Antioxidant and photoprotective potential of *Polypodium leucotomos*

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Academic Editor: Md Noushad Javed, K.R. Mangalam University, India

Received: September 9, 2022 Accepted: November 14, 2022 Published: December 29, 2022


Abstract

In recent years, *Polypodium leucotomos* has emerged with a great interest for having medicinal and therapeutic potential. It is producing very promising results due to the presence of antioxidant and photoprotective properties. Electronic libraries and databases, including Scopus, PubMed, Google Scholar, Science Direct, and Web of Science were searched to identify relevant studies; 79 publications contributed to this review regarding *Polypodium leucotomos* botanical aspects, chemical composition, antioxidant and photoprotective activity. It is used in complementary and alternative therapies with various pharmaceutical dosage forms (systemic or topical). Thanks to the composition of phytochemical constituents present in the leaves and rhizomes which confer antioxidant and photoprotective activity that has clinical therapeutic potential to be used as systemic and topical sunscreen of natural origin for the prevention of different types of skin diseases caused by harmful ultraviolet A and ultraviolet B radiations. However, more studies are needed in the future to test the ability and enhance the capacity of sunscreen and sunblock in cosmetic formulations. To conclude, it is recommended to carry out scientific studies based on different analytical methods to evaluate the phytoconstituents potential and to develop stable pharmaceutical formulations according to the skin phototype.

Keywords

*Polypodium leucotomos*, antioxidant, photoprotective

Introduction

*Polypodium leucotomos*—a tropical fern belonging to the genus *Polypodium* and to the family Polypodiaceae—originated from South and Central America [1, 2] which was traditionally used due to its anti-tumor and anti-inflammatory properties [3]. In 1788, this species was first introduced in Europe after the botanical
expedition in Peru and Chile by Hipólito Ruiz López (botanist) funded by the Spanish Crown and later spread to other areas [4]. It has been shown to contain saponins [1] and phenolic compounds: vinyl acid, chlorogenic acid, ferulic acid, caffeic acid, and coumaric acid [5–7] extracted from rhizomes [1, 8] and leaves [9, 10]. It is beneficial for specific dermatological pathologies [11] such as skin tumors [3, 12, 13], rash [14], erythema and pigmentation [12, 13, 15], melanoma [16], photodermatosis [13, 17, 18], vitiligo [19, 20], melasma, psoriasis, and atopic dermatitis [2, 21, 22]. It particularly reduces the skin deterioration induced by exposed ultraviolet (UV) rays [11, 23, 24] to minimize photoaging [25], therefore, it gained considerable interest in cosmetic and dermatological research. Further, the research demonstrated the positive effects in tonsillitis [26], trichomoniasis [4], infectious diseases [27], acute colitis [28], scalp keratosis [29, 30], polymorphic light eruption [14, 31] as well as immunomodulation of lymphocytes and cytokines [32] and it was also used as a dietary supplement [33].

The Polypodium leucotomos pharmaceutical preparations are available as oral capsule (act as a systemic antioxidizing agent), topical gel, cream, spray and compact makeup powder to protect the skin from sunlight (or invisible UV rays) exposure [2]. Besides, it is one of the global public health problems. Overexposure to solar radiation has a significant impact on skin health [34] such as sunburn, photoaging, photodermatosis, photosensitivity, immunosuppression and photocarcinogenesis [35, 36]; the latter being of great concern due to the increase in cases [37, 38]. Therefore, it is highly beneficial due to its chemoprotective, immunomodulatory, anti-inflammatory and antioxidant properties. In addition, it is attributed for the inhibition of photoisomerization as well as apoptosis that leads directly to DNA damage, and it also prevents immunosuppression [7, 25, 39, 40] which were proven in in vitro and in vivo studies, involving human, cell and animal studies [22, 41].

It is necessary to highlight that the harmful biological effects of UV radiation will depend on the energy that it diffuses [42]; while UVA, UVB and UVC spectral ranges of solar radiation comprise from 100 to 400 nm. Among them, UVA and UVB radiations are of great biological importance as they are concerned with mild to chronic skin damage and compromise the skin integrity [43]. Hence, the skin is the primary organ that eventually receives the most exposure [44], as there is a direct relationship between skin and UV radiation and this relationship generates reactive oxygen species that alter the structure and function of the skin [45]. For this reason, the dermatological studies carried out on Polypodium leucotomos have demonstrated its potential antioxidant activity [5, 10] due to the presence of phenolic compounds. Since, they have the ability to bind with free radicals, which are agents that prevent or delay oxidation by inhibiting the initiation of oxidative reactions and thus producing beneficial effects on human health [46, 47].

Free radicals are highly reactive unstable species and when reacting with UV rays, they can even lead to cell death [48] which implies they are responsible for photoaging, immunosuppression, phototoxicity, photoallergenic and photocarcinogenesis [9, 47, 49, 50]. To avoid these damages, strategies are sought out such as photoprotection with natural antioxidants to limit them thus preventing erythema, inflammation, wrinkles, photoaging and skin cancer [51].

The area of cosmetic science has emerged in the last three decades to maintain cutaneous homeostasis and to neutralize the free radicals induced by damaging UV rays. The researchers are trying their best to formulate the skin preparation without causing toxicity or unwanted effects [52]. Some traditional sunscreen contains inorganic compounds such as titanium dioxide and zinc oxide [33] that dissociate UVA and UVB rays. Perhaps they are often visible as an undesirable opaque layer on the skin, though these are metallic particles that are considered highly toxic for the skin [53].

Therefore, researchers have been studying the compounds present in the Polypodium leucotomos which is considered as a UV protector. In recent years, there is a very high demand for its oral formulation as antioxidant capsules [41]. It should be important to highlight that the Polypodium leucotomos extract has been patented with the name Fernblock® XP [54].

The aim of this review is to gather the information from published studies to evaluate the antioxidant and photoprotective properties. The databases of Scopus, PubMed, Google Scholar, Science Direct and Web of Science were searched and an exhaustive review was carried out with publications from the year 2010.
to 2022. A total of 117 reviews and research articles were collected, 79 contributing to this review with a topic of interest to carry out this work. In English, the following search words were used and mentioned here: “Polypodium leucotomos”; and other word combinations were also made like “Polypodium leucotomos” with “antioxidant”, “photoprotective”, “cancer”, “anti-inflammatory”, “photoaging”, “UV radiation”, “phenolic compounds”, “reactive oxygen species”, “skin” and “Fernblock”. After thorough evaluation, a discussion was held to highlight its antioxidant and photoprotective properties.

**Taxonomy**

The taxonomic classification is shown in Table 1.

**Table 1. Taxonomic classification of Polypodium leucotomos**

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class</td>
<td>Equitopsida</td>
</tr>
<tr>
<td>Order</td>
<td>Polypodiales</td>
</tr>
<tr>
<td>Suborder</td>
<td>Polypodiineae</td>
</tr>
<tr>
<td>Family</td>
<td>Polypodiaceae</td>
</tr>
<tr>
<td>Genus</td>
<td>Polypodium</td>
</tr>
<tr>
<td>Species</td>
<td>leucotomos</td>
</tr>
</tbody>
</table>

**Distribution**

The geographical distribution ranges from Central America to South America, mainly in Bolivia, Brazil, Mexico and Peru [10, 26]. Besides, it cultivates in humid environment, and it grows on developed tree trunks. Its adaptation and vegetation reach the height of 1,200 to 2,200 meters above sea level [8].

**Phytochemical constituents**

The phytochemical constituents are presented in Table 2 and the chemical structures are shown in Figure 1.

**Table 2. Phytochemical constituents**

<table>
<thead>
<tr>
<th>Phytochemical constituents</th>
<th>Chemical compound</th>
<th>Plant part</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saponins</td>
<td>Osladin, calagualine</td>
<td>Rhizome</td>
<td>[8, 55]</td>
</tr>
<tr>
<td>Phenolic compounds</td>
<td>Caffeic acid: 3,4-dihydroxycinnamic acid, Ferulic acid: 3-methoxy-4-hydroxycinnamic acid</td>
<td>Leaves</td>
<td>[56]</td>
</tr>
<tr>
<td>Biological acid molecules</td>
<td>Shikimic acid, glucuronic acid, malic acid, coumaric acid: 4-hydroxycinnamic acid, vanillic acid: 3-methoxy-4-hydroxybenzoic acid, chlorogenic acid: 3-caffeylquinic acid, lactic acid, protocatechuic acid: 3,4-dihydroxybenzoic acid, citric acid</td>
<td>Rhizome and leaves</td>
<td>[56]</td>
</tr>
<tr>
<td>Monosaccharides</td>
<td>Fructose, glucose</td>
<td>Rhizome and leaves</td>
<td>[56]</td>
</tr>
<tr>
<td>Steroids</td>
<td>Ecdysone</td>
<td>Rhizome</td>
<td>[8]</td>
</tr>
<tr>
<td>Others</td>
<td>Oleoresin, deoxyhexose, potassium nitrate</td>
<td>Rhizome</td>
<td>[8]</td>
</tr>
</tbody>
</table>

**Antioxidant activity**

Antioxidants are substances that can neutralize the actions of oxidants that cause free radicals, thus endogenous cellular antioxidants are released into the bloodstream that is subsequently trapped by free radicals, which maintains oxidant-antioxidant homeostasis [57]. The free radical is an atom that has an unpaired (free) electron; this characteristic makes them very reactive to capture an electron from molecules to become stable, thus reaching their electrochemical stability. Usually, the free radical tends to initiate a chain reaction and lead to the destruction and damage to cell membranes and tissues. In our body, this action occurs continuously and we need antioxidants to control this process [48, 58]. It will not be beneficial for health when our body has to tolerate excess free radicals that are produced by endogenous and exogenous...
oxidant species such as solar radiation [57, 59, 60]. The latter is considered as the major source of free radical production that causes inflammation, acceleration of cellular aging, and initiation of skin cancer [61].

![Chemical structure](image)

**Figure 1.** Chemical structure

The phytochemical extracts were demonstrated to have antioxidant activity and photoprotective properties [6]. However, if we compare the activities between the rhizomes and the leaves, the leaves showed high activity due to the presence of phenols, tannins and flavonoids [8, 13, 62], which was determined using oxygen radical scavenging methods such as ferric reducing antioxidant power (FRAP), 2,2-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS), and oxygen radical absorbance capacity (ORAC) [3, 11, 63]. Of note, health benefits of polyphenols using human skin cells demonstrated to be good skin photo protectors and photocarcinogenesis inhibitors, therefore, widely incorporated in medicinal and cosmetic products [64, 65].

Reactive oxygen species (superoxide anion, hydroxyl radical, hydrogen peroxide, and singlet oxygen) are important oxidizing agents that have been considered to be involved in skin aging and various diseases such as cerebrovascular, Parkinson’s, multiple sclerosis, heart, cancer, and others [57, 66, 67]. This plant demonstrated its antioxidant effect by eliminating reactive species [6, 68] while inactivating the oxidative stress response that is a precursor of inflammation, aging, androgenic alopecia and skin cancer [68]. Further, it is not limited to reactive oxygen species, but it also prevents the synthesis of nitric oxide that participates in cell damage [69].

**Photoprotective activity**

The skin is highly sensitive to UV rays which cause sunburn, photoaging, immunosuppression and photocarcinogenesis. It has caught the attention of researchers to develop alternatives in photoprotection that may have a filtering system for UVA and UVB radiations [35]. We are familiar that our body undergoes series of preventive mechanisms to counteract short- and long-term solar damage, but they are not enough due to the increase in intensity and duration of solar radiation exposure, whether due to the environmental pollution or ozone layer thinning that is subsequently responsible for skin cancer which considered a global health problem [70, 71].
In this scenario, the most affected people are those that have fair skin and even more if they live in the regions closest to the earth equator that has a higher solar irradiance [72]. The use of sunscreen and sunblock is one of the protective measures. Hence, the efficient development of skin products should be with high protection factors that are less irritating, with lower amounts of synthetic agents and above all easy accessibility in the market [73]. The skin products should not cause adverse reactions such as dermatitis or causing skin sensitivity and thinning. The adverse reaction usually happens when we use sunscreens in a very concentrated way that have phototoxic effects and thus a high risk for consumers [74]. To resolve this problem, the researchers are trying to introduce phytocosmetics from natural compounds that have proven scientific quality, safety and efficacy established during different studies [75].

This has been proven to successfully inhibit skin damage induced by UVA and UVB rays by reducing DNA mutations, inhibiting inflammation, improving the immune response and ultimately decreasing the photo-induced erythema. Recently, in vitro and in vivo studies that include animal models and human clinical trials proved that phytotherapeutic treatments are of great interest and hence beneficial for humans [38, 40, 76].

## Polypodium preparation

The Polypodium preparations are mentioned in Table 3.

<table>
<thead>
<tr>
<th>Polypodium preparation</th>
<th>Result of interest</th>
<th>Photoprotective activity (assays)</th>
<th>Radiation type</th>
<th>Route and dose</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsule</td>
<td>Significant reduction of cutaneous reaction and symptoms/photoprotection treatment in idiopathic photodermatosis</td>
<td>In vivo—human</td>
<td>UVA/UVB</td>
<td>Oral</td>
<td>[18]</td>
</tr>
<tr>
<td>Capsule</td>
<td>Decreased erythema/increased minimal erythema dose (MED)</td>
<td>In vivo—human</td>
<td>UVB</td>
<td>Oral</td>
<td>[16, 40, 77]</td>
</tr>
<tr>
<td>Hydrophilic extract</td>
<td>Prevention and delay of typical lesions (eruptions) caused by UVR</td>
<td>In vivo—human</td>
<td>UVA/UVB</td>
<td>Oral</td>
<td>[14]</td>
</tr>
<tr>
<td>Extract</td>
<td>Inhibition of elastase activity/stimulation of cell expression/strengthening cell matrix/prevention in photoaging</td>
<td>In vitro—enzymes and substrate</td>
<td>UVA/UVB</td>
<td>Enzyme (starting concentration of 1 µg/µL) with its substrate 0.5 mM</td>
<td>[78]</td>
</tr>
<tr>
<td>Extract</td>
<td>Negative photobiological effects/reduction of UVB rays</td>
<td>In vivo—human</td>
<td>UVB</td>
<td>Oral</td>
<td>[7]</td>
</tr>
<tr>
<td>Hydrophilic extract (Fernblock)</td>
<td>Cell damage prevention/ increased expression of matrix metalloproteinase-1 and cathepsin K/ slowing expression of fibrillin 1, 2 and elastin</td>
<td>In vitro—cell cultures (human dermal fibroblasts)</td>
<td>Infrared A and visible light</td>
<td>Incubation</td>
<td>[11]</td>
</tr>
<tr>
<td>Extract (Fernblock)</td>
<td>Decrease in darkening, cyclooxygenase-2 (marker of cell damage)</td>
<td>In vivo—human</td>
<td>Visible light</td>
<td>Oral</td>
<td>[79]</td>
</tr>
<tr>
<td>Extract (Fernblock)</td>
<td>Protective activity against oxidative stress and aging</td>
<td>In vitro—non-tumorigenic human keratinocyte cells</td>
<td>UVB</td>
<td>Incubation</td>
<td>[68]</td>
</tr>
</tbody>
</table>

## Conclusions

Different studies have demonstrated that this plant extract possesses anti-inflammatory, antioxidant, photoprotective and immunomodulatory activities making this species a powerful agent against solar induced aging and skin cancer. The capsule dosage form is very popular, widely accessible, and viable for all people around the globe. Hence, its antioxidant activity greatly facilitates its usage and thus preventing the skin damage caused by harmful UV radiation.
After an exhaustive review, no studies have been found for this plant based on its phytochemical performance, whether taken from leaves or rhizomes. It is recommended to carry out these studies for better evaluation of this plant. Likewise, it is worth mentioning that no scientific study carried out to determine the antioxidant capacity by 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) free radical electron-transfer method, while stability studies are required for different pharmaceutical formulations as there is no widely approved dose according to the skin phototype. Hence, nowadays it is necessary to carry out these studies on damaging UVC rays to make better formulations with other active ingredients to produce synergy in the photoprotective and antioxidant capacity.

**Abbreviations**

UV: ultraviolet

**Declarations**

**Author contributions**

RYMSC and SVA: Investigation, Methodology, Formal analysis, Visualization, Writing—original draft. MRAJ: Supervision. AR and MSAP: Conceptualization, Methodology, Formal analysis, Writing—review & editing, Project administration, Supervision.

**Conflicts of interest**

The authors declare that they have no conflicts of interest.

**Ethical approval**

Not applicable.

**Consent to participate**

Not applicable.

**Consent to publication**

Not applicable.

**Availability of data and materials**

Not applicable.

**Funding**

Not applicable.

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