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Goji Berry (*Lycium barbarum*) Extract as a Potential Anti-Photoaging Agent: A Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author LMS design the study, wrote the protocol, and wrote the first draft of the manuscript. Authors IWS and IWJS managed the analyses of the study and literature searches. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Tropical countries worldwide are frequently subjected to high levels of sunlight year-round. This leads to concerns about potential harmful effects, including skin damage resulting from oxidative stress caused by free radicals due to prolonged sun exposure. This results in extrinsic skin aging, or photoaging. Sunscreen, as a primary photoprotection, is commonly recommended to protect the skin from sunlight. However, even sunscreens with high SPF cannot provide 100% protection from damage caused by free radicals generated by UV rays. Therefore, secondary photoprotection such as natural antioxidants are needed. Goji berry is a natural antioxidant known as a superfruit

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because it contains many compounds with high antioxidant activity, such as *lycium barbarum* polysaccharides, flavonoids, carotenoids, and phenols. The antioxidant compounds in goji berries can act as scavengers or neutralize excess free radicals on the skin, and they can also stimulate the production of endogenous antioxidants in the skin to prevent oxidative damage caused by sunlight. This literature review utilized electronic databases on Google Scholar, PubMed, ScienceDirect, and SpringerLink using the keyword "Goji Berry", "*Lycium barbarum*", "Photoaging", "Skin Aging" and "Photoprotection". We found six studies on the treatment using goji berry extract related to skin aging caused by UV radiation (photoaging). In conclusion, the studies suggest that goji berry extract has great potential as an antioxidant in combating photoaging. Further research is needed to determine the best method of administration and the optimal dosage as an anti-photoaging agent.

Keywords: Goji berry; photoaging; skin aging; Lycium barbarum; photoprotection.

1. INTRODUCTION

Tropical countries around the world are often exposed to large amounts of sunlight throughout the year. This raises concerns about the negative effects that can occur, such as skin damage due to oxidative stress from free radicals caused by excessive sun exposure. For example, the UV-index study in one of the cities in Indonesia, as one of the tropical country showed extreme ultraviolet index values (≥ 10) 46% of the time, and there were no days with a maximum ultraviolet index below two (Fauziyyah et al., 2023; Hamdi, 2019). Consequently, its population is continuously exposed to UV-rays and is at risk of photoaging (Jusuf et al., 2022). Photoaging symptoms on the face were most frequently observed in individuals of Javanese ethnicity (30,5%) and in the 30-39 age group (59,1%). Additionally, 62% experienced over 34 hours of sun exposure per week and 65% had a Fitzpatrick IV skin type (moderate brown skin) (Muslim et al., 2021; Respati et al., 2022).

Photoaging, or extrinsic skin aging, refers to early damage to the skin resulting from exposure to sunlight (UV-radiation) (A. H. Huang & Chien, 2020). Sunlight releases ultraviolet (UV) rays which are divided into three categories: UVA with wavelengths ranging from 320-400nm, UVB with 280-320nm, and UVC between 100-280nm (Mayangsari et al., 2024). Unlike UVA and UVB radiation, UVC radiation is nearly entirely absorbed by the ozone layer. In contrast, UVA and UVB rays penetrate through to the earth's surface in amounts that can harm skin structures (Gromkowska-Kępka et al., 2021). UVA penetrates deeply into the dermis and subcutaneous layer, and it can trigger the production of reactive oxygen species (ROS) as free radical, leading to photoaging (Mayangsari et al., 2024). UVB radiation can lead to skin redness, DNA damage, photoaging, and suppression of the immune system (Holick, 2017). UV radiation is the primary factor responsible for DNA damage in stem cells. This damage can result in a reduction of stem cell numbers and harm to the stem cell niche, ultimately contributing to skin aging caused by exposure to sunlight (Petruk et al., 2018).

Free radicals are small, diffusible molecules that are highly reactive due to their unpaired electron. Initially, they were believed to be primarily oxygen-centered radicals known as reactive oxygen species (ROS) (Obeagu, 2018). Exposure to ultraviolet light can indirectly result in the generation of various reactive oxygen species (ROS), such as superoxide, singlet oxygen, hydroxyl radicals, and hydrogen peroxide, through two main mechanisms, namely direct absorption and photosensitization. The mechanisms can be seen in Fig. 1. (de Jager et al., 2017).

Photoprotection is recommended to help minimize skin damage and the risk of skin cancers caused by ultraviolet (UV) radiation. Photoprotection encompasses both primary and secondary protective measures (Krutmann et al., 2020). The primary includes wearing protective clothing, hats, sunglasses, and apply sunscreen (Lim et al., 2017). Sunscreen should be applied to the skin 15 minutes prior to sun exposure and should be reapplied every two hours, as well as after swimming or sweating (Gabros et al., 2023). But no sunscreen available can completely block 100% UVB rays, and products with an SPF higher than 100 do not offer extra protection (Bravo & Negbenebor, 2023). Thus, secondary protection is needed, such as the administration of natural antioxidants to prevent the damaging effect from free radical caused by UV-radiation (Petruk et al., 2018). Natural antioxidants are compounds found in foods and plants, particularly in red or orange fruits and vegetables, which exhibit strong antioxidant activity. Key groups of natural antioxidants include tocopherols, tocotrienols, ascorbic acid, flavonoids, carotenoids, and phenolic acids (Zehiroglu & Ozturk Sarikaya, 2019). Increasing the consumption of natural antioxidants can help sustain an acceptable level of antioxidant activity, as these compounds engage in one-electron reactions with free radicals *In vitro*, thereby preventing oxidative damage (Nimse & Pal, 2015).

Goji berries, originating from China, are called a superfruit due to their high nutrient content and significant biological antioxidant activity (Kulczyński & Gramza-Michałowska, 2016). Goji berries presented more antioxidant capacity than other fruits such as kiwifruit, raspberry, apple, and orange. This is supported by a study that states the ORAC value of goji berries is 188,52 µmol TE/g of dry weight (higher than other fruits) (Vidović et al., 2022). Goji berries are oval-shaped, reddish-orange in color, and are typically dried for consumption or processed into food, desserts, or mixed into other dishes (can be seen in Fig. 2). The components in goji berries that exhibit high biological activity include polysaccharides, carotenoids, and phenolic compounds such as phenolic acids and flavonoids (Ma et al., 2019).

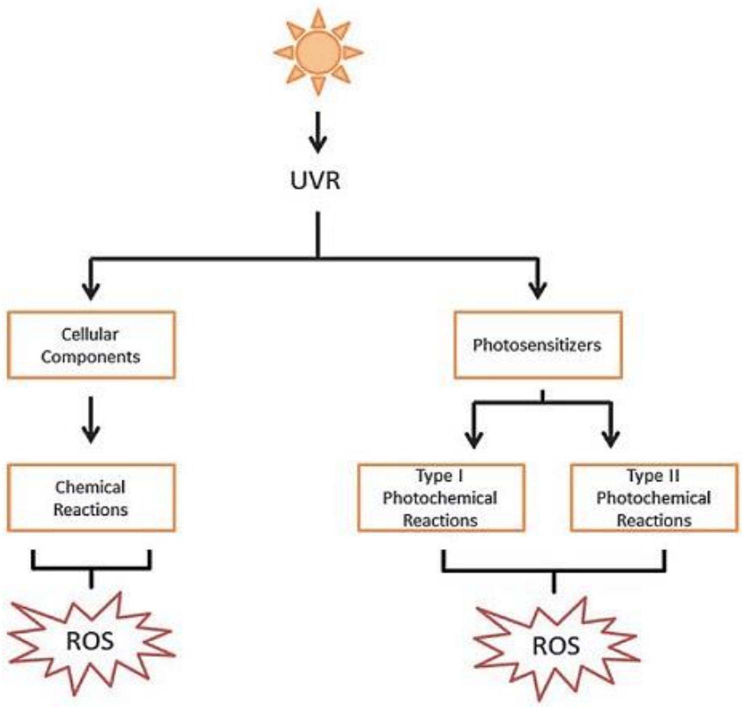

Fig. 1. Ultraviolet Light Mechanism Produces ROS (de Jager et al., 2017)

Fig. 2. The fresh and dried of *Lycium barbarum* fruit (Tian et al., 2019)

Goji berries have a range health benefits, including antioxidant, anti-inflammatory, antimicrobial, immune-boosting, anti-diabetic, neuroprotective, anti-cancer, prebiotic, and anti-obesity effects. The antioxidant properties of goji berries are closely linked to their content of polysaccharides, carotenoids, ascorbic acid, and flavonoids which can act as a radical scavenging via electron transfer and increase endogen antioxidant levels (Vidović et al., 2022). This superfruit markedly raise serum levels of SOD and GSH-Px while lowering MDA levels. Moreover, goji berries boost macrophage nitric oxide production, phagocytic ability, and acid phosphatase activity, demonstrating strong antioxidant properties in vitro (Tian et al., 2019). The various contents in goji berries are known to have a protective effect against oxidative damage to the skin, especially that caused by exposure to UV radiation (Ma et al., 2019; Tian et al., 2019). This literature review aims to analyze the potential effect of goji berry extract on skin photoaging.

2. METHODS

The methods used for this literature review is an article review, which involves gathering information and theories from research articles collected from the internet, extensive journal research, journal reviews, and publications. The search engines employed include Google Scholar, PubMed, ScienceDirect, and SpringerLink. The search utilized the keywords: "Goji Berry", "*Lycium barbarum*", "Photoaging", "Skin Aging" and "Photoprotection", focusing on literature from 2014 to 2024 (or the last ten years). The article eligibility criteria used for the results are described as follows: research articles written in English, published in the last ten years and in academic journal, and also that examine goji berry extract on skin photoaging. Exclusion criteria such as: scientific articles that are not fully accessible, conference proceedings, and case report or case series. Articles that did not meet the criteria were excluded from this study. Results and information were compiled by summarizing details about participants, interventions, control groups, outcome measurements, results, and the assessment of study quality.

3. RESULTS AND DISCUSSION

The initial literature search for research paper, utilizing the specified keywords, yielded 57 articles. After removing duplicate entries and screening the abstract, 17 full-text articles were assessed for eligibility. Ultimately, the final review comprised six (6) articles, as shown in Table 1. The sixth scientific article evaluates the effect of goji berry extract on skin photoaging.

Table 1. Research investigates the effects of goji berry extract on skin photoaging

Author	Sample	Intervention	Result	Conclusion
Neves, et al.,2020 (Neves et al., 2020)	Female hairless mice, six weeks old, were split into six groups (n= eight/group): (i) PA-photoaged (ii) PA+LBP-photoaged + polysaccharide-rich hydrogel formulation (LBP) (iii) PA+La-photoaged + laser (iv) PA+LBP+La, (v) PA+La+LBP, (vi) untreated control (UC) All treatments were administered following the induction of photodamage.	All experimental group (except UC group), were exposed to 100mJ/cm^2 for seven sessions a week (16 minutes per session) during first week, followed by exposure to 200mJ/cm^2 for three sessions a week (33 minutes per session) over the course of five weeks, total of six weeks of photo exposure. The treatments were conducted after the induction of photoaging (six weeks), three times a week, totaling	• The skin in the group treated with LBP showed decreased fragmentation and disorganization of collagen fibers in the dermis, when compared to all other groups. • Both LBP and laser application treatments, whether used separately or in combination, significantly reduced the expression of c-Jun and c-Fos transcription factors and also the level of MMP-1, MMP-2, and MMP-9 in treated group.	The administration of LBP, whether used alone or in combination with PBM (red laser), shows promise as an effective approach for repairing photodamaged skin, indicating its potential for clinical use in skin rejuvenation.

Author	Sample	Intervention	Result	Conclusion
		three weeks of treatment across nine sessions. On each treatment, 50mg of the polysaccharide-rich hydrogel formulation—LBP was applied using the tip of the index finger until fully absorbed, covering an area of 3 cm × 2 cm (6 cm^2) on the dorsal region of the animals.	• PA+La+LBP group promoted a significantly increase in the expression of collagen I and II, as well as FGF2, when compared to the photoaged group.	
Huang, et al.,2020 (X. Huang et al., 2020)	HaCaT cells in the logarithmic growth phase were inoculated in a DMEM containing 10% FBS and cultured in an incubator at 37°C with 5% CO_2. The cells were then divided into a control group (no treatment) and LBP groups (which were treated with 12.5, 25, 50, and 100 µg/mL of LBP for four hours).	Following the treatments, the control and LBP groups received UVB exposure at doses of 0, 20, 40, and 60 mJ/cm^2 for 24 hours, and were then cultured for two hours. The irradiation dose (mJ/cm^2) is calculated by multiplying the irradiation intensity (W/cm^2) by the duration of exposure.	• At the same radiation dose, the survival rate or cell viability of the LBP groups was higher than that of the control group. • At the same radiation dose, the SOD activity in the LBP groups was higher than that in the blank group. • mRNA level with RT-PCR analysis in LBP groups was decreased than the control group. • The protein expression levels of HIF-1α and VEGF was significantly reduced at a concentration of 50 µg/mL of LBP.	LBP significantly enhanced the survival rate of HaCaT cells and SOD activity under UVB irradiation, and it effectively reduced mRNA and protein expression with statistical significance. Consequently, LBP could serve as a potential pharmaceutical and cosmetic agent for preventing UVB damage.
Neves, et al.,2021 (Neves et al., 2021)	HRS/J female mice, eight weeks old were divided into six subgroups (n=8 per group). (i) CTRL-control (ii) PC-photoaged (iii) LBPF- photoaged and treated with LBPF	The first two weeks, the animals only given UV-irradiation. Treatments were conducted three times a week following each session of photoaging induction over a period of four	• The group treated with LBPF exhibited a thinning of the epidermis and more organized collagen fibers in the reticular dermis, featuring parallel bundles aligned with the epidermis and longer,	LBP provide a photo-protective effect on the skin of hairless mice, preventing epidermal thickening

Author	Sample	Intervention	Result	Conclusion
	(iv) PBM-photoaged + photobiomodulation (v) LBPF+PBM (vi) PBM+LBPF	weeks (the third to the sixth week). A dosage of 50 mg of the LBPF 5% was applied to a 3×2 cm area of the dorsal skin of the animals, then gently spread without rubbing, until fully absorbed.	less fragmented fibers. • The LBPF + PBM group showed a reduced quantity of birefringent collagen fibers in comparison to the control group.	and reducing collagen density. Both approaches (LBP or PBM), wheather used separately or together, can effectively reduce cutaneous photoaging caused by UV radiation.
Fan, et al.,2024 (Fan et al., 2024)	Human foreskin fibroblast cells (HFF-1) were cultured in high-glucose DMEM. Treatments began once the cells achieved 80% to 90% confluence. The cells were categorized into four groups: control group, LBP group, UVB group, and LBP + UVB group.	The cells were pretreated with LBP at different concentrations or 3-TYP (a selective inhibitor of SIRT3) for 24 hours before being exposed to UVB radiation. HFF-1 were categorized into groups and subjected to UVB radiation at varying doses over a period of five consecutive days. Radiation was delivered using UVB phototherapy devices that emitted UVB light within a wavelength range of 295–320 nm.	• At a concentration of 100 μg/mL, LBP significantly increased cell viability ($P < 0.05$) compared to the control group. • When HFF-1 cells were pre-treated with LBP before UVB radiation, the percentage of senescent cells significantly decreased • The group receiving pretreatment LBP had lower ROS level than UVB group. • The cells pre-treated with LBP showed decrease in γ-H2AX expression. • LBP group showed a significant decrease in senescence-related proteins and pro-inflammatory cytokines, along with a notable increase in intracellular collagen compared to the UVB group. • LBP shields HFF-1 from UVB-induced photoaging by	LBP is a natural compound capable of reducing oxidative stress and combating the effects of photoaging.

Author	Sample	Intervention	Result	Conclusion
			boosting SIRT3 expression and enhancing SOD activity, rather than increasing SOD2 expression.	
Jung, et al.,2023 (Jung et al., 2023)	Hs68 human skin fibroblasts and HaCaT human skin keratinocytes for examination of collagen, hyaluronic acid, and matrix metalloproteinase (MMP-1) production. Skh:HR-1 hairless male mice, five week old, were adapted for 1 week, then divided into four group (10 mice per group): (i) Control group (ii) UVB-group (iii) UVB+AB20 group (iv) UVB+AB200 group AB is an AGEs Blocker made up of a mixture of korean mint extract (KE), fig fruits extract (FE), and Goji Berry extract (GE).	Hs68 cells were exposed to UVB radiation (30 mJ/cm^2, 312nm), then incubated for 24 hours in DMEM, with or without the addition of 200 µg/ml of KE, FE, GE, or AB. HaCaT cells were exposed to UVB radiation (5 mJ/cm^2, 312nm), then incubated for 24 hours in DMEM, with or without the addition of 200 µg/ml of KE, FE, GE, or AB. All mice, except in control group, were given UVB irradiation three times per week for 12 weeks with variation doses, as follows : • 60 mJ/cm^2 (week 1-2) • 120 mJ/cm^2 (week 3-4) • 180 mJ/cm^2 (week 5-6) • 240 mJ/cm^2 (week 7-12)	• AB significantly increased collagen levels and reduced the secretion of MMP-1. • Goji berry extract, either alone or in an AB, significantly increased hyaluronic acid content. • The AB group had a significantly lower erythema index and higher skin moisture than UVB group. • Skin elasticity index were significantly higher in AB group than UVB group. • The level of skin roughness in the AB group was lower than UVB group, which indicates that AB can reduce the formation of wrinkles. • AB group showed had decreased MDA level and increased catalase and GPx level in skin tissue.	Goji berry extract as one of the ingredients of AGEs Blocker (AB) prevents wrinkle formation in UVB-irradiated hairless mice, increases collagen content and moisturizes the skin by stimulating hyaluronic acid production. Consequently, AB may serve as a promising antiphotoaging and moisturizing ingredient in skin functional foods.
Liang, et al., 2018 (Liang et al., 2018)	Human skin fibroblast (HSF) cell lines were cultured with DMEM containing 10% FBS and incubated at 37°C with 5% CO_2 for 24 hours.	The cells were treated with 0 (control), 100, 300, and 600 µg/ml LBP. After 24 hours, the supernatant was removed, and the cells were washed with PBS. They were then incubated for 6 hours with	• LBP enhances the phosphorylation and nuclear translocation of Nrf2, which is essential for its protective functions. • LBP treatment increases levels of important antioxidants,	This study highlighted the crucial role of LBP in activating Nrf2 to safeguard HSF cells from UV damage.

Author	Sample	Intervention	Result	Conclusion
		DMEM at 37°C and 5% CO_2. For UV irradiation, UVA and UVB lamps emitted light in the ranges of 320–430 nm and 290–320 nm, respectively, with dosages of 30 J/cm² and 400 mJ/cm². The exposure time was determined by dividing the UV irradiation dose by UV intensity. After irradiation, PBS was replaced with fresh medium.	specifically superoxide dismutase (SOD) and glutathione peroxidase (GSH-PX), leading to a reduction in reactive oxygen species (ROS) and lipid peroxidation (LPO). • Silencing Nrf2 results in decreased cell viability, increased ROS levels, and elevated lipid peroxidation, indicating that Nrf2 is crucial for mediating LBP's protective effects against UV damage. • The optimal concentration of LBP for protective effects was determined to be 300 µg/ml for 3 hours.	

As we age, the normal chronological aging process of skin occurs. The levels of collagen and elastin decline and become fragmented, along with changes in glycosaminoglycan and proteoglycan levels in the dermis, diminished blood circulation, lower fat content, and a loss of rete ridges (Karim et al., 2021). The alterations in the amount of extracellular matrix components as we age, lead to various visible signs of aging skin, including wrinkles and reduced elasticity (Guan et al., 2021). Prolonged or repeated exposure to sunlight can accelerate the aging process, especially of the skin because it is the largest and outermost organ that is most easily exposed (Salminen et al., 2022). Skin aging or photoaging results from a combination of genetic and environmental influences, primarily shaped by the accumulated damage caused by exposure to ultraviolet (UV) radiation (Poon et al., 2015). Prolonged sun exposure is well-established as a cause of photoaging, which involves alterations in skin structure, such as changes in epidermal thickness, increased pigment variation, dermal elastosis, collagen breakdown in the dermis, the formation of dilated blood vessels, and heightened mutagenesis in keratinocytes and melanocytes (Guan et al., 2021). There is strong evidence that exposure to UV radiation exacerbates the process that can accelerate the natural aging of the skin (Salminen et al., 2022).

The wavelength and intensity of radiation, such as sunlight, play a crucial role in influencing the responses triggered by UV radiation. Repeated exposure to UVA (320-400 nm) and UVB (280-320 nm) can harm the skin, including its DNA and extracellular matrix (ECM), leading to immunosuppression (Salminen et al., 2022). UV radiation also induces oxidative stress in the skin due to an imbalance between antioxidants and free radicals. One of the mechanisms involves the formation of reactive oxygen species (ROS) which causes oxidative stress, leading to collagen degradation and DNA strand breaks (Kaddurah et al., 2018; Poon et al., 2015). ROS can activate NF-κB, resulting in the production of various proinflammatory cytokine, including TNFα, IL-1, IL-6, VEGF, and EGF, which can increase MMP-1 expression, and also trigger the senescence-associated secretory phenotype (SASP) independently of DNA damage and cellular senescence pathways. Oxidative damage to proteins and lipids accelerates the aging process, resulting in alterations to dermal structure and observable signs of skin aging, such as collagen degradation, epidermal thickness, etc (Kaddurah et al., 2018).

As previously known, UV radiation can produce excess free radicals and trigger oxidative stress in the skin, so antioxidants are needed to balance the levels of excess free radicals. Antioxidants can be categorized into 2 types, namely endogenous antioxidants (which are produced within the body) and exogenous antioxidants (which are obtained from outside) (Francenia Santos-Sánchez et al., 2019). Antioxidants can balance or neutralize free radicals and ROS in the cell and it can scavenge these free radicals and thus protect cells from damage. If endogenous antioxidants are not enough to balance excess free radicals, there will be a deficit/imbalance which will trigger oxidative stress and damage to the epidermis and dermis layers of the skin. To make up for this deficit of antioxidants, the body can utilize external sources of antioxidants obtained from food, dietary supplements, or medications (Francenia Santos-Sánchez et al., 2019).

Natural antioxidants are compounds found in foods, primarily sourced from plants especially red, orange, or purple colored fruits and vegetables that exhibit strong antioxidant properties. The primary groups of natural antioxidants include tocopherols and tocotrienols, ascorbic acid, flavonoids, carotenoids, and phenolic acids (Zehiroglu & Ozturk Sarikaya, 2019). Research by Popoola, et al showed ten flavonoid-related structures has potent antioxidant that can help prevent the buildup of free radicals in the body and may be effective in preventing skin-related issues, such as photoaging (Popoola et al., 2015). The findings are supported by the theory that states that flavonoids are recognized for their ability to absorb ultraviolet radiation, which is attributed to the chromophores present in their structure (Nunes et al., 2018). The photoprotective effects of several carotenoids have been studied for their potential to reduce the size of erythema following exposure to UV radiation (Petruk et al., 2018). Recent studies have shown that carotenoids offer photoprotection against UVA-induced pigmentation and inhibit markers of oxidative stress at the molecular level (Baswan et al., 2021). Polyphenol compounds have been proven to protect the skin from photoaging due to UV radiation with anti-melanogenic, anti-wrinkle and antioxidant mechanisms (Zehiroglu & Ozturk Sarikaya, 2019). In this case, secondary metabolite compounds produced by plants can serve as natural antioxidants that help protect the skin from photoaging (Petruk et al., 2018).

Goji berries, also known as wolfberries or gouqizi, are a fruit that has been used as a traditional Chinese medicinal plant and food supplement for more than 2000 years in various Asian countries (Cheng et al., 2015). Goji berry (*Lycium barbarum*) comes from a shrub plant that belongs to the Solanaceae family. Its tree can reach a height of 1-2.5 meters, with green leaves on the upper surface and grayish-green on the lower surface, measuring 2-3 cm in length. The plant has pale purple flowers. The fruit produced by the goji berry is oval or elliptical in shape, with a length between 8-18 mm and a diameter of 5-10 mm, and is orange or dark red in color. The goji berry seeds are yellowish, kidney-shaped, and 2.5-3 mm in diameter. Goji berry plants typically flower from June to September, and the fruit ripens from July to October (Serebryanaya et al., 2018).

Goji berries are also called “superfruit” because they contain many active compounds with high biological activity and antioxidant potential, such as *Lycium barbarum* polysaccharide (LBP), carotenoid, flavonoid, phenolic compounds, and ascorbic acid (Ma et al., 2019). The most important and abundant compounds in Goji Berry fruits are *Lycium barbarum* polysaccharides (LBP) which make up 5-8% of the total dry matter in the fruit. Their structure consists of six kinds of monosaccharides: arabinose, rhamnose, xylose, mannose, galactose, glucose, galacturonic acid, along with eighteen amino acids (Donno et al., 2015). Carotenoids found in Goji are the second most important group of biologically active compounds, contributing to the distinct orange-red color of the berries and make up 0.03–0.5% of the fruit's dry matter. Dipalmitin zeaxanthin is a form of carotenoid, and goji berry is considered the best natural source of dipalmitin zeaxanthin. Studies on various Chinese medicinal herbs have confirmed the presence of phenylpropanoids with a concentration of 22.7 mg and has a strong antioxidant properties. The presence of vitamin C, betaine, and taurine has also been confirmed. The vitamin C concentration was measured at 42 mg per 100 g (Kulczyński & Gramza-Michałowska, 2016).

There are many health benefits that can be obtained from goji berries, such as anti-aging, as an antioxidant, improving visual health, having hypolipidemic and hypoglycemic activity, as an immunomodulatory, and preventing from cancer (Kocyigit & Sanlier, 2017). In addition, goji berries are also known to have a protective effect on skin cells exposed to UV radiation due to its high antioxidant properties, anti-inflammatory and immunomodulatory activities. A study evaluated the potential of consuming Goji Berry (GB) juice to mitigate sun damage caused by ultraviolet (UV) radiation in rats. The results showed that drinking 5% GB juice helped reduce edema caused by sunburn (Leite et al., 2019). Other study showed that protective effect of LBPs, through the activation of Nrf2, likely helps protect the skin from ultraviolet radiation by neutralizing active radicals, reducing DNA damage, and suppressing the UV-induced P38 MAP pathway (Skenderidis et al., 2022). This is in line with the research by Liang, et al which states that *lycium barbarum* polysaccharides protect cells from UV damage through the regulation of Nrf2.

UVB radiation can cause an excessive buildup of intracellular ROS, leading to cellular dysfunction, oxidative stress, inflammation, cell apoptosis, and aging (Kleszczyński et al., 2018). A study by Fan et al. showed that LBP, as a natural compound, has the ability to reduce oxidative stress and combat the effects of photoaging by activating the mitochondrial SIRT3-SOD2 pathway (Fan et al., 2024). This aligns with the study conducted by Huang et al which stated that LBP significantly increased SOD activity which has the ability to scavenge ROS directly (X. Huang et al., 2020). Other study by Huaping Li, et al showed that pretreatment with goji berry notably reduced UVB-induce p38 phosphorylation, caspase-3 activation, and MMP-9 expression in HaCaT cells. The p38 MAPK pathway is strongly activated by solar UV exposure and plays a crucial role in UVB-induced skin carcinogenesis. Phosphorylation of p38 triggers the activation of caspases and the upregulation of MMP expression. Caspase-3, which interacts with caspase-8 and caspase-9, is a key mediator of apoptosis, leading to chromatin condensation, DNA fragmentation, and the formation of apoptotic bodies. The association of MMP with collagen degradation contributes to photoaging, which is marked by the buildup of abnormal elastin and a loss of skin tone and elasticity (Li et al., 2017). The study by Neves et al. also presented similar results, indicating that goji berry has protective effects against UVR-induced damage. It provided protection against epidermal thickening, collagen fiber fragmentation in the dermis, and biomodulated the synthesis and degradation of birefringent collagen fibers in the reticular dermis (Neves et al., 2021). There is also research that uses a combination of Goji Berry, Fig, and Korean Mint extracts, also known as AGE's Blocker extract/AB, which shows significant effects on skin quality. According to a study by Yo et al., skin elasticity and hydration levels improved with the AB extract. In addition, there was an increase in antioxidant enzymes, a decrease in inflammatory cytokines, and a suppression of MMP expression in the skin (Yoo et al., 2023). Similar results were shown in a study by Jung et al., where the AB/AGEs blocker extract was able to inhibit the formation of skin wrinkles, the reduction of collagen, and skin hydration in mice exposed to UV radiation. It was also explained that the Goji Berry extract in the combination was dominant and provided significant results, making it a potential agent for anti-photoaging in the future (Jung et al., 2023).

In addition, other components in Goji Berry, such as phenolic acids, flavonoids, carotenoids, and betaine, are also known to act as antioxidants that can neutralize free radicals in the body. Phenolic compounds serve as a protective mechanism, helping the skin adapt and survive in harsh environmental conditions, such as shielding it from ultraviolet (UV) radiation (Teixeira et al., 2023). Phenolic compounds, such as flavonoids and phenolic acids, can block the penetration of radiation into the skin. Furthermore, they help reduce inflammation, oxidative stress, and affect various signaling pathways to protect the skin from UV damage (Petruk et al., 2018). Zeaxanthin, one form of carotenoid, is also known to have cytoprotective effects on the skin (Cenariu et al., 2021). β-carotene and lycopene have also been shown to protect the skin from UV damage, such as reducing erythema and lipid peroxidation (Zerres & Stahl, 2020). Additionally, betaine compounds also prevents UVB-induced skin damage by reducing the elevated expression of MMP-9 (Im et al., 2016).

4. CONCLUSION

In conclusion, it shows that Goji Berry (*Lycium barbarum*) extract has a great potential as anti-photoaging. It can act as a powerful antioxidant, reducing oxidative stress caused by free radicals from excessive UV exposure. It also maintain skin thickness, increase collagen levels, reduce secretion of MMP-1, also improve skin hydration and elasticity. Therefore, based on these findings, goji berries have potential implications, as they can be utilized/consumed by the general public as a source of antioxidants for the skin and can also be developed for the cosmetic/skin care industry. Further research is needed to determine the best method of administration and the optimal dosage as an anti-photoaging agent.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc. have been used during the writing or editing of manuscripts.

Details of the AI usage are given below:

1. I used Large Language Models, specifically ChatGPT, only around 2-3 times. I accessed it from chatgpt.com and only used it to paraphrase sentences in order to avoid plagiarism of the text I quoted from the reference journals.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Baswan, S. M., Klosner, A. E., Weir, C., Salter-Venzon, D., Gellenbeck, K. W., Leverett, J., & Krutmann, J. (2021). Role of ingestible carotenoids in skin protection: A review of clinical evidence. In *Photodermatology Photoimmunology and Photomedicine* (Vol. 37, Issue 6, pp. 490–504). John Wiley and Sons Inc. https://doi.org/10.1111/phpp.12690

Bravo, C. G., & Negbenebor, N. A. (2023). *Sunblock Uncovered: Essentials for Optimal Protection*. Iowa Cancer Consortium. https://canceriowa.org/sunblock-uncovered-essentials-for-optimal-protection/

Cenariu, D., Fischer-Fodor, E., Țigu, A. B., Bunea, A., Virág, P., Perde-Schrepler, M., Toma, V. A., Mocan, A., Berindan-Neagoe, I., Pintea, A., Crișan, G., Cenariu, M., & Maniu, A. (2021). Zeaxanthin-rich extract from superfood *lycium barbarum* selectively modulates the cellular adhesion and mapk signaling in melanoma versus normal skin cells in vitro. *Molecules*, *26*(2). https://doi.org/10.3390/molecules26020333

Cheng, J., Zhou, Z. W., Sheng, H. P., He, L. J., Fan, X. W., He, Z. X., Sun, T., Zhang, X., Zhao, R. J., Gu, L., Cao, C., & Zhou, S. F. (2015). An evidence-based update on the pharmacological activities and possible molecular targets of *lycium barbarum* polysaccharides. In *Drug Design, Development and Therapy* (Vol. 9, pp. 33–78). Dove Medical Press Ltd. https://doi.org/10.2147/DDDT.S72892

de Jager, T. L., Cockrell, A. E., & Du Plessis, S. S. (2017). Ultraviolet light induced generation of reactive oxygen species. In *Advances in Experimental Medicine and Biology* (Vol. 996, pp. 15–23). Springer New York LLC. https://doi.org/10.1007/978-3-319-56017-5_2

Donno, D., Beccaro, G. L., Mellano, M. G., Cerutti, A. K., & Bounous, G. (2015). Goji berry fruit (Lycium spp.): Antioxidant compound fingerprint and bioactivity evaluation. *Journal of Functional Foods*, *18*, 1070–1085. https://doi.org/10.1016/j.jff.2014.05.020

Fan, L., Luan, X., Jia, Y., Ma, L., Wang, Z., Yang, Y., Chen, Q., Cui, X., & Luo, D. (2024). Protective effect and mechanism of *lycium barbarum* polysaccharide against UVB-induced skin photoaging. *Photochemical & Photobiological Sciences*. https://doi.org/10.1007/s43630-024-00642-2

Fauziyyah, R. N. P., Komariah, M., & Herliani, Y. K. (2023). Sunlight Exposure and Protection Behavior as Prevention of Skin Cancer in Nursing Students. *Indonesian Journal of Cancer*, *17*(1), 1. https://doi.org/10.33371/ijoc.v17i1.921

Francenia Santos-Sánchez, N., Salas-Coronado, R., Villanueva-Cañongo, C., & Hernández-Carlos, B. (2019). Antioxidant Compounds and Their Antioxidant Mechanism. In *Antioxidants*. IntechOpen. https://doi.org/10.5772/intechopen.85270

Gabros, S., Nessel, T. A., & Zito, P. M. (2023). Sunscreen and Photoprotection. In *StatPearls [Internet]*. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK537164/

Gromkowska-Kępka, K. J., Puścion-Jakubik, A., Markiewicz-Żukowska, R., & Socha, K. (2021). The impact of ultraviolet radiation on skin photoaging — review of in vitro studies. In *Journal of Cosmetic Dermatology* (Vol. 20, Issue 11, pp. 3427–3431). John Wiley and Sons Inc. https://doi.org/10.1111/jocd.14033

Guan, L. L., Lim, H. W., & Mohammad, T. F. (2021). Sunscreens and Photoaging: A Review of Current Literature. In *American Journal of Clinical Dermatology* (Vol. 22, Issue 6, pp. 819–828). Adis. https://doi.org/10.1007/s40257-021-00632-5

Hamdi, S. (2019). Analysis of ultraviolet index, ultraviolet B insolation, and sunshine duration at Bandung in year 2017. *IOP Conference Series: Earth and Environmental Science*, *303*(1). https://doi.org/10.1088/1755-1315/303/1/012018

Holick, M. F. (2017). Ultraviolet B Radiation: The Vitamin D Connection. In S. I. Ahmad (Ed.), *Ultraviolet Light in Human Health, Diseases and Environment* (Vol. 996, pp. 1–360). Springer, Cham. https://doi.org/https://doi.org/10.1007/978-3-319-56017-5_12

Huang, A. H., & Chien, A. L. (2020). Photoaging: a Review of Current Literature. In *Current Dermatology Reports* (Vol. 9, Issue 1, pp. 22–29). Springer. https://doi.org/10.1007/s13671-020-00288-0

Huang, X., Liu, Y., Ye, H., Lin, Z., Ma, C., Lin, H., Zhang, H., Chen, H., Ren, J., Yue, H., & Lv, G. (2020). Effects of *Lycium barbarum* polysaccharides on expression of hypoxia inducible factor 1α and vascular endothelial growth factor in human immortalized keratinocytes cells irradiated by ultraviolet B. *Materials Express*, *10*(12), 2154–2159. https://doi.org/10.1166/mex.2020.1839

Im, A. R., Lee, H. J., Youn, U. J., Hyun, J. W., & Chae, S. (2016). Orally administered betaine reduces photodamage caused by UVB irradiation through the regulation of matrix metalloproteinase-9 activity in hairless mice. *Molecular Medicine Reports*, *13*(1),823–828. https://doi.org/10.3892/mmr.2015.4613

Jung, J. I., Choi, Y. J., Yoo, J. H., Choi, S. Y., & Kim, E. J. (2023). Antiphotoaging Effect of AGEs Blocker™ in UVB-Irradiated Cells and Skh:HR-1 Hairless Mice. *Current Issues in Molecular Biology*, *45*(5), 4181–4199. https://doi.org/10.3390/cimb45050266

Jusuf, N. K., Putra, I. B., & Muslim, M. (2022). Evaluation of dermoscopic photoaging score among multiethnic in Medan, Indonesia. *Bali Medical Journal*, *11*(3), 1919–1923. https://doi.org/10.15562/bmj.v11i3.3810

Kaddurah, H., Braunberger, T. L., Vellaichamy, G., Nahhas, A. F., Lim, H. W., & Hamzavi, I. H. (2018). The Impact of Sunlight on Skin Aging. In *Current Geriatrics Reports* (Vol. 7, Issue 4, pp. 228–237). Springer New York LLC. https://doi.org/10.1007/s13670-018-0262-0

Karim, P. L., Inda Astri Aryani, & Nopriyati. (2021). Anatomy and Histologic of Intrinsic Aging Skin. *Bioscientia Medicina : Journal of Biomedicine and Translational Research*, *5*(11), 1165–1177. https://doi.org/10.32539/bsm.v5i11.417

Kleszczyński, K., Bilska, B., Stegemann, A., Flis, D. J., Ziolkowski, W., Pyza, E., Luger, T. A., Reiter, R. J., Böhm, M., & Slominski, A. T. (2018). Melatonin and Its Metabolites Ameliorate UVR-Induced Mitochondrial Oxidative Stress in Human MNT-1 Melanoma Cells. *International Journal of Molecular Sciences*, *19*(12), 3786. https://doi.org/10.3390/ijms19123786

Kocyigit, E., & Sanlier, N. (2017). Emine Kocyigit, Nevin Sanlier. A Review of Composition and Health Effects of *Lycium barbarum*. *International Journal of Chinese Medicine*, *1*(1), 1–9. https://doi.org/10.11648/j.ijcm.20170101.11

Krutmann, J., Passeron, T., Gilaberte, Y., Granger, C., Leone, G., Narda, M., Schalka, S., Trullas, C., Masson, P., & Lim, H. W. (2020). Photoprotection of the future: challenges and opportunities. *Journal of the European Academy of Dermatology and Venereology*, *34*(3), 447–454. https://doi.org/10.1111/jdv.16030

Kulczyński, B., & Gramza-Michałowska, A. (2016). Goji Berry (*Lycium barbarum*): Composition and Health Effects - A Review. *Polish Journal of Food and Nutrition Sciences*, *66*(2), 67–75. https://doi.org/10.1515/pjfns-2015-0040

Leite, F. de G., Júnior, J. A. O., Chiavacci, L. A., & Chiari-Andréo, B. G. (2019). Assessment of an anti-ageing structured cosmetic formulation containing goji berry. *Brazilian Journal of Pharmaceutical Sciences*, *55*. https://doi.org/10.1590/s2175-97902019000217412

Li, H., Li, Z., Peng, L., Jiang, N., Liu, Q., Zhang, E., Liang, B., Li, R., & Zhu, H. (2017). *Lycium barbarum* polysaccharide protects human keratinocytes against UVB-induced photo-damage. *Free Radical Research*, *51*(2), 200–210. https://doi.org/10.1080/10715762.2017.1294755

Liang, B., Peng, L., Li, R., Li, H., Mo, Z., Dai, X., Jiang, N., Liu, Q., Zhang, E., Deng, H., Li, Z., & Zhu, H. (2018). *Lycium barbarum* polysaccharide protects HSF cells against ultraviolet-induced damage through the activation of Nrf2. *Cellular and Molecular Biology Letters*, *23*(1). https://doi.org/10.1186/s11658-018-0084-2

Lim, H. W., Arellano-Mendoza, M. I., & Stengel, F. (2017). Current challenges in photoprotection. *Journal of the American Academy of Dermatology*, *76*(3), S91–S99. https://doi.org/10.1016/j.jaad.2016.09.040

Ma, Z. F., Zhang, H., Teh, S. S., Wang, C. W., Zhang, Y., Hayford, F., Wang, L., Ma, T., Dong, Z., Zhang, Y., & Zhu, Y. (2019). Goji berries as a potential natural antioxidant medicine: An insight into their molecular mechanisms of action. In *Oxidative Medicine and Cellular Longevity* (Vol. 2019). Hindawi Limited. https://doi.org/10.1155/2019/2437397

Mayangsari, E., Mustika, A., Nurdiana, N., & Samad, N. A. (2024). *Comparison of UVA vs UVB Photoaging Rat Models in Short-term Exposure*. https://www.orcid.org/0000-0001-6461-

Muslim, M., Jusuf, N. K., & Putra, I. B. (2021). *Gambaran Dermoskopi Penuaan Kulit Wajah pada Berbagai Etnis di Medan* [Universitas Sumatera Utara]. https://repositori.usu.ac.id/handle/123456789/32547

Neves, L. M. G., Parizotto, N. A., Tim, C. R., Floriano, E. M., Lopez, R. F. V., Venâncio, T., Fernandes, J. B., & Cominetti, M. R. (2020). Polysaccharide-rich hydrogel formulation combined with photobiomodulation repairs UV-induced photodamage in mice skin. *Wound Repair and Regeneration*, *28*(5), 645–655. https://doi.org/10.1111/wrr.12826

Neves, L. M. G., Tim, C. R., Floriano, E. M., da Silva de Avo, L. R., Fernandes, J. B., Parizotto, N. A., & Cominetti, M. R. (2021). *Lycium barbarum* polysaccharide fraction associated with photobiomodulation protects from epithelium thickness and collagen fragmentation in a model of cutaneous photodamage. *Lasers in Medical Sciences*, *36*, 863–870. https://doi.org/10.1007/s10103-020-03132-w/Published

Nimse, S. B., & Pal, D. (2015). Free radicals, natural antioxidants, and their reaction mechanisms. *RSC Advances*, *5*(35), 27986–28006. https://doi.org/10.1039/c4ra13315c

Nunes, A. R., Vieira, Í. G. P., Queiroz, D. B., Leal, A. L. A. B., Maia Morais, S., Muniz, D. F., Calixto-Junior, J. T., & Coutinho, H. D. M. (2018). Use of Flavonoids and Cinnamates, the Main Photoprotectors with Natural Origin. *Advances in Pharmacological Sciences*, *2018*. https://doi.org/10.1155/2018/5341487

Obeagu, E. I. (2018). *A Review on Free Radicals and Antioxidants*. https://doi.org/10.22192/ijcrms.2018.04.02.019

Petruk, G., Giudice, R. Del, Rigano, M. M., & Monti, D. M. (2018). Antioxidants from plants protect against skin photoaging. In *Oxidative Medicine and Cellular Longevity* (Vol. 2018). Hindawi Limited. https://doi.org/10.1155/2018/1454936

Poon, F., Kang, S., & Chien, A. L. (2015). Mechanisms and treatments of photoaging. In *Photodermatology Photoimmunology and Photomedicine* (Vol. 31, Issue 2, pp. 65–74). Blackwell Publishing Ltd. https://doi.org/10.1111/phpp.12145

Popoola, O. K., Marnewick, J. L., Rautenbach, F., Ameer, F., Iwuoha, E. I., & Hussein, A. A. (2015). Inhibition of oxidative stress and skin aging-related enzymes by prenylated chalcones and other flavonoids from Helichrysum teretifolium. *Molecules*, *20*(4), 7143–7155. https://doi.org/10.3390/molecules20047143

Respati, R. A., Yusharyahya, S. N., Wibawa, L. P., & Widaty, S. (2022). The Dermoscopic Features of Photoaging and Its Association with Sun Index Score in the Coastal Population at Cilincing, Jakarta: A Cross-Sectional Study. *Clinical, Cosmetic and Investigational Dermatology*, *15*, 939–946. https://doi.org/10.2147/CCID.S355260

Salminen, A., Kaarniranta, K., & Kauppinen, A. (2022). Photoaging: UV radiation-induced inflammation and immunosuppression accelerate the aging process in the skin. In *Inflammation Research* (Vol. 71, Issues 7–8, pp. 817–831). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s00011-022-01598-8

Serebryanaya, F. K., Sekinaeva, M. A., & Denisenko, O. N. (2018). Comparative micromorphological investigations of red godji berries (*Lycium barbarum* L.) and black godji berries (Lycium ruthenicum Murr.). *Pharmacognosy Journal*, *10*(5), 911–915. https://doi.org/10.5530/pj.2018.5.153

Skenderidis, P., Leontopoulos, S., & Lampakis, D. (2022). Goji Berry: Health Promoting Properties. *Nutraceuticals*, *2*(1), 32–48. https://doi.org/10.3390/nutraceuticals2010003

Teixeira, F., Silva, A. M., Delerue-Matos, C., & Rodrigues, F. (2023). *Lycium barbarum* Berries (Solanaceae) as Source of Bioactive Compounds for Healthy Purposes: A Review. In *International Journal of Molecular Sciences* (Vol. 24, Issue 5). Multidisciplinary Digital Publishing Institute (MDPI). https://doi.org/10.3390/ijms24054777

Tian, X., Liang, T., Liu, Y., Ding, G., Zhang, F., & Ma, Z. (2019). Extraction, structural characterization, and biological functions of *lycium barbarum* polysaccharides: A review. *Biomolecules*, *9*(9). https://doi.org/10.3390/biom9090389

Vidović, B. B., Milinčić, D. D., Marčetić, M. D., Djuriš, J. D., Ilić, T. D., Kostić, A., & Pešić, M. B. (2022). Health Benefits and Applications of Goji Berries in Functional Food Products Development: A Review. In *Antioxidants* (Vol. 11, Issue 2). MDPI. https://doi.org/10.3390/antiox11020248

Yoo, J. H., Lee, J. S., Jang, J. H., Jung, J. I., Kim, E. J., & Choi, S. Y. (2023). AGEs BlockerTM (Goji Berry, Fig, and Korean Mint Mixed Extract) Inhibits Skin Aging Caused by Streptozotocin-Induced Glycation in Hairless Mice. *Preventive Nutrition and Food Science*, *28*(2), 130–140. https://doi.org/10.3746/pnf.2023.28.2.134

Zehiroglu, C., & Ozturk Sarikaya, S. B. (2019). The importance of antioxidants and place in today's scientific and technological studies. In *Journal of Food Science and Technology* (Vol. 56, Issue 11, pp. 4757–4774). Springer. https://doi.org/10.1007/s13197-019-03952-x

Zerres, S., & Stahl, W. (2020). Carotenoids in human skin. In *Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids* (Vol. 1865, Issue 11). Elsevier B.V. https://doi.org/10.1016/j.bbalip.2019.158588

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