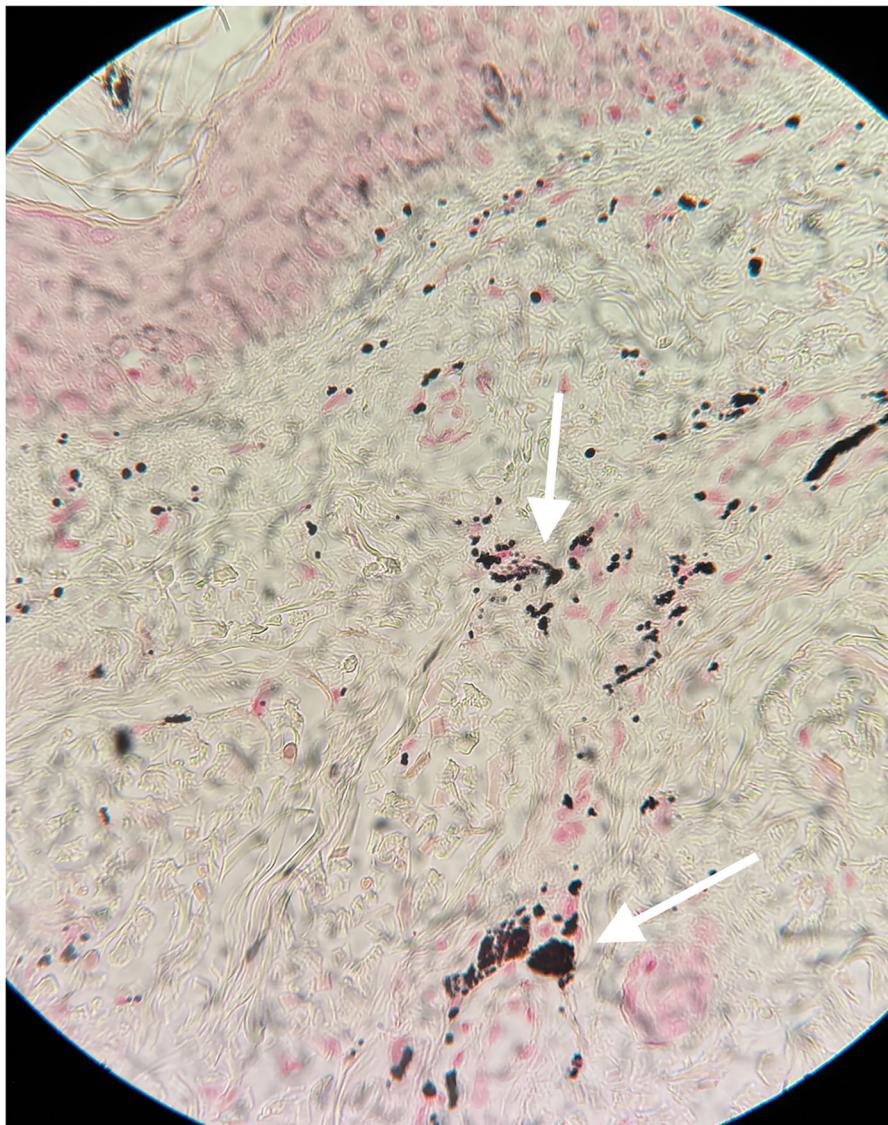


FIGURE 12 | Pigment deposition positive for melanin content (arrows) (Fontana-Masson stain; original magnification: $\times 400$).



FIGURE 13 | Chest spot test post picosecond 730 nm laser test showing significant response.

positively with Fontana-Masson, confirming the presence of melanin, but negatively to iron stains, which rules out hemosiderin deposition. This pattern suggests that the pigmentation is indeed melanin-based, but the exact nature of the pigment granules remains unclear [3–5]. Further histopathological studies, including more detailed analysis of

the pigment composition and its interaction with kratom's bioactive compounds, are crucial to fully understand the underlying mechanisms of this adverse reaction. Additionally, identifying potential risk factors for developing kratom-induced hyperpigmentation—such as dosage, duration of use, and individual predispositions—will be important in managing this condition in clinical practice.

To date, there are no established treatments for kratom-induced hyperpigmentation in the literature. However, the introduction of picosecond lasers, particularly the 730 nm titanium-sapphire laser, has significantly advanced the management of various pigmentary disorders, including tattoos and benign pigmented lesions [7, 8]. Picosecond lasers offer several advantages over traditional laser systems. Their very short pulse durations allow for precise targeting of pigment particles, leading to faster pigment clearance, shorter treatment times, and reduced recovery periods. Additionally, picosecond lasers generate a combination of photomechanical and photothermal effects, with photothermal effects playing a role in enabling the photomechanical effects in tissue, particularly at very short pulse durations [9],

enhancing the esthetic outcome. Importantly, the high precision and extremely short pulse duration of the picosecond laser minimize the risk of damage to surrounding tissues, reducing the likelihood of scarring or other adverse effects. Thus, the 730 nm picosecond laser offers a safe and highly effective approach for treating dermal hyperpigmentation by selectively targeting and fragmenting melanin, while also stimulating skin rejuvenation through collagen induction.

In this report, we present the first documented use of the 730 nm picosecond titanium-sapphire laser for the treatment of kratom-induced hyperpigmentation. Both patients treated with this laser showed significant improvement in pigmentation, with no reported adverse effects following treatment. The treatment parameters were selected based on results from initial test spots and were adjusted during subsequent treatments to optimize efficacy. For both patients, light-to-moderate frosting of the treated areas with or without edema was considered the clinical endpoint, indicating adequate

thus minimizing the risk of heat-induced damage to surrounding tissues. This is especially beneficial for treating conditions like drug-induced hyperpigmentation, where heat confinement and the risk of post-inflammatory hyperpigmentation are significant concerns [7].

In contrast to traditional nanosecond lasers, picosecond lasers deliver higher energy in a shorter time frame, creating pressure waves that fragment pigment with greater precision and efficiency. This has been shown to reduce the risk of adverse effects, such as scarring and post-inflammatory hyperpigmentation [10, 11]. Furthermore, the 730 nm picosecond laser has demonstrated efficacy in the removal of multicolored tattoos, including black, blue, green, and purple inks [12], suggesting its versatility in targeting a broad spectrum of pigments. These properties make the 730 nm picosecond laser an ideal candidate for treating kratom-induced hyperpigmentation, where pigment is often deposited in the dermis and may be resistant to conventional treatments.



FIGURE 14 | Left profile of the patient's face, illustrating the endpoint posttreatment, showing immediate light to moderate pigment whitening in the treated areas, along with edema.

A 730 nm picosecond laser can be an effective treatment for hyperpigmentation caused by melanin deposition in the dermis, utilizing a selective photothermal effect. Although wavelengths around 500–700 nm (such as 532 or 755 nm) are more commonly used for targeting melanin, 730 nm still falls within an effective absorption range for melanin, particularly in deposition which is deeper in the dermis. The 730 nm wavelength in this platform is delivered at a pulse duration ranging from 240 to 500 picoseconds [12], and is preferentially absorbed by melanin, enabling the laser to specifically target pigmented lesions in the dermis. The picosecond pulse duration (10^{-12} s) delivers energy in ultra-short bursts, resulting in selective photothermal fragmentation of melanin granules into smaller particles with a lower risk of collateral injury to surrounding tissue. The fragmented melanin particles are then cleared by the body's immune system, leading to a gradual reduction in pigmentation. In addition to its primary effect on melanin, the energy delivered by the picosecond laser can induce a mild inflammatory response in the dermis, stimulating fibroblasts and promoting collagen production. This collagen remodeling can improve skin texture and tone, further



FIGURE 15 | (A) kratom hyperpigmentation pretreatment and (B) kratom hyperpigmentation posttreatment with picosecond 730-nm laser.

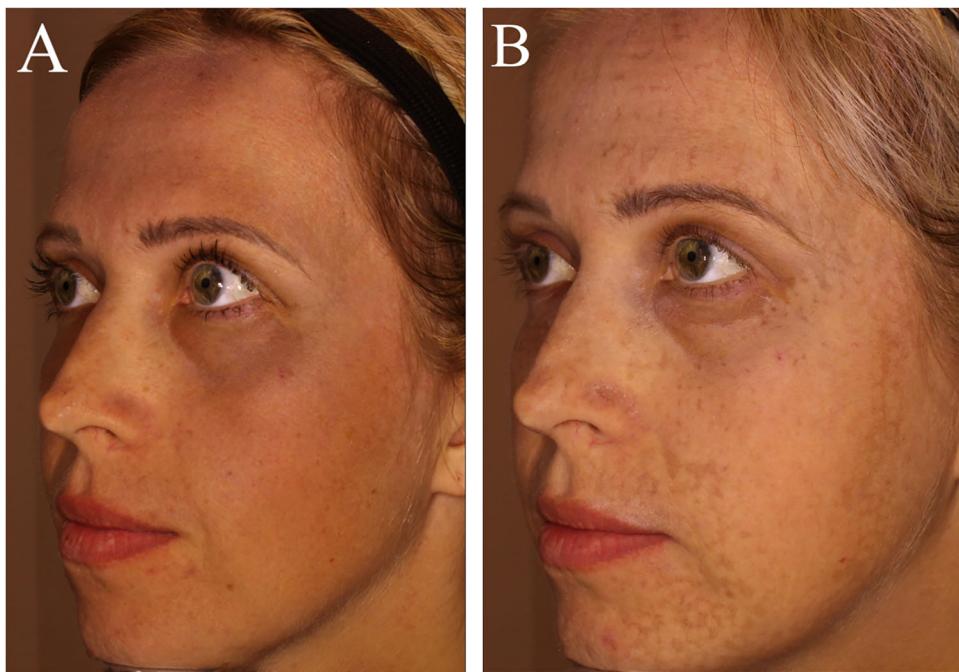


FIGURE 16 | (A) kratom hyperpigmentation pretreatment and (B) kratom hyperpigmentation posttreatment with picosecond 730-nm laser (polarizing camera filter used).

pigment disruption. Fluence levels were gradually increased for each subsequent session, based on patient tolerance and the absence of adverse effects in follow-up visits.

The first case showed no signs of recurrence of hyperpigmentation 10 months after the final session. The second case demonstrated significant improvement in the appearance of the hyperpigmentation, with continued favorable responses to therapy (Figures 8 and 9). The results from both cases suggest that picosecond 730 nm laser therapy is a promising and safe treatment option for kratom-induced hyperpigmentation, offering a viable solution to a previously underreported dermatological complication.

Further clinical studies, including larger patient cohorts and long-term follow-up, are needed to better define the role of picosecond lasers in treating drug-induced pigmentation disorders, including those caused by kratom. Such research will help refine treatment protocols and ensure that this technology can be optimally utilized for patients with pigmentary changes linked to various pharmacological agents.

4 | Conclusion

The 730-nm picosecond titanium sapphire laser represents a promising and safe treatment option for improving the cosmetic appearance of hyperpigmentation associated with kratom use. This advanced laser technology has shown efficacy in addressing various types of pigmentary disorders, and in this case, it appears to offer a viable solution for mitigating the discoloration caused by kratom-induced hyperpigmentation. To the best of our knowledge, this is the first reported use of a picosecond laser specifically to treat hyperpigmentation linked to kratom use. Given the growing interest in the dermatological effects of kratom, further clinical studies are warranted to better understand the laser's potential and optimize

treatment protocols for drug-induced pigmentation disorders. Such research could pave the way for more targeted and effective approaches in managing pigmentation complications related to various substances.

Ethics Statement

This case series was conducted with the informed consent of both patients. Written informed consent was obtained before treatment, and both patients were fully informed about the nature of the procedure, potential risks, and benefits. The patients also provided consent for the publication of their anonymized case details and images for academic and research purposes. The study adhered to all applicable local ethical guidelines and principles.

Consent

The authors have nothing to report.

Conflicts of Interest

Girish S. Munavalli has received research funding from Candela Medical Company, and he is on the medical advisory board.

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