# Effective Treatment of Post-Inflammatory Hyperpigmentation in People with Skin of Colour

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**Abstract**

People with skin of colour (Fitz-Patrick skin types IV-VI) have an increased tendency to develop post-inflammatory hyperpigmentation. Constitutional features make the treatment of PIH in skin of colour more difficult. This systematic review summarizes various treatment options for PIH and other hyperpigmentation conditions available for people with skin of colour.

## INTRODUCTION

Post-inflammatory hyperpigmentation (PIH) is a reactive hypermelanosis usually precipitated by skin inflammation from acne, rosacea, eczema and allergies or traumatic events from surgery or aesthetic procedures. Shenoy and Madan[1] described it as a reactive process that culminates in increased melanin or abnormal distribution of melanin, also attributable to inflammatory skin conditions as mentioned earlier. The study by Shenoy and Madan[1] concedes that therapeutic options exist for hyperpigmentation conditions despite little focus on PIH treatment strategies. Another conceptualization of the condition, as posited by Lawrence and Aboud[2] is that PIH is a result of abnormal melanin deposition in the epidermis or dermis as a result of an inflammation. Mediators of inflammation initiate melanocyte hypertrophy and activity, thus raising melanin production in the epidermis[2].

Melanin is the pigment responsible for skin colour. It is synthesized and stored in organelles called melanosomes, which are produced by melanocytes. Melanocytes are found in the basal layer of the epidermis, the outermost of the three layers of the skin. Melanocyte activity, rather than density, is said to be the major determinant of skin colour[3]. Inflammatory skin conditions like acne and rosacea, and other factors such as trauma, allergy, and prolonged exposure to sunlight trigger the release of inflammatory cells which in turn triggers increased activity of melanocytes, resulting in the production of melanin[4]. Furthermore, Suarez-Bigetti[5] explains that the skin increases pigmentation as a corrective response to induced inflammation which can be from skin rejuvenating modalities such as full and fractional ablative lasers, intense pulsed light (IPL), percutaneous collagen induction, and superficial chemical peel[5].

The tendency of the inflammatory process described above to be triggered is greater in people with skin of colour[5,6]. That is, inflammatory skin conditions are more likely to kick-start the inflammatory process and cause greater hyperpigmentation in people with skin of colour, thus contributing to the increased prevalence of dyschromia in this group of people. For instance, Dlova, Akintilo, & Taylor[6] in their study on pigmentary disorders found that PIH is among the three most occurring pigmentary diagnoses among a Durban, South African population of African and Indian descent.

Skin of colour, also known as ethnic skin, refers to Fitzpatrick skin types IV-VI. These higher Fitz-Patrick skin types are relatively rich in melanin which serves a major function of absorbing ultraviolet rays and blocking the generation of free radicals, in the process protecting the skin from sun damage and aging[7]. The anatomic location of melanosomes differs among different races, being found mostly in the basal layer in blacks, as opposed to white persons in whom they are found mostly in the stratum corneum[7]. In addition, the degradation of melanosomes within keratinocytes is said to be slower in ethnic or darkly pigmented skin[8], thus making the treatment of PIH in people of colour somewhat slower and more difficult. In this systemic review, we explored various treatment modalities

for induced post-inflammatory hyperpigmentation or pigmentation disorders and their effectiveness in people with skin of colour.

## METHODOLOGY

### Study Design

This systematic review was conducted according to the Cochrane methodology and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

### Literature Search

Three primary databases were searched for useful articles that could be included in this study. PubMed, Cochrane Central Library, and Embase were the main databases searched in an effort to discover studies for this systematic review. Additional searches for grey literature were done in Google Scholar and a hand search through reference lists of former reviews and meta-analyses was also done. The study search was made possible by the use of keyword combinations and the incorporation of Boolean operators AND/OR. Keywords "treatment", "post-inflammatory hyperpigmentation", AND "melanin" were used as the basis of building search strings. Strings included search techniques such as Medical Subject Heading (MeSH) terms and truncations by the introduction of asterisks (*). The search string was emboldened by the following MeSH terms (("Therapeutics"[Mesh]) AND "Melanins"[Mesh]) AND "Hyperpigmentation"[Mesh]. Bringing every search mechanism together, generated the search string represented in table 1 below. In October 2022, we applied the search string to the bibliographic databases.

**Table 1**

Search string executed for the main study search for this systematic review

*Table 1: Search string executed for the main study search for this systematic review*

| |
|---|
| ("Therapeutics"[MeSH Terms] OR "treat*"[All Fields] OR "therap*"[All Fields] OR ("drug discov today ther strateg"[Journal] OR ("therapeutic"[All Fields] AND "strategies"[All Fields]) OR "therapeutic strategies"[All Fields])) AND ("Melanins"[MeSH Terms] OR (("skin"[MeSH Terms] OR "skin"[All Fields]) AND ("colorant"[All Fields] OR "colorants"[All Fields] OR "coloration"[All Fields] OR "colorations"[All Fields] OR "colored"[All Fields] OR "coloreds"[All Fields] OR "colorful"[All Fields] OR "colorfulness"[All Fields] OR "coloring"[All Fields] OR "colorings"[All Fields] OR "colorization"[All Fields] OR "colorized"[All Fields] OR "colour"[All Fields] OR "color"[MeSH Terms] OR "color"[All Fields] OR "colourant"[All Fields] OR "colourants"[All Fields] OR "colouration"[All Fields] OR "colourations"[All Fields] OR "coloured"[All Fields] OR "coloureds"[All Fields] OR "colourful"[All Fields] OR "colourfulness"[All Fields] OR "colouring"[All Fields] OR "colourings"[All Fields] OR "colours"[All Fields] OR "colors"[All Fields])) OR ("eumelanin"[Supplementary Concept] OR "eumelanin"[All Fields] OR "eumelanins"[All Fields]) OR ("pheomelanin"[Supplementary Concept] OR "pheomelanin"[All Fields] OR "pheomelanins"[All Fields])) AND ("Hyperpigmentation"[MeSH Terms] OR ("post-inflammatory"[All Fields] AND ("hyperpigmentated"[All Fields] OR "Hyperpigmentation"[MeSH Terms] OR "Hyperpigmentation"[All Fields] OR "hyperpigmentations"[All Fields] OR "hyperpigmention"[All Fields])) OR "pih"[All Fields] OR ("post"[All Fields] AND "inflammat*"[All Fields] AND "hyperpigment*"[All Fields])) |

### Eligibility Criteria

Two independent reviewers assessed the retrieved studies using predesigned items for eligibility. In addition, the PECOS inclusion and exclusion criteria were implemented to sieve through the pool of discovered studies. Table 2 below outlines the criteria of eligibility used in the selection of studies for the present systematic review.

**Table 2**

The criteria of eligibility used to determine inclusions and exclusion of studies from the present systematic review

*Table 2: The criteria of eligibility used to determine inclusions and exclusion of studies from the present systematic review*

| *PECOS* | *Inclusion* | *Exclusion* |
|---|---|---|
| *Population* | Participants of the study should be persons that can be described as having a skin of colour. Patients with Fitzpatrick skin phototypes IV-VI. They should also have a diagnosis of PIH. | Participants that do not have a skin of colour or don't fall under skin types IV-VI. Persons without a positive diagnosis of PIH. |
| *Exposure* | Therapeutic strategies for post-inflammatory hyperpigmentation and/or melasma. This can either be physical, chemical, mechanical or laser treatments. | Any other therapeutic modalities. |
| *Comparator* | A comparator was not a necessity. | Studies were not excluded either for having a comparator or not. |
| *Outcome* | Successful management of PIH and/or melasma | Lack of a description detailing the management of PIH and/or melasma. |
| *Study design* | The study designs were not a major consideration for the inclusion and exclusion of studies | |

In addition, the language of publication was also a consideration for eligibility. Only articles with full-text versions published or translated into English language were included in the systematic review. Independent results of the eligibility assessment were brought together and amended by the consultation of a third party.

### Data Extraction

Selected studies were scoured through for data extraction into a predesigned excel sheet. The findings from the extraction process were moderated by a third party. The process of extraction majorly focused on outcomes that indicated the success of management of PIH among the study subjects. The first items of extraction were identifiers of the study; the name of the first author and the year, the study design, and the aim of the study. Other items extracted were the number of participants studied, the treatment strategy applied, the success rate of the strategy, and the authors' conclusive findings.

### Results Analysis

This systematic review employed a narrative synthesis of key findings from primary outcomes. Additionally, the review conducted a thematic analysis based on the efficacy and safety of using specific therapeutic approaches to treat PIH. It also attempted to juxtapose the pathophysiology of PIH and melasma. Finally, it elucidated the merits and demerits of each mode of treatment being adopted for PIH management.

## RESULTS

### Study Selection

A total of 642 articles (604 from PubMed, 25 from Cochrane Central, and 13 from Embase) were discovered from the three primary databases. An additional 2 studies were identified from grey literature and hand searching through reference lists making the total outcome 644 articles. The selection process was conducted on EndNote 20. Duplicates (21) were eliminated before the screening, and 623 articles were brought forward for inclusion consideration. The screening reviewers removed 144 articles in the first screening phase for being incompatible with the purpose of the systematic review. The title and abstract screening process was continued for the remaining 479 studies. At this stage, 291 studies were eliminated leaving 188 studies for full-text screening. At the end of the selection process 11 studies qualified for inclusion in the systematic review. Figure 1 below shows a PRISMA flow chart detailing the selection process.

**Figure 1**

A PRISMA flow-chart diagram showing the process of study selection for this systematic review

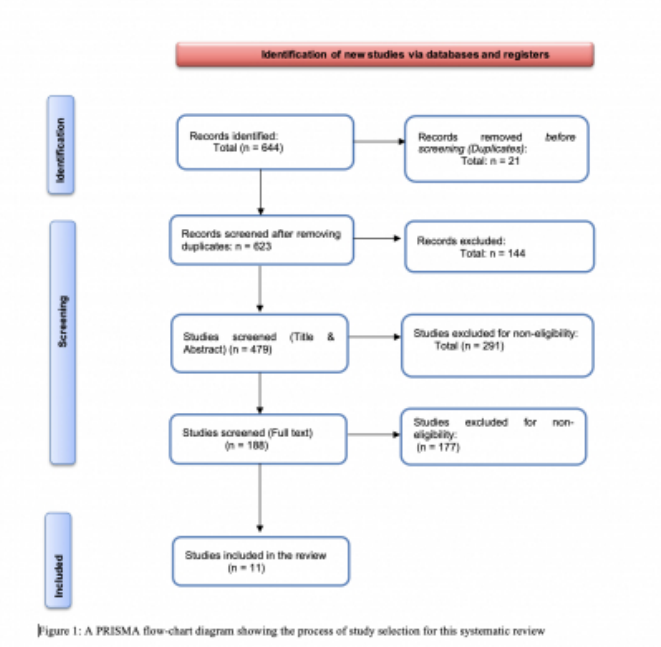


Figure 1: A PRISMA flow-chart diagram showing the process of study selection for this systematic review

### Study Characteristics

**Table 3**

Summary of the Extracted Data from the 11 Included Studies

## RESULTS ANALYSIS

### Laser Treatment

Laser and light therapy can also be used to lighten hyperpigmented lesions[13]. However, there are specific wavelengths recommended for various types of lesions and not all the wavelengths are suitable for use on people with skin of colour.

A review of the eleven studies that met the eligibility criteria for this study has presented a new angle of discussing the therapeutics available for PIH in patients with a skin of

colour. Articles with varying study designs were included in the present review, all positing different interventions with a certain degree of effectiveness. Alharbi et al[9] and Bae et al[10] investigated the usage of nonablative fractional 1927 nm diode laser treatment. The studies report similar outcomes in that this is an effective and safe method of managing PIH. The laser treatments involved the application of a topical anesthetic ointment, half an hour before the procedure. The intervention used a nonablative fractional 1927 nm diode laser with a 30% surface area coverage at pulse energy of 20mJ per microthermal zone [9,10]. A photographic review was then done to elucidate the therapeutic effectiveness of the treatment [9,10].

An earlier laser treatment study by Taylor and Anderson[19], conducted in 1994, used Q-switched ruby laser pulses (694 nm, 40 nanoseconds) at fluences of 15-7.5 J/cm$^2$ on PIH and melasma patients[19]. The laser delivered contiguous pulses of 1.5, 4.5, and 7.5 J/cm$^2$ with a 40 nanoseconds pulse duration in 5-mm-diameter round exposure per pulse[19]. Photographic biopsies obtained after exposure to this laser treatment revealed that the Q-switched ruby laser pulses produce fluence-related injuries to the cells that carry pigmentation in the epidermis and dermis. In this intervention, we get to see an intersection between the treatment modalities for PIH and melasma. The three studies have demonstrated that while some laser wavelengths are an effective treatment approach for PIH, certain wavelengths may not effectively treat hyperpigmentation on their own. [9,10,19].

**Topical Regimens**

The reviewed studies additionally revealed that PIH patients have been treated successfully by various forms of topical regimens in form of ointments and gels. According to five studies[11,12,15,16,18], such regimens used topical agents either solely or in combination with other treatment modalities. In 2012, Callender et al[12] published a study investigating the potentialities of using clindamycin phosphate/tretinoin gel in combination with a factor 30 sunscreen in the treatment of acne and PIH patients. Researchers used a chromameter and photographic images to assess the changes in hyperpigmentation and skin erythema. The mean (SD) baseline noninflammatory lesion count for patients receiving clindamycin/tretinoin gel was 48.6 (46.10), and it dropped by 21.3 (22.60) after 12 weeks. In contrast, it dropped by 12.8 (40.08) for patients receiving placebo, and whose mean baseline noninflammatory lesion count was 64.7 (73.08)[12]. Similar levels of efficacy were demonstrated in a more recent study (2022) by Callender et al[11] who used tazarotene 0.045% lotion on PIH patients for 12 weeks. Tazarotene is a topical retinoid which works by unclogging skin pores and reinforcing the rejuvenation of new skin cells[20]. To achieve this, retinoid molecules, which have anti-inflammatory properties, bind and activate retinoic acid receptors thus influencing the differentiation and proliferation of cells[21]. Using tazarotene, Callender et al[11] found it an effective adjunctive treatment in patients with Fitzpatrick skin types III-VI.

Kasraee et al[15], Roggenkamp et al[16], and Sarkar et al[18] posited three different topical regimens that can be considered as therapeutic alternatives for PIH patients. A case report of a 27-year-old male was analyzed after being treated with a depigmenting skin agent (peroxidase inhibitor methimazole (1-methyl-2-mercapto imidazole; MMI))[15]. The author found it safe and effective in improving hyperpigmented lesions on the patient's skin. Depigmenting agents are not commonly used for treating PIH. However, among those experimented on, MMI rises above hydroquinone (HQ) and biphenol antioxidants, which have been found to have moderate efficacy. MMI has been recommended as a novel solution for its noncytotoxic and nonmutagenic properties[15]. Another recommendation investigated was a formulation containing Thiamidol[16]. Thiamidol is a tyrosinase inhibitor isobutylamido-thiazolyl-resorcinol which translates into a decrease in enzyme Tyrosinase hence preventing overproduction of pigments in the skin[16]. The use of Thiamidol for acne induced PIH proved better than placebo treatments. Researchers even observed a continued improvement throughout the treatment without any significant side effects. Similarly, a combination of glycolic acid (GA) peels with a modified Kligman formula (MKF), made up of 2% hydroquinone, 0.05% tretinoin, and 1% hydrocortisone is yet another regimen tested by Sarkar et al.[18]. Using Hyperpigmentation Area and Severity Index (HASI) scores to measure the severity of hyperpigmentation, Sarkar et al[18] found that there was a high mean change in HASI scores in the groups that used GA peels and MKF treatment combination (11.16 ± 6 3.43) [18]. The effectiveness and safety of this regimen is recommendable for other PIH patients with Fitzpatrick skin Types III-V.

Combination treatments resulted in significantly better outcomes when compared with treatments with single agents or modes of treatment. This is supported by Suarez-Bigetti[5] who asserts that synergism of the various treatment modalities is of paramount importance in the treatment of

PIH. Some other studies involved combinations like glycolic acid peels with 2% hydroquinone, 1% tretinoin and hydrocortisone[18], salicylic acid and 0.1% tretinoin[27], niacinamide and tranexamic acid[22]. Prior conditioning of the skin, is said to increase cell turnover and improve the penetration of depigmenting agents5, thus enhancing the effectiveness of treatment.

**Other Effective Treatments of PIH**

Available treatment modalities for PIH include physical, chemical, mechanical treatment. Physical exfoliation with abrasive scrubs and resurfacing procedures like microdermabrasion, dermabrasion and micro-needling have been demonstrated to treat PIH disorders safely and effectively in all skin types if properly done.

Resurfacing procedures such as exfoliation achieved using abrasive scrubs, microdermabrasion, dermabrasion, and micro-needling are safe for use and effectively treat hyperpigmentation in all skin types [23,24].

Chemical exfoliants, topical retinoids, and tyrosinase inhibitors all showed significant pigmentation improvement and tolerability in people with skin of colour. Chemical exfoliation can be achieved through peeling with alpha- and beta-hydroxy acids such as glycolic acid, lactic acid, and salicylic acid, through depigmentation via tyrosinase inhibition achieved using drugs like hydroquinone, kojic acid, resorcinol, and retinoids, plant extracts like Tyrostat®, Thiamidol®, Resveratrol, Bakuchiol oil, and through anti-oxidations achieved with substances like Resveratrol, L-ascorbic acid, and Tocopherol[25–28].

A systematic review of several clinical trials on the effectiveness of natural ingredients in the management of hyperpigmentation concluded that ascorbic acid, soy, lignin peroxidase, ascorbic acid iontophoresis, arbutin, ellagic acid, licorice extracts, niacinamide, and mulberry all show promise in the treatment of hyperpigmentation[28]. Similarly, a prospective, randomized, double-blind study comparing the effectiveness of the plant extract Bakuchiol to retinol in the treatment of wrinkles and hyperpigmentation revealed that bakuchiol and retinol both significantly decreased wrinkle surface area and hyperpigmentation, with no statistically significant difference between the compounds, with retinol users reporting more facial skin scaling and stinging[29]. However, these clinical trials were not exclusively conducted with people with skin of colour.

**Skincare**

Besides sunscreen usage, Health [14] also puts forward the idea of using gentle skincare routine and skin lightening treatments as alternative strategies. It is advised to use mild cleansers and moisturizers each day to keep the skin hydrated and free of any irritation and dryness that could cause itching or flare-ups of an underlying skin disease[14]. Topical drugs that could be irritating should only be used if there is no itching, erythema, or other symptoms of inflammation [14].

**Sunscreen/Photoprotection**

Sun protection, including that provided through sunscreens, is significant and essential in the treatment of PIH in people with skin of colour [13,18]. We have seen sunscreen incorporated into treatment by Alharbi et al[9], but Fatima et al[13] reviewed the sole use of sunscreen as an alternative therapeutic option. In that review, findings from about 600 PIH and melasma patients, researched by 9 studies, were synthesized. Polypodium leucotomos extract (PLE) was the most used sunscreen during all these trials. The reviewers arrived at the notion that due to the diverse nature of sunscreens, there needed to be specific properties such as protection from ultraviolet (UV) and visible light (VL), and other broader spectra to make the sunscreen effective in managing PIH and melasma. Few studies have identified sunscreen as a viable option for managing PIH ad melasma. In the present systematic review, a recent (2019) review article by Health[14], cited the use of sunscreen as one of the alternative management strategies. For skin protection, Health[14] opines that proper sunscreen usage can be as effective in managing and preventing PIH and melasma as other modalities.

Therefore, in addition to the categories of PIH treatment methods already mentioned, an important aspect of the management of PIH is the prevention of PIH lesions through sun protection and behaviour modification. Sun protection can be achieved by means of sun protection factor and sun blocking acquired through topical skin care products, protective clothes, eyewear, and wide-brimmed hats. Personal care products that provide sunscreen should be broad spectrum (UVA & UVB), can be physical or chemical, and should have a sun protection factor (SPF) of 30 and above. In addition to sun protection, avoiding or stopping undesirable habits such as skin picking (excoriation) that promote the occurrence of PIH will help reduce the occurrence of new lesions.

**Advantages and Disadvantages of the Various Treatment**

**Modalities**

Laser treatments utilize beams of light of specific wavelengths to reduce hyperpigmentation. This modality is preferred because it is quick and relatively easy to achieve the target skin condition. The laser removes thin layers of the skin and, by so doing, eliminates hyperpigmentation. Usually, PIH removed in this manner does not recur. While lasers have a high level of effectiveness, there is a downside to this treatment option. For one, Q-switched ruby laser pulses produce fluence-related injuries to the cells that carry pigmentation in the dermis and the epidermis. In other cases, using laser to treat melasma and PIH has been found to lead to worsening of hyperpigmentation especially in black and brown patients. Acne patients with skin of colour also tend to run a risk of worsened PIH when they undergo laser treatment.

Topical regimens such as retinoids are advantageous in PIH treatment for properties such as being comedolytic, anti-inflammatory, and their ability to eradicate the precursor microcomedone. Despite their proven potentials, majority regimens are usually adjuvant PIH treatment alternatives. Having so many options in this category also means the patient risks using a regimen with unpalatable side effects. Hydroquinone has been the golden standard of PIH treatment; however, it is associated with skin irritation, contact dermatitis, and exogenous ochronosis in persons with the skin of colour. Relatively new substances like Tyrostat® (an extract from the plant Rumex occidentalis) and Bakuchiol oil were found to be as effective as hydroquinone and retinol respectively in the treatment of hyperpigmentation[30,31]. However, they are yet to be studied in people with skin of colour.

Other treatment alternatives such as sunscreen/photoprotection and skincare routines present a very natural and mostly non-irritable alternatives of treating PIH. These treatment options are not only cheaper but also have almost less adverse side-effects. However, they do not present fast solutions to PIH and other hyperpigmentation conditions. Therefore, these treatment options are useful to patients as additional therapies and other primary therapies. Alharbi et al[9] demonstrated this better in the treatment strategy used in their trial.

## CONCLUSION

People with skin of colour (Fitz-Patrick skin types IV-VI) have an increased tendency to develop post-inflammatory hyperpigmentation. Constitutional features make the treatment of PIH in skin of colour more difficult. This systematic review has demonstrated that there are various treatment options for PIH and other hyperpigmentation conditions available for people with skin of colour, and these modalities of treatment have been demonstrated to treat PIH effectively and safely in this group of people. However, combination of these modalities, including sun protection, appear to result in significantly better improvement of pigmentation in skin of colour.

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