



Review Article

Herbal products as skincare therapeutic agents against ultraviolet radiation-induced skin disorders

Raghu Rai Sharma ^{a, b}, Aakash Deep ^c, Sheikh Tasduq Abdullah ^{a, b, *}^a PK-PD and Toxicology Division, CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu Tawi, Jammu and Kashmir, India^b Academy of Scientific & Innovative Research (AcSIR), Ghaziabad, India^c Department of Pharmaceutical Sciences, Chaudhary Bansi Lal University, Bhiwani, Haryana, India

ARTICLE INFO

Article history:

Received 27 January 2021

Received in revised form

13 July 2021

Accepted 23 July 2021

Available online 29 December 2021

Keywords:

Ultraviolet radiation

Skin disorders

Traditional plants

Herbal products

Skincare products

ABSTRACT

This paper aims to highlight the pharmacological aspects of listed herbal skincare products used for the treatment of various disorders caused due to ultraviolet radiation. The pharmacological aspects include safety and efficacy validation as per regulatory guidelines following internationally accepted scientific principles for their development of skincare products. Herbal products have always been used traditionally for the treatment of various skin ailments and have become more prevalent because of their safety and high efficacy benefits. The incorporation of synthetic molecules and chemical substances in the different medicinal and pharmaceutical formulations is the leading cause of the dermal toxicity. Therefore, the developments of herbal skincare products containing scientifically validated herbal ingredients have better acceptance, respect, and belief in the society. The listed herbal products in this review can help take forward the commercial development of skincare products for therapeutic as well as beauty care purposes from such plants.

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1. Introduction

The human skin plays a significant role in physiological functions of sensation, protection, thermoregulation, defense system, and metabolic mechanisms to help in maintaining homeostasis [1,2]. It is mostly exposed to different environmental factors such as harmful radiation, toxic chemicals, and pathogens [3]. The ultraviolet (UV) portion of sunlight is responsible for various skin disorders [4]. Continuous exposure to UVB leads to various adverse effects on the skin [5]. The increase in awareness about the photoaging and carcinogenic effects of UV radiation (UVR) resulted in tremendous increase in the demand for herbal skincare products. The most frequently used inorganic filters in the market possess titanium dioxide (TiO₂) and zinc oxide (ZnO). These UV filters are suggested to be the most frequent cause of dermal toxicity and contact allergy, which is caused by a wide range of chemicals present in sunscreens [6]. The herbal products exhibit various therapeutic properties and have always been used for centuries in the

treatment of many skin disorders [7]. Several herbal products have been uncovered for their therapeutic potential and are gaining considerable attention in the market as skincare products [8]. Internationally, numerous studies have been conducted on many herbal products to reveal their therapeutic potential via various *in vivo* and *in vitro* models. However, future long-term studies and new approaches are required in this area [9].

2. Methodology

The literature published between 2003 and 2018 was searched on Pubmed and Google Scholar databases and as included in this review. The main keywords used were “skin”, “ultraviolet radiation”, “UVB”, “skin disorders”, “photodamage”, “photoaging”, “skin cancer”, “natural products”, “herbal products”, “photo-protection”, “sunscreens” and “skincare products”. The present review summarizes the published data over a hundred scientifically validated herbal products that include their biological and

* Corresponding author.

E-mail: stabdullah@iiim.res.in

Peer review under responsibility of Transdisciplinary University, Bangalore.

pharmacological information and various experimental models used to study skin photodamage.

3. Ultraviolet radiation (UVR)

Ultraviolet radiation is divided into three subtypes as UVA, UVB, and UVC as based on wavelengths and biological effects which are accountable for various skin disorders [4]. UVA has wavelengths between 320 and 400 nm and termed as long-wave radiation is absorbed by the deep dermis. UVB, also known as mid-UV, has wavelengths between 290 and 320 nm and is mostly consumed or dissipated within the epidermis and is significantly responsible for skin photodamage. UVB is a complete mutagen and more efficient than UVA in contributing most of the hazardous effects associated with sun exposure [10,11]. UVC, known as shorter UV, has wavelengths between 200 and 290 nm and is also absorbed within the epidermis and has germicidal property [12]. UVR can be both beneficial and harmful to human skin. The extent of UVR reaching into the earth's surface depends on latitude, altitude, season, daytime, cloudiness, and the ozone layer. The beneficial effects include Vitamin D production, killing different pathogens, and treating certain skin diseases like Psoriasis vulgaris and vitiligo. The damaging effects mostly include degradation of the extracellular matrix and all the significant risk factors associated with sunlight include sunburn, tanning, photoaging, and skin cancer development [13–15] (Fig. 1).

4. Environmental skin disorders

Photodamage is a type of skin disorder that arises from the exposure of the skin to solar light or UVR which includes erythema, edema, hypermelanogenesis, oxidative stress, inflammation, immunosuppression, and further development of cutaneous malignancies.

4.1. Erythema (sunburn)

Erythema is an acute inflammatory response to continuous UVR exposure. The severity of erythema depends upon the rate and extent of skin exposure to UVR [16].

4.2. Hypermelanogenesis

UVR exposure to the skin may result in immediate pigmentation or delayed pigmentation response. UVR exposure to the skin elevates melanin synthesis, which increases number and activity of melanocytes, leading to the deposition of melanin granules in the upper layers of the epidermis [16].

4.3. UVR-induced epigenetic alterations

Epigenetics is the modification in gene expression, function, and generation of a heritable phenotype irrespective of change in DNA sequence. UVR-induced histone acetylation contributes to the UVR transcriptional response [17]. Epigenetic alterations are reversible, and therefore dietary food or bioactive compounds may have the ability to reverse, inhibit or delay the epigenetic modifications for the prevention of the disease [18].

4.4. UVR-induced microRNAs regulation

MicroRNAs (miRNAs) are small non-coding RNAs which act as a regulator in post-transcriptional modifications. Recent studies show that miRNAs have been explored as a therapeutic target against UVR-induced cellular responses [19]. The diversity of miRNA targets determines their involvement in various cellular networks. miRNAs have shown to regulate many biological processes such as cell differentiation, proliferation, and apoptosis [20].

4.5. UVR-induced DNA damage and repair

Reactive oxygen species (ROS) generated by UVR irradiation can indirectly damage DNA bases which lead to dimerization and is considered as the biomarker of oxidative DNA damage [21]. The injury persists beyond repair leading to cell death by induction of the apoptosis pathway. If the DNA damage continues in the S-phase of the cell cycle, there is an increase in proliferation, which ultimately leads to skin carcinogenesis [22].

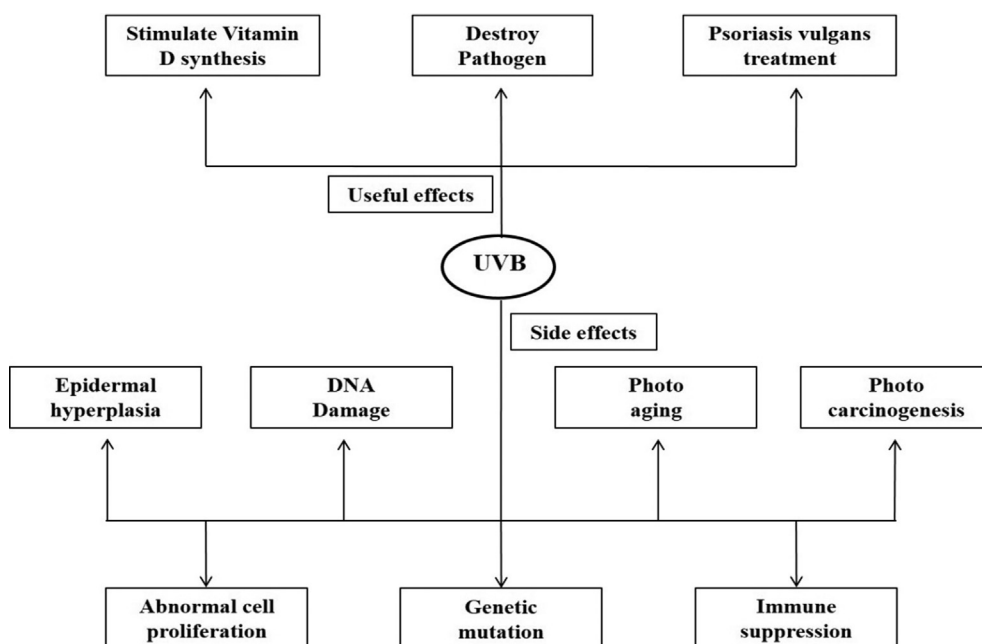


Fig. 1. Effects of UVR on the skin [12].

4.6. Immunological responses

UV radiation also affects the immune system and its exposure results in the generation of T-suppressor cells. UVR passes on suppressive effects on many immune parameters. The decrease in cellular immunity is responsible for various pathogens and loss of immune surveillance against tumors [23].

4.7. Photoaging

Aging is a natural and complicated process of progressive deterioration in the functioning of all organs in the body, including the skin. Intrinsic aging is a genetic phenomenon that occurs with time [24,25]. The onset of aging and its severity is exacerbated by exposure of skin to environmental factors. UVR is the most harmful factor which induces aging-like skin changes termed photoaging. Intrinsic photoaging is a time-dependent phenomenon that mainly depends on the extent of sun exposure and skin color [26,27]. Photoaging has more profound effects than an intrinsic one, accounting for about 90% of all the visible aging changes [28].

4.8. Photocarcinogenesis

Photocarcinogenesis is the unlimited growth of cells in the skin and is categorized into basal cell carcinomas (BCC), squamous cells carcinoma (SCC) (both specifically called non-melanocytic carcinomas), and cutaneous malignant melanomas. Cancer prevailing in basal layers of the epidermis is called basal cell carcinoma. It grows slowly and rarely spreads to other parts. SCC occurs in the middle layer of the epidermis and is considered more aggressive than BCC. Melanomas arise in the melanocytes; the cells are involved in melanin production and are responsible for 75% of all skin-related deaths. The survey from the past several years has found that there has been an increase in the prevalence of skin cancer. It has been assessed that approximately 1 in 5 Americans will develop skin cancer. It has been surveyed that over 2–3 million new cases of non-melanoma skin cancer (NMSC) appear per year globally, the highest rate among the Caucasian population [29–31].

Various natural products with their detailed molecular mechanism have been explored for their cellular photoprotective effects against UVR by utilizing different experimental models. Various studies revealed that topical application of almond oil has been found capable of preventing the structural damage caused by UV irradiation [32]. The inhibitory effect of encapsulated curcumin on UV-induced photoaging in mice has been examined [33]. *Amla* (*Emblica officinalis*) has been studied for its protective effect against UVB-induced photoaging [34]. Curcumin prevented UVR-induced transcriptional response in human keratinocytes [17]. A recent study showed the decreased expression of miRNAs in epigallocatechin gallate-mediated UVB protection in human dermal fibroblasts [35]. Glycyrrhizic acid prevented the oxidative stress-mediated DNA damage response through modulation of autophagy in UVB-irradiated human primary dermal fibroblasts [36].

5. Molecular signaling pathways induced by UVR

UVR exposure stimulates the production of ROS which overwhelms the defense mechanism of the skin, making endogenous cytoprotectants insufficient and causes alterations in inflammatory mediators, vascularity, and infiltration of inflammatory cells [7]. ROS stimulates various intracellular signaling pathways including mitogen-activated protein kinases (MAPK) and alters primarily the mitochondrial pathway, leading to cell death [37,38]. The generation of ROS by UVR acts as a mediator to activate several signaling cascades for various cellular responses. Therefore, the inhibition of

ROS-induced signaling pathways can help to protect skin cells from UVR [39,40]. Moreover, the altered expression of various components (MMPs, cytokines) leads to various pathophysiological conditions. This will provide an ideal framework for more specific targets for the assessment of risk factors, diagnostic biomarkers, and effective therapeutic alternatives for studying various molecular signalling pathways induced by UVR [41] (Fig. 2).

6. Traditionally used plants for skin disorders

Plant-derived products have been used for medicinal purposes for centuries and the earliest records from 2900–2600 BC document the use of approximately 1000 plants, such as oil of *Cedrus species* (cedar), *Commiphora myrrha* (myrrh), *Cupressus sempervirens* (cypress), *Glycyrrhiza glabra* (Liquorice), and *Papaver somniferum* (opium) [42]. Various natural phytoingredients (curcumin, silymarin, ginkgo biloba) have been exploited for their cellular protective effects with the detailed mechanisms in different experimental models [41]. Herbal products from the plant's sources for cosmetic or skin pathological states have always been popular because of several advantages such as fewer side-effects, better patient tolerance, being cheaper and acceptable due to the long history of use. These include aloe vera, grapevine, ginseng, green tea, tea tree oil, rosemary, lemon, soybean, papaya, garlic, ginkgo, olive oil, and *Ocimum* [43] (Table 1).

7. Pros and cons of commercially available sunscreens

Currently, cosmeceuticals, wherein biocative ingredients are used, are more preferred over synthetic molecules or chemical substances mainly due to safety issues in long-term treatment, which leads to dermal toxicity. The increase in awareness about the carcinogenic and photoaging effects of UVR and socio-economic upliftment of the society has resulted in a tremendous increase in the demand of herbal skincare products, especially sunscreen products by the society. The sunscreens mostly employ inorganic UV filters and show protection against solar radiation, which involves physical phenomena, i.e., scattering and reflection of UVR. The most frequently used inorganic filters are titanium dioxide (TiO₂) and zinc oxide (ZnO) which reflects the UV light, and tend to be opaque and white on the skin, and consequently is unacceptable for cosmetic use. The other oxides used are alumina, ceria, and zirconia. These oxides are formulated as nanoparticles, which decreases the reflection of visible radiation and, thereby, produces less white coloration when applied to the skin, and confers additional beneficial and efficacious photoprotection. According to Balogh et al., although sunscreens report several advantages, they also have numerous safety challenges that need to be overcome [53,54].

These inorganic UV filters are suggested to be the most frequent cause of dermal toxicity, such as photo-contact allergy which is caused by a wide range of synthetic molecules or chemical substances present in sunscreens [6]. The photo-toxicity of TiO₂ nanoparticles has been a severe concern [55]. Benzophenone-3 is one of the major causes of allergic reactions, especially contact dermatitis. The research on the use of herbal products is steadily increasing to overcome the occurrence of harmful effects associated with sunscreen products [56].

The use of safe cosmetic agents is essential for the prevention and treatment of UVR-induced skin disorders. There is a need to develop new herbal formulations that are safe and efficient. The history of the use of herbal products for the treatment of various dermatological agents for skincare purposes is as old as human civilization. Therefore, there is a wide scope for the development of new herbal formulations based on herbal ingredients which are efficient and scientifically validated in various *in vivo* and *in vitro* systems.

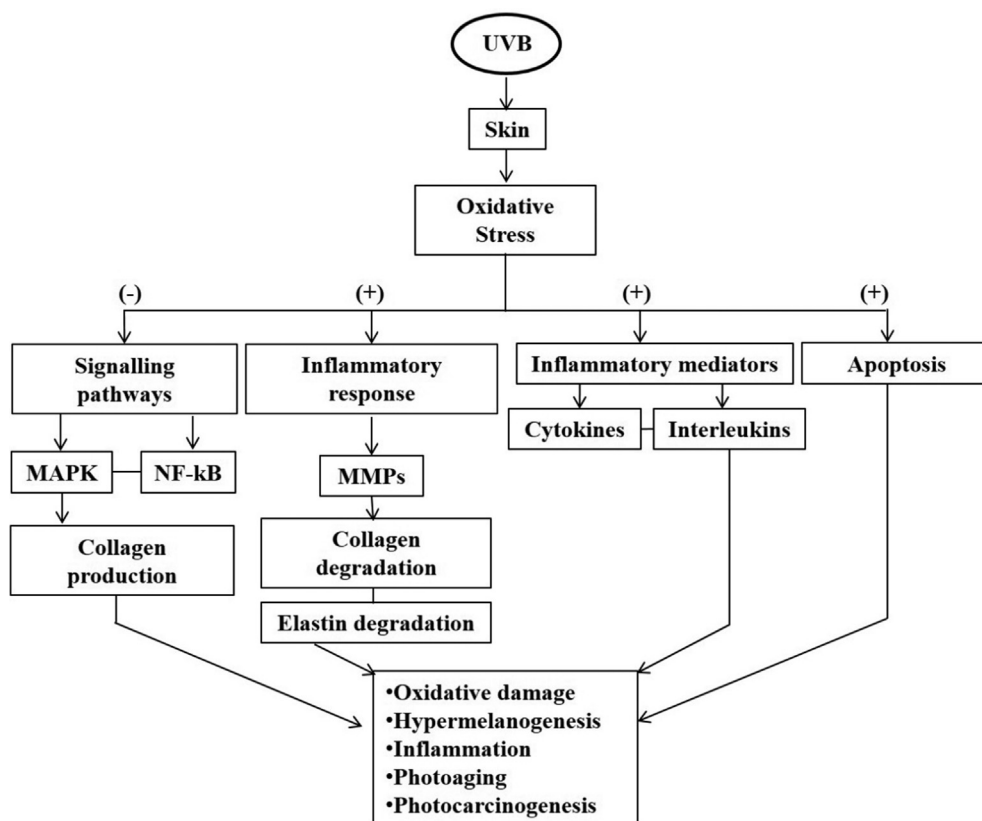


Fig. 2. Mechanism of UVB induced skin photodamage and central pathways affected by chronic exposure of the skin to UVB radiation [40].

8. Herbal skincare products as a therapeutic alternative

Herbal skincare products are now-a-days more preferred and chosen by people because of their fewer side-effects and cost-effectiveness [57]. Traditionally, herbal products are applied to a particular area or a part of the skin for the treatment of various skin ailments. The topical formulations can be classified into creams, gels, ointments, lotions, and foams [58,59].

The herbal products exhibit various therapeutic properties such as anti-oxidant, anti-inflammatory, anti-viral, cardio-protective, neuroprotective, and hepato-protective properties [7]. Many plants-derived natural molecules such as alkaloids, flavonoids, isoflavones, proanthocyanidins, phenolic compounds, and

essential oils are associated with the treatment of many dermatological disorders. Several herbal products have been uncovered for their therapeutic potential against UV irradiation and are gaining considerable attention [8]. The photoprotective properties of such herbal products regarding safety and efficacy need to be validated as per the regulatory guidelines which follows internationally accepted scientific principles. It is requisite for the development of such herbal skincare products possessing strong therapeutic potential for the treatment of UVB-induced skin disorders and a better quality of life [60]. The combination of different herbal products may result in their synergistic effect. This will further help in pre-clinical and clinical investigations in the area of dermatology.

Table 1

Represents traditionally used plants for various skin disorders.

S. No.	Plant binomial name	Common name	Family	Therapeutic use	Reference
1.	<i>Aloe barbadensis</i>	Aloe vera	Asphodelaceae	Cuts, burns and eczema	[44]
2.	<i>Azadirachta indica</i>	Neem	Meliaceae	Immuno-modulator, anti-inflammatory, anti-malarial, anti-fungal, anti-bacterial, anti-viral, anti-oxidant, anti-mutagenic and anti-carcinogenic.	[45]
3.	<i>Carica papaya L.</i>	Papaya	Caricaceae	Eczema, dermatitis and psoriasis	[46]
4.	<i>Curcuma longa</i>	Turmeric	Zingiberaceae	Scleroderma and anti-inflammatory	[47]
5.	<i>Emblica officinalis</i>	Amla	Phyllanthaceae	Anti-aging and skin disorders	[48]
6.	<i>Ginkgo biloba</i>	Ginkgo	Ginkgoaceae	Wound healing	[49]
7.	<i>Glycyrrhiza glabra</i>	Liquorice	Fabaceae	Anti-inflammatory, anti-microbial, anti-oxidative, anti-cancer and immune-modulator	[50]
8.	<i>Ocimum sanctum</i>	Tulsi	Labiatae	Anti-microbial, immune-modulator, anti-stress and anti-inflammatory	[51]
9.	<i>Psoralea corylifolia</i>	Babchi	Leguminosae	Psoriasis, leukoderma, and leprosy	[52]
10.	<i>Santalum album L.</i>	Sandalwood	Santalaceae	Acne, eczema, atopic dermatitis, psoriasis, anti-inflammatory, anti-microbial and anti-proliferative	[41]

9. Scientific investigation of herbal products against UVR-induced skin disorders

UVR has many deleterious effects on human skin. Among these results, photoaging and skin cancer are of great concern [56]. Due to changes in lifestyle and awareness about the dangers of the UVR, there has been a significant upsurge in research in the area of the use of herbal products for the prevention and treatment of UVR-induced skin disorders. There is a need to understand novel therapeutic targets which are involved in the progression of UVR-induced skin disorders [61]. These herbal products are mostly rich in polyphenols, flavonoids, and have a noticeable activity that can impede the skin from the deleterious effects of UVR. These herbal products should be incorporated for the development of herbal skincare products [62]. Internationally, many herbal products have been studied which had shown novel therapeutic potential for the prevention and treatment of UVR-induced skin disorders (Refer to [supplementary table 2](#)).

However, scanty reports are available on the skin beneficial effects of herbal products on skin photodamage, photoaging, and photo-carcinogenesis. These findings help in understanding the fact that there is a tremendous need to study various herbal products for their skin beneficial effects. There is a need for the development of herbal formulation based on scientifically validated herbal products for therapeutic as well as beautification purposes.

10. Discussion

Skin is the largest organ and continuous exposure to UVR leads to different pathological and dermatological conditions. UVR acts as a mediator to activate several signaling cascades for various cellular responses. The increase in consciousness about the carcinogenic and photoaging effects of UVR and socio-economic improvement of the society has resulted in the increased demand for herbal skincare products, especially sunscreen products. Currently, cosmeceuticals, are more preferred over synthetic molecule or chemical substances due to safety issues related to dermal toxicity. The research on the use of herbal products is steadily increasing to overcome the occurrence of harmful effects associated with sunscreen products using inorganic filters. Herbal products have always been used traditionally for the treatment of various skin ailments. There is a need to develop new herbal formulations that are safe and efficient. The listed herbal products in this paper have shown skin beneficial effects against UVR-induced skin disorders in various experimental models which recapitulate the same in humans. It is requisite for the development of such herbal skincare products possessing strong therapeutic potential for the treatment of UVB-induced skin disorders and a better quality of life. A lot has been done in the last decade for the safety and efficacy of herbal products for discussing more active natural products for skincare.

11. Conclusion

This review provides the summarized information of listed herbal skincare products used for the treatment of various disorders caused due to UVR. These products were scientifically validated as per the regulatory guidelines which follow internationally accepted scientific principles. The data of these listed herbal products including biological, pharmacological information, and experimental models have been summarized and transformed into tabular forms. These herbal products can be taken forward for formulation and development purposes as skincare products for therapeutic as well as beauty care uses.

Source(s) of funding

Department of Science and Technology (DST), New Delhi For Senior Research Fellowship to RRS (IF180691) and Council of Scientific and Industrial Research (CSIR), New Delhi For Research Grant (HCP-007) are acknowledged for financial assistance.

Conflict of interest

None.

Author contributions

RRS: Contributed to the literature review, writing of MS, and its formatting.

AD: Contributed to the writing of MS.

STA: Contributed to the design of MS, Literature review, Writing, Editing, and Formatting of the MS.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jaim.2021.07.016>.

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