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Herbal Compounds for the Treatment of Vitiligo: A Review

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Abstract

An overview of unconventional therapies for vitiligo is presented. Some herbal compounds may be considered as valid therapeutic tools for the treatment of vitiligo.

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Introduction

Since ancient time, herbal products of different nature and effects had been used for the treatment of vitiligo. The Authors provide a brief overview of the herbal products available for the treatment of the pigmentary disease.

Ginkgo biloba

Ginkgo biloba (also known as “maidenhair tree”), is one of the oldest trees on Earth and its leaves and seeds had been largely used in medicine

for a very long time. Ginkgo extracts have been shown to be effective for the treatment of different diseases, such as allergies, varicose vein, premenstrual syndrome, headache, vertigo and others [1]. In the last few years, ginkgo extracts have also been used for the treatment of vitiligo. The drug is formulated into a tablet of different dosage, which must be taken orally once to three times daily, for more than three months.

The exact mechanism of action of Ginkgo biloba in vitiligo is still unknown, but it seems to be related to the anti-inflammatory, immunomodulatory and antioxidant properties of the drug [2].

Many data support the efficacy of the herbal compound in controlling the activity of vitiligo and in inducing repigmentation of the white macules, especially if administrated with other conventional

therapies (e.g. corticosteroids, phototherapies) [3][4]. Moreover, recent studies underline how the drug is also effective when administrated alone [2][5]. Unfortunately, the results in term of repigmentation are not uniform. This fact may be explained by different factors: the genetic differences of the analysed populations, the different type of Ginkgo biloba extracts, the treatment duration, the number of administrated doses per day [5]. The drug is safe and well-tolerated at therapeutic dosages (normal value: 120 mg/day). Only daily dosage > 240 mg may result in restlessness and gastrointestinal disorders. Patients on anticoagulants should only take ginkgo under medical supervision for a correct prescription, to avoid over-thinning of their blood and haemorrhaging.

Cucumis melo

Cucumis melo (also known as “Muskmelon”) is a species of Cucumis, plants of the Cucurbitaceae family. Cucumis melo extract is rich in antioxidants that naturally contain a high superoxide dismutase (SOD) (Table 1) activity, which has been proposed to be important in stopping the melanocytes de construction by the oxidative stress in the first step of vitiligo. Recently, preliminary studies were conducted to evaluate the efficacy of a topical preparation, containing Cucumis melo superoxide dismutase (SOD) and catalase, in the treatment of vitiligo [6][7]. In each study, the gel preparation was applied to the skin lesions followed by irradiation with natural UV or artificial narrow band UVB. Even though the drug has been shown to be safe, there was no difference in repigmentation rate recorded compared to the patients treated only with the phototherapy. More interesting and promising is the use of a different topical formulation, containing phenylalanine, Cucumis melo extract, and acetyl cysteine. The association of the gel with nb - UVB target phototherapy has been observed to be safe and effective, leading to a better repigmentation of cutaneous lesions [8].

Khellin

Khellin is a naturally occurring furanochromone, derived from the plant *Amni visnaga*. The plant has been used as a herbal medicine for different purposes (e.g. kidney diseases, asthma and others), since ancient Egyptian times. Because of khellin side effects, including liver dysfunction and allergic reactions, analogues of khellin, with safer profiles and better efficacy, have been developed and introduced in medicine in the last decades for the

treatment of vitiligo, where they provide good results in combination with UVA phototherapy. Even if the exact mechanism of action is unclear, khellin acts by stimulating melanocytes proliferation and melanogenesis [9]. Khellin may be administrated both systemically (oral administration) or topically. The association of oral Khellin to UVA is better known as KUVA therapy [10]. The treatment consists in the oral intake of khellin gelatin capsules and, after about 2.5 hours, in the patient's irradiation with UVA. The therapeutic session is repeated 2 - 3 times a week. The treatment is quite safe and provides clinical results similar to PUVA therapy. Unlike psoralens, Khellins have less phototoxic, and DNA mutagenic effects but the long-term risk of carcinogenesis has to be determinate [11]. Like topical - PUVA, khellin may be applied topically and associated with UVA radiation (topical KUVA therapy) or natural UVR (sol - KUVA therapy). Even in this case, the risk of carcinogenesis has to be yet determinate [12]. More recently, topical khellin 4% has been successfully used in association to monochromatic excimer light 308 nm [13]. The clinical results regarding repigmentation rate and safe profile suggest how this combination may be useful for vitiligo treatment.

Ayurvedic medicine: Picrorhiza kurroa

Also, Ayurvedic medicine had tried to treat vitiligo with herbal products, such as Picrorhiza kurroa. Picrorhiza kurroa (also known as “Kutki” or “Kutaki”) is another khellin extract, with well - known hepatoprotective properties. More recently, researchers have proposed how the herbal extract has antioxidant and immune-modulating activities too (Table 1).

Table 1: Some of the most common herbal products used for vitiligo treatments, and their main components

Herbs	Active components
Cucumis melo	Cucumis melo superoxide dismutase
Green Tea	Epicatechin, epicatechin-3-gallate, epigallocatechin
Picrorhiza kurroa	Picroside I and picroside II
Polypodium leucotomos	p-coumaric, ferulic, caffeic, vanillic, 3,4 - dihydroxybenzoic, 4 - hydroxybenzoic, 4 - hydroxycinnamic, 4 - hydroxycinnamoyl - quinic, chlorogenic acids

Recently, a study investigated Picrorhiza Kuroda's potential use in association with phototherapy, in the treatment of vitiligo. The drug was administrated twice a day orally for three months. At the same time, patients were treated with methoxsalen photochemotherapy. The association of the two therapies has seen to provide a better result regarding repigmentation [14]. Another Ayurvedic herbal product which had been used for the treatment of vitiligo is the anarchic [15], topical concentrated pharmaceutical preparations of plants in the

Anacardiaceae family. The drug seems to act as a photosensitizing agent. Unfortunately, more data and research are needed.

Polypodium leucotomos

Polypodium leucotomos (also known as “Calaguala”) is a species of tropical fern in the family Polypodiaceae. Its extracts, famous for their antioxidant and photoprotective properties (Table 1) [16], are used for the treatment of various skin diseases, such as psoriasis, atopic dermatitis and others [17][18]. In the last few years, *Polypodium leucotomos* has been used as adjuvant therapy for vitiligo patients who were being treated with phototherapy. An interesting study underlines how PUVA therapy plus oral *Polypodium leucotomos* led to a higher repigmentation than the photochemotherapy alone. A different study showed similar results with the combination of nb - UVB/oral *Polypodium leucotomos* in comparison to the single phototherapy [18][19].

Traditional Chinese Medicine (TCM)

Since ancient time, TCM had tried to treat vitiligo with different herbal products, used alone or, more often, in combination. Among the traditional Chinese products, psoralen plus UVA (PUVA therapy) had been considered as the first vitiligo treatment for several decades. Psoralen is a photosensitising compound, derived from *Psoralea Cordyfolia*, a Chinese herb, and other plants. TCM used to treat vitiligo by combining topical or systemic *Psoralea* seed extract, in association to UVA exposure for a long time. The mechanism of action of therapeutic protocols, such as the beneficial effects and the collaterals are well - known. Another well - known and characterized treatment option is the topical PUVA, based on the topical application of *Psoralea* extract or derived products, and in the successive exposure to a UVA source [20]. Among the other herbal products, many are the formulations available for the treatment of the pigmentary disorders (Table 2) (Table 3) [21][22][23][24].

Table 2: The most commonly prescribed Chinese herbs for vitiligo

Angelica Sinensis, *Ligusticum wallichii*, *Tribulus Terrestris*, *Polygonum multiflorum*, *Fructus psoraleae*, *Radix Paeoniae Rubra*, *Rehmannia glutinosa*, Glossy Privet Fruit, *Eclipta Alba*, *Salvia miltiorrhiza*, *Liquorice*, *Angelica dahurica*

They can be administered alone or in association with phototherapy. Unfortunately, for most

of them, clinical trials are of poor quality or missing [25]. A particular mention is due to the “Barresi complex prescription”, one of the most used for vitiligo treatment in the Uyghur medicine, which is an important part of TCM [26]. The formulation is composed of the hot water extract of five herbs (*Psoralea corylifolia*, *Plumbago zeylanica*, *Brassica juncea*, *Nigella glandulifera*, *Vernonia anthelmintic*). The efficacy of the drugs has been evaluated both in vivo and in vitro. In both studies, a good repigmentation has been observed, as the result of melanogenesis stimulation [27].

Table 3: Examples of TCM for vitiligo treatments

Main components:	
Treatment 1	Systemic treatment: walnut, red flower, black sesame, black beans, zhi bei fu ping, lu lu tong, and plums
Treatment 2	Systemic treatment: ligustrum, lycium, morus fruit, cuscuta, eclipta, epimedium (to restore liver and kidney), plus tang - kwei, red peony, cnidium, carthamus, persica, moutan, lithospermum (to promote circulation); plus tribulus, psoralea, cuscuta, black sesame seed, ho-shou-wu, angelica (to promote cutaneous pigmentation). Topical treatment: psoralea, cuscuta, tribulus, angelica, mume, sulfur, and various toxic metals
Treatment 3	Systemic treatment: Phase 1: bupleurum, tang-kuei, red peony, dalbergia, and pangolin scale (to regulate circulation and vitalize blood), plus ligustrum and eclipta (to nourish liver and kidney). Duration treatment: 3-6 months. Phase 2: astragalus, ginseng, tang-kuei, rehmannia, cnidium, cinnamon bark, millettia, psoralea, and epimedium (to regulate circulation and stimulate skin pigmentation). Treatment duration: several months. Topical therapy: psoralea.

Green Tea Polyphenols

Green Tea polyphenols are extracts of green tea leaves, which are used in medicine since ancient time. They act as anti - inflammatory, anti - oxidant, and immunomodulatory agents, mainly because of their composition in Epigallocatechin – 3 - gallate (EGCG) (Table 1) [28]. The drug can be administered both systemically and topically [29]. Recent data suggest how Green Tea polyphenols may be useful for vitiligo treatment, in stopping the oxidative stress of the melanocyte-unit [30].

Capsaicin

Capsaicin is one of the active component of chili peppers, plants of the genus *Capsicum*. Because its antiinflammatory and antioxidant properties, the drug has been proposed as a therapeutic tool for

vitiligo treatments. An experimental study recently confirmed how the incubation of keratinocytes, taken by the perilesional skin of a vitiliginous patient, with capsaicin stopped the cellular damage by ROS [31].

Curcumin

Curcumin is a polyphenol derived from the golden spice turmeric (“*Curcuma longa*”).

Because of its numerous properties (e.g. antioxidant, anti - proliferative, anti - inflammatory, antiviral, antibacterial and antifungal properties), curcumin has been used for the treatment of different diseases [32].

Recently, a tetrahydrocurcumide cream has been used in association with nb - UVB for vitiligo treatments. The phototherapy was performed twice a week for 12 weeks. At the end of the therapeutic protocol, patients showed a slightly better repigmentation compared to the ones treated only with nb-UVB [33]. Finally, as with other antioxidants, curcumin may be orally administered as adjuvant therapy in vitiligo patients.

Pyrostegia venusta

Pyrostegia venusta (also known as “cipó – de – são - João”) is a herb of the family Bignoniaceae, widely distributed in southern Brazil, where topical formulations are commonly used for the treatment of vitiligo. Even if its mechanisms of action are still under investigations, the herb seems to be effective for its antioxidant, anti-inflammatory and melanogenic properties [34].

Conclusions

Some herbal compounds may be considered as valid therapeutic tools for the treatment of vitiligo.

References

1. PDR for Herbal Medicines. Montvale, NJ: Medical Economics Company, 1998.
2. Parsad D, Pandhi R, Juneja A. Effectiveness of oral Ginkgo biloba in treating limited, slowly spreading vitiligo. *Clin Exp Dermatol.* 2003; 28(3):285-7. <https://doi.org/10.1046/j.1365-2230.2003.01207.x> PMID:12780716
3. Cohen BE, Elbuluk N, Mu EW, et Al. Alternative Systemic Treatments for Vitiligo: A Review. *Am J Clin Dermatol.* 2015; 16(6):463 - 74. <https://doi.org/10.1007/s40257-015-0153-5> PMID:26329814
4. Grimes PE, Nashawati R. The Role of Diet and Supplements in Vitiligo Management. *Dermatol Clin.* 2017; 35(2):235 - 243. <https://doi.org/10.1016/j.det.2016.11.012> PMID:28317532
5. Szczurko O, Shear N, Taddio A. et Al. Ginkgo biloba for the treatment of vitiligo vulgaris: an open label pilot clinical trial. *BMC Complementary and Alternative Medicine.* 2011; 11:21. <https://doi.org/10.1186/1472-6882-11-21> PMID:21406109 PMCid:PMC3065445
6. Naini FF, Shooshtari AV, Ebrahimi B et Al. The effect of pseudocatalase/superoxide dismutase in the treatment of vitiligo: A pilot study. *J Res Pharm Pract.* 2012; 1(2):77-80. <https://doi.org/10.4103/2279-042X.108375> PMID:24991594 PMCid:PMC4076862
7. Yuksel EP, Aydin F, Senturk N et Al. Comparison of the efficacy of narrow band ultraviolet B and narrow band ultraviolet B plus topical catalase-superoxide dismutase treatment in vitiligo patients. *Eur J Dermatol.* 2009; 19(4):341 -4. PMID:19467974
8. Buggiani G, Tsampau D, Hercogová J et Al. Clinical efficacy of a novel topical formulation for vitiligo: compared evaluation of different treatment modalities in 149 patients. *Dermatol Ther.* 2012; 25(5):472-6. <https://doi.org/10.1111/j.1529-8019.2012.01484.x> PMID:23046028
9. Carlie G, Ntusi NB, Hulley PA et Al. KUVVA (khellin plus ultraviolet A) stimulates proliferation and melanogenesis in normal human melanocytes and melanoma cells in vitro. *Br J Dermatol.* 2003; 149(4):707-17. <https://doi.org/10.1046/j.1365-2133.2003.05577.x> PMID:14616361
10. Morliere P, Hönigsmann H, Averbeck D et Al. Phototherapeutic, photobiologic, and photosensitizing properties of khellin. *J Invest Dermatol.* 1988; 90(5):720-4. <https://doi.org/10.1111/1523-1747.ep13083852> PMID:3283251
11. Ortel B, Tanew A, Hönigsmann H. Treatment of vitiligo with khellin and ultraviolet A. *J Am Acad Dermatol.* 1988; 18(4 Pt 1):693-701. [https://doi.org/10.1016/S0190-9622\(88\)70092-4](https://doi.org/10.1016/S0190-9622(88)70092-4)
12. Bech - Thomsen N, Wulf HC. Treatment with topical khellin in combination with ultraviolet A or solar-simulated radiation is carcinogenic to lightly pigmented hairless mice. *Photodermatol Photoimmunol Photomed.* 1996; 11(5-6):204-8. PMID:8738715
13. Saraceno R, Nisticò SP, Capriotti E, et Al. Monochromatic excimer light 308 nm in monotherapy and combined with topical khellin 4% in the treatment of vitiligo: a controlled study. *Dermatol Ther.* 2009; 22(4):391 -4. <https://doi.org/10.1111/j.1529-8019.2009.01252.x> PMID:19580584
14. Bedi KL, Zutshi U, Chopra CL, et Al. Picrorhiza kurroa, an ayurvedic herb, may potentiate photochemotherapy in vitiligo. *J Ethnopharmacol.* 1989; 27(3):347-52. [https://doi.org/10.1016/0378-8741\(89\)90009-3](https://doi.org/10.1016/0378-8741(89)90009-3)
15. Punshi SK. Topical use of anacarcin forte (R) oil in vitiligo. *Indian J Dermatol Venereol Leprol.* 1980; 46(2):102-103. PMID:28218142
16. Edlich RF, Winters KL, Lim HW. Photoprotection by sunscreens with topical antioxidants and systemic antioxidants to reduce sun exposure. *Journal of Long - Term effects of Medical Implants.* 2004;14: 317 - 340. <https://doi.org/10.1615/JLongTermEffMedImplants.v14.i4.40> PMID:15447629
17. Berman B, Ellis C, Elmets C. Polypodium Leucotomos - An Overview of Basic Investigative Findings. *J Drugs Dermatol.* 2016; 15(2):224-8. PMID:26885792 PMCid:PMC5189711
18. Nestor M, Bucay V, Callender V, et Al. Polypodium leucotomos as an Adjunct Treatment of Pigmentary Disorders. *J Clin Aesthet Dermatol.* 2014; 7(3):13-7. PMID:24688621 PMCid:PMC3970827
19. Middelkamp - Hup MA, Bos JD, Rius-Diaz F, et Al. 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*. 2007; 21(7):942-50. <https://doi.org/10.1111/j.1468-3083.2006.02132.x> PMID:17659004
20. Hussain I, Hussain N, Manan A, et Al. Fabrication of anti-vitiligo ointment containing *Psoralea corylifolia*: in vitro and in vivo characterization. *Drug Des Devel Ther*. 2016; 10:3805- 3816. <https://doi.org/10.2147/DDDT.S114328> PMID:27920496 PMID:PMC5125804
21. Gao C, Yang L, Chen M et al.: Principles of Differentiation and Prescription for Vitiligo in Traditional Chinese Medicine Based on a Literature Investigation. *Integr Med Int*. 2015; 2:149–156. <https://doi.org/10.1159/000441845>
22. Liu ZJ, Xiang YP. [Clinical observation on treatment of vitiligo with xiaobai mixture]. *Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi/Chinese Journal of Integrated Traditional & Western Medicine/Zhongguo Zhong Xi Yi Jie He Xue Hui, Zhongguo Zhong Yi Yan Jiu Yuan Zhu Ban*. 2003; 23(8):596-598.
23. Yin Ping, A review of 14 works on treatment of vitiligo. *Yunnan Journal of Traditional Chinese Medicine*. 1994; 15(5): 36-38.
24. Xue Changlian, et al., A clinical report on 800 cases of vitiligo treated with Chinese herb therapy, *Acta Medica Sinica*. 1991; 6(4): 28-29.
25. Szczurko O, Boon HS. A systematic review of natural health product treatment for vitiligo. *BMC Dermatol*. 2008; 8:2. <https://doi.org/10.1186/1471-5945-8-2> PMID:18498646 PMID:PMC2432048
26. Ma ZQ, Hu H, He TT et al., *Afr J Tradit Complement Altern Med*. 2014; 11(2):301-314. <https://doi.org/10.4314/ajtcam.v11i2.13>
27. Huang X, Ishikawa M, Mansur A et Al. The Effects of Bairesi Complex Prescription (a Uyghur Medicine Prescription) and Its Five Crude Herbal Extracts on Melanogenesis in G-361 Cells. *Evid Based Complement Alternat Med*. 2016; 2016:8415359. <https://doi.org/10.1155/2016/8415359> PMID:27069495 PMID:PMC4812344
28. Zhu Y, Wang S, Lin F et Al. The therapeutic effects of EGCG on vitiligo. *Fitoterapia*. 2014; 99:243-51. <https://doi.org/10.1016/j.fitote.2014.08.007> PMID:25128425
29. Eken ZE. Antioxidants. *Pigmentary Disorders*. 2015; 2: 163.
30. Jeong YM, Choi YG, Kim DS et Al. Cytoprotective effect of green tea extract and quercetin against hydrogen peroxide-induced oxidative stress. *Arch Pharm Res*. 2005; 28(11):1251 -6. <https://doi.org/10.1007/BF02978208> PMID:16350851
31. Becatti M, Prignano F, Fiorillo C, et Al. The involvement of Smac/DIABLO, p53, NF - kB, and MAPK pathways in apoptosis of keratinocytes from perilesional vitiligo skin: Protective effects of curcumin and capsaicin. *Antioxid Redox Signal*. 2010; 13(9):1309-21. <https://doi.org/10.1089/ars.2009.2779> PMID:20085492
32. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti - inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. *Int J Biochem Cell Biol*. 2009; 41(1):40 – 59. <https://doi.org/10.1016/j.biocel.2008.06.010> PMID:18662800 PMID:PMC2637808
33. Asawanonda P, Klahan SO. Tetrahydrocurcuminoid cream plus targeted narrowband UVB phototherapy for vitiligo: a preliminary randomized controlled study. *Photomed Laser Surg*. 2010; 28(5):679 – 84. <https://doi.org/10.1089/pho.2009.2637> PMID:20961233
34. Moreira CG, Carrenho LZB, Pawloski PL et al. Pre-clinical evidences of *Pyrostegia venusta* in the treatment of vitiligo. *Journal of Ethnopharmacology* 2015; 168: 315 – 325. <https://doi.org/10.1016/j.jep.2015.03.080> PMID:25862965