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Systematic Review

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Systematic Review of Oral and Topical Botanicals in Reducing Photosensitivity

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ABSTRACT

Objectives: Various treatment options are available for the management of photosensitivity. The objective of this review is to evaluate the use of botanicals rich in antioxidants for photosensitivity reduction.
Design: Embase and Ovid/MEDLINE databases were searched for clinical studies evaluating antioxidants from botanical sources in the management of photosensitivity.
Results: Of 339 citations, 10 met the inclusion criteria. Four studies evaluated *Polypodium leucotomos*, two evaluated *Camelia sinensis*, while *Hamamelis*, *Pistacia vera L.*, *Citrus sinensis* varieties Moro, Tarocco and Sanguinello, and *Capparis spinosa* were investigated in one study each. Five studies evaluated oral supplementation, four evaluated topical formulations, and one study evaluated both oral and topical antioxidants. Main results were summarized.
Conclusions: There is some evidence that antioxidants derived from botanical sources may be beneficial in reducing skin erythema and photosensitivity. However, the studies included in this review have methodological limitations and large scale randomized, placebo controlled trials are needed to further evaluate the efficacy and safety of botanical antioxidants in photosensitivity reduction.

KEY WORDS: Botanical; Plant; Antioxidant; Erythema; Photosensitivity; Ultraviolet; Ultraviolet-A (UVA); Ultraviolet-B (UVB); Photoprotection; *Polypodium leucotomos*.

ABBREVIATIONS: UV: Ultraviolet; UVA: Ultraviolet-A; UVB: Ultraviolet-B; MED: Minimal Erythema Dose; MPD: Minimal Phototoxic Dose; IP: Idiopathic Photodermatoses; PL: *Polypodium leucotomos*; PLE: Polymorphic Light Eruption; IBS: Irritable Bowel Syndrome.

INTRODUCTION

Photosensitivity, commonly referred to as sun sensitivity, is a term used to describe inflammation triggered by ultraviolet (UV) rays from the sun. The American College of Rheumatology explains that photosensitivity is a 'skin rash as a result of unusual reaction to sunlight, by patient history or physician observation.'[1] Specifically, photosensitivity is caused by an abnormal reaction to a component of the electromagnetic spectrum of sunlight and a chromophore (reactive compound) within the skin. The characteristics of photosensitivity vary with the type of photosensitivity. The presentation can manifest as macular erythema, papules, plaques, vesicles, bullae, telangiectasias, or eczematous patches usually in sun-exposed areas of the skin. The differential diagnosis of photosensitivity is large and includes genetic and metabolic diseases, photochemical sensitivity, idiopathic photosensitivity and other systemic and cutaneous diseases where photosensitivity is a part of a larger symptom complex. Aggravation of skin symptoms from sunlight exposure is a common presentation of various rheumatologic diseases.[2] There have been recent advances in the understanding of photosensitive rheumatic diseases, especially cutaneous lupus erythematosus and dermatomyositis.[3] Studies suggest mechanisms for photosensitivity include: modulation of autoantibodies, production of free radicals, cytotoxic effects, apoptosis induction, upregulation cytokines, induction of nitric oxide

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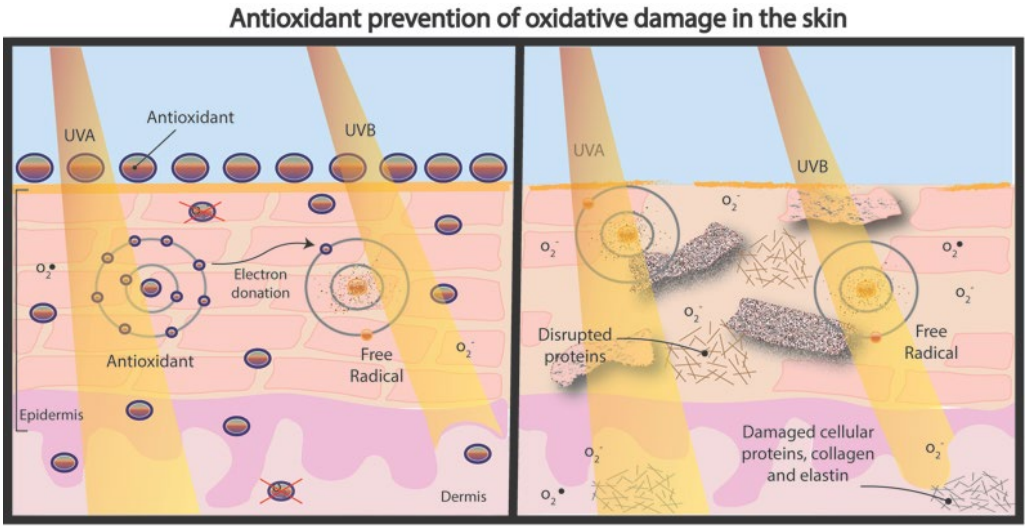
Figure 1: Plant Extract Antioxidants are a Promising Approach to Protecting Photosensitive Skin from Damaging UV Radiation. Free Radicals can Adversely Alter Lipids, Proteins, and DNA and Trigger a Number of Human Diseases. Antioxidants are Involved in the Prevention of Cellular Damage by Safely Interacting with Free Radicals and Halting Damage. The Application of External Sources of Antioxidants can Assist in Managing the Oxidative Stress.



synthase expression and ultraviolet-generated antigenic DNA.[1,4] In concert with the mechanisms discussed, some studies suggest that supplementation with antioxidants may be beneficial. Plant extract antioxidants and immune modulating mechanisms are a promising approach to protecting photosensitive skin from damaging UV radiation (Figure 1).

Current therapy for photosensitivity involves symptom specific relief, sun protection and treatment of the underlying disorder. Sun-protective measures such as sun avoidance and sunscreen are essential. If possible, any drugs or chemicals that could cause photosensitivity should be discontinued after consulting with a doctor. When a skin reaction has already developed, topical corticosteroids may be prescribed to reduce inflammation. Topical application of calcineurin inhibitor tacrolimus has also shown to be efficacious in some patients.[5] For more severe reactions, oral glucocorticoids may improve symptoms during acute exacerbations.[6] The use of steroids leads to numerous unwanted side effects such as skin thinning and bruising, weight gain, acne, and osteoporosis.[7] Given these adverse effects there is a need for safe and effective alternatives to treat photosensitivity. Our understanding of medicinal botanical extract efficacy and their mechanisms is growing, as is the demand for natural approaches for treatments. Here we review and discuss the evidence for the use of plant-derived components and their mechanisms in reducing photosensitivity.

MATERIALS AND METHODS

Search Strategy

Embase and Ovid/MEDLINE databases were searched in January 2017 for clinical studies examining the effects of plant based antioxidants on photosensitivity. A controlled vocabulary was used in the search, as outlined in Appendix Table A1.

Eligibility Criteria

Clinical studies that used antioxidants from botanical sources were included. Additionally, studies focusing on photosensitivity with outcome measures evaluating the change in skin erythema were included. Reports that did not describe human clinical studies (such as reviews, abstracts, and editorials), as well as those that did not study photosensitivity or did not evaluate a plant-derived antioxidant were excluded.

RESULTS AND DISCUSSION

Our search yielded 339 articles of which ten manuscripts met the inclusion criteria (Figure 2). The botanical sources of antioxidants included *Polypodium leucotomos* (tropical fern; four reports), *Camelia sinensis* (green tea, two reports), *Hamamelis* (witch hazel, one report), *Pistacia vera* L. (pistachio, one report), *Citrus sinensis* varieties Moro, Tarocco and Sanguinello (red orange, one report), and *Capparis spinosa* (one report) (Table 1). Five studies evaluated antioxidants in oral formulation, four studies evaluated topical formulations, and one study evaluated both oral and topical antioxidants. Main results are summarized in Table 2.

Polipodium leucotomos

Polypodium leucotomos (PL) is a tropical fern plant native to Central America. The benefits of PL have been reported in the treatment and prevention of skin conditions including psoriasis, sunburn, and polymorphic light eruption.[8] PL possesses potent antioxidant, photoprotective, and immune modulatory activities.[9]

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Table 1: Botanicals Used for Photosensitivity Reduction.

Scientific name	Common name
Polypodium leucotomos[10-13]	Tropical fern
Camelia sinensis[16,17]	Green tea
Hamamelis virginiana L.[21]	Witch hazel
Pistacia vera L.[23]	Pistachio
Citrus sinensis[24]	Red orange
Capparis spinosa L.[27]	Caper bush

Gonzalez et al[10] conducted a non-blinded randomized controlled trial to investigate the photoprotective activity of PL when applied topically or consumed orally among 21 healthy subjects aged 18-46 years (8 men, 13 women), with skin type III and IV. The subjects were either non-sensitized or psoralen-sensitized [oral 8-methoxy psoralen (8-MOP) or 5-methoxy psoralen (5-MOP)] and then randomized to receive topical PL (10%, 25%, 50%) or oral PL (1080 mg). Topical treatment was applied to subjects' backs once, in the amount of 2 µL/cm^2, at least 15-30 minutes prior to sun exposure. In the group receiving oral PL, a total of 720 mg PL in the form of capsules was consumed one day prior to sun exposure and 360 mg PL three hours prior to sun exposure. The outcome measures were minimal erythema dose (MED) and minimal phototoxic dose (MPD) before and after PL administration. MED is the minimal UV dose that leads to sunburn; MPD is the minimal ultraviolet-A (UVA) dose that leads to phototoxic reaction in the skin. The MED and MPD outcomes were evaluated visually and reported as minutes of sun exposure until visible skin reaction occurred. Subjective determination of MED was done 20-24 hours post-exposure to solar radiation; MPD was determined 48-72 hours post-exposure. The following criteria was used for evaluating erythema reaction: 0=none, ±= trace, +=pink, ++=pink red without edema, +++=strong red with edema, ++++=violaceous with painful edema. MED was reported as minutes of solar exposure until there was visible erythema; similarly, MPD values were reported as minutes of sun exposure until phototoxic reaction. The results showed that both topical and oral PL provided skin photoprotection. Specifically, PL significantly increased MED (p<0.001) and MPD (p<0.001). Oral PL provided better photoprotection than 10% PL topical (MED: 98±15.4 and 80±0, respectively; p<0.05). No adverse effects were reported.

Although, this study shows that PL in topical or oral formulation may provide photoprotective benefits, while not causing side effects, the results should be interpreted with cau-

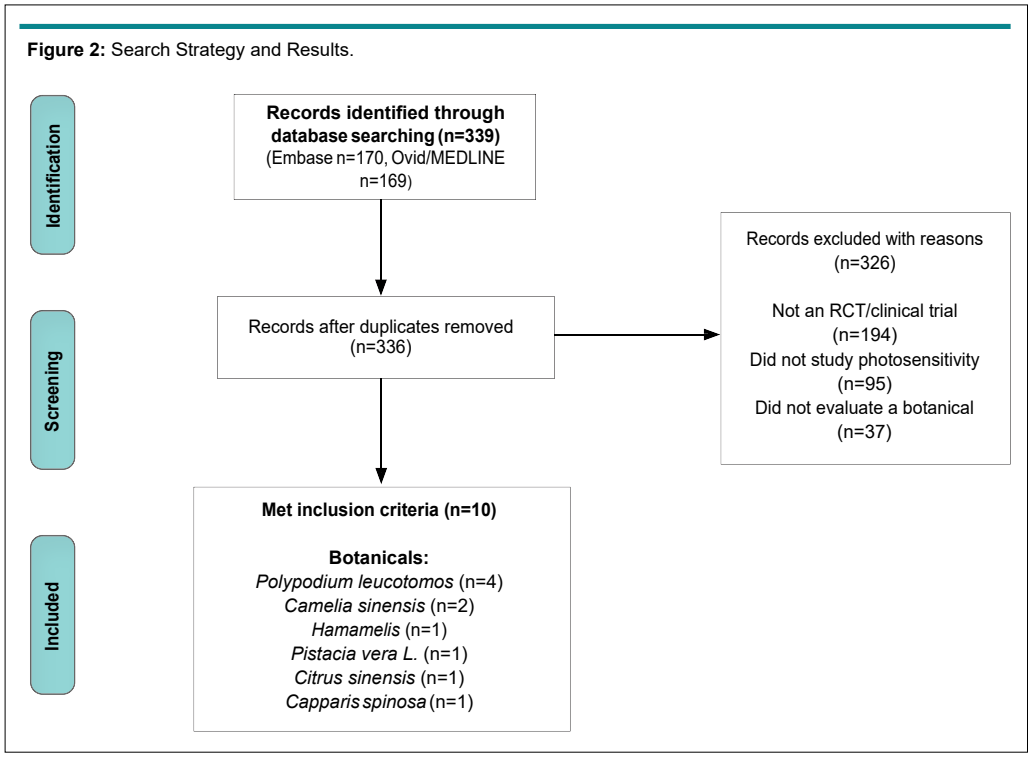

Figure 2: Search Strategy and Results.

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Table 2: Summary of Clinical Studies.

Author	Intervention	Study design	Comparison	Subjects	Affected region	Period of treatment	Outcome measure	Major results
Gonzalez et al[10]	*P. leucotomos* (PL) topical (10%, 25%, 50%)	Randomized trial	Oral PL (1080 mg daily) Sunscreen SPF 15 Control (no treatment)	N=21 Age 18-46 Skin type III and IV Subjects untreated or treated with oral psoralens [oral 8-methoxy psoralen (8-MOP) or 5-methoxy psoralen (5-MOP)]	Back	Topical–one time application 15-30 minutes before sun exposure Oral PL–one time consumption (720 mg day before sun exposure, 360mg three hours before sun exposure)	MED[a] MPD[b]	PL significantly increased MED (p<0.001) and MPD (p<0.001)
Caccialanza et al[12]	*P. leucotomos* (PL) extract 480mg daily for 15	Single group	None	N=28 subjects Age 21-68 with idiopathic photodermatoses	Sun exposed body areas	For 15 days prior to sun exposure	% improvement in skin condition[c]	80% had improvement in skin condition after PL consumption (p<0.05)
Caccialanza et al[11]	*P. leucotomos* (PL) extract 480mg daily for 15	Single group	None	N=57 Age 21-74 With idiopathic photodermatoses (IP)	Sun exposed body areas	For 15 days prior to sun exposure	% improvement in skin condition	74% had improvement in skin condition after PL consumption (p<0.05)
Tanew et al[13]	*P. leucotomos* (PL) extract 720 to 1200 mg daily for 2 weeks	Open, uncontrolled bicenter study	None	N=35 Skin type III, IV With polymorphic light eruption (PLE) Age not specified	Extensor surface of upper arms; alternatively, upper back	3 weeks	Photoprovocation of PLE lesions	Threshold for induction of PLE lesions increased significantly (p<0.05)
Farrar et al[16]	*Camelia sinensis* 1080mg daily for 12 weeks	RCT	Placebo capsules	N=50 Age 18-65	Buttocks	12 weeks	MED	MED not different between green tea and placebo group (p=0.47) MED not different at baseline vs post-green tea supplementation (p=0.17)
Li et al[17]	*Camelia sinensis* extract 2-5% topical	Single group, intra patient	None	N=20 Skin type III, IV Age not specified	Dorsal skin	6 days	Erythema index measured by chromamtery	2% and 3% green tea extracts were most protective from erythema
Hughes-Formella et al[21]	*Hamamelis (witch hazel)* aftersun lotions (distillate 1, 2, 3 each from different supplier)	Double blind, controlled trial	Vehicle 1 and 2 Dimethindene maleate 0.1% topical Hydrocorticone lotion 0.1%, 0.25%, 1% Control (no topical)	N=41 Age 19-50	Back	48 hours	Erythema suppression (assessed by visual inspection and chromametry)	Hamamelis lotions led to maximal erythema suppression at 72 hours (which is 36% that of hydrocortisone response at 1.2 MED, 66% at 1.4 MED, 56% at 1.7 MED)
Martorana et al[23]	*Pistacia vera L.* extracts TP–extract from pistachio skins SP–extract from decorticated seeds	Single group, intra patient	Tocopheryl acetate (TOC) Vehicle Control (no treatment)	N=12 Age 25-35	Ventral surface of each forearm	One time application	Percent induced erythema (PIE) (monitored by reflectance spectrophotometry)	PIE for TP, SP, and TOC were 66.8%, 33.2%, and 22.6% respectively TP formulation was significantly more protective than SP formulation (p<0.05) Difference between SP and TOC formulations was not significant (p>0.05)

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Puglia et al[24]	*Citrus sinensis* varieties Moro, Tarocco and Sanguinello (red orange) extract 100mg daily for 15 days	Single group, intra patient	None	N=20 Age 26-47 Skin type II, III	Ventral surface of each forearm	15 days	Erythema (monitored by reflectance spectrophotom-etry)	40% reduction in UV induced erythema compared to baseline
Bonina et al[27]	2% Lyophi-lized extract of *Capparis spinosa* (LECS)	Single group, intra-patient	Tocopheryl acetate (TOC) gel Control gel	N=6 Age 25-35	Ventral sur-face of each forearm	One time application	Percentage of erythema inhibition (PIE) (monitored by reflectance spectrophotom-etry)	60% PIE by LECS *vs.* 22% PIE by TOC gel (p<0.01)

[a]MED: minimal erythema dose (minimal UV dose that produces visible erythema)
[b]MPD: minimal phototoxic dose
[c]Normalization – no symptoms after UV exposure; clear improvement; slight improvement; no improvement
RCT: Randomized, controlled trial.

tion. First, subjects only received a one-time treatment with topical or oral PL. Long-term topical application, oral consumption, and potential side effects were not evaluated. Additionally, the non-sensitized group consisted mostly of women (1 man, 12 women) aged 18-46 years, while psoralen-sensitized group consisted mostly of men (7 men, 1 woman) aged 18-21 years. The small sample size and unequal gender distribution in the two groups are limitations of this study. Combined with the relatively narrow age range, the results of the study may not be generalizable. Lastly, no blinding was implemented in the study. Double-blinded-randomized controlled studies in healthy subjects, as well as those with skin disorders, are needed to further investigate the long-term effects and safety profile of topical and oral PL.

Idiopathic photodermatoses (IP) are a group of skin disorders in which skin reacts abnormally to sunlight.[11] The most common IP are polymorphic light eruption (PLE), actinic prurigo, chronic actinic dermatitis, and solar urticaria.[11] Caccialanza et al[11] conducted an uncontrolled, single arm clinical study to investigate the photoprotective activity of PL extract in 57 subjects (12 men, 45 women) with IP (PLE and solar urticaria) aged 21-74 years. Subjects consumed 480 mg PL extract daily for 15 days before UV exposure. The outcome was assessed by clinical evaluation and subjective assessment of improvement. Overall, 74% found it beneficial to consume PL extract during exposure to sunlight, which was significant at p<0.05. There were no reported adverse effects. Similarly, in another uncontrolled single arm study, Caccialanza et al[12] evaluated whether oral PL extract would provide photoprotection in 28 subjects (9 men, 19 women) with IP (PLE and solar urticaria), aged 21 to 68 years who consumed 480 mg PL extract daily for 15 days. Overall, 80% found it beneficial to consume oral PL extract during the summer (p<0.05). One subject with irritable bowel syndrome (IBS) stopped treatment due to worsening of symptoms. No other adverse effects were reported. The limitations of both studies include small sample size and no placebo control. Although both studies included a wide age range, the small sample size and lack of equal gender distribution make the results not generalizable to broader population. The lack of a placebo control prevents differentiation between the effects of the PL compared to the natural phenomenon of "hardening" that occurs with PLE and may account for the improvement in symptoms. Further controlled studies with a larger sample size and a placebo control are needed to investigate the benefits and potential side effects of PL extract supplementation.

Tanew et al[13] investigated whether PL extract would prevent or delay photoinduction of polymorphic light eruption (PLE) lesions by UV radiation. A total of 35 subjects of skin type III and IV and with PLE participated in an open, uncontrolled bicenter study. Age range and gender of study subjects were not specified. For one week, PLE lesions were induced *via* UVA and ultraviolet-B (UVB) photoprovocation, after which subjects initiated PL extract supplementation for three weeks (720 to 1200 mg daily, according to body weight). Subjects returned for second photoprovocation during week three of PL supplementation. Outcome measure was reported as the number of UVA and UVB exposures needed to induce PLE lesions before and after treatment. The results showed that the number of UVA exposures required to induce PLE increased significantly after the two-week PL extract supplementation (1.95±1.07 to 2.62±1.02, p<0.01). Additionally, the number of required UVB exposures also increased significantly after oral PL supplementation (2.38±1.19 to 2.92±0.95, p<0.05). There were no reported side effects and tolerance of PL extract was excellent. The limitations of this study include the open, uncontrolled study design. Like previously described studies, this study allowed for early UV exposure, which can lead to hardening of the skin and may account for the changes noted in the study. Age range and gender of study subjects were not specified; therefore, it would be difficult to make generalizations based on the results of this study. Further blinded, controlled studies are needed to investigate the efficacy, optimum dosage, and duration of treatment with PL extract.

Green Tea

Camelia sinensis is the plant that gives rise to a variety of teas, including green tea. Green tea contains polyphenols, which are naturally occurring compounds known for their antioxidant activity, including prevention of oxidative damage in the skin

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induced by UV radiation.[14] Catechins are polyphenolic compounds that are found in green tea, of which epigallocatechin-3-gallate (EGCG) is the most abundant and is thought to provide skin protection.[15]

Farrar et al[16] conducted a randomized, placebo-controlled trial using systemic green tea to evaluate its effects on minimal erythema dose (MED). MED is the lowest UV dose that produces visually detectable skin erythema. Fifty subjects aged 18-65 years ("nearly all females")[16] were randomly assigned to consume 1080 mg green tea catechins daily or placebo capsules. At baseline and 12 weeks post-supplementation, buttock skin was exposed to UV radiation and MED was recorded. After supplementation, the difference in MED between green tea and placebo group was not significant (p=0.47). Additionally, the difference between MED at baseline and post green tea supplementation was not significant (p=0.17). The study failed to demonstrate that oral supplementation with green tea catechins protects from UV induced erythema. The limitation of this study is that it did not compare the effects of green tea supplementation at different dosages. Additionally, the study included mostly white female subjects, thus results cannot be generalized and may raise the possibility of sex-specific effect. Future studies are needed to compare how different dosages affect the efficacy and adverse effects of green tea.

Li et al[17] conducted a single group controlled trial among 20 Chinese women (age not specified) to investigate the efficacy of 2-5% green tea extract for skin protection from UV induced erythema. Green tea extracts were applied to skin before and after UV irradiation (6 days total). The erythema intensity was measured by chromametry. The results showed that green tea extracts protected the skin from UV damage, with 2% and 3% green tea extract being the most effective. The study showed promise for the use of green tea extract in sunscreens and other topical formulations for skin photoprotection. The authors found that higher concentration was not protective and hypothesized that higher concentrations of green tea extracts may lead to cutaneous irritation and make the skin more sensitive. More studies are needed to assess how the concentration of green tea may relate to cutaneous irritation before the cost-benefit assessment can be made. The limitation of this study is that it only included a small sample of Chinese women, making generalizations difficult.

Hamamelis

Hamamelis virginiana L. (Hamamelidaceae) is a medicinal plant commonly known as witch hazel.[18] It has been used in the treatment of various conditions including rash, sunburn, swelling, inflammation, erythema, eczema, rheumatism, and tumors.[19] Hamamelis has anti-inflammatory, astringent, hydrating, and barrier stabilizing properties, which make it beneficial in the treatment of skin conditions.[20]

A double-blind study of 41 subjects (9 men, 32 women) aged 19-50 years, was conducted in order to optimize the development of hamamelis topical for after sun use.[21] Three lotions containing 10% hamamelis distillates from different suppliers were compared to 2 hamamelis free vehicles, 0.1% dimethindene maleate gel, 1% hydrocortisone cream, 0.25% hydrocortisone lotion, and control (no topical). Topicals were applied to the skin for 48 hours after skin irradiation with three UV doses (1.2 MED, 1.4 MED, 1.7 MED). The hamamelis topicals resulted in maximal erythema suppression at 72 hours which was 36% that of hydrocortisone response at 1.2 MED, 66% at 1.4 MED, and 56% at 1.7 MED. Overall, the study showed that the three hamamelis lotions exerted anti-inflammatory effects, and one of the distillates appeared more effective than the others although differences among the 3 distillates was not large. Although hamamelis topical formulations seem to be beneficial, all formulations were less effective than 1% hydrocortisone. Further, studies are needed to elicit the advantage of hamamelis formulations compared to currently available therapies for photosensitivity. As has been the case in other studies reviewed here, this study enrolled mostly women.

Pistachio

Pistachio nuts are thought to have high antioxidant potential.[22] Both the pistachio seeds and skins contain bioactive compounds which, when taken orally or applied topically, may protect human skin from damaging effects of UV radiation.

Martorana et al[23] investigated the antioxidant properties of two polyphenol-rich extracts from skins (TP) and decorticated seeds (SP) of Bronte pistachios. The results showed that both TP and SP had high levels of phenolic compounds, but TP had 10 times more phenols than SP. It was concluded that TP extract had higher antioxidant activity than SP. Due to their antioxidants properties, TP and SP extracts were investigated further for their ability to ameliorate skin erythema induced by acute UVB irradiation in 12 healthy subjects aged 25-35 years (gender not specified). The skin of both forearms was exposed to UVB radiation, and immediately treated with topical formulations containing SP, TP, TOC (tocopheryl acetate), or vehicle (blank formulation). Control site received no treatment. Induced erythema was monitored for 58 hours by reflectance spectrophotometry. Percentage inhibition of UVB-induced erythema (PIE) was calculated for each formulation in order to better compare their efficacy. The PIE values for TP, SP, and TOC formulations were 66.8%, 33.2%, and 22.6% respectively. The TP formulation was significantly more protective than SP formulation (p<0.05), while the difference between SP and TOC formulations was not significant (p>0.05). Overall, the results showed that both TP and SP extracts were protective against UVB induced skin damage and inflammation. The skin from pistachio nuts is typically industrially removed and becomes waste. This study points to the potential benefits of using this low cost ingredient in cosmetics for photoprotective applications. The limitation of this study is its small sample size and that it was only conducted on volunteers with healthy skin. Further studies investigating the

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protective effects of TP and SP extracts in individuals with photodermatoses may be beneficial.

Red Orange Extract

The red orange extract (ROE) comes from blood oranges (*Citrus sinensis* varieties Moro, Tarocco, Sanguinello)[24], which are a type of fruit with blood colored flesh. The extract possesses antioxidant properties and may protect the skin from UV damage.[25] The antioxidant and photoprotective properties of ROE are thought to be due to its content of phenolic compounds including anthocyanins, flavones, and hydroxycinnamic acids.[25]

Puglia et al[24] investigated the protective effects of ROE on UV induced skin erythema. Twenty healthy, Caucasian subjects aged 26-47 years (gender not stated) of skin types II and III were enrolled in the study. Two sites on ventral forearms were irradiated with UVB to induce skin erythema and the erythema was monitored for 48 hours by reflectance spectrophotometery. After a three-week rest period, the same subjects consumed ROE capsules in the amount of 100 mg daily for 15 days. At the end of supplementation period, the skin on ventral forearms was again irradiated and skin erythema monitored for 48 hours. After 15 days of oral supplementation with ROE there was a 40% mean reduction in UV-induced skin erythema. This study points to ROE may be a good candidate as an ingredient in skin products aimed at photoprotection. The limitation of this study is small sample size, lack of gender characterization, and that it did not report if the subjects experienced adverse effects from the supplement. Information on side effects would help in weighing the risks and benefits of such treatment.

Capparis spinosa L.

Capparis spinosa L. (CS) is a small shrub that is found in the Mediterranean and some parts of West and Central Asia.[26] It has been used in traditional medicine for the treatment of various diseases. It possesses antioxidant, anti-inflammatory, antimicrobial, antiviral, and immunomodulatory properties.[26]

Bonina et al[27] conducted an *in vitro* study showing that CS does possess antioxidant properties. They then evaluated the ability of topically applied lyophilized extract of CS (LECS) to reduce UVB induced skin erythema in six healthy subjects of both sexes, aged 25-35 years. The 2% LECS topical was compared with tocopheryl acetate (TOC; an antioxidant used in cosmetic formulations) and a control. The skin was irradiated with UV light and then the topicals were applied and remained on the skin for 3 hours, after which they were washed off and skin dried. The induced erythema was monitored for 58 hours using reflectance spectrophotometry and percentage of erythema inhibition (PIE) was determined. The PIE was approximately 60% for LECS and 22% for TOC gel formulations. These findings are not surprising considering that LECS is rich in flavonols, which have a rich antioxidant and anti-inflammatory profile. The limitation of this study is a small sample size. Additionally, the study did not provide the subject gender breakdown and it only enrolled individuals within a narrow age range of 25-35 years. Further studies with larger sample size and perhaps various LECS concentrations could help further determine the benefits of this antioxidant rich topical for skin photoprotection.

CONCLUSION

Overall, there is some evidence suggesting that botanical therapies rich in antioxidants may be beneficial in reducing skin erythema and photosensitivity when used topically or orally. Botanicals that are known to be rich sources of antioxidants include *Polypodium leucotomos* (tropical fern), *Camelia sinensis* (green tea), red orange, Hamamelis (witch hazel), pistachio, and *Capparis spinosa*, as reviewed here. It is important for clinicians to be aware of such studies evaluating plant sources of antioxidants as they could be used as adjunctive supplements in skincare. Our search produced a limited number of studies evaluating botanical antioxidants in reducing photosensitivity. Many of the studies had a small sample size and enrolled mostly women; therefore, it is difficult to generalize the results. Further, clinical studies involving larger sample sizes are needed to assess the use of botanically derived antioxidants in reducing photosensitivity. Regardless of the findings presented here, it is important that all individuals, including those with photosensitive skin, follow sun protective measures as their first line of protection, including the use of sun protective clothing, broad spectrum sunscreens, and limit their sun exposure. Supplements should only be used as adjunctive approaches and should not replace good sun protection hygiene.

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AUTHOR CONTRIBUTION

Suzana Saric and Ashley K. Clark wrote the first draft of this manuscript; Raja K. Sivamani performed critical editing and provided overall oversight for the review.

CONFLICTS OF INTEREST

The authors declare no conflict of interest. Dr. Sivamani serves as a scientific advisor for Dermveda.

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Appendix

Table A1: Search Strategies used on January 28, 2017 in Embase and Ovid Databases.

Database	Search syntax
Embase	1. 'photosensitivity disorder'/exp OR 'photosensitivity'/exp OR 'photodermatosis'/exp OR 'skin protection'/exp OR 'sunscreen'/exp 2. 'plant extract'/exp/dd_dt OR 'plant extract' OR 'herbaceous agent'/exp 3. 'antioxidant'/exp 4. 'phytotherapy'/exp OR 'chinese medicine'/exp OR 'dietary supplement'/exp 5. ('plant extract'/exp/dd_dt OR 'plant extract' OR 'herbaceous agent'/exp) OR ('phytotherapy'/exp OR 'chinese medicine'/exp OR 'dietary supplement'/exp) 6. 'antioxidant'/exp AND (('plant extract'/exp/dd_dt OR 'plant extract' OR 'herbaceous agent'/exp) OR ('phyto-therapy'/exp OR 'chinese medicine'/exp OR 'dietary supplement'/exp)) 7. ('photosensitivity disorder'/exp OR 'photosensitivity'/exp OR 'photodermatosis'/exp OR 'skin protection'/exp OR 'sunscreen'/exp) AND ('antioxidant'/exp AND (('plant extract'/exp/dd_dt OR 'plant extract' OR 'herbaceous agent'/exp) OR ('phytotherapy'/exp OR 'chinese medicine'/exp OR 'dietary supplement'/exp))) 8. ('photosensitivity disorder'/exp OR 'photosensitivity'/exp OR 'photodermatosis'/exp OR 'skin protection'/exp OR 'sunscreen'/exp) AND ('antioxidant'/exp AND (('plant extract'/exp/dd_dt OR 'plant extract' OR 'herbaceous agent'/exp) OR ('phytotherapy'/exp OR 'chinese medicine'/exp OR 'dietary supplement'/exp))) AND [humans]/lim AND [english]/lim
Ovid	1. exp Photosensitivity Disorders/dt [Drug Therapy] (803) 2. exp Antioxidants/ (443711) 3. 1 and 2 (93) 4. limit 3 to (english language and humans) (71) 5. remove duplicates from 4 (66) 6. photosensitiv*.mp. (14260) 7. 1 or 6 (14528) 8. 2 and 7 (549) 9. limit 8 to (english language and humans) (240) 10. remove duplicates from 9 (224) 11. Drugs, Chinese Herbal/ or Plants, Medicinal/ or Dietary Supplements/ or Plant Extracts/ or botanicals.mp. or Phytotherapy/ (231765) 12. 7 and 11 (155) 13. limit 12 to (english language and humans) (101) 14. remove duplicates from 13 (90) 15. Skin/ or skin.mp. or Skin Diseases/ (733988) 16. 10 and 15 (89) 17. remove duplicates from 16 (89) 18. 14 or 17 (169)