



Research article

A systematic approach of efficacy and safety of herbal medicine in the treatment of Vitiligo

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ABSTRACT

Vitiligo is a chronic dermatological disorder caused by the loss of melanin. Conventional therapies for vitiligo require prolonged treatments, have low efficacy, and are complicated by side effects. This study aimed to review the role of herbal medicine in the treatment of vitiligo. A comprehensive search was conducted in PubMed, Embase, and Google Scholar for studies conducted till December 2023 using related keywords linked with Boolean operators such as AND, OR, and NOT. Subsequently, a more comprehensive search was performed using the name of each specific herb. A variety of herbs were used to treat vitiligo. The most widely used herbal therapies among vitiligo populations were Khellin, Ginkgo biloba L., Picrorhiza kurroa, Polypodium leucotomos, Cucumis melo, Psoralea corylifolia L., Turmeric, Curcumin, and Nigella sativa L. were used either alone or in combination with other therapies. The majority of herbs were found to be efficacious with negligible side effects. No severe toxicities were reported. Most herbal medicines showed a positive impact on vitiligo. Therefore, healthcare providers may consider herbal medicine as an option for patient's refractory to conventional therapies.



Keywords: Vitiligo, Herbal Medicine, Conventional Therapy, Literature Review, Efficacy, Safety.

INTRODUCTION

Vitiligo is a chronic autoimmune depigmented dermatological disorder. The disease appears as white macules or patches on the skin due to the loss of skin pigment melanin. Patches can appear on any part of the body, including the scalp and inside the mouth ^[1]. It affects all skin types; however, it is more apparent in persons with a dark complexion. Vitiligo is mainly categorized into unilateral (also known as segmental) and bilateral (also known as generalized). Bilateral vitiligo can appear at any age and progresses in stages throughout the patient's life. It produces symmetrical depigmentation; a lesion matches a lesion on the right side of the body in a similar area on the left. Unilateral or segmental vitiligo commonly occurs in children and young adults. It progresses for a limited period, usually 1 to 2 years, and remains constant throughout the individual's life ^[2]. The exact etiopathogenesis of vitiligo is not yet explored. Multiple factors were involved in the development of vitiligo, including disorders of the immune system (autoimmune conditions), genetic factors, inflammatory mediators, oxidative stress, severe sunburn, and skin trauma ^[1]. Vitiligo does not cause any physical limitation, but the psychosocial impact due to physical disfigurement devastates many patients and poses a significant healthcare burden ^[3].

Various therapeutic options for managing vitiligo are corticosteroids, immunomodulators, phototherapy (UVB), photochemotherapy (PUVA), and surgery. These conventional therapies have several limitations regarding success rate, cost of medicine, and ADRs. Treatment with PUVA increases the risk of skin cancer, corticosteroids induce skin atrophy, and UVB therapy is associated with skin boils ^[4,5]. Topical corticosteroids are recommended for treating vitiligo as first-line therapy. Tacrolimus or pimecrolimus are excellent immunomodulatory for patients with minor depigmentation, notably on the face and neck ^[6]. When vitiligo is severe, rapidly spreading, or does not respond to topical treatment, phototherapy alone or in combination is the basis of therapy ^[7]. For isolated, stable lesions that have not responded to prior therapies, surgery is an effective option. The low benefit-to-risk ratios of the current therapeutic approaches have led to the search for safe and effective alternative treatments ^[8]. In clinical and preclinical studies, herbal drugs have been reported to promote melanin synthesis and prevent damage ^[9-11]. Herbal medicines are relatively safe, reliable, easy to access, and affordable to the general public ^[12]. For thousands of years, herbal drugs have been widely used for the management of many skin diseases such as acne, alopecia, dermatitis, herpes simplex, herpes zoster, pruritus, psoriasis, scabies, skin cancer, wounds, burns, as well as vitiligo ^[13]. Some of the herbal products shown to have good therapeutic effects in the treatment of vitiligo are ginkgo biloba L., khellin, cucumis melo, green tea polyphenols, capsaicin, and

picrorhiza kurroa K ^[14]. This study comprehensively reviews all the existing clinical data related to applying herbal drugs in managing vitiligo.

MATERIALS AND METHODS

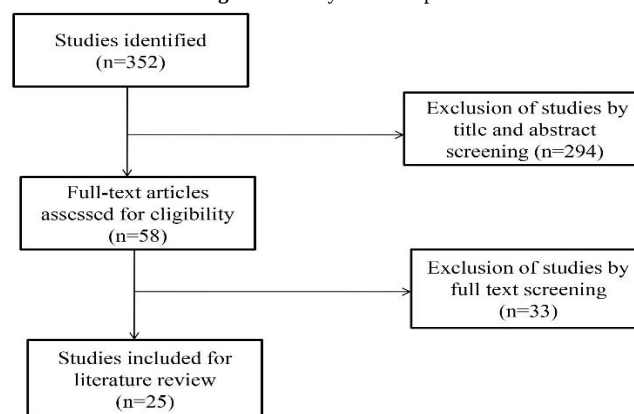
Literature Search

This literature review was performed using the following databases: PubMed, Embase, and Google Scholar for studies conducted until December 2023. The following keywords were used: “vitiligo,” “herbal therapy,” “herbal drugs,” “herbs,” “herbal medicines,” “herbal products,” “alternative medicine,” “medicinal plants,” traditional medicine,” and “herbal plants,” linked with Boolean operators such as AND, OR, and NOT. Subsequently, a more comprehensive search was performed by using the names of each specific herb, including Khellin, Turmeric, Curcumin, Picrorhiza kurroa, Polypodium leucotomos, Cucumis melo, Psoralea corylifolia L., Ginkgo biloba L., and Nigella sativa L. in combination with the terms “vitiligo” or “leukoderma”. Two independent investigators reviewed the titles and abstracts of articles from databases. A predetermined set of criteria is used as part of the initial screening to identify potentially relevant papers. Following the initial screening, the full texts of potentially relevant articles were evaluated for inclusion in the review based on eligibility criteria. Finally, we checked the bibliographies of all included articles for further relevant studies.

Eligibility Criteria

All human studies that reported the effects of herbal drugs in treating vitiligo, herbal medications in combination with or in comparison with any other topical or oral medications, phototherapy, or UV therapy and published in English were included. Review articles, meta-analyses, studies with insufficient data, conference presentations, editorials, and expert opinions were excluded. The study selection process is shown in Figure 1.

Figure: 1 Study selection process



Data Extraction

A well-structured data collection form was used to collect data from all selected studies. The form should have been designed to collect the information needed to address the research question or objective of the review. The extracted data typically include general characteristics of

the studies (e.g., author, publication year), sample size, study design, dose/ duration, assessment tools, treatment and safety outcomes.

RESULTS AND DISCUSSION

A total of 25 articles comprised of 23 clinical trials and 2 case reports were eligible to be included in this study. The study

consisted of data from clinical studies done across various countries such as India, Brazil, Canada, Turkey, Iran, Algeria, Pakistan, Austria, Italy, Bulgaria, Tunisia, Egypt, Thailand, and Spain. A detailed summary of the study characteristics and the effectiveness of the herbal drug in the treatment of vitiligo is presented in Table 1.

Table 1: Summary of collected data included in this review

Author, Year of publication, country	Sample Size	Study design	Drugs/Dose/Duration	Assessment tools	Treatment outcomes	Safety Outcomes
Szczurko et al. (2011), Canada ^[9]	12	Open-label pilot clinical trial	Ginkgo biloba (60mg) capsule, BID for 3 months	VASI and VETF	25% of participants achieved 30% re-pigmentation	Mild watery diarrhoea
Parsad et al. (2003), India ^[15]	52	Placebo-controlled trial	Group A: Ginkgo biloba (40mg) capsule, TID for 6 months Group B: Placebo, TID for 6 months	Comparison of paper tracings, measurement of the vitiligo patchy areas, and written descriptions	Complete re-pigmentation of the existing lesions in 50% of patients	Mild nausea
Abu-Raghif et al. (2013), Iraq ^[16]	50	Randomized, single-blind and placebo-controlled trial	Group A: Ginkgo biloba (75mg) capsule, BID for 2 months Group B: Placebo (sucrose) capsule with food for 2 months	VASI	No difference in VASI between the test and placebo group	NM
Sarac et al. (2019), Turkey ^[17]	33	Clinical trial	Nigella sativa topical cream, BID for 6 months	Digital photography	Re-pigmentation $\geq 50\%$ was achieved in facial, hand, and genital involvement	No adverse reactions
Ghorbanibargani et al. (2014), Iran ^[18]	52	Randomized Double-blind clinical trial	Group A: Nigella sativa oil, BID for 6 months Group B: Fish oil, BID for 6 months	VASI	The average VASI score reduced from 4.98 ± 4.81 to 3.75 ± 3.91 in group A, Where 4.98 ± 4.80 to 4.62 ± 4.36 in group B	No adverse reactions
Deshmukh et al. (2020), India ^[11]	15	Pilot clinical trial	Vishakalpa (Shwetralepa), BID for 1 month	VETI score	Patchy size was reduced in 26.6% of patients (3mm reduction).	Mild irritation and pustules
Hussain et al. (2016), Pakistan ^[19]	20	Self-controlled clinical trial	Psoralea corylifolia (10% w/w) ointment, OD+ expose to sunlight for 3 months	Photographs	Reduced white patch diameter and pigmentation from the corner to the center	Mild to moderate irritation
Jalalmanesh et al. (2022), Iran ^[21]	30	Randomized placebo-controlled trial	Turmeric cream BID for 4 months	VASI, VNS, PGA	Compared with placebo, turmeric cream reduced the size and improved lesions	No adverse reactions
Resende et al. (2015), Brazil ^[22]	12	Clinical trial	Herbal oral infusion containing- Solanum paniculatum, Jacaranda brasiliensis, Sonchus oleraceus (800ml), OD for 12 months	Photography	Re-pigmentation was observed in the left foot, knee, elbows, and mouth lips	No adverse reactions
Djerrou (2015), Algeria ^[40]	1	A case study	A topical application containing- honey bee, a decoction of dry oat stems, and red onion juice, OD for 11months+ Exposure to sunlight for 15–20 min, OD for 11 months, and Citrus lemon fruit juice was used occasionally	Photography	Complete re-pigmentation on the face	No adverse effects
Hussain et al. (2019), Larkana ^[20]	1	Case study	Psoralea corylifolia (5grams) oral powder, OD for 6 months + Psoralea corylifolia (5%w/w) topical cream, OD for 6 months+ sun exposure for 2-3 hours, OD for 6 months	Photography	Re-pigmentation was started after 15 days. Full facial pigmentation was observed after 24 weeks of therapy	No adverse reactions
Orecchia G et al. (1998), Italy ^[10]	36	Double blind clinical trial	Group A: Topical gel containing khellin (1%)-WPG+UVA thrice weekly for 6 months Group B: Topical gel containing WPG+UVA thrice weekly for 6 months	Photographs and following criteria: re-pigmentation, >51% (excellent), 26-50% (good), 11-25% (moderate), <10% (poor), 0 (none)	Re-pigmentation (>10%) of 86.1% in group A whereas 66.6% in group B	No adverse reactions

Ortel et al. (1988), Austria ^[23]	28	Clinical trial	Khellin (2%) topical solution+ Khellin oral (100 mg) +UVA (10–15 Joules/cm ²) thrice weekly for 18 weeks	Photographs	Re-pigmentation of >70% was achieved in 41% of patients	Nausea orthostatic complaints, and mild rise in liver transaminases
De Leeuw et al. (2003), Netherland ^[24]	74	Case study	Group A: Khellin (0.005%) and phenylalanine topical solution, BID for 12 months+ UVA/UVB one minute daily, 5 times weekly for 12 months Group B: UVA/UVB one minute daily, 5 times weekly for 12 months	Photographs	Re-pigmentation of 50% to 100% was observed in 72% of treated locations	No adverse reactions
Saracenoet al. (2009), Italy ^[25]	48	Open prospective, controlled study	Group A: MEL 308 nm once-weekly + oral vit. E capsule (400 IU), OD for 3 months Group B: MEL 308 nm once weekly + khellin (4%) ointment (MEL-K) + oral vit. E capsule (400 IU), OD for 3 months Group C: oral vit. E capsule (400 IU), OD for 3 months	Re-pigmentation was categorized as No re-pigmentation, moderate (<50% lesions healed), good (51– 75% of lesions healed), and excellent (76-100%of lesions healed).	Group I- moderate re-pigmentation in 12.5%, good in 62.5%, and excellent in 25% patients Group II- moderate re-pigmentation in 12.5% of patients, good in 31.25%, and excellent in 56.25%, Group III- moderate re-pigmentation in 18.75%, a good in 6.25%, and 62.5% patients didn't show re-pigmentation.	Erythema, pain/ burning, perilesional hyperpigmentation, was observed in group A and B No adverse reactions in group C
Valkova et al. (2004), Bulgaria ^[26]	33	Pilot study	Group A: khellin (5%) topical (emulsion)+ KUVA (12 J/cm ²), 3-5 times weekly for 7 months Group B: PUVA (1.5 J/cm ²), thrice weekly for months	Planimetry methods and using criteria of re-pigmentation 90-100% (significant improvement), 60–80% (moderate), 20–50% (slight), no effect (no re-pigmentation)	Significant improvement was observed in 18.7% of the patients treated with KUVA and 11.8% with systemic PUVA	No adverse reactions Erythema, with a mild or moderate itch, stomach pain, vomiting or dizziness patients from group
De Leeuw et al. (2011), Netherland ^[27]	19	Double-blind observation study	Khellin (0.005%) BID+ UV therapy thrice weekly	Photographs	A re-pigmentation of 75–100% was achieved in 2 patients, 50–75% in 6 patients	Not mentioned
Hofer et al. (2001), Austria ^[28]	28	Retrospective observational study	khellin +UVAfor 3months	Photographs	70% of re-pigmentation rate in 41%patients	Mild nausea
Fenniche et al. (2017), Tunisia ^[29]	20	Open-label prospective study	Topical khellin + Excimer lamp (308 nm) therapy (250 mJ/cm ²) twice weekly for 6 months	Percentage of lesions area re-pigmented grouped as ER (>75%), GR (50%–75%), MR (25%–50%), and PR (<25%)	45% of patients achieved ER, GR in 25% of patients achieved GR	Mild transitory burning and erythema
Abdel-Fattah et al. (1982), Egypt ^[30]	60	Double-blind clinical study	Group A: Khellin (100mg) tablet, OD for 4 months + Sunlight exposure for 15 minutes Group B: No treatment	Photography	16.6% patients' re-pigment with 90-100%, 23.3% with 50-60%, 36.6% with 25% or less	No adverse reactions
Bedi et al. (1989), India ^[31]	30	Randomized, placebo-controlled trial	Picrorhizakurroa (200 mg) capsule, BID+ Methoxsalen (10–20 mg) tablet, OD+ methoxsalen (0.75%) lotion, BID for 7 months	Clinical examination of lesions	26.6% of patients were completely cured, 53.3% showed rapid and continuous decreases in the number and size of lesions	Erythema, itching, and pruritus
Asawanonda et al. (2010), Thailand ^[35]	10	Randomized control trial	Group A: topical tetrahydrocurcuminoid (THC) cream, BD + TNB-UVB (100 mJ/cm ²) twice weekly for 3 months Group B: TNB-UVB (100 mJ/cm ²) followed by 50 mJ/cm ² increments at each session, twice weekly for 3 months	Digital photography	90% of the lesions repigmented in group A	Erythema, itching, burning sensation, and hyperpigmentation
Middelkamp-Hup et al. (2007), Netherlands ^[33]	50	Randomized double-blind placebo-controlled trial	Group A: Polypodium leucotomos (250mg) TID+ NB-UVB two times a week for 25-26 weeks Group B: Placebo+NB-UVB (210 and 360 mJ/cm ²) two	Photography, Physician Global Assessment (PGA)	Re-pigmentation was observed in 72% of cases in the P. leucotomos group, whereas 43% in the placebo group.	Mild to transient itching and skin dryness

			times a week for 25-26 weeks			
Reyes et al. (2006), Spain [32]	19	A pilot study	Group A: PUVA + Polypodium leucotomos (720 mg) capsule OD for 3 months Group B: PUVA+ Placebo (720mg) OD for 3 months	Clinical examination	The percentage of subjects with a skin re-pigmentation of >50% was higher in group A	No adverse reactions
Buggiani et al. (2012), Italy [34]	149	Open observational study	Group A: Re-Pigmenta® gel (Phenylalanine + Cucumis melo extract + acetylcysteine) TID for 12 weeks. Group B: UVB phototherapy once weekly for 12 weeks Group C: Pigmenta® gel TID + UVB once weekly for 12 weeks. Group D: Clobetasol propionate (0.05%) TID for 12 weeks	Photography	Re-pigmentation (>75 %) was seen in 38.4% of Group A, 61.14% of Group B, 73.54% of Group C, and 56.24% of Group D patients.	Hypertrichosis, skin atrophy, telangiectasias, experienced by people in group D

VASI-Vitiligo Area Scoring Index; VETF-Vitiligo European Task Force; VNS- Vitiligo Noticeability Scale; PGA- Physician Global Assessment; WPG-water/2-propanol/propylene glycol; ER- excellent repigmentation; GR-good repigmentation; MR- moderate repigmentation; PR- poor repigmentation; UV-ultraviolet; UVA-ultraviolet A; UVB-ultraviolet B; KUVA-khellin and UVA; PUVA- psoralen and UVA; NM- Not mentioned; MEL- Monochromatic Excimer Light; NB-UVB-Narrow-band ultraviolet B; TNB-UVB-targeted narrowband UVB phototherapy; TID- three times a day; BID- twice a day; RCT- randomized controlled trial.

Figure 2: Photographs of herbal plants used in the treatment of vitiligo. (a) Ginkgo biloba (b) Nigella sativa L. (c) Turmeric (d) Cucumis melo (e) Polypodium Leucotoms (f) Picrorhiza Kurroa (g) Ammi Visnaga (h) Psoralea Corylifolia L.



Ginkgo Biloba L.

Ginkgo biloba is one of the ancient plants on the earth, and its leaves and seeds have long been utilized in herbal treatments [13]. It contains flavone glycosides and terpene lactones. The mechanism of action of Ginkgo biloba in vitiligo is not known, however, it appears to be related to its anti-inflammatory, antioxidant, and immunomodulatory properties. These properties probably play a role in the treatment of vitiligo. Its antioxidant effect is valuable in the treatment of vitiligo and other free radical-induced disorders [15]. Many studies reported that this herb controls the spread of vitiligo and induces repigmentation [9, 15].

In a clinical trial, 12 vitiligo patients were treated with a

Ginkgo biloba capsule of 60 mg two times daily for 3 months [9]. This study reported poor treatment outcomes in which 25% of patients achieved 30% repigmentation. Mild watery diarrhea was experienced by one patient. Treatment response was improved (50% repigmentation) by prolonging the duration of therapy to 6 months [15]. In this study, Ginkgo biloba was used at a dose of 40 mg thrice daily in 52 patients. Mild nausea was developed in 2 patients [15]. Another study was carried out by Abu Raghib et al. by administering 75 mg of Ginkgo biloba twice daily for 2 months. No difference in treatment outcome over placebo was observed [16].

Nigella Sativa L.

Nigella sativa L. belongs to the family of Ranunculaceae and

can be found all over the globe. It has tapering green leaves and rosaceous white and purplish flowers. Thymoquinone is the main component of the seed that has anti-inflammatory, and antioxidant properties. It also strengthens the immune system [35]. Thymoquinone can mimic the acetylcholine activity, which causes the release of melanin and the darkening of the skin by stimulating cholinergic receptors [18]. *Nigella sativa* L. was also found to be effective in the disorders of respiratory, digestive, kidney, liver, cardiovascular, and immune systems.

Nigella sativa oil is well-tolerated, safe, and efficacious in treating vitiligo [18]. A clinical trial study was conducted by Sarac et al., in which 33 patients received *nigella sativa* twice daily for 6 months. Repigmentation was observed in more than 50% of the area in the face, hands, and genital regions, and none of the patients developed any adverse reactions [18]. *Nigella sativa* was also found to be effective in animal studies [17].

Turmeric

Turmeric is a rhizomatous plant of the family Zingiberaceae. Since turmeric has high anti-oxidant and anti-inflammatory properties, it also helps to synthesize melanin, which is crucial to the treatment of vitiligo. It is effective in a wide variety of conditions, such as diseases of the skin, respiratory tract, joints, and digestive system. It is also promoted as a dietary supplement [21]. Asawanonda et al., conducted a study using topical tetrahydro curcuminoid (THC) cream, in combination with TNB-UVB resulting in 90% repigmentation of the vitiligo lesions [35].

Despite widespread application in many diseases, only one study is available for vitiligo. In this study, 30 vitiligo patients received treatment with turmeric cream twice daily for 4 months and showed a good result by significantly decreasing the size of the lesions on the affected part of the body when compared to a placebo [21].

Polypodium Leucotomos

The *Polypodium leucotomos* is a tropical fern that can be found in Central and South America. Researchers have demonstrated over the past 30 years that extracts from *P. leucotomos* have beneficial properties in both clinical and non-clinical research. Numerous antioxidants and photoprotective compounds are believed to be responsible for this effect. It is effective for the treatment of vitiligo, and melasma [37].

Middelkamp-Hup et al. performed an RCT to see if the antioxidative and immunomodulatory effect of *Polypodium leucotomos* improves NB-UVB-induced repigmentation in vitiligo patients [33]. A total of 50 vitiligo patients randomly received 250 mg oral *P. leucotomos* or placebo thrice daily, in combination with NB-UVB two times weekly for 25 – 26 weeks. Increased repigmentation was observed when phototherapy was administered in combination with oral *P. leucotomos*. Itching, dryness of the skin, and

gastrointestinal upset were common adverse events reported in the study [33]. In another study, a combination of PUVA + *polypodium leucotomos* 720 mg once daily for 3 months was administered to 19 vitiligo patients, whereas patients in the other arm were treated with PUVA + placebo in the same dose and duration. Repigmentation was more prominent in the *Polypodium leucotomos* treated group than placebo [32].

Picrorhiza kurroa

Picrorhiza kurroa is also known as “Kutki” or “Kutaki”. There is limited scientific research specifically examining the effects of kutki extract on vitiligo. However, the antioxidant and immunomodulatory properties might help manage the condition. By reducing oxidative stress, kutki extract may support melanocyte survival and function, which could slow vitiligo progression [13]. Oral administration of *picrorhiza kurroa* in combination with methoxsalen was found to be useful in vitiligo [31]. An RCT by Bedi et al. administered a *picrorhiza kurroa* (200 mg) capsule in combination with methoxsalen (0.75%) two times daily for 7 months in 30 vitiligo patients [31]. Results revealed that 26.6% of patients were completely cured with a progress score of +4, whereas 53.3% showed a rapid and continuous reduction of patches with a progress score of +3.42. Erythema, itching, and pruritis were experienced by 16 patients. No serious toxicities were observed [31].

Khellin

Khellin is a furanochromone obtained from the plant *Ammi Visnaga*. Chemically, it is similar to psoralens, and it exerts similar photobiological, photochemical, and phototherapeutic properties. However, it is less carcinogenic and less phototoxic because it mainly forms mono-adducts. It has already been demonstrated that systemic khellin and UVA (Kuva) are effective in treating vitiligo [26].

Saraceno et al. conducted a study using Monochromatic excimer light 308 nm in monotherapy and combined with topical khellin 4% on vitiligo population and found that excellent response (>75%) was achieved in approximately half of the studied population. Treatment response was further improved upon the addition of antioxidant therapy (vitamin-E) to topical khellin and excimer light, in which 76-100% repigmentation was observed in more than half of the studied patients, and none of the patients developed any severe toxicities [25].

Two different studies reported good treatment response with minimal adverse effects when khellin was given with UV therapy in various doses and duration [10, 23, 24, 27, and 28]. In a retrospective study, khellin 100mg was administered orally in combination with UVA therapy in 28 vitiligo patients [28]. Forty-one percent of patients reported 70% repigmentation after receiving 3 months of treatment. No severe toxicity was reported; however, nausea was experienced by one-third of patients. No actinic damage or skin cancer was observed up to 9.2 years of follow-up (mean 3.3 years) [28]. Another similar observation

was also reported by Ortel et al., in which UVA phototherapy thrice weekly in combination with oral (n = 25) or topical (n = 3) khellin was given in 28 patients. At least 70% or higher repigmentation was achieved among 41% of patients after 6 months of therapy [23].

In another study, 60 patients received treatment with 100 mg of khellin or a placebo, along with natural sunlight exposure given daily for 15 minutes [30]. After 4 months, 16.6% of patients had 90–100% repigmentation, and 23.3% showed 50–60% repigmentation. No repigmentation was reported in the control group. Khellin was also tried in combination with phenylalanine and UVA/UVB therapy for 12 months; repigmentation of 50–100% was observed in 72% of treated locations [24].

A clinical trial study was done using a triple combination of khellin (1%) gel + WPG + UVA thrice weekly for 6 months. In comparison, patients in the other arm were treated with a topical gel containing only WPG + UVA for the same frequency and duration. Excellent repigmentation was observed in the khellin-containing triple combination regimen [10].

Psoralea Corylifolia L.

Psoralea corylifolia, also known as Babchi, is a well-known herb that has been used for centuries to treat leprosy, psoriasis, and vitiligo. This plant's chemoprotective, antioxidant, antimicrobial, and anti-inflammatory properties are also being studied pharmacologically. *Psoralea corylifolia* extract exhibits immunomodulatory and antioxidant properties, which can treat vitiligo. It may regulate the immune response and reduce oxidative stress. Both are believed to play a role in the development and progression of vitiligo [19]. A significant reduction in patch diameter was noted when *Psoralea corylifolia* (10% w/w) was given along with sunlight exposure for 3 months [19]. Similarly, a complete facial repigmentation was observed when *Psoralea corylifolia* oral and topical form in combination with daily sunlight exposure was given daily for 6 months [20].

Other Herbs

Cucumbers (*Cucumis sativus*) contain antioxidants and free radical scavenging properties. The presence of carotenoids, phenolic flavonoids, tannins, polyphenols, and lycopene contributes to its antioxidant activity. Cucumber juice can help to improve skin texture and treat skin infections and eczema. According to Liu et al. rubbing vitiligo lesion areas with sulfur powder adhered to fresh cucumber slices provided significant benefits [38]. *Sonchus oleraceus* is an herbal plant of the Asteraceae family, a natural source of antioxidants, and is rich in vitamins A, D, and E [39]. An infusion of *S. oleraceus* causes the pigmentation of white spots in patients with vitiligo [39]. Resende et al. studied 12 vitiligo patients using an oral infusion of leaves extract of *Solanum paniculatum*, *Jacaranda brasiliensis*, and *Sonchus oleraceus* (800ml) OD for 12 months and observed re-pigmentation on

the left foot, knee, elbows, and lips [22]. Djerrou et al. used a new formulation on a patient suffering from facial vitiligo, containing honey bee, a decoction of dry oat stems, and red onion juice [40]. The formulation is rich with antioxidant components, anti-inflammatory activity, and complete regimentation on the face after 11 months [40].

CONCLUSION

Most of the herbal drugs were found to have favorable therapeutic outcomes in the treatment of vitiligo. Therefore, herbs alone or in combination can be considered as one of the options for patients who are contraindicated to conventional therapies. However, a randomized controlled trial with a larger sample size is warranted to find out the position of these herbs in the treatment hierarchy.

REFERENCES

1. Rodrigues M, Ezzedine K, Hamzavi I, et al, 2017. Vitiligo Working Group. New discoveries in the pathogenesis and classification of vitiligo. *J Am Acad Dermatol*. 77(1), Pages 1-13. Doi: <https://doi.org/10.1016/j.jaad.2016.10.048>.
2. Hann SK, 2000. Clinical features of segmental vitiligo. In: Hann SK, James J, Nordlund MD et al (edition). *Vitiligo: A Monograph on the Basic and Clinical Science*, Oxford; Blackwell Scientific Publishers, Pages 49–60.
3. Rzepecki AK, McLellan BN, Elbuluk N, 2018. Beyond Traditional Treatment: The Importance of Psychosocial Therapy in Vitiligo. *J Drugs Dermatol* 17(6), Pages 688-691.
4. Whitton ME, Ashcroft DM, Barrett CW, et al, 2007. Interventions for vitiligo. *Cochrane Database of Systematic Reviews* 3, Pages 149-156. Doi: <https://doi.org/10.1002/14651858.CD003263.pub5>.
5. Grimes PE, 2005. New insights and new therapies in vitiligo. *Clin Cosmet Investig Dermatol* 293(6), Pages 730-735. Doi: 10.1001/jama.293.6.730.
6. Wong R, Lin AN, 2013. Efficacy of topical calcineurin inhibitors in vitiligo. *Int J Dermatol* 52, Pages 491-496. Doi: <https://doi.org/10.1111/j.1365-4632.2012.05697.x>.
7. Rodrigues M, Ezzedine K, Hamzavi I, et al, 2017. Current and emerging treatments for vitiligo. *J Am Acad Dermatol* 77(1), Pages 17-29. Doi: <https://doi.org/10.1016/j.jaad.2016.11.010>.
8. Orschner T, Buchholtz S, Stockfleth E, 2007. Current state of vitiligo therapy-evidence-based analysis of the literature. *J Dtsch Dermatol Ges* 5(6), Pages 467–475. Doi: <https://doi.org/10.1111/j.1610-0387.2007.06280.x>.
9. Szczurko O, Shear N, Taddio A, et al, 2011. Ginkgo biloba for the treatment of vitiligo vulgaris: an open label pilot clinical trial. *BMC Complement Altern Med* 11(1), Pages 1-9. Doi: <http://www.biomedcentral.com/1472-6882/11/21>.
10. Orecchia G, Sangalli ME, Gazzaniga A, et al, 1998. Topical photochemotherapy of vitiligo with a new khellin formulation: preliminary clinical results. *J Dermatolog Treat* 9(2), Pages 65-69. Doi: <https://doi.org/10.3109/09546639809161375>.

11. Deshmukh A, Wadnerwar N, Gaikwad A, 2020. A pilot study on efficacy of vishakalpa (shwetralepa) in shwetra (vitiligo). *IJAM* 11(4), Pages 747-753.
12. Szczurko O, Boon HS, 2008. A systematic review of natural health product treatment for vitiligo. *BMC Dermatol* 8(1), Pages 1-2. Doi: 10.1186/1471-5945-8-2.
13. Gianfaldoni S, Wollina U, Tirant M, et al, 2018. Herbal Compounds for the Treatment of Vitiligo: A Review. *Open Access Maced J Med Sci* 6(1), Pages 203-207. Doi: 10.3889/oamjms.2018.048.
14. Narayanaswamy R, Ismail IS, 2018. Role of herbal medicines in vitiligo treatment-current status and future perspectives. *Asian J Pharm Clin Res* 11, Pages 19-23. Doi: <https://doi.org/10.22159/ajpcr.2018.v11i9.26830>.
15. Parsad D, Pandhi R, Juneja A, 2003. Effectiveness of oral Ginkgo biloba in treating limited, slowly spreading vitiligo. *Clin Exp Dermatol* 28(3), Pages 285-287. Doi: <https://doi.org/10.1046/j.1365-2230.2003.01207.x>.
16. Abu-Raghif AR, Ali NM, Farhood IG, et al, 2013. Hameed HB et al. Evaluation of a standardized extract of ginkgo biloba in vitiligo remedy. *Asian J Pharm Clin Res* 6(5), Pages 127-130. Doi: 10.1186/1472-6882-11-21.
17. Sarac G, Kapicioglu Y, Sener S, et al, 2019. Effectiveness of topical *Nigella sativa* for vitiligo treatment. *Dermatol Ther* 32(4), Page e12949. Doi: <https://doi.org/10.1111/dth.12949>.
18. Ghorbanibirgani A, Khalili A, Rokhafrooz D, 2014. Comparing *Nigella sativa* oil and fish oil in treatment of vitiligo. *Iran Red Crescent Med J* 16(6), Page 4515. Doi: 10.5812/ircmj.4515.
19. Hussain I, Hussain N, Manan A, et al, 2016. Fabrication of anti-vitiligo ointment containing *Psoralea corylifolia*: in vitro and in vivo characterization. *Drug Des Devel and Ther* 10, Pages 3805-3816. Doi: <https://doi.org/10.2147/DDDT.S114328>.
20. Hussain I, Abro HA, Mubarak N, 2019. Skin Pigmentation Effects of *Psoralea Corylifolia*: A Case Study of Vitiligo. *J Islam Int Med Coll* 14(1), Pages Pages 48-50.
21. Jalalmanesh S, Mansouri P, Rajabi M, 2022. Therapeutic effects of turmeric topical cream in vitiligo: A randomized, double-blind, placebo-controlled pilot study. *J Cosmet Dermatol* 21(10), Pages 4454-4461. Doi: <https://doi.org/10.1111/jocd.14814>.
22. Resende JH, de Aquino GS, do Nascimento FR et al, 2015. Oral Use of an Infusion of Leaves of *Solanum paniculatum* L., *Jacaranda brasiliensis* and *Sonchus oleraceus* for Treatment of Vitiligo. *Journal of Cosmetics, Dermatological Sciences and Applications* 5(4), Page 317. Doi: 10.4236/jcdsa.2015.54039.
23. Ortel B, Tanew A, Hönigsmann H, 1988. Treatment of vitiligo with khellin and ultraviolet A. *J Am Acad Dermatol* 18(4), Pages 693-701. Doi: [https://doi.org/10.1016/S0190-9622\(88\)70092-4](https://doi.org/10.1016/S0190-9622(88)70092-4).
24. De Leeuw J, van der Beek N, Maierhofer G, et al, 2003. A case study to evaluate the treatment of vitiligo with khellin encapsulated in L-phenylalanine-stabilised phosphatidylcholine liposomes in combination with ultraviolet light therapy. *Eur J Dermatol* 13(5), Pages 474-477.
25. Saraceno R, Nistico SP, Capriotti E, et al, 2009. Monochromatic excimer light 308 nm in monotherapy and combined with topical khellin 4% in the treatment of vitiligo: a controlled study. *Dermatol Ther* 22(4), Pages 391-394. Doi: <https://doi.org/10.1111/j.1529-8019.2009.01252.x>.
26. Valkova S, Trashlieva M, Christova P, 2004. Treatment of vitiligo with local khellin and UVA: comparison with systemic PUVA. *Clin Exp Dermatol* 29(2), Pages 180-184. Doi: <https://doi.org/10.1111/j.1365-2230.2004.01462.x>.
27. De Leeuw J, Assen YJ, Van Der Beek N, et al, 2011. Treatment of vitiligo with khellin liposomes, ultraviolet light and blister roof transplantation. *J Euro Acad Dermatol Venereal* 25(1), Pages 74-81. Doi: <https://doi.org/10.1111/j.1468-3083.2010.03701.x>.
28. Hofer A, Kerl H, Wolf P, 2001. Long-term results in the treatment of vitiligo with oral khellin plus UVA. *Eur J Dermatol* 11(3), Pages 225-229.
29. Fenniche S, Zaouak A, Tanfous AB, et al, 2018. Successful treatment of refractory vitiligo with a combination of khellin and 308-nm excimer lamp: An open-label, 1-year prospective study. *Dermatol Ther* 8(1), Pages 127-135. Doi: <https://doi.org/10.1007/s13555-017-0218-x>.
30. Abdel-Fattah A, Aboul-Enein MN, Wasset GM, 1982, et al. An approach to the treatment of vitiligo by khellin. *Dermatologica* 165(2), Pages 136-140. Doi: <https://doi.org/10.1159/000249932>.
31. Bedi KL, Zutshi U, Chopra CL, et al, 1982. Picrorhiza kurroa, an ayurvedic herb, may potentiate photochemotherapy in vitiligo. *J Ethnopharmacol* 27(3), Pages 347-352. Doi: [https://doi.org/10.1016/0378-8741\(89\)90009-3](https://doi.org/10.1016/0378-8741(89)90009-3).
32. Reyes E, Jaén P, de las Heras E, et al, 2006. Systemic immunomodulatory effects of *Polypodium leucotomos* as an adjuvant to PUVA therapy in generalized vitiligo: A pilot study. *J. Dermatol. Sci.* 41(3), Pages 213-216. Doi: <https://doi.org/10.1016/j.jdermsci.2005.12.006>.
33. Middelkamp-Hup MA, Bos JD, Rius-Diaz F, et al, 2007. Treatment of vitiligo vulgaris with narrow-band UVB and oral *Polypodium leucotomos* extract: a randomized double-blind placebo-controlled study. *J Eur Acad Dermatol Venereol* 21(7), Pages 942-950. Doi: <https://doi.org/10.1111/j.1468-3083.2006.02132.x>.
34. Buggiani G, Tsampau D, Hercogová J, et al, 2012. Clinical efficacy of a novel topical formulation for vitiligo: compared evaluation of different treatment modalities in 149 patients. *Dermatol Ther* 25(5), Pages 472-476. Doi: <https://doi.org/10.1111/j.1529-8019.2012.01484.x>.
35. Zohary D, Hopf M, Weiss R, 2012. Domestication of plants in the old world. 4th ed., New York: Oxford University Press. Pages 1–264.
36. Asawanonda P, Klahan SO, 2010. Tetrahydrocurcuminoid cream plus targeted narrowband UVB phototherapy for vitiligo: a preliminary randomized controlled study. *Photomed Laser Surg* 28(5), Pages 679-84. Doi: <https://doi.org/10.1089/pho.2009.2637>.

37. Nestor M, Bucay V, Callender V, et al, 2014. Polypodium leucotomos as an adjunct treatment of pigmentary disorders. J Clin Aesthet Dermatol 7(3), Page 13.
38. Liu Z, Wang R, Zhang C, et al, 2019. A case of vitiligo cured with cucumber and sulfur. Phytother. Res. 33(4), Pages 1241-1242. Doi: <https://doi.org/10.1002/ptr.6309>.
39. Eibel GS, Zilly A, da Silva RM, et al, 2021. Use of the infusion of Sonchus oleraceus leaves for the treatment of vitiligo. Res. Soc. Dev. 10(4), Page e141041382. Doi: <https://doi.org/10.33448/rsd-v10i4.13824>.
40. Djerrou Z, 2015. Successful treatment of facial vitiligo with honey bee, Allium cepa and Avena sativa combined to sun light exposure: A case clinical trial. Int. J. Pharm. Clin. Res. 7(1), Pages 9-14.