ISSN-e 1984-8773

Surgical & Cosmetic Dermatology

SOCIEDADE BRASILEIRA DE DERMATOLOGIA

APOIO CIENTÍFICO:

www.surgicalcosmetic.org.br/

Treatment modalities for exogenous ochronosis: A narrative review of current and emerging therapeutic approaches. (Treatment of exogenous ochronosis)

Modalidades de tratamento para ocronose exógena: Uma revisão narrativa das abordagens terapêuticas atuais e emergentes. (Tratamento para ocronose exógena)

DOI: http://www.dx.doi.org/10.5935/scd1984-8773.2026180541

ABSTRACT

Exogenous ochronosis is a chronic skin disorder characterized by dermal hyperpigmentation, often resulting from prolonged use of hydroquinone. This review analyzed 29 studies (2000-2025) assessing treatments for exogenous ochronosis. Laser and light-based therapies, particularly in combination regimens, showed the greatest efficacy, while microneedling and chemical peels provided moderate improvement. Topical agents alone offered limited benefit. Post-inflammatory hyperpigmentation was the most frequent adverse event. Emerging modalities, including intradermal vitamin C, exosome therapy, and platelet-rich fibrin lysate, demonstrated promising early results. Overall, multimodal and light-based therapies appear to be the most effective; however, further controlled studies are essential to confirm their safety and long-term outcomes.

Keywords: Ochronosis; Hyperpigmentation; Dermabrasion

RESUMO

A ocronose exógena é uma doença cutânea crônica caracterizada por hiperpigmentação dérmica, geralmente causada pelo uso prolongado de hidroquinona. Esta revisão analisou 29 estudos (2000-2025) sobre tratamentos para a ocronose exógena. As terapias baseadas em laser e luz, especialmente em combinações, apresentaram maior eficácia, enquanto o microagulhamento e peelings químicos proporcionaram melhoria moderada. Os agentes tópicos isolados tiveram benefício limitado. A hiperpigmentação pós-inflamatória foi o evento adverso mais comum. Modalidades emergentes, como vitamina C intradérmica, terapia com exossomos e lisado de fibrina rica em plaquetas, tiveram resultados promissores. Terapias multimodais parecem mais eficazes, exigindo estudos controlados adicionais para confirmar sua segurança e eficácia.

Palavras-chave: *Ocronose; Lasers; Hiperpigmentação*

Review Article

Authors:

Emmanuela Dapomaa Asante[1]

Hsuan Hsiang Chen[2]

[1] Tema General Hospital, Internal Medicine Department, Tema, Greater Accra, Ghana

[2] University of South Wales, Department of Dermatology, Wales, United Kingdom

Correspondence:

Emmanuela Dapomaa Asante

E-mail: nuelasante11@gmail.com / emmanuela.asante@ghs.gov.gh

Funding: None

Conflict of interest: None

Submitted on: 11/30/2025

Final decision: 12/21/2025

How to cite this article:

Asante ED, Chen HH. Treatment modalities for exogenous ochronosis: A narrative review of current and emerging therapeutic approaches. (Treatment of exogenous ochronosis). Surg Cosmet Dermatol. 2026;18(2):e20260541.

INTRODUCTION

The term "ochronosis" is derived from the Greek word ochre, meaning yellow discoloration, and was first described in the 18th century by Virchow, who noted the ochre-like pigmentation in tissues.[1-3]

Ochronosis refers to a bluish-gray discoloration of connective tissues caused by pigment deposition and is classified into endogenous and exogenous forms.[4] Endogenous ochronosis, or alkaptonuria, is a rare autosomal recessive disorder resulting from homogentisic acid oxidase deficiency,[5-10] which leads to systemic manifestations such as arthropathy, pigmentation, and organ calcification.[11-19]

Exogenous ochronosis (EO), by contrast, is an acquired disorder characterized by blue-black pigmentation of the skin, typically induced by chronic application of topical skin-lightening agents. Hydroquinone is the most commonly implicated compound, though resorcinol, phenol, quinine, picric acid, and mercury have also been linked to the condition.[3] First described by Pick in 1906 and later associated with hydroquinone use by Findlay and De Beer in 1975, EO has since been recognized as an important adverse effect of long-term skin-lightening practices.[3]

EO is increasingly prevalent, particularly in populations with darker skin phototypes, where demand for skin-lightening is high and products are often unregulated. Notably, the risk of EO is not solely determined by hydroquinone concentration, as cases have been reported with low-strength formulations (2%), implicating cumulative dose and duration of exposure as central risk factors.[14]

Alcohol-based formulations may further heighten risk by enhancing percutaneous absorption.[3] Additional predisposing factors include extensive or prolonged sun exposure, application over large body surface areas, and the presence of active melanocytes that interact with hydroquinone-induced metabolic pathways.[15-17]

The pathogenesis of EO remains incompletely understood. Several mechanisms have been proposed, including hydroquinone-induced stimulation of melanogenesis, its oxidation to quinones and melanin-like intermediates, and its inhibition of homogentisic acid oxidase leading to pigment polymerization in the dermis.[20-23]

Clinically, EO presents as bilaterally symmetric blue--black macules, predominantly over the malar regions, temples, and cheeks, progressing through 3 stages: mild erythema and pigmentation (stage I), hyperpigmentation with colloid milia (stage II), and papulonodular lesions (stage III).[24-30]

Diagnosis can be challenging, particularly in the early stages, when EO may mimic melasma. Dermoscopy may reveal gray-blue amorphous areas with obliteration of follicular openings, while reflectance confocal microscopy has found characteristic dermal structures.

Histopathology remains the gold standard for diagnosis, with hallmark ochre-colored, banana-shaped fibers in the dermis.[3]

Epidemiological data are limited due to underrecognition and misdiagnosis. Early reports suggested prevalence rates of up to 35% among Black populations in South Africa, but more recent evidence shows that EO also affects lighter skin phototypes, including Hispanic, European, and Asian populations.[31-34]

In the United States, a dermatology survey identified 512 suspected cases, of which 130 were biopsy-confirmed.[30]

Management of EO is difficult, as pigmentation is often persistent and sometimes irreversible. Discontinuation of hydroquinone and strict photoprotection are essential first steps, but improvement may take years. Pharmacological interventions such as retinoids, corticosteroids, antioxidants, and systemic agents yield variable results, while procedural approaches—including chemical peels, dermabrasion, microneedling, and energy-based devices such as Q-switched and Nd:YAG lasers—have shown promise but lack standardization.[24,30]

Given its growing prevalence, diagnostic challenges, and limited treatment success, EO represents an important dermatological concern. This review critically evaluates current pharmacological and non-pharmacological treatment modalities for EO, with emphasis on evidence from clinical case series, procedural outcomes, and emerging therapies, to guide future practice and research.

METHODS

Study Design

This study employed a narrative literature review to explore and evaluate treatment modalities for EO, with emphasis on effectiveness, safety, and emerging therapies. The review was guided by 3 objectives: (1) to identify the most effective treatment modalities, (2) to evaluate safety concerns and adverse effects, and (3) to highlight promising novel interventions.

The narrative review approach was chosen because it allows the integration of diverse sources of evidence, including case reports, case series, and retrospective studies, which constitute the majority of the EO literature. Unlike systematic reviews, which require homogeneous data, this method facilitates a broad overview of treatment trends, knowledge gaps, and potential innovations, making it particularly valuable for under-researched conditions.[35-37]

Search Strategy

An extensive search was performed across PubMed, Scopus, Google Scholar, ScienceDirect, JAMA, the University of South Wales FINDit tool, and Surgical & Cosmetic Dermatology. The search covered publications from January 2000 to May 2025 using keywords and combinations such as "Exogenous Ochronosis," "Hydroquinone-induced ochronosis," "Treatment," "Laser therapy," "Microneedling," "Dermabrasion," and "Oral medication." Boolean operators ("AND," "OR") were used to refine the search, and reference lists of key articles were

screened to identify additional studies.

Inclusion and Exclusion Criteria

Included studies comprised peer-reviewed case reports, case series, retrospective studies, or systematic reviews reporting treatment outcomes in patients with clinically or histopathologically confirmed EO. Only English-language publications involving human subjects were considered. Studies exclusively on endogenous ochronosis, animal or in vitro research, studies not focusing primarily on treatment modalities, and non-English works without usable abstracts were excluded.

Data Extraction and Synthesis

Twenty-nine articles met the inclusion criteria: 2 retrospective studies, 8 case series, and 19 case reports. Data were extracted into tables capturing author and year, study design, treatment modality, outcomes, and adverse effects. Findings were synthesized qualitatively, with particular attention to combination therapies and emerging approaches. A systematic review or meta-analysis was not feasible due to the heterogeneity in study designs and outcome measures.

RESULTS

The treatment of EO encompasses non-pharmacological measures, pharmacological approaches such as topical and oral medications, and procedural interventions like dermabrasion, microneedling, and energy-based device therapies.

Non-Pharmacological Approaches

A key step in the management of EO is the immediate discontinuation of the offending agent, although visible improvement may take years.[19]

Strict photoprotection, including broad-spectrum sunscreens, hats, UV-protective sunglasses and protective clothing, is also critical to prevent further pigmentation.[3]

Several case reports highlight the benefit of sunscreen as an adjunctive therapy. For example, Tekgöz et al.[7] reported reduced hyperpigmentation after 7 months of sunscreen use and discontinuation of hydroxychloroquine. Similarly, Ceglio et al.,[5] Bellew and Alster,[2] and Gulwani et al.[28] emphasized the use of broad-spectrum sunscreen during EO treatment. A narrative review by Simmons et al.[30] also reported improved outcomes with sunscreen use in some cases. These findings underscore the importance of photoprotection in preventing disease progression and for protecting the skin during treatment.

Pharmacological Approaches

Topical Medications

Topical treatments alone have shown limited effectiveness in the management of EO. However, when combined with other therapies, they may provide clinical improvement. Commonly used topical agents include corticosteroids, retinoic acid, azelaic acid, kojic acid, topical calcineurin inhibitors, and tyrosinase inhibitors.

A 2007 case series by Charlín et al.[6] described 4 women (skin phototypes IV–V) with long-standing melasma who developed progressive facial hyperpigmentation after 10–25 years of hydroquinone-based cream use (2%–6%). Clinical signs included blue-brown macules, caviar-like papules, and confetti-like depigmentation, consistent with Dogliotti Stage II EO. Histopathology confirmed pigment incontinence and yellow-brown banana-shaped fibers in the dermis.

Treatment with combinations of 0.05% retinoic acid, 20% azelaic acid, and kojic acid led to only partial or minimal improvement.[6]

Singh and Ramesh[31] reported the case of a 44-year-old woman who developed bluish-black pigmentation after 1 year of skin-lightening cream use. Histopathology confirmed EO. Despite discontinuing the cream and using 0.05% topical retinoic acid with strict photoprotection, there was no notable improvement after 3 months.

Similarly, Qorbani et al.[27] described 2 patients with EO secondary to hydroquinone and tretinoin use. In one case, desonide 0.5% lotion with photoprotection reduced inflammation but did not improve pigmentation. The second patient was treated with tazarotene 0.1% gel and pimecrolimus cream in conjunction with photoprotection, but pigmentation persisted for more than 1 year.

Patel and Shah[24] reported the case of a 55-year-old woman with EO following 2 years of daily use of hydroquinone-containing cream. Clinical examination showed bluish-brown patches with erythema and telangiectasia. Despite discontinuing the cream, applying topical emollients and retinoid gel, and practicing strict photoprotection, only minimal improvement was observed after 2 months.

A recent retrospective study by Keshavamurthy Vinay et al.[12] evaluated 29 patients with EO, predominantly women (93%) with skin phototypes III–VI. Most had a history of hydroquinone use for melasma, averaging 16 months. The malar region was the most commonly affected, with 41% of cases classified as Dogliotti stage I and 59% as stage II. Among 11 patients for whom treatment data were available, combination therapies demonstrated variable outcomes. Chemical peels with topical tacrolimus 0.1% led to moderate improvement over 6 months in 6 patients. A regimen of kojic acid, arbutin, and glycolic acid resulted in minimal improvement, while 1 patient receiving topical tacrolimus combined with oral medication achieved moderate improvement over 6 months.

Overall, topical pharmacological treatments for EO are largely adjunctive. Monotherapy rarely produces substantial improvements, and outcomes are generally enhanced when topical agents are combined with photoprotection, chemical peels, or systemic treatments. Despite limited efficacy, topical agents remain a cornerstone of EO management, particularly for patients with mild disease or as part of multimodal therapeutic strategies.

Oral Medications

Oral medications are infrequently used in EO, generally alongside other therapies. Agents include tranexamic acid, corticosteroids, glutathione, and systemic retinoids.

Moche et al.[22] reported 2 Black female patients with EO from prolonged hydroquinone use who developed cutaneous and systemic sarcoidosis. Treatment with oral prednisone (30 mg/day) and chloroquine (200 mg/day) led to improvement in both systemic and skin symptoms.

Pirrone et al.[25] described a 51-year-old Filipino woman with histologically confirmed EO who received oral isotretinoin 20 mg 4 times daily, resulting in mild improvement.

Sunkara et al.[32] reported the case of a 39-year-old woman with EO after 3 months of using a 4% hydroquinone cream. Oral glutathione was administered, leading to a 50% reduction in pigmentation after 4 months.

In a retrospective study by Keshavamurthy Vinay et al.,[12] one patient received oral tranexamic acid as part of the treatment, achieving moderate improvement.

Procedural Treatments

Procedural therapies for EO are typically considered when topical or oral medications provide limited benefit. These include dermabrasion, microneedling, and chemical peels, all of which aim to reduce dermal pigmentation through controlled skin injury or tissue remodeling. The available evidence is largely based on case reports, case series, and small retrospective studies, reflecting both the rarity and treatment-resistant nature of EO.

Dermabrasion

Dermabrasion induces superficial skin injury, triggering wound healing and dermal remodeling, which can improve skin appearance. It has demonstrated moderate to substantial success in selected EO cases, particularly when topical therapies fail. Sunkara et al.[32] reported the case of a 39-year-old woman with EO from 3 months of 4% hydroquinone use who underwent microdermabrasion alongside photoprotection, achieving a 50% reduction in pigmentation after 4 months. Similarly, Lamas et al.[15] described a 70-year-old woman with a 10-year history of EO who underwent facial dermabrasion with water sandpaper, combined with a nighttime topical regimen (0.05% desonide, 0.01% tretinoin, 2% alpha-bisabolol) and strict photoprotection. After 3 months, the patient exhibited a marked reduction in hyperpigmentation, highlighting the role of dermabrasion in achieving substantial pigment clearance when combined with adjunctive measures.

Microneedling

Microneedling involves the creation of micro-injuries within the dermis to stimulate collagen production and facilitate pigment reduction. Moerbono Mochtar et al.[23] reported the cases of 3 women aged 45–50 years with long-standing EO who underwent biweekly microneedling using a 1-mm dermaroller over an 8-week period, associated with daily SPF 30 use. Improvements in pigmentation and vascular changes were noted by week 4, accompanied by increased patient satisfaction and physician-rated appearance scores. A larger 10-year retrospective study by Lazar et al.[16] involving 25 patients with EO demonstrated that microneedling promoted dermal remodeling and achieved visible pigment reduction without substantial adverse effects, particularly in patients with darker skin types, indicating its safety and effectiveness as a procedural option.

Chemical Peels

Chemical peels employ caustic agents such as glycolic acid, salicylic acid, and trichloroacetic acid (TCA) to remove the epidermal and superficial dermal layers, promoting pigment reduction.

Franca et al.[8] reported the case of a 40-year-old woman with EO who initially underwent a combination peel consisting of 5% hydroquinone, 5% retinoic acid, and 14% salicylic acid, which resulted in minimal improvement. A subsequent 20% TCA peel in combination with other treatment modalities led to complete resolution of the lesions.

Similarly, Keshavamurthy Vinay et al.[12] reported moderate improvement in patients with EO treated with 30% glycolic acid peels. When glycolic acid peels were combined with topical medications, 6 patients experienced moderate pigment reduction over a 6-month period. These findings underscore that chemical peels may be more effective when used in combination with other treatment modalities rather than as monotherapy.

Overall, procedural treatments for EO provide valuable therapeutic options when conventional pharmacological approaches fail. Dermabrasion, microneedling, and chemical peels promote dermal remodeling and pigment reduction, with outcomes often enhanced when combined with topical agents and strict photoprotection. Although the available evidence is limited, these interventions have consistently demonstrated the potential to achieve partial to substantial improvement, particularly in long-standing or treatment-resistant cases. Further studies are needed to standardize protocols, optimize treatment combinations, and determine long-term efficacy and safety across diverse skin phototypes.

Energy-Based Device Therapy

Kramer et al.[14] described a case of a Hispanic woman with EO unresponsive to topical treatments who underwent treatment with a Q-switched ruby laser (694 nm, 7 J/cm^2 fluence, 5-mm spot size). The patient had noticeable clinical improvement, suggesting that Q-switched ruby lasers may represent a promising option for refractory EO.

Alster and Bellew[2] reported the use of a Q-switched 755-nm alexandrite laser in 2 patients with hydroquinone-induced EO. The first patient underwent 6 sessions at 2-month intervals with a mean fluence of 7.8 J/cm^2, while the second patient un-

derwent 4 sessions at 4-month intervals with a mean fluence of 6.9 J/cm². Both exhibited substantial lightening of pigmented areas without scarring or textural changes, and histopathological examination confirmed a reduction in dermal pigmentation.

Gil et al.[9] assessed the use of intense pulsed light (IPL) therapy in a 63-year-old woman with Fitzpatrick skin phototype V diagnosed with EO. She underwent 6 IPL sessions (645 nm, pulse duration 6 ms, fluence 20–22 J/cm²), alongside topical therapy with 4% kojic acid and 0.2% salicylic acid and strict photoprotection. After 2 months, only mild clinical improvement had been achieved. Dermoscopic features of EO persisted, and reflectance confocal microscopy found unchanged subepidermal banana-shaped bodies, indicating IPL efficacy was limited.

França et al.[8] reported the case of a 40-year-old woman with EO after prolonged hydroquinone use who underwent multiple treatment modalities. Four sessions of Q-switched Nd:YAG laser (1064 nm, 2.9–3.05 J/cm², 4-mm spot size) resulted in limited response. Subsequent treatment with ultrapulse CO_2 laser (5 W, 30-day intervals) resulted in partial improvement, particularly in the left malar region. IPL therapy (36 J, 10 ms) was then administered, followed by microdermabrasion and a chemical peel combining 5% hydroquinone, 5% retinoic acid, and 14% salicylic acid. Complete lesion clearance was achieved after 3 additional IPL sessions (36 J, 10 ms) in conjunction with 20% TCA peels.

Kanechorn-Na-Ayuthaya et al.[11] described 3 patients with EO treated with Q-switched Nd:YAG (1064 nm) and fractional CO_2 lasers. In the first case, a 67-year-old Thai woman (skin phototype V) underwent 4 Q-switched Nd:YAG laser sessions (1.9–2.2 J/cm²) and 1 fractional CO_2 laser session, achieving progressive fading and smoother skin texture by the third session, despite transient post-inflammatory hyperpigmentation (PIH). The second case, that of a 58-year-old woman (skin phototype III) who underwent 4 Nd:YAG sessions and one CO_2 laser session, achieved noticeable improvement in pigmentation and skin tone after the third session, accompanied by temporary PIH. In the third case, a 66-year-old woman (skin phototype IV) underwent 2 Nd:YAG laser sessions followed by fractional CO_2 laser treatment, with minimal PIH and visible skin lightening and mild rejuvenation at 5 months. Overall, combination laser therapy resulted in gradual improvement of lesions and high patient satisfaction.

Tan[33] evaluated 6 ethnic Chinese patients with histologically confirmed EO and concomitant melasma, classified according to Dogliotti staging: 4 with Stage I disease, 1 with Stage II, and 1 with Stage III. Treatment consisted of fortnightly Q-switched Nd:YAG (1064 nm) laser sessions using a low-fluence first pass (1.2 J/cm², 8- mm spot size) and targeted high-fluence passes (4–6 J/cm², 4-mm spot size) until petechiae or erythema appeared. Topical EMLA cream was applied before treatment, and post-treatment care included topical tetracycline and continuation of non-hydroquinone lightening agents. Patients with stage II and III disease showed marked improvement after 8 and 16 sessions, respectively, while patients with stage I disease demonstrated mild-to-moderate improvement. Pigment clearance was maintained, and no serious adverse events occurred, supporting the use of Q-switched Nd:YAG lasers, particularly with a multi-pass low-fluence and targeted high-fluence technique, for moderate-to-severe EO in darker skin phototypes.

Lee and Weiss[17] reported the case of a 48-year-old woman with EO treated with IPL (570 nm, 12 J/cm², 15 ms) at 6-week intervals, with lightening of pigmentation after the initial session.

Liu et al.[21] described a 50-year-old Chinese man (skin phototype IV) with Stage II EO who underwent 6 sessions of Q-switched Nd:YAG laser (1064 nm, 6–9 J/cm²) with no improvement, despite treatment adherence and discontinuation of hydroquinone.

Ko and Wang[13] reported the case of a 50-year-old Chinese woman with EO treated with Q-switched Nd:YAG (1064 nm, 5.3 J/cm²) and Q-switched alexandrite (755 nm, 8.5 J/cm²) lasers. Pigmentation worsened after 2 sessions; the use of fractional CO_2 laser was recommended, but declined. Carvalho et al.[4] described a 46-year-old woman (skin phototype V) treated with monthly fractional CO_2 laser sessions for 12 months, achieving substantial improvement. Pirrone et al.[25] reported the case of a 51-year-old Filipino woman who experienced mild improvement with oral isotretinoin and topical corticosteroids, but subsequent fractional laser therapy over 3 sessions achieved marked lightening of the hyperpigmented lesions. Baca et al.[1] described a 55-year-old woman (skin phototype IV) with long-standing EO refractory to multiple prior therapies, who underwent 9 sessions of fractional nonablative picosecond laser (1064/532 nm), achieving clear improvement in lesion color and texture.

Qian[26] presented 2 cases of EO treated with microneedle pulsed radiofrequency adjunctive to laser therapy, with satisfactory outcomes.

Lee et al.[18] reported the case of a 66-year-old woman treated with fractional CO_2 and Q-switched Nd:YAG lasers, with no clinical improvement after 3 sessions. Ceglio et al.[5] described a 52-year-old man (skin phototype V) treated sequentially with Q-switched Nd:YAG laser (12 sessions), IPL (7 sessions), and fractional CO_2 laser (5 sessions), with the most notable improvement achieved after fractional CO_2 laser therapy. Lazar et al.[16] conducted a 10-year review of 25 patients with EO (88% women, skin phototypes IV–VI) and found Q-switched alexandrite (755 nm) laser effective, with marked improvement in observed in 3 patients after a mean of 4.66 sessions.

Li and Zhang[20] reported the case of a 28-year-old woman with concomitant EO and vitiligo who achieved improvement after 4 chemical peels and one IPL session.

Almutairi et al.[38] reported the case of a 31-year-old man with refractory EO who responded to 3 sessions of picosecond alexandrite laser (755 nm) following prior unsuccessful treatment with Q-switched and 1064-nm picosecond laser therapy. The man achieved marked lesion improvement after 6 months with no complications.

NEW AND EMERGING TREATMENT MODALITIES

Emerging treatment modalities for EO aim to improve therapeutic outcomes and patient satisfaction. One such novel approach involves intradermal vitamin C injections, which act as antioxidants and may reduce pigmentation. Another innovative modality is platelet-rich fibrin lysate (PRF-L), an autologous derivative of platelet-rich fibrin that is rich in growth factors and cytokines and may promote skin rejuvenation and pigment regulation.

A case series involving 3 healthy Javanese women aged 45–50 years explored the potential of PRF-L in the management of EO. Each patient had progressive facial hyperpigmentation previously diagnosed as melasma, with disease durations of 2, 5, and 6 years, a history of prolonged use of dermatologist-prescribed skin-lightening creams without follow-up or knowledge of their ingredients. Clinical examination revealed patchy hyperpigmentation, facial erythema, hypopigmented macules, and telangiectasia.

The diagnosis of EO was supported by skin stretching tests, Wood's lamp, and dermoscopy. After informed consent was obtained, autologous PRF-L was prepared by collecting peripheral blood in 10-mL sterile tubes without anticoagulant, centrifugation at 2700 rpm (~400 g) for 12 minutes, and incubation of the isolated PRF gel at 4 °C for 24 hours to obtain the PRF-L supernatant. Facial skin was cleansed and anesthetized topically for 1 hour. PRF-L was administered using 2 methods: topical application followed by dermarolling (1-mm depth) on the right side of the face and intradermal injection with a 1-mL syringe on the left. Patients were instructed to apply SPF 30 sunscreen daily. The 2-month follow-up period included biweekly clinical photography, with 2 blinded physicians assessing improvement using a 10-point scale. Early improvements were noted on dermoscopic examination, and 1 patient demonstrated visible clinical improvement.[23]

Rajesh Gulwani et al.[28] described a 45-year-old Indian man with bilateral cheek hyperpigmentation following intermittent use of multiple skin-lightening agents over a 9-year period, including a triple-combination cream (2% hydroquinone, 0.05% tretinoin, 0.1% mometasone) over 3 years. Clinical examination revealed blue-black macules on an erythematous background, and dermoscopy found dark globules in annular, arciform, and curvilinear patterns, follicular obliteration, and telangiectasia. Histopathological examination confirmed EO, revealing epidermal thinning, elastotic degeneration, and banana-shaped ochronotic bodies within the dermis. The patient underwent intradermal vitamin C (ascorbic acid) injections: 1 mL (100 mg) at 1-cm intervals across affected areas, repeated every 4 weeks for 3 sessions. Sunscreen to protect against ultraviolet, infrared, and visible light and a barrier-repair moisturizer containing hyaluronic acid, ceramide, squalene, and lecithin were prescribed. The treatment resulted in complete resolution of erythema within 1 month and approximately 80% improvement in hyperpigmentation after 3 months. The treatment regimen was well tolerated, with mild-to-moderate discomfort at injection sites.[28]

Plant-based exosome therapy represents another emerging therapeutic option. Widjaja et al.[35] reported the case of a 39-year-old Indonesian woman with widespread facial hyperpigmentation following 8 months of using a 4% hydroquinone cream. She developed erythema and patchy pigmentation and had never used sunscreen. Clinical examination revealed dry, sallow skin with hyperpigmented macules, hypopigmented areas, and telangiectasia, supporting the diagnosis of EO. Treatment consisted of intradermal injections of 6 mL of a plant-derived exosome skin booster across facial zones, followed by topical application of 1.2 mL of exosome serum and dual-light photodynamic therapy (PDT) for 10 minutes per light source. A comprehensive skincare regimen was instituted, including a morning routine consisting of facial cleanser, toner, serum, and cream containing niacinamide, alpha-arbutin, 3-O-ethyl ascorbic acid, and tranexamic acid, as well as nighttime cream containing retinol. An SPF 50 hybrid sunscreen was introduced for photoprotection. At the 36-day follow-up, improvements in skin texture and tone were evident, with brighter, better-hydrated skin and a notable reduction in hyperpigmented patches, particularly on the cheeks.

These emerging therapies reflect a trend toward minimally invasive, regenerative, and targeted approaches for EO. PRF-L offers autologous growth factor–mediated modulation of pigmentation and dermal remodeling, demonstrating early dermoscopic and clinical improvements. Intradermal vitamin C provides antioxidant-mediated pigment reduction and skin repair, achieving substantial clinical improvement in severe EO. Plant-based exosome therapy, combined with topical agents and PDT, represents a multimodal approach that addresses pigmentation, inflammation, and skin barrier restoration.

Across these modalities, photoprotection remains a critical adjunctive measure, emphasizing the importance of using sunscreen to prevent further pigmentary changes and protect against ultraviolet, infrared, and visible light–induced skin damage. In addition, supportive skincare with barrier repair and antioxidant components may enhance overall treatment outcomes. Case reports and small case series suggest that these therapies are generally well tolerated, with minimal adverse effects such as mild injection-site pain and transient erythema, while resulting in measurable improvements in hyperpigmentation, erythema, telangiectasia, and skin texture.

Collectively, early evidence suggests that these innovative approaches can complement conventional EO management strategies, offering the potential for faster clinical improvement, greater patient satisfaction, and expanded therapeutic options for individuals with treatment-resistant cases. Long-term follow-up and larger studies are needed to establish standardized protocols, determine optimal dosing schedules, and compare efficacy with established procedural and pharmacological therapies. Nonetheless, PRF-L, intradermal vitamin C, and plant-based exosome therapy represent promising additions to the evolving therapeutic armamentarium for EO.

Table 1: TOPICAL TREATMENT

	AUTHORS	STUDY DESIGN	TREATMENT	OUTCOME	ADVERSE EFFECTS
1.	Charlín et al., 2007	Case series	Retinoic acid + azelaic acid + kojic acid Retinoic acid + azelaic acid	Partial improvement No improvement	Not documented Not documented
2.	Singh and Ramesh, 2014	Case report	Retinoic acid + sunscreen	No improvement	Not documented
3.	Qorbani et al., 2020	Case series	Desonide lotion + sunscreen Tazarotene 0.1% gel + pimecrolimus cream + photoprotection	Minimal improvement Minimal to no improvement	Not documented Not documented
4.	Lazar et al., 2023	Retrospective study	Triluma Tretinoin Ammonium lactate	Not helpful	Not documented
5.	Patel and Shah, 2024	Case report	Emollient + retinoid gel	Minimal improvement	Not documented
6	Keshavamurthy Vinay et al., 2025)	Retrospective study	Kojic acid+ arbutin + glycolic acid + sunscreen	Minimal improvement	Not documented

Table 2: ORAL TREATMENT

	AUTHORS	STUDY DESIGN	TREATMENT	OUTCOME	ADVERSE EFFECTS
1.	Moche et al., 2010	Case series	Tab prednisone 30 mg + Tab chloroquine 200 mg	Marked improvement	Not documented

Table 3: PROCEDURAL TREATMENT

	AUTHORS	STUDY DESIGN	TREATMENT	OUTCOME	ADVERSE EFFECTS
1.	Lamas et al., 2023	Case report	Dermabrasion	Significant lightening	Not documented
2.	Lazar et al., 2023	Retrospective Study	Microneedling	Marked improvement	None reported
3.	Keshavamurthy Vinay et al., 2025	Retrospective study	Chemical peel with 30% glycolic acid	Moderate improvement	Not documented

Table 4: TOPICAL TREATMENT

	AUTHORS	STUDY DESIGN	TREATMENT	OUTCOME	ADVERSE EFFECTS
1.	Kramer et al., 2000	Case report	Q-switched ruby laser (694 nm, 7 J/cm2, 5-mm spot size)	Marked improvement	Not documented
2.	Bellew and Alster, 2004	Case series	Q-switched alexandrite laser (755 nm, initial fluence 7.0 J/cm2, final fluence 8.0 J/ cm2, mean fluence 7.8 J/cm2) Q-switched alexandrite laser (755 nm, initial fluence 6.0 J/cm2 and final fluence 7.0 J/ cm2, mean fluence 6.9 J/cm2)	Significant improvement Marked improvement	Not documented Post inflammatory hyperpigmentation
3.	Charlín et al., 2007	Case series	Q-switched Nd:YAG laser (1064 nm)	No improvement	Not documented
4.	Kanechorn-Na-Ayutha-ya et al., 2013	Case series	Q-switched Nd:YAG laser (1064 nm, 1.9-2.2 J/cm2 fluence) + Fractional CO2 laser Q-Switched Nd:YAG laser (1064 nm, initial fluence 1.9 J/cm2) + fractional CO2 laser + pulsed-dye laser Q-switched Nd:YAG laser (1064 nm) + fractional CO2 laser	Significant improvement Significant improvement Significant improvement	Post inflammatory hyperpigmentation + purpura Post inflammatory hyperpigmentation + purpura Post inflammatory hyperpigmentation + purpura
5.	Tan, 2013	Case series	Q-switched Nd:YAG laser (1064 nm)	2 patients showed relevant improvement and 4 of them showed mild improvement.	Petechiae and pinpoint bleeding
6	Liu et al., 2014	Case report	Q-switched Nd:YAG laser (1064 nm, 6-9 J/cm2 fluence)	No improvement	Not documented

Continuation…

	AUTHORS	STUDY DESIGN	TREATMENT	OUTCOME	ADVERSE EFFECTS
7	Lee and Weiss, 2014	Case report	Intense pulsed light (570 nm waves, 12 J/cm2 fluence, 15 ms pulse duration)	Marked improvement	Not documented
8	Ko and Wang, 2015	Case report	Q-switched Nd:YAG laser (1064 nm, 5.3 J/cm2 fluence, right zygomatic region) Q-switched alexandrite laser (755 nm, 8.5 J/cm2 fluence, right zygomatic region)	Significant improvement Marked improvement	Not documented Post inflammatory hyperpigmentation
9	Carvalho et al., 2016	Case report	Fractional CO2 laser (120 mm tip, 120 mJ, 150 points stitches per cm2)	No improvement	Not documented
10	Baca et al., 2018	Case report	Fractional picosecond laser (1064 nm and 532 nm, initial fluence 1.30 and 0.18 J/cm2, increased by 0.20/0.02 J/cm2 per application up to a maximum fluences of 2.9/0.30 J/cm2)	Significant improvement Significant improvement Significant improvement	Post inflammatory hyperpigmentation + purpura Post inflammatory hyperpigmentation + purpura Post inflammatory hyperpigmentation + purpura
11	Qian, 2018	Case series	Microneedle pulsed radiofrequency + Q-switched Nd:YAG laser + copper bromide laser therapy	2 patients showed relevant improvement and 4 of them showed mild improvement.	Petechiae and pinpoint bleeding
12	Lee et al., 2019	Case report	CO2 fractional laser + Q-Switched Nd:YAG laser	No improvement	Not documented
13	Ceglio et al., 2022	Case report	Q-switched Nd:YAG laser (1064 nm) + intense pulsed light+ fractional CO_2 laser (10,600 nm)		
14	Lazar et al., 2023	Retrospective study	Q-switched alexandrite laser (755 nm)		
15	Almutairi et al., 2024	Case report	Picosecond alexandrite laser (755 nm)		

Table 5: COMBINATION TREATMENTS

	AUTHORS	STUDY DESIGN	TREATMENT	OUTCOME	ADVERSE EFFECTS
1.	Keshavamurthy Vinay et al., 2025	Retrospective study	Tacrolimus ointment + oral tranexamic acid Glycolic acid peel + tacrolimus ointment	Moderate improvement Moderate improvement	Not reported
2.	Pirrone et al., 2017	Case report	Oral isotretinoin + topical corticosteroids + fractional laser	Marked improvement	Not documented
3.	Sunkara et al., 2020	Case report	Microdermabrasion + chemical peels (50% glycolic acid and yellow cosmelan) + oral glutathione + kojic acid cream + sunscreen	50% reduction in pigmentation	Not documented
4.	Gil et al., 2010	Case report	Intense pulsed light (645 nm, 6 ms, 20-22 J/cm2) + 4% kojic acid and 0.2% salicylic acid cream	Mild improvement	Not documented
5.	Franca et al, 2010	Case report	Q-switched Nd:YAG laser (1064 nm) + ultrapulse CO_2 laser + intense pulsed light + microdermabrasion + chemical Peels (5% hydroquinone, 5% retinoic acid, 14% salicylic acid, and 20% trichloroacetic acid)	Complete resolution of lesions	Not documented
6.	Liu et al, 2014	Case report	Tretinoin cream + niacinamide cream + Q-switched Nd:YAG laser (1064 nm)	No improvement	Not documented
7.	Li and Zhang, 2024		Chemical peel (salicylic acid) + intense pulsed light	Reduced pigmentation	Not documented

Table 6: NEW AND EMERGING TREATMENTS

	AUTHORS	STUDY DESIGN	TREATMENT	OUTCOME	ADVERSE EFFECTS
1.	Moerbono Mochtar et al., 2019	Case series	Platelet-rich fibrin lysate (PRF-L)	Visible clinical improvement	None reported
2.	Rajesh Gulwani et al., 2024	Case report	Intradermal vitamin C injections	80% reduction in hyperpigmentation	Mild to moderate injection pain
3.	Widjaja et al., 2025	Case report	Plant-based exosome therapy + photodynamic therapy	Visible improvement in pigmentation	None reported

DISCUSSION

Photoprotection is widely recommended, as EO is exacerbated by exposure to ultraviolet radiation. Bhattar et al.[3] highlight its role in limiting disease progression, while Simmons et al.[30] caution that sunscreen alone does not result in substantial cosmetic improvement. Across the literature, photoprotection is mostly used as an adjunctive therapy, suggesting that optimal outcomes are achieved when combining it with active therapies.

Topical agents, particularly in early-stage EO, demonstrate modest efficacy. Studies by Charlín et al.,[6] Singh and Ramesh,[31] and Qorbani et al.[27] report limited response to retinoic acid, azelaic acid, corticosteroids, and calcineurin inhibitors. Although these agents theoretically target melanin production and inflammation, poor dermal penetration likely limits their effectiveness given the deep pigment deposits found in EO. Keshavamurthy Vinay et al.[12] further demonstrated minimal improvement with topical monotherapy unless it was combined with peels or systemic agents. Thus, topicals should generally be considered adjunctive rather than definitive treatments.

A consistent observation across multiple studies[4–6,9,12,13,15,24,27,31,33] is the near-universal history of hydroquinone use in patients who develop EO. This highlights a potentially underrecognized association between melasma management and the onset of EO, raising concerns about long-term safety, particularly in individuals with darker skin phototypes or prolonged hydroquinone use. Reevaluation of melasma guidelines and development of safer alternatives or stricter protocols may help reduce the incidence of EO.

Oral medications are used sporadically, primarily for atypical presentations or experimental purposes. Moche et al.[22] reported corticosteroids and chloroquine for sarcoid-like EO, suggesting a possible role for systemic immunomodulation in inflammatory variants. More conventional agents, such as isotretinoin[25] and glutathione,[32] yield mild-to-moderate improvements in pigmentation, likely through cell turnover and reduction of oxidative stress. Oral tranexamic acid, traditionally prescribed for melasma, was modestly effective in one case,[12] possibly due to anti-inflammatory effects. However, these findings are isolated, highlighting the need for controlled studies to assess safety and dosing.

Procedural interventions appear more promising, particularly for patients who do not respond to pharmacologic therapy. Dermabrasion has demonstrated notable reduction in pigmentation, especially when combined with topical agents and photoprotection.[15] Microdermabrasion[32] and microneedling[16,23] have also shown favorable outcomes, particularly in individuals with darker skin phototypes, in whom dermal pigmentation is more pronounced. Microneedling offers the advantages of promoting dermal remodeling and enhancing topical drug absorption.

Chemical peels, particularly TCA, seem to outperform superficial peels such as glycolic acid. França et al.[8] reported complete lesion resolution with 20% TCA after failure of treatment with superficial agents, whereas Vinay et al.[12] observed only moderate improvement with 30% glycolic acid, underscoring the importance of peel depth. Sequential or combination approaches may further enhance efficacy, although variability in formulations, techniques, and patient factors complicate direct comparisons.

Laser and light-based therapies provide compelling but variable results. Q-switched lasers (ruby, Nd:YAG, alexandrite) have shown efficacy but may induce PIH or even worsen pigmentation, particularly in patients with darker skin phototypes.[13] Fractional CO_2 lasers, alone or combined with Q-switched devices, have resulted in more consistent outcomes.[4,5] IPL appears to be the most effective when added to multimodal regimens. Picosecond lasers have shown encouraging preliminary results with fewer adverse effects,[38] but further validation is required.

Emerging regenerative therapies, including intradermal vitamin C injections, plant-based exosomes, and PRF-L, aim to restore dermal integrity while reducing pigmentation. Vitamin C injections achieved reductions in pigmentation of up to 80%,[28] while plant exosomes and PRF-L were associated with improvements in skin quality and lightening.[23,35] While promising, these early-stage studies have small sample sizes and limited long-term safety data.

Few studies report adverse effects. PIH is the most frequent, especially after laser-based therapies, posing particular risk for patients with darker phototypes, who represent a large share of EO cases. Reports of worsening pigmentation with Q-swit-

ched and alexandrite lasers[13] underscore the need for caution. Microneedling, picosecond lasers, and select chemical peels, on the other hand, are generally well tolerated.

In conclusion, the management of EO requires a multimodal, individualized approach. Non-pharmacological measures remain foundational, topicals therapies provide adjunctive benefits, and procedural or energy-based interventions achieve the most consistent reduction in pigmentation. Emerging regenerative strategies may further expand treatment options, but high-quality studies are needed to optimize treatment protocols, minimize adverse events, and identify predictive factors for treatment response, particularly in individuals with darker skin phototypes.

CONCLUSION

This review underscores the complexity of managing EO, a challenging pigmentary disorder. Among available therapeutic options, laser and light-based therapies—particularly when used in combination with other modalities—demonstrate the most consistent clinical efficacy, supporting a multimodal approach over monotherapy. Procedural treatments such as microneedling and chemical peels provide moderate improvement, whereas topical agents alone are generally ineffective, especially in long-standing disease or cases involving deep dermal pigmentation.

Regarding safety, PIH is the most frequently reported complication, particularly following laser-based therapies. Microneedling and picosecond lasers are generally well tolerated and may represent safer options for patients with darker skin phototypes, who are more susceptible to pigmentary rebound and adverse effects.

Emerging interventions, including intradermal vitamin C, plant-derived exosomes, and PRF-L, have shown promising preliminary results, potentially combining pigment reduction with dermal remodeling, barrier restoration, and local antioxidant and anti-inflammatory effects.

Overall, the management of EO remains multifaceted and requires individualized treatment plans based on pigmentation depth, histopathological severity, skin phototype, and treatment tolerance. Combination therapies appear to be the most effective, but further controlled studies are required to establish standardized protocols, confirm long-term safety, and validate emerging approaches for broader clinical application.

ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to the Almighty God for the gift of life, strength, and wisdom that enabled me to undertake and complete this project.

My sincere thanks also go to my supervisor, Dr. Hsuan-Hsiang Chen, for his guidance, support, and encouragement throughout this work.

Finally, I would like to extend my heartfelt appreciation to the Merck Foundation for sponsoring my studies and making this academic journey possible.

This work was completed in partial fulfillment of the requirements for the Master of Science (MSc) in Dermatology in Clinical Practice at the University of South Wales. ●

REFERENCES:

1. Baca IM, Firas Al-Niaimi, Colina C, Anuzita A. A Case of Ochronosis Successfully Treated with the Picosecond Laser. J Cosmet Dermatol. 2018;18(5):1322–5.
2. Bellew SG, Alster TS. Treatment of Exogenous Ochronosis with a Q-Switched Alexandrite (755 nm) Laser. Dermatol Surg. 2004;30(4):555–8.
3. Bhattar P, Zawar V, Godse K, Patil S, Nadkarni N, Gautam M. Exogenous Ochronosis. Indian J Dermatol. 2015;60(6):537.
4. Carvalho CGS, Vilela VN, Rocha AEA, Carvalho GSM, França ER, Rodrigues AGA. Exogenous Ochronosis Treated with CO2 Laser. Surg Cosmet Dermatol. 2016;8(4).
5. Ceglio WW, Careta MF, Regia Patriota, Luís Antônio Torezan. Exogenous Ochronosis Successfully Treated with the Combination of Intense Pulsed Light and Fractional CO2 Laser. Ann Bras Dermatol. 2022;98(1):138–40.
6. Charlín R, Barcaui CB, Kac BK, Soares DB, Rabello-Fonseca R, Azulay-Abulafia L. Hydroquinone-induced Exogenous ochronosis: a Report of Four Cases and Usefulness of Dermoscopy. Int J Dermatol. 2007;47(1):19–23.
7. Emre T, Egemen A, Muhammet Ç, Sedat Y. A Case of Exogenous Ochronosis Associated with Hydroxychloroquine. European Journal of Rheumatology. 2018;5(3):206–8.
8. França ER, Paiva V, Toscano LPN, Nunes GJB, Rodrigues TFA. Exogenous ochronosis: a Case Report. Surg Cosmet Dermatol. 2010;2(4):319–21.
9. Gil I, Segura S, Martínez-Escala E, Lloreta J, Puig S, Vélez M, et al. Dermoscopic and Reflectance Confocal Microscopic Features of Exogenous Ochronosis. Arch Dermatol. 2010;146(9).
10. Hull PR, Procter PR. The melanocyte: an Essential Link in hydroquinone-induced Ochronosis. J Am Acad Dermatol. 1990;22(3):529–31.
11. Kanechorn NAP, Niumphradit N, Aunhachoke K, Nakakes A, Sittiwangkul R, Srisuttiyakorn C. Effect of Combination of 1064 Nm Q-switched Nd:YAG and Fractional Carbon Dioxide Lasers for Treating Exogenous Ochronosis. J Cosmet Laser Ther. 2013;15(1):42–5.
12. Keshavamurthy V, Mehta H, Bhat YJ, Khare S, Nkechi AE, Chauhan P, et al. Clinical and Dermoscopic Characteristics of Exogenous ochronosis: Results of a Multicenter Study by the International Dermoscopy Society Task Force on "Imaging in Skin of Color." Clin Exp Dermatol. 2025.

13. Ko WL, Wang KH. Exogenous Ochronosis. Dermatol Sinica. 2015;33(1):29–30.
14. Kramer KE, Lopez A, Stefanato CM, Phillips TJ. Exogenous Ochronosis. J Am Acad Dermatol. 2000;42(5):869–71.
15. Lamas CN, Maria F, Manfredini E, Regina Ferreira F, Santos P, Gonçalves F. Dermabrasion in Exogenous ochronosis: a Therapeutic Option. Surg Cosmet Dermatol. 2023;15.
16. Lazar M, Garza H, Vashi NA. Exogenous Ochronosis: Characterizing a Rare Disorder in Skin of Color. J Clin Med. 2023;12(13):4341.
17. Lee MD, Weiss E. Treatment of Exogenous Ochronosis with Advanced Fluorescence Technology. Dermatol Surg [Internet]. 2014;40(9):1046–8.
18. Lee MY, Yun SJ, Lee SC, Won YH, Lee JB. A Case of Ochronosis with Atypical Manifestations Involving the Perioral Area and Sclera. Ann Dermatol. 2019;31(1):106–6.
19. Levin CY, Maibach H. Exogenous Ochronosis. Am J Clin Dermatol. 2001;2(4):213–7.
20. Li ZZ, Zhang C. Exogenous Ochronosis with Vitiligo: a Therapeutic Challenge. Skin Res Technol. 2024;30(10).
21. Liu W, Tey H, Lee S, Goh B. Exogenous Ochronosis in a Chinese patient: Use of Dermoscopy Aids Early Diagnosis and Selection of Biopsy Site. Singapore Med J. 2014;55(1).
22. Moche MJ, Glassman SJ, Modi D, Grayson W. Cutaneous Annular Sarcoidosis Developing on a Background of Exogenous ochronosis: a Report of Two Cases and Review of the Literature. Clin Exp Dermatol. 2010;35(4):399–402.
23. Moerbono M, Sri EI, Dendy Z, Ammarilis M, Suci W. A split-face of Dermaroller and Intradermal Injection with the Autologous Platelet Rich Fibrin Lysate in the Treatment of Exogenous ocronosis: a Case Series. Dermatol Rep. 2019.
24. Patel N, Shah H. Exogenous Ochronosis from Skin-Lightening Cream. New England journal of medicine/ New Engl J Med. 2024;390(3):254–4.
25. Pirrone J, Broyer J, Otte N, Reich K, Almut BA. Extensive Hyperpigmentation of the Face in a Filipina. JDDG J Deutschen Dermatol Gesell. 2017;15(11):1167–8.
26. Qian YH. Micro-needling Pulsed Radiofrequency as an Adjuvant to Lasers for Exogenous Ochronosis. J Clin Exp Dermatol Res. 201809.
27. Qorbani A, Mubasher A, Sarantopoulos GP, Nelson S, Fung MA. Exogenous Ochronosis (EO): Skin Lightening Cream Causing Rare caviar-like Lesion with banana-like pigments; Review of Literature and Histological Comparison with Endogenous Counterpart. Autopsy Case Rep. 2020;10(4):e2020197.
28. Rajesh Gulwani P, Parekh AR, Shah HA. Intradermal Vitamin C: a New Paradigm in the Treatment of Exogenous Ochronosis. Indian J Dermatol, Venereol Leprol. 2024;90:378–80.
29. Rocha MDN, Aguiar C, Saraiva MJ. Exogenous ochronosis: Case Report and Literature Review. Ann Bras Dermatol. 2012;87(4):633–6.
30. Simmons BJ, Griffith RD, Bray FN, Falto-Aizpurua LA, Nouri K. Exogenous Ochronosis: a Comprehensive Review of the Diagnosis, Epidemiology, Causes, and Treatments. Am J Clin Dermatol. 2015;16(3):205–12.
31. Singh A, Ramesh V. Exogenous Ochronosis. Indian J Med Res. 2014;139(2):327.
32. Sunkara HP, Kilaru KR, Kumar AP, Ramineni HB, Krishna PR. A Case Report on Hydroquinone Induced Exogenous Ochronosis. Int J Adv Med. 2020;7(2):337.
33. Tan SK (SK). Exogenous Ochronosis – Successful Outcome after Treatment with Q-switched Nd:YAG Laser. J Cosmet Laser Ther. 2013;15(5):274–8.
34. Tan SKS. Exogenous Ochronosis - a Diagnostic Challenge. J Dermatol. 20109(4):313–7.
35. Widjaja DK, Ruma IMW, Widianti IGA, Kwanda V. Administration of Exosome-based Treatment for Exogenous Ochronosis Caused by Prolonged Use of Topical Hydroquinone. J Adv Med Pharm Sci. 2025;27(2):1–7.
36. Wilhelm KP, Zhai H, Maibach HI. Dermatotoxicology. Crc Press; 2007.
37. Sukhera J. Narrative Reviews: Flexible, Rigorous, and Practical. J Grad Med Educ. 2022;14(4):414–7.
38. Almutairi R, Usmani S, Mubarak S, Aldaraji W. Novel Picosecond 755 nm Alexandrite Laser for Treating Exogenous Ochronosis. Int J Dermatol. 2024.

AUTHOR'S CONTRIBUTION:

Emmanuela Dapomaa Asante ORCID 0009-0006-8831-7943
Conception and design of the study, Preparation and writing of the manuscript, Critical review of the literature, Critical revision of the manuscript

Hsuan Hsiang Chen ORCID 0000-0003-2642-5114
Approval of the final version of the manuscript, Critical revision of the manuscript