Review Article

The Photoprotective Effect of Curcumin on Skin Exposed to Ultraviolet Radiation

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Abstract

Introduction: Curcumin is an active ingredient mainly found in the *Curcuma* species' rhizomes. It is a phenol with biological effects, such as anti-inflammatory, antioxidant, antimicrobial, wound healing, and antineoplastic. This paper aims to provide a systematic review of the literature on the photoprotective effect of curcumin on skin irradiated by ultraviolet (UV) light (*in vivo* studies). **Methods:** This systematic review was done in compliance with PRISMA guidelines. We searched articles from Science Direct, Web of Science, Scopus, and PUBMED databases using specific search strategies. **Results:** Of the 805 articles identified, nine articles met the inclusion criteria. Curcumin, given orally or topically, was found to have a photoprotective effect on UV-exposed skin. Researchers found that curcumin protects against oxidants, reduces inflammation, prevents aging due to UV exposure, reduces epidermal thickness, reduces wrinkles, decreases inflammatory cytokines, and increases collagen density. Administration of curcumin in its pure form or from the extraction of *Curcuma* species showed similar good results. **Conclusion:** These review results show that curcumin can be an effective photoprotective compound used on UV-irradiated skin. Therefore, curcumin usage as an adjuvant along with sunscreen and other cosmetic products should be considered.

Keywords: *Aging, curcumin, human and health, photoprotective, ultraviolet radiation*

Introduction

Ultraviolet (UV) rays, encompassing UVA and UVB with wavelengths (320–400 nm) and (290–320 nm), respectively, can lead to various skin injuries. Although ambient light contains UVA in quantities 10–100 times greater than UVB, UVB has more energy.[1] UV rays are said to be the main cause of skin aging on the face.[2] The premature skin aging caused by sun exposure in the long term is called photoaging. Photoaging is characterized by the presence of deep wrinkles, coarse texture, and reduced elasticity of the skin.[3] To prevent this premature aging, cosmetic products have been launched, with various herbal ingredients added to the formula. The well-known herbal ingredient used for skin routines is *Curcuma* genus, with approximately 93–100 *Curcuma* species,[4] such as *Curcuma longa* (turmeric) and other *Curcuma* spp., which contain the main active component, curcumin.s[5] Over the past century, curcumin has exhibited various activities, such as anti-inflammatory,[6] antioxidant,[7] and antimicrobial activities.[8] On the skin, curcumin was reported to have healing effect on skin inflammatory disorders, such as psoriasis, atopic dermatitis, wounds, and even skin cancer. Curcumin was also reported to have a positive effect on aging caused by inflammation (inflammaging).[9] Although curcumin is a well-studied herbal ingredient, its effects in photoaging have not been summarized and reviewed thoroughly. Therefore, the aim of this article is to present a systematic review of animal studies on the effects of curcumin on skin irradiated by UV light.

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Methods

A systematic review of published studies reporting Curcumin's effect on UV-irradiated skin was conducted using a prespecified protocol (population, interventions, comparisons, and outcomes [PICO]) in agreement with PRISMA.[10] PROSPERO registration number is CRD42023391685.

Sources of data and methods of searching

A thorough literature search was completed on June 30, 2020. Articles published in the English language were evaluated through Pubmed, ScienceDirect, Web of Science, and Scopus databases using the key terms "curcumin, turmeric yellow, photoaging, photodamage, skin aging, UV, radiation, and UV irradiation." According to NCBI's PubChem compound summary of curcumin, turmeric yellow is one of the synonyms of curcumin.[11] Primary research studies included for comparison involve only animal experimental.

Selection criteria

PICO protocol was used to clarify the eligibility criteria for the inclusion and exclusion of relevant articles. Regardless of randomization, we included experimental studies investigating the effect of curcumin on UV-irradiated skin. We included articles that were available in full copy.

The study included all types of UV irradiation at various doses. No publication date limit was set. Animal models, specifically mice or rats, whose skins receive UV irradiation treatment and curcumin supplementation (oral or topical) were included. Animal models of photoaging which received curcumin, via any method, were included. The study included all types of UV irradiation at various doses. All kinds of curcumin application, via oral or topical, with different doses were included. Application of turmeric extract in any form and doses was also included. Published articles that did not meet the inclusion criteria were removed from the study.

Data extraction

First, we searched the article in the databases using the following keywords in the title: Curcumin, turmeric yellow, photoaging, photodamage, skin aging, UV, radiation, and UV irradiation. A total of 805 articles were found during searches conducted in June 2022. Among these, 130 articles were removed as duplicates and 675 articles remained. Second, we screened the titles and the abstracts of the articles using several keywords (curcumin, turmeric, UV, UV, photo, and aging), and only the related 112 articles that contained the keywords were included. Third, of 112 articles, the title and the abstract were screened one by one, and 68 unrelated articles were excluded, leaving 44 articles remained to be assessed for eligibility. Out of these 44 articles, 15 were reviews, 10 were not animal studies, 7 were irrelevant, and 3 were inaccessible. At the end, only 9 studies remained for further analysis [Figure 1].

Results

Sample diversity

In this review, to be able to know the effect of curcumin on photoaging, we included studies in which animals were subjected to UV irradiation. Of 9 studies, 8 studies used mice and only 1 study used rats as animal models for photoaging. The most common strain of mice used was hairless SKH-1 mice.[12-14] The other hairless mice used were hairless Hos,[15] BALB/c derived Uncovered (*Uncv*) hairless mice,[16] and nude mice.[17] The rest of the animals were hairy and their dorsal back was shaved before intervention/treatment which was Laca mice,[18] Inbred Research Colony (IRC) rats,[19] and BALB/C mice.[20]

Ultraviolet treatment

UV type used in the studies investigating the effect of curcumin on photoaging mostly was UVB with wavelength 290–320 nm, although there was a study using broad spectrum UV (UVA and UVB) with wavelength 260–400 nm. The UV doses used in the studies varied, where most of the time, the doses were often increased several times throughout the study.

Intervention

The route of curcumin administration in the animal models varies with topical application being the most used route. The curcumin given in the studies was in its herbal *Curcuma* spp. Table 1 summarizes the use of curcumin in various forms such as extract, nanoparticles, conjugate, and vesicles. The studies also used a variety of doses.

Outcomes measures

The studies used a variety of outcomes or variables as measurements. The outcomes could be divided into two groups, macroscopic and microscopic outcomes. The macroscopic outcomes included skin thickness, wrinkles formation, erythema, and diameter/length of the blood vessel. The microscopic outcomes included the expression of dermal cells and substance (sunburn cells, fibroblast cells, collagen, and elastic fiber), the expression of proinflammation cytokines and matrix metalloproteinase (MMP), the existence of apoptosis, tumor suppressor activity, lipid peroxidation, and many more. The most assessed outcome was skin/epidermal thickness.

The summary of the results is presented in Table 1.

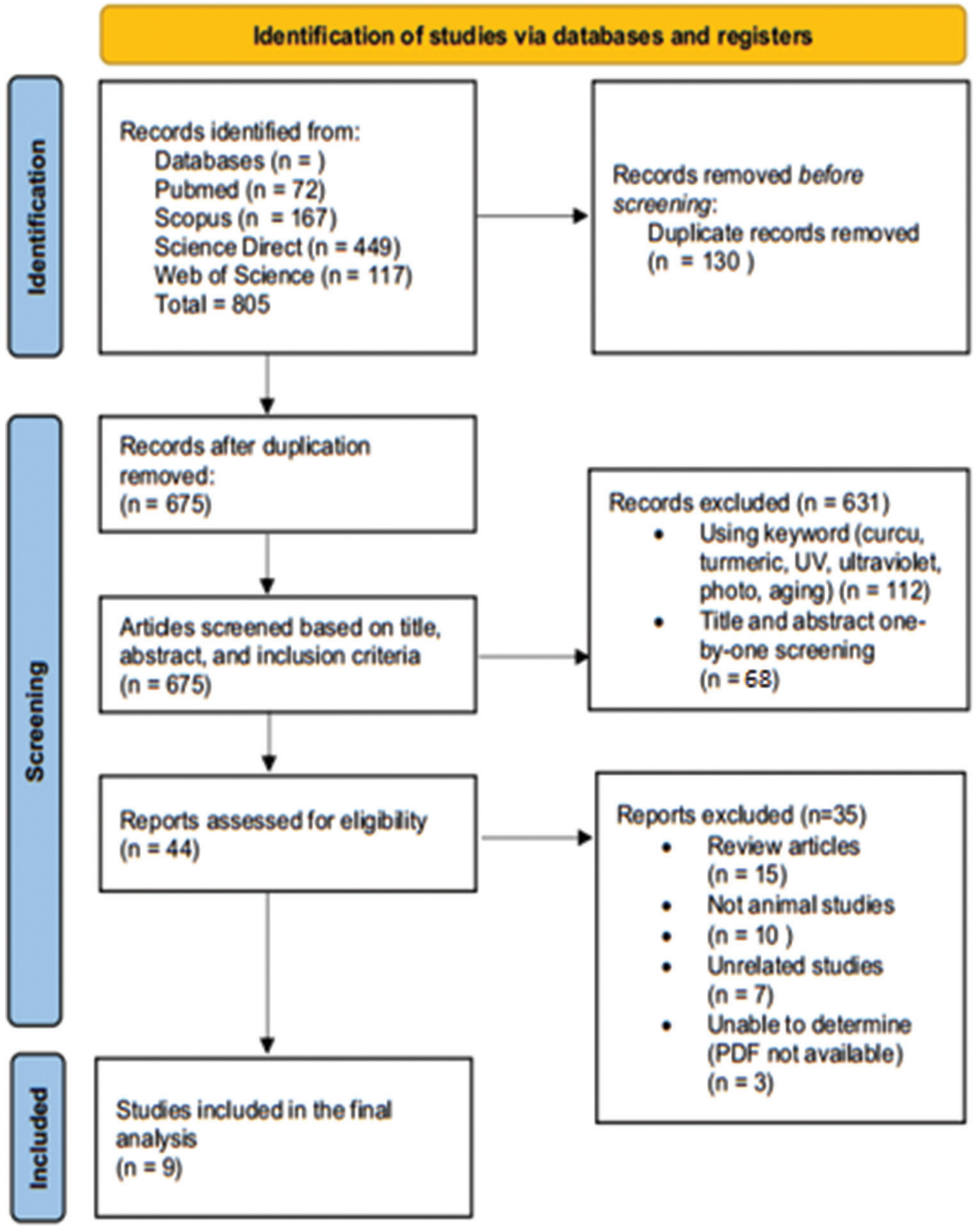

Figure 1: PRISMA diagram flow. UV: Ultraviolet

Discussion

Researchers have replicated various pathological conditions linked to cognitive decline due to aging caused by exposure to sunlight in animals. The initial study in the 1960s discovered elastosis, examining the histological changes occurring in the dermal connective tissue as actinic damage (now known as photoaging) progresses. Subsequent ultrastructural and biochemical studies focused on advanced photodamage. *In vitro* research helped overcome challenges related to obtaining biopsies from diverse age groups and the labor-intensive nature of examining tissues with advanced technology. Nonetheless, a comprehensive study of the photoaging process with precise exposure measurements remains impractical for human skin. Animal models, where the aging process is accelerated, are therefore preferred. The first trial to investigate UV-induced connective tissue damage in an animal model occurred in 1964 using the shaved dorsal trunk skin of a haired mouse. The hairless mouse emerged as the primary model for UV-induced cancer in 1948, and in 1980, the first experiment to induce elastosis in a hairless mouse was conducted. By the 1990s, the albino Skh-hairless-1 mouse became the most commonly used model for studying photoaging. In addition, in 2014, the nude mouse was also identified as a suitable model for studying the progression of photoaging.[22]

Curcumin is the main biologically active polyphenol constituent in the Curcuma genus.[23] Over the past

Table 1: Reported outcomes of turmeric/curcumin application after ultraviolet irradiation

Authors	Country	Population	Methods	Outcomes
Sumiyoshi and Kimura[15]	Japan	Hairless Hos: HRM mice	Oral turmeric extract	Inhibition of the increased skin thickness Reduced wrinkles Inhibition of the increased diameter and length of vessels Reduced pro-MMP2, MMP-2 and pro-MMP-9
Agrawal and Kaur[18]	India	Laca mice	Topical curcumin elastic vesicles	Macroscopic changes and lesion formation prevention Recovery time reduction Normal MDA levels of restoration The reduction of increased catalase activity
Li *et al*.[16]	China/USA	BALB/c derived Uncovered hairless mice	Topical curcumin	Minimalization of dramatic infiltration of inflammatory cells and collagen accrementition derangement Decreased oxidative damage Increased Nrf2 protein expression
Jeong *et al*.[12]	South Korea	SKH-1 hairless mice	Topical CZE	Inhibition of wrinkle formation Inhibition of COX-2 and MMP-13 expression
Kusumawati *et al*.[19]	Indonesia	IRC rats	Topical *C. heyneana* ethanolic extract	Reduction of the epidermal thickness Decreased SBC Distance reduction between collagen Increased fibroblast and elastic fibers
Cho *et al*.[13]	South Korea	SHK-1 mice	Topical *C. longa* extract	Reversal of increased epidermal thickness Reduced oxidative stress Increased SOD activities and decreased MDA Upregulate Akt and Nrf2 activities Prevention of skin damage, collagen degradation, and mast cell infiltration
Zheng *et al*.[21]	China	Nude mice	Topical CL-EO	Decreased epidermal skin thickness Reduced wrinkles Better symptoms (rough skin, erythema, and edema) Decreased IL-1β and TNF-α levels
Adusumilli *et al*.[20]	USA	Balb/c mice	Topical curcnp	Less erythema Fewer sunburn cells and less dermal inflammatory infiltrate Less p53 tumor suppressor Lower expression of pro-inflammatory IL-6 Higher expression of anti-inflammatory IL-10
Hur *et al*.[14]	Korea	SKH-1 mice	Chlorin e6–curcumin conjugate	Reduced skin roughness Attenuation of increased epidermal thickness Attenuation of collagen loss

Nrf2: NF-E2-related factor 2, MMP 2: Matrix metalloproteinase-2, MMP-13: Matrix metalloproteinase-13, SBC: Sunburn cell, CL-EO: *Curcuma longa* rhizome-derived essential oil, IL: Interleukin, IL-1β: IL-1 beta, TNF-α: Tumor necrosis factor alpha, CZE: *Curcuma zedoaria* extract, curcnp: Curcumin nanoparticles, IRC: Inbred research colony, SOD: Superoxide dismutase, HRM: High-resolution melting, MDA: Malondialdehyde

century, curcumin has been reported to have anti-inflammatory, antioxidant, antimicrobial, wound-healing, and antineoplastic activities.[24] Clinical trials have tested curcumin for various types of diseases by administering oral doses, due to its many therapeutic targets. However, curcumin's potential for clinical application is still limited because of its rapid degradation,[25] poor water solubility,[26] and low oral bioavailability,[27] and data regarding the application of turmeric extract under the photoaging concept is still scarce.

Sumiyoshi and Kimura investigated the protective effects of *C. longa* against chronic UVB-induced skin damage. They studied a *C. longa* extract's impact on skin characteristics in melanin-bearing hairless mice subjected to long-term, low-dose UVB exposure, focusing on changes in skin thickness, elasticity, pigmentation, and wrinkle formation. Their findings demonstrated that administration of the extract (at different doses, twice daily) prevented UVB-induced increases in skin thickness and reductions in skin elasticity. In addition, the extract inhibited wrinkle formation and melanin production, along with the diameter and length decrease of skin blood vessels. These protective effects are thought to involve the suppression of MMP-2 expression induced by chronic UVB exposure.[15]

Agrawal and Kaur formulated curcumin in elastic vehicles (EVs) and carried out experiments on mice using different doses (1, 3, 5, and 10 mmol) to assess its potential in mitigating the effects of aging. VICCO turmeric served as the commercial reference, while free curcumin mixed in an ointment base acted as another control. The mice's skin on the back was exposed to full-spectrum UV radiation (UVA and UVB with wavelength 260–400 nm) for 6 weeks (5 s, five times per week). Subsequently, each exposure site was treated with curcumin EVs at varying doses, free curcumin ointment, or VICCO turmeric. Evaluations of skin appearance, histopathology, pinch tests, and analysis of redox balance in skin homogenates confirmed the efficacy of the treatments. Skin assessments demonstrated that curcumin EVs at doses of 5 and 10 mmol, in addition to the commercial formulation, effectively prevented lesion formation and other changes. The pinch test showed a significantly faster healing time with the highest dose of curcumin EVs. Histopathological examinations further supported the protective properties of curcumin in EVs. The highest dose of curcumin in the EV restored redox balance, similar to the significant effects observed with the commercial formulation. Conversely, the group treated with free curcumin ointment did not exhibit any improvement in redox levels.[18]

Li *et al*. (2016) examined the photoprotective properties of curcumin against acute UVB-induced photodamage in hairless mice. They found that topical application of curcumin significantly suppressed UVB-induced inflammation, collagen disorder, and lipid peroxidation following exposure to UVB (540 mJ/cm^2 for 3 consecutive days). Moreover, curcumin effectively promoted nuclear accumulation of NF-E2-related factor 2 in the skin of hairless mice. The study suggests that curcumin has the potential as an agent for preventing and/or treating acute inflammation and photoaging induced by UV radiation.[16]

In their study published in 2018, Jeong Ha *et al*. utilized a model of chronic skin inflammation and photoaging to investigate the effects of *Curcuma zedoaria* extract (CZE). They observed that CZE notably inhibited the formation of wrinkles induced by repetitive UVB exposure and reduced the expression of Cyclooxygenase-2 (COX-2) and MMP-13 *in vivo*. Among the compounds studied, curcumin exhibited the most significant inhibition of UVB-induced MMP-1 promoter activity. These findings underscore the potent preventive properties of CZE against UVB-induced skin inflammation and photoaging.[12]

In their study, Kusumawati *et al*. (2018) explored the antiaging potential of *Curcuma heyneana* to validate its traditional medicinal application. They conducted *in vivo* experiments to observe histomorphological changes in rat skin exposed to UV radiation. Total curcuminoid content and chromatographic profiles were analyzed using thin-layer chromatography with densitometry. Results from the *in vivo* assays demonstrated that topical application of C. *heyneana*'s crude extract significantly ameliorated UV-induced damage to skin structure. The study revealed a direct association between the total curcuminoid content and the observed antiaging effects of *C. heyneana*. These findings underscore the presence of antioxidant compounds in *C. heyneana*, highlighting its robust antiaging properties and suggesting its potential application as a candidate for developing antiaging drugs or as a phyto-cosmeceutical.[19]

Cho *et al*. (2018) explored the ethanolic extracts of *C. longa* rhizomes and Diospyros lotus leaves to investigate their synergistic effects in shielding against chronic UVB-triggered skin photodamage in SHK-1 mice. The research evaluated the protective capabilities using biochemical indicators. *C. longa* rhizomes, diospyros lotus leaves, and their blend notably shielded against photodamage by boosting natural antioxidants in mouse skin through Akt and Nrf2 activation. They also hindered epidermal thickening, mast cell infiltration, and collagen degradation. The combined extract exhibited superior effectiveness compared to individual extracts, with the synergistic effects of discoid lupus erythematosus / cutaneous lupus erythematosus (DLE/CLE) being on par with the standard drug. This investigation underscores the synergistic protective potential of the combination against UVB-triggered photodamage.[13]

Zheng *et al*. (2020) assessed the effectiveness of *C. longa* rhizome-derived essential oil (CL-EO) in combating skin aging caused by UVB exposure. The CL-EO was obtained through hydrodistillation and analyzed using gas chromatography–mass spectrometry. Different concentrations of CL-EO were applied topically to nude mice's backs exposed to daily UVB light for 8 weeks, except on Sundays, to evaluate its antiaging properties. Histological and immunohistochemical analyses were performed. A total of 56 compounds were identified, constituting 94.36% of the CL-EO content. Hematoxylin and eosin staining indicated a reduction in skin thickness due to CL-EO application. Immunohistochemistry results showed that CL-EO suppressed the expression of interleukin-1 β and tumor necrosis factor-α. These results suggest that CL-EO has the potential to alleviate skin aging induced by UVB exposure in nude mice, indicating its possible use in skin care products and cosmetics.[21]

Adusumilli *et al*. (2021) tackled the curcumin limitation, such as its poor solubility in water and fast breakdown in the body, by creating curcumin nanoparticles (curc-np) to improve its delivery and effectiveness when applied topically. In their research, they applied curc-np or control substances on the BALB/c mice's skin before exposing them to UVB radiation. After a day, mice treated with control substances showed reduced redness, swelling, and flaking compared to the control group. Examination of skin tissue revealed fewer cells damaged by sunburn and lower cell death in the mice treated by curc-np. The analysis also indicated decreased levels of p53 protein in the skin treated with curc-np. Furthermore, the study demonstrated lower levels of IL-6 as an inflammatory cytokine and higher levels of IL-10 as an anti-inflammatory in the skin of mice treated with curc-np, highlighting the known curcumin's anti-inflammatory effects of on the skin and its potential as a protective agent against UV damage when delivered through nanoparticles. Further investigation, especially in conjunction with sunscreens, is necessary to effectively counteract UV-induced harm.[20]

Hur *et al*. (2022) examined the effectiveness of a chlorin e6 (Ce6) –curcumin conjugate, a photosensitizer made up of Ce6 and curcumin connected by polyethylene glycol (PEG), in animal models (SKH-1 mice). The photodynamic therapy using this photosensitizer inhibited the expression of MMPs and boosted levels of procollagen Type I in the skin of the mice exposed to UVB radiation. Moreover, this treatment notably decreased skin roughness caused by UVB exposure. Analysis of skin tissue through methods like H and E staining and Masson's trichrome staining indicated a decrease in skin thickness and an increase in collagen fiber density. Overall, this treatment shows the potential in delaying and enhancing the effects of skin aging induced by UV radiation.[14]

Conclusion

Curcumin, given orally or topically, was found to have a photoprotective effect on UV-exposed skin. From this review, Curcumin is reported to attenuate the photoaging effect of UV irradiation, especially in animal models. Curcumin can act as antioxidant, anti-inflammation, and antiaging caused by UV exposure. Besides, Curcumin also can reduce epidermal thickness, wrinkles, and inflammatory cytokines, and increases collagen density. Administration of curcumin in its pure form or from the extraction of *Curcuma* species showed similar good results. Although additional information about the best method and dose of curcumin administrated is still limited, these review results show that curcumin can be an effective photoprotective compound used in UV-irradiated skin. Therefore, the use of curcumin as an adjuvant along with sunscreen and other cosmetic products should be considered.

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Conflicts of interest

There are no conflicts of interest.

Author contribution

AT was responsible for the concept and manuscript writing. SK contributed to the revision and proofreading. AKA handled the design and proofreading. ISM defined the intellectual content and performed the final proofreading.

Data availability

The data is available upon request from the corresponding author.

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