Scoping Review

Treatment of Melasma on Darker Skin Types: a Scoping Review

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Abstract: Melasma is a challenging chronic skin condition associated with hyperpigmentation and unknown etiology. This scoping review mapped evidence of available treatments and their effectiveness in darker skin types. A comprehensive, systematic online search was conducted in Scopus, PubMed, CINAHL Complete, Cochrane, ScienceDirect, and Web of Science Core Collection. All eligible titles were exported to an Endnote20 library. Thematic content analysis was performed to summarise data on current melasma treatments for darker skin types. The quality of included articles was appraised using the Mixed Methods Appraisal Tool (MMAT) 2018 version. A total of 2863 articles were retrieved from the databases, and 10 met the eligibility criteria following abstract and full-text screening. Our findings demonstrate that topical treatments, chemical peels, lasers, and tranexamic acid are common treatment modalities used in darker skin types. Although these treatments may be effective in the short term, they bring about undesirable side effects and sometimes worsen or result in reoccurrences of melasma. Based on the evidence mapped, current treatment modalities are not suitable for darker skin types. There are very few studies conducted on individuals of African descent. Further research is necessary to investigate treatment interventions which may be user-friendly when dealing with darker skin types.

Keywords: Melasma; Treatment; Darker skin types; Fitzpatrick skin types IV-VI; Mapping review

1. Introduction

Melasma is a common, acquired human melanogenesis dysfunction, characterised by symmetric hyper-pigmented macules with irregular borders, and light to dark brown

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patches on the forehead, cheeks, upper lip, and chin areas of the face [1-3]. While being characterized as a facial disorder, melasma also occurs in non-facial areas like the chest, arms, and neck [4]. Although no specific gene has been identified in the pathogenesis of melasma, it is found to be more common in females and males of Hispanic, Asian, and African descent. [5-8]. A study conducted in South Africa reported that pigmentation disorders are in the top five skin conditions, with melasma accounting for most of the cases [9].

The specific cause of melasma is not known, however, its onset is often linked to various etiological factors. Pregnancy, use of oral contraceptives, improper safe sun practices, pollution, stress, genetic predisposition, hormonal changes, some cosmetic ingredients, phototoxic drugs, and hypothyroidism have been associated with the onset of melasma [10, 11]. Some studies show the genetic association of melasma with African ancestry [12, 13]. Exposure to ultraviolet (UV) rays is another risk factor for melasma as it is more common in countries near the equator. Due to its complex pathogenesis, melasma is challenging to treat, particularly in dark-skinned people [14, 15]. It has been traditionally managed with a combination of photo-protection, avoidance of triggers, and topical medications such as hydroquinone and Kligman's formula, with variable success rates [1, 10, 16, 17].

Being a facial disfiguring lesion, melasma has been reported to impact negatively upon patients' overall well-being. Quality of life (QoL) studies have revealed that melasma affects interpersonal interactions [18-22]. According to the World Health Organization (WHO), "quality of life refers to the individuals' perceptions of their position in life within their cultural context, value systems, goals, expectations, standards, and concerns" [22-24]. Due to constant visibility, facial melasma has an unsightly effect on a person's appearance resulting in a negative impact on interpersonal interaction [3, 15] with feelings of shame, frustration, embarrassment, low self-esteem, lack of motivation to go out, and suicidal ideas being reported [19, 25]. In a desperate attempt to solve their melasma problem, people may spend a fortune on medical and cosmetic treatments, though unfortunately most treatment results are often suboptimal and do not meet expectations.

Challenges in treating melasma have resulted in a plethora of anti-melanogenesis treatments. Hydroquinone is a first-line topical medical depigmentation therapy, that is used alone or in conjunction with other treatment modalities such as laser and or tranexamic acid [26-28]. Most documented treatments have primarily relied on the use of chemical methods [29-32], laser therapy [33-38], and topical creams [39-43]. However, the effectiveness of these treatment modalities is limited due to their adverse effects, especially in darker skin types [44]. For this study, darker skin types refer to the Fitzpatrick skin type scale (*i.e.* types IV-VI). Recent studies have demonstrated the effectiveness of tranexamic acid (TA) against hyper-melanosis, however, shortfalls in the number of controlled studies, lack of follow-up treatment periods, and establishment of optimum doses remain under-explored and provide scope for further investigation. Most documented studies are performed with Indian and Asian patients making it a challenge to generalise the results [11, 45-48].

Despite numerous treatment options available to treat melasma, it remains a medical concern as the problem still exists. There is increasing interest in the potential use of medicinal plants in managing hypermelanosis and uneven skin tone, as they are perceived as being safe [49]. Historically, one of the most medicinally beneficial plants in rural areas of the Eastern Cape and KwaZulu-Natal provinces in South Africa is the *Cassipourea flanaganii (C. flanaganii).* The ground crude bark is used to protect the skin from the sun, enhance the complexion, and even out the skin tone [49-52]. Therefore, the extensive use of *C. flanaganii* as a hypopigmentation therapy warrants further studies to investigate its potential

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as a safer alternative to hydroquinone. Recently, *C. flanaganii* isolates showed low cytotoxicity towards melanin-producing skin cells, *in vitro,* as demonstrated by a significant decrease in melanin content in these cells [50]. This scoping review aims to identify and summarise the most effective, tolerable, and safe treatment interventions for melasma in darker skin types. Gleaned evidence will be used to promote best practice and add value to the development of products specifically for darker skin individuals.

2. Materials and Methods

2.1 Overview

This scoping review is aimed at developing a novel approach to enhance the scientific understanding of the use of medicinal plants for the treatment of hypermelanosis, which can be locally manufactured in South Africa, and which may help address melasma in darker skin types.

A scoping review protocol entitled *"The prevalence and treatment options of melasma as well as its association with quality of life in darker skin types: A scoping review protocol"* was registered on the open science framework (OSF) and made available on 05 October 2021 for public comment *via* the link https://osf.io/ru3jc/. The review was guided by the Arksey and O'Malley framework [53], further advanced by Levac *et al.* and the Joanna Briggs Institute 2020 guidelines [54]. By this methodological framework, the review was conducted in the following five stages: 1. identifying the research question, 2. identifying relevant studies, 3. study selection, 4. charting the data, 5. collating, summarising, and reporting the articles. The sixth optional stage involving consultation (knowledge translation) with stakeholders to provide more insights beyond those found in the literature Arksey and O'Malley (2005) [53]) was not required as this scoping review did not include consultation with stakeholders. The findings of the study were reported by Table 1 of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist [55].

Identifying the research question

This paper aims to systematically evaluate evidence from the literature on treatment interventions used for melasma in darker skin type individuals and to answer the research question: *What are the most effective, tolerable, and safe treatment interventions for melasma in darker skin types?* To answer this research question, the Population, Exposure, and Outcome (PEO) framework, as illustrated in table 2 below, was used to determine the eligibility of the research question for the review. Studies on both males and females classified as having darker skin types and who suffered from facial melasma were included in the population. For exposure, all studies of treatments used for melasma were included. In the outcomes, the efficacy of treatment reported toxicity, and side effects were all considered.

Table 2 PEO framework for determining the eligibility of the research question.

Criteria	Determinants
Population	Darker skin type patients (skin type IV-VI) with diagnosed epidermal, dermal, or mixed melasma
Exposure	All types of treatment for melasma e.g. self-applied topical interventions, or combinations of topical interventions and oral interventions.
Outcome	(1) Was the treatment effective? (2) Was the treatment safe? (3) Reported toxicity or relapse

Identifying relevant studies

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We conducted a comprehensive and reproducible literature search using six academic databases, namely Scopus, PubMed, Cochrane, CINAHL Complete, ScienceDirect, and the Web of Science Core Collection (file S2) to retrieve published peer-reviewed articles which reported on primary research based on experiment, observation, or simulation [56]. All articles published from database inception to November 2021 were considered. Search strategies were developed by the principal investigator (PI) together with a librarian. A combination of free text keywords as well as Medical Subject Headings (MeSH) was used when conducting the literature searches. Search terms used included “melanosis”, “melasma”, "skin pigmentation", “dyschromia”, “hyperpigmentation”, “chloasma”, “Fitzpatrick skin IV to VI”, “Fitzpatrick skin IV–VI”, “Fitzpatrick VI”, “Fitzpatrick IV”, “Black”, “Indian”, “mixed ancestry”, "darker skin type*", "African Continental Ancestry Group", "mixed race”, "quality of life", “prevalence”, “therapy”, “therapeutics”, “treatment”. The Boolean terms, OR and AND were used to combine the keywords into search strings. For example (melasma OR pigmentation OR dyschromia OR hyperpigmentation OR chloasma) AND (“quality of life” OR prevalence OR therapy OR therapeutics OR treatment).

Peer-reviewed articles in any language were selected if they met the following inclusion criteria:

- evidence of facial melasma
- evidence of treatment interventions used for facial melasma
- evidence of the prevalence of facial melasma
- evidence of the effects of facial melasma on quality of life

Studies were excluded if they were review studies or grey literature and if they did not meet any of the criteria for inclusion.

Selecting studies

Eligible articles were saved in an EndNote20 library where duplicates were identified and removed. Articles were screened in three stages according to the title, abstract and full text. A screening tool (file 1), which factored the inclusion/exclusion criteria and the PEO elements, was developed by the PI and piloted by the reviewers using 10 articles. The tool was then adjusted accordingly.

In the second phase of selection, the PI, in parallel with the co-reviewer (TV), screened the abstracts of the included articles using the screening tool. Following this, the reviewers discussed the selected articles, and any discrepancies were resolved by consensus. In the last phase, two reviewers (NM) and (TV) screened the full-text articles for all eligible abstracts. A third screener (SG) resolved any discrepancies at this stage. The level of the agreement after the full-text screening was determined using Kappa statistics. The Kappa statistics were interpreted as follows: values <0.1 indicate no agreement and 0.10–0.20 indicate none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial and 0.81–1.00 as almost perfect agreement.

Charting the data

Data were captured from each included article using an electronic data charting form. For consistency, the data charting form was piloted by the two independent reviewers using a random sample of five included articles. All recommended modifications were implemented by the feedback provided by the two independent reviewers. Data extracted from the included studies summarised the most effective, tolerable, and safe treatment interventions for melasma on darker skin types.

2.2 Quality Appraisal

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The methodological quality of the included studies was determined using the Mixed Methods Appraisal Tool (MMAT) version 2018 [57]. As stipulated in the MMAT guidelines, the study design used in each article was appraised. Scores for each study were calculated as a percentage after which a specific rank was assigned. Studies were ranked as low in quality if their score was below or equal to 50%, deemed average quality if their score was between 51–75%, and were given a high-quality score if they ranged from 76–100% (file S 6 and S7).

2.3 Collating, Summarising, and Reporting Results

To address the research question, we employed thematic analysis to extract all relevant evidence from the included articles. Emerging themes from the data were narratively summarised.

2.3 Ethical Consideration

Ethical approval was not required for this scoping review, as the review relied on the synthesis of existing literature available in the public domain.

3. Results

3.1 Screening Results

PRISMA-ScR flow chart (Figure 1) reports on the inclusion and exclusion of studies in this review. Initially, the literature search yielded a total of 2853 articles (table 3, file S2) from six different databases. Following the removal of 867 duplicate titles, 1986 titles were identified to be eligible. A further 1566 records were removed. The remaining 420 articles were included for abstract screening. Of the 420 articles, 341 articles did not meet the inclusion criteria as some studies were conducted on all skin types and some were conducted on animals or they investigated extra-facial melasma, and were excluded. Meeting the inclusion criteria for full article screening were the remaining 79 articles. Ultimately data was extracted from 10 articles as 69 articles were excluded after full article screening due to the following reasons: 42 articles included all skin types; 20 articles did not meet the inclusion criteria, one article was based on an animal study, four articles were reviews (not original research) and one was a case report.

2853 records identified by CINHAL (n=87), Cochrane (n=104), PubMed (n=888), Science Direct (n=413), Scopus (n=1000) and Web of Science (n=361)

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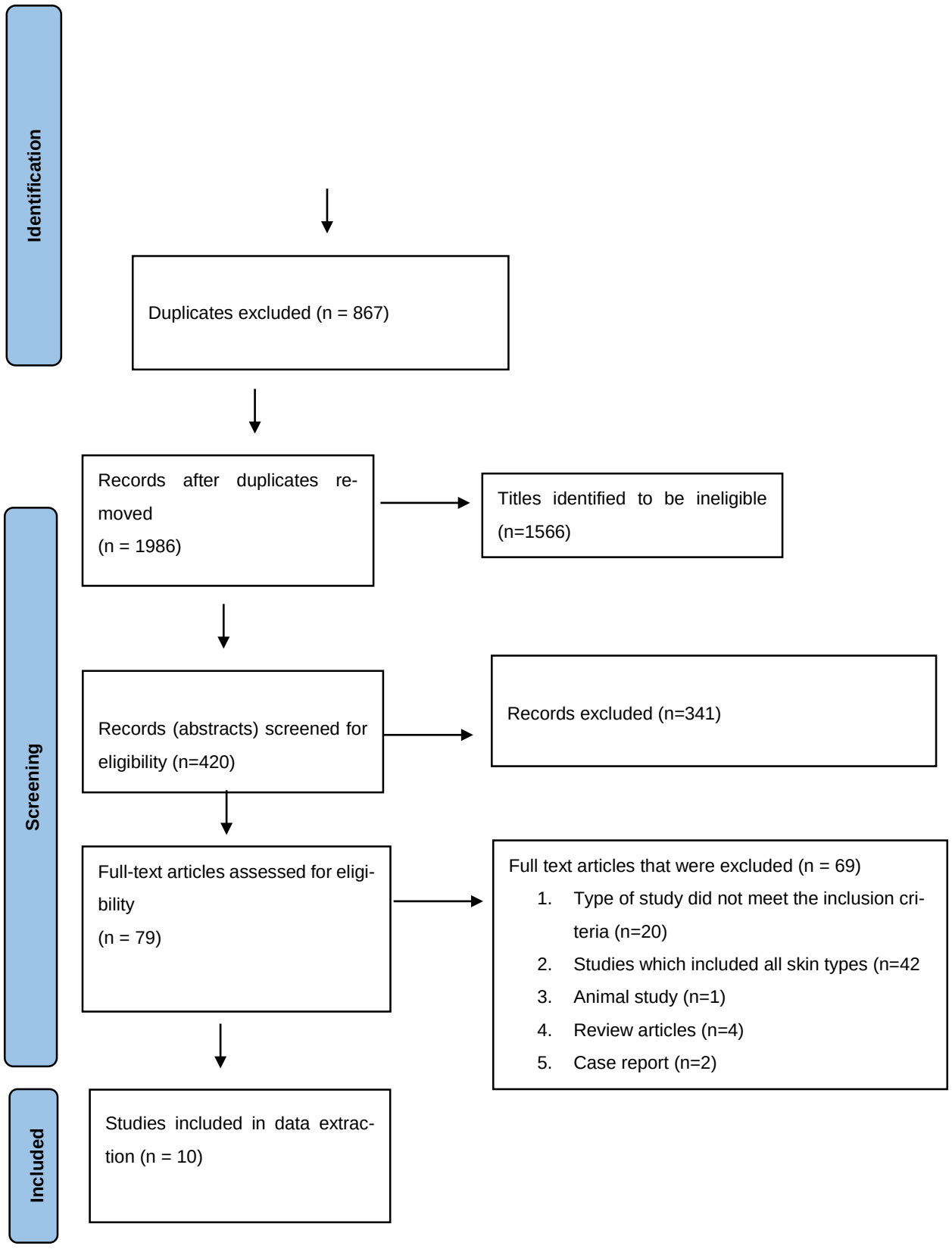

Figure 1: flow diagram demonstrates the literature searches and study selection

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There was 96.2% agreement versus 50.0% expected by chance which according to the Cohen Kappa value of 0.901 (SE = 0.056, t = 7.960, p < 0.001) is indicative of "almost perfect" agreement" [58]. Similarly, McNemar's Chi-squared statistic, $\chi^2 = .333$, suggests that there is not a statistically significant difference in the proportions of yes/no answers by the reviewers with a p-value = 0.564. This confirms the agreement between the reviewers.

3.2 Characteristics of the Included Studies

The characteristics of the included articles are summarised in Table 4. The eligible studies were published between 1994 and 2020. These articles presented evidence of research conducted in the following countries: India [6, 11, 59-61], USA [62], Thailand [63], South Africa [15], Korea [64], and China [65]. Findings from these articles were conveyed as randomised comparative study [11, 60], prospective randomised single-blind [6], prospective single-blind [6, 59], randomised vehicle-controlled [62], prospective pilot [65], randomised controlled trial [66] and experimental studies [15, 63, 64]. The primary healthcare settings included dermatology outpatient clinics, medical schools, tertiary care hospitals, as well as private practice rooms. Study participants were mainly Indian [6, 11, 59-61]. The total number of participants from all included studies is 420 of which 398 were female participants while 22 were male (table 2). Drop-outs, due to side effects did not make a significant difference in any of the included studies as the number was very low [6].

3.3 Quality of Evidence

All included articles were appraised for methodological quality using the MMAT tool version 2018 [57]. The 10 studies that were appraised for methodological quality scored between 70% and 90%, which indicated high methodological quality. Seven studies scored the highest quality score of 90%. Two studies scored 80%. The remaining article scored 70% (File S2).

3.4 Main Findings

The themes that emerged from the included studies were topical treatments, chemexfoliation, lasers and lights, and oral treatments. All the included articles presented evidence of at least one aspect of PEO on melasma. Findings from all included studies are summarised in table 5.

3.4.1 Topical Treatments

1. AZA cream

One study reported the efficacy of the topical application of 20% AZA cream as a monotherapy compared to sequential therapy with a steroid when treating melasma in Indian patients [59]. A comparative study of 20% azelaic acid cream monotherapy versus a sequential therapy in the treatment of melasma in dark-skinned patients was conducted [59]. The overall response, which included clinical evaluation and photography, revealed melasma lightening. The improvement was significantly greater on the side that received sequential therapy than on the side that received only 20% AZA cream. However, even though the difference was still significant at 24 weeks, as many as 96.7 and 90% of patients in each group (sequential therapy and AZA) had good to excellent treatment responses. Although there were side effects, they were regarded as local irritant effects. Six patients reported itching and burning after using the 20% AZA cream, although this subsided with continued usage. In five cases, topical strong steroids were used, but the symptoms resolved once the steroids were stopped, and the patients were put on AZA cream after eight weeks as the side effects were temporal. It was not conclusive whether continuous treatment was required to manage melasma after the end of the study period.

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2. Retinol/Tretinoin

In a randomised, vehicle-controlled clinical trial, the effects of topical Retinoic acid (RA) on melasma in Black patients (African American) were studied. The study trial was started with moderate to severe face hypermelanosis that was clinically compatible with melasma [62]. Follow-up evaluations were carried out at 2 and 4 weeks of therapy and monthly intervals, thereafter. At each visit, the change in clinical appearance was compared with the baseline. The overall response showed improvement in the tretinoin treatment group compared with a 10% improvement in the vehicle group. Colorimetric measurements indicated lightening of melasma after 40 weeks of tretinoin treatments. Histologic examination of the involved skin revealed a significant decrease in epidermal pigmentation in the tretinoin group compared with the vehicle group. Side effects were limited to a mild "retinoid dermatitis" occurring in 67% of tretinoin-treated patients (table 5).

3.4.2 Chemical Peels

Three studies investigated the use of different chemical peels in the treatment of melasma. A comparative study evaluated the efficacy and tolerability of Glycolic Acid (GA), Salicylic Acid (SA), Mandelic Acid (MA), and phytic combination peels [6]. In this study, participants were divided into three groups. Group A used glycolic acid (35%), Group B used SM acid (20% salicylic/10% mandelic acid), and Group C used phytic combination peel. It was evident from the results that both glycolic and SM acid peels are equally efficient and a safe treatment choice for melasma in Indian skin and are more effective compared to phytic acid peels [6]. Several undesirable side effects including post-peel pigmentary changes were reported as mild (table 5).

The focal Trichloroacetic Acid (TCA) peel method presented a safe and effective modality for the treatment of melasma, with no significant complications [64]. Periocular melasma was treated with 10% to 20% TCA, while the rest of the facial melasma lesions received 30% - 50% TCA. Also, the choice of concentration was determined by the caustic chemical used, the concentration, the mode and number of applications, the skin type, and the dermatologic condition being treated, thus the intensity of keratocoagulation and the effectiveness of the peel are modulated by the concentration and amount of each agent used. The TCA peel was applied to a focal pigmented area by pressing firmly with a sharpened wooden applicator. Coagulation of the epidermal and dermal proteins, which is characterised by a frosted appearance was used to monitor the peel depth and marked the endpoint. Focal application of TCA produced evenly frosted spots on each pigmented lesion. For independent clinical assessment, independent two blinded physicians evaluated the photographs taken before treatment and 6 months after completion of the treatment. Six patients rated the results as excellent (over 70% of the lesions disappeared), five patients indicated the results as good (50% to 70% of the lesions disappeared), five obtained fair results (30% to 50% of the lesions disappeared) and four experienced poor results (less than 30% of the lesions disappeared). Although the complications were regarded as insignificant, transient post-inflammatory hyperpigmentation occurred which necessitated the use of 5% hydroquinone treatment (table 5).

A study compared the therapeutic response of melasma in Indian women to GA (20–35%) versus TCA (10–20%) for chemical peeling [60]. Both men and women with epidermal melasma were enrolled in the study. Participants were divided into two groups. Group 1 was treated with concentrations of GA (20–35%) and Group 2 with TCA (10–20%). Before the commencement of the study, both groups were enrolled in a pre-peel program that involved the daily application of 1% tretinoin at night before the peel procedure. The faces were divided into two sections right forehead, left forehead, left cheek, right cheek, nose and glabella, and perioral area. A 20% glycolic acid peel and 10% TCA were applied for 2 minutes; the second peel: 20% GA/10%TCA was applied for 4 minutes; the third peel application comprised: 35% GA/20% TCA for 2 minutes; the fourth peel:

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35% GA/20% TCA for 4 minutes. Both groups were treated the same, but t difference was the peel concentration as group 1 was treated with GA (20–35%) and Group 2 with TCA (10–20%). All peels were applied at 2-week intervals. The results of the study showed that the application of 20% GA cream at night for 2 weeks, followed by an increase in GA and TCA concentrations of facial peel for a duration of 2–4 minutes once every 2 weeks for three consecutive months proved to be an equally effective treatment. There was no difference in the peels in six weeks, however, improvement of the TCA Group was noted after two weeks, compared with an improvement only after six weeks in the GA Group. Side effects were well treated (table 5).

3.4.3 Lasers and Lights

Four studies evaluated the use of different lasers and lights as monotherapy or used with other therapies. One study looked at the efficacy of LED [15], another investigated the use of Q-switched neodymium-doped yttrium aluminium garnet (Nd-YAG) lasers combined with Kligman's triple combination [61] and the last two evaluated the efficacy and safety of the picosecond alexandrite laser [63, 65].

In a prospective trial, refractory melasma was treated with the picosecond alexandrite laser (755 nm) using a diffraction lens array and a flat optic [63]. In this study, all patients had ceased all previous treatments/medications for at least one month prior to treatment with the picosecond alexandrite laser. Participants were divided into two groups. Group 1 participants were treated with the picosecond alexandrite laser flat optic while Group 2 participants were treated with the picosecond alexandrite laser with a diffractive lens array. At the completion of the study, there was a significant improvement in patients with the diffractive lens array compared to the flat optic lens. Both groups reported side effects ranging from macular hypopigmentation dissatisfaction (table 5).

A split-face randomised controlled trial examined the effectiveness and safety of Q-Switched neodymium-doped yttrium aluminum garnet laser (QSNYL) and Topical Creams (TC) in treating melasma compared efficacy of 1,064 nm Q-switched Nd-YAG laser and modified Klugman's formulation [61]. Both QSNYL and TC were administered as monotherapy to study their efficacy. Seventeen patients (37.8%) had epidermal melasma, and the remaining had a dermal or mixed type. Participants were randomised into two groups. Group A was treated with QSNL while Group B was treated daily with TC. After the study period, an assessment of treatment efficacy was done by four different outcome measures. The results revealed an overall improvement in both groups after 16 weeks. No statistically significant differences were observed between low fluence QSNYL and TC as monotherapy. The reappearance of melasma after stopping the therapy was one of the reported side effects experienced (table 5).

Omnilux LED showed improvement in melasma in individuals with skin types V-VI [15]. In this study, participants were purposefully divided into two groups based on their skin tone. Both groups received two LED treatments twice weekly for 12 weeks. After the study period, both groups showed improvement. Participants with skin type V rated their melasma to have improved more compared with that of skin type VI participants. In this study, no side effects were reported, however, the study period was long as it was nine months and people who suffer from melasma tend to be less patient (table 5).

3.4.4 Tranexamic Acid

One study evaluated the effects of oral tranexamic acid (TXA) compared to intradermal microinjections of TXA in the treatment of melasma [11]. In this comparative study, patients were randomly allocated to one of two groups (intradermal or oral) which comprised 50 participants [11]. The results of the study revealed that both treatment methods

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were equally effective. Some patients reported adverse effects which necessitated treatment with oral ranitidine 150 mg twice daily and some reported relapse (table 5).

4. Discussion

We conducted a scoping review to map the evidence of treatments used for melasma in darker skin types. In this review, all participants were adults aged between 18-67 (Table 4). Many of the studies included both male and female participants [6, 11, 59, 60, 62, 64], while four studies were conducted with only females [15, 61, 63, 65]. The smallest sample size was 20 [64, 65] and the maximum was 100 [11]. The included studies were carried out on skin types IVI-VI, only four studies investigated skin type VI [15, 60, 62, 63]. Reported treatment interventions included topical creams and solutions [59, 61], chemical peels [6, 60, 64], lasers: picosecond alexandrite [63, 65], Q-switched Nd-YAG [61], LEDs [15], and TXA different routes [11] (n=1). All patients used daily SPF as part of their routine melasma on top of their daily moisturiser.

Melasma is a common disfiguring skin condition that is more common in women with darker skin types [15]. Due to its pathogenesis which is poorly understood, melasma is difficult to treat and is refractory [7]. In one cross-sectional, multi-centric clinico-epidemiological study of melasma in India [67], a strong correlation between family history and prevalence of melasma was observed, suggesting genetic predisposition [68]. Sun exposure is a major precipitating factor in melasma and as such a broad-spectrum sunscreen with an SPF of 50 or higher was always recommended [1, 5, 15]. Other factors such as concomitant medication, chronicity of disease, multiple pregnancies, and use of oral contraceptives might precipitate melasma [67].

4.1 Topical Treatments

TC cream is considered the first-line treatment of melasma. Kligman's formula which employs a combination of 4% hydroquinone, 0.05% tretinoin, and 0.01% fluocinolone acetonide is the most widely used depigmenting agent at present [69]. TC shows better results as Hydroquinone (HQ) inhibits melanin production by blocking the tyrosinase, while tretinoin has exfoliating properties which help enhance better penetration, however, with this combination it has been observed that it is easy to re-pigment due to the inflammation caused by tretinoin [70]. HQ 2–4% cream is often used; however, it has been reported to cause uneven depigmentation, contact dermatitis, post-inflammatory hyperpigmentation, temporary erythema, burning, and ochronosis [59, 71].

Another commonly used TC is Tretinoin. It is either used with other topical whitening creams as a penetration enhancer or alone. It reduces pigmentation by inhibiting tyrosinase induction as it causes interference with pigment transfer, and acceleration of epidermal turnover [62, 72]. The use of tretinoin has proved to be effective, however, lightening requires more than 24 weeks, which is rather a long period and thus inconvenient for patients. Additionally, being a corticosteroid, it brings about undesirable side effects such as local irreversible thinning of the skin, burning, stinging, erythema, dryness, and scaling, contact dermatitis, perioral dermatitis, or acne rosacea and hypertrichosis in some cases [62, 71]. Although the adverse effects are reversible, retinoid dermatitis may lead to hyperpigmentation, especially in dark-skinned individuals [62].

4.2 Chemical Peels

Superficial and medium-depth chemical peels, especially glycolic acid, are effective in melasma but are not ideal in the therapy of melasma, especially when used as monotherapy [6, 7, 60]. There is a tendency for irritation, increased dryness, photosensitivity, and pigmentation changes, including areas of hypopigmentation and hyperpigmentation, to develop in darker skin typed patients after chemical peels [10, 69]. TCA has been widely used as a peeling agent for the treatment of several pigmented lesions including melasma

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and photo-aging. The application of TCA causes coagulative necrosis of cells through extensive protein denaturation and resultant structural cell death [64]. The depth of necrosis correlates with the concentration of TCA, which at medium-level concentrations of 35% to 50% will penetrate between the superficial papillary and midreticular dermis. Over 5 to 7 days, the epidermis and superficial dermis slough, carrying away cytologically atypical keratinocytes and structurally compromised dermal connective tissue. As the wound heals by second intention, it is repopulated by deep follicular epithelium and newly generated connective tissue; thus, the skin is rejuvenated both clinically and histologically [64]. There are increased risks associated with the use of higher TCA concentrations for deeper peels, especially in dark-skinned patients whose skin is known to possibly develop post-inflammatory hyperpigmentation [64].

4.3 Lasers and Lights

Both ablative and non-ablative lasers can have a profound effect on melasma [15, 61, 63, 65], however, the results are not always consistent, and problems have been reported. The use of lasers has proved both demanding and frustrating to both patients and operators. These devices inevitably may activate melanocyte by different irritation, inflammation, or by injuries to keratinocyte that lead to recurrence or PIH [63, 73, 74]. Adverse effects such as significant epidermal damage and peripheral hyperpigmentation, rebound hyperpigmentation, mottled hypopigmentation, and petechiae have been recorded in varying degrees of frequency [75] more especially for those with darker skin tones [76].

4.4 Tranexamic Acid

TXA can be used safely and effectively in the treatment of melasma in various forms such as oral, intradermal, or topical application. Its safety profile has been thoroughly explored and elucidated [11, 26, 40, 47, 77], however, there is no controlled trial study in other ethnic groups, such as Africans, so further data collection and risk assessment is necessary for these groups [78].

4.5 Sun Protection

Sun exposure is completely prohibited when treating melasma. Daily sun exposure, which occurs with typical daily activities in sunny climates, has a detrimental effect on therapies for melasma [63, 79]. In some countries, myths that darker skin types do not get sun damage still exist [15] and there is a need for education on the importance of sun protection in darker skin types.

Implication for Research and Practise

In this study, we found there are a variety of treatment interventions to treat melasma. Despite the excessive availability of treatment, melasma remains a huge frustration both to the people suffering from it and the skin specialists managing it, as there is currently no cure for it. Melasma is not just a cosmetic concern as it affects the quality of life as well. We found that most research done on darker skin types has been overwhelmingly conducted on Indian skin types. There is limited research done on Africans or Mixed Ancestry Groups of people, so further data collection and risk assessment is necessary for these groups. We recommend primary studies and clinical trials investigating the use of medicinal plants to treat melasma. We also recommend that the psychological aspect should be considered when dealing with melasma.

Strengths and Limitations

The use of a scoping review to map evidence allowed the incorporation of a methodological framework which is a transparent and reproducible method to identify, chart, analyse and appraise the articles [53]. There were no language limitations or time frames

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applied to the study which allowed us to comprehensively cover the available peer-reviewed literature. Review articles and sources from grey literature were excluded. The range of evidence included both qualitative and quantitative methodologies.

5. Conclusions

Melasma remains a huge medical burden. It is not only a cosmetic concern. Treating melasma is cumbersome since the therapy options typically include risks of pigmentary change, especially when dealing with darker skin types. Due to its high recurrence rate, many therapy techniques have been explored with minimal effectiveness but greater side effects. Chemical peels, tretinoin, tranexamic acid, lasers, and lights, are all options for therapy, however, while providing brief minor relief, are associated with a high incidence of complications and, in many cases, worsening of melasma. Additionally, they are not suitable for all darker skin types. We have observed in this review that most studies have been conducted up to skin type V. We hope that this review can bring more insight into the need for a suitable treatment for all skin types. There is a need for controlled trial studies in darker ethnic groups as most studies have been conducted on Indians. Exploring the effects of *Cassipourea flanaganii*, as it has demonstrated anti-tyrosinase effects *in-vitro* may be beneficial and may add to the melasma treatment armamentarium. *Cassipourea flanaganii* could make more targeted therapy available for all skin types in the future as there is a dire need for a novel relief that will be suitable for all skin types.

Supplementary Materials: The following supporting information can be downloaded from figshare at: https://doi.org/10.6084/m9.figshare.21730970, File S1: Electronic database search results. File S2: Full article screening results and agreement. File S3: MMAT quality appraisal reviewer 1. File S4: MMAT quality appraisal reviewer 2. File S 5: Preferred reporting items for systematic reviews and meta-analyses extensions for scoping reviews (PRISMA-ScR) checklist.

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Appendix A

Table A1: Table 4 Study Characteristics

Appendix B

Table A2: Table 5 Summary of included studies

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