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The Photoprotective Effect of Curcumin on Skin Exposed to UV Radiation: A Systematic Review

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, anti-microbial, 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: Curcumin, UV Radiation, Aging, Photoprotective, Human and Health

Introduction

Ultraviolet rays, encompassing ultraviolet A (UVA) and ultraviolet B (UVB) with wavelength (320–400 nm) and (290–320 nm), respectively, can lead to various skin injuries. Although ambient light contains UVA in quantities 10 to 100 times greater than UVB, UVB has more energy.[1] Ultraviolet rays are said to be the main cause of skin aging on the face.[2] The premature skin aging caused by sun exposure in a 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 skin, curcumin was reported to have healing effect on skin inflamatory disoders, such as psoriasis, atopic dermatitis, wound, and even skin cancer. Curcumin was also reported to have 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.

Methods

A systematic review of published studies reporting the Curcumin's effect on UV-irradiated skin was conducted using a pre-specified 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 30 June 2020. Articles published in the English language were evaluated through Pubmed, ScienceDirect, Web of science, and Scopus database using the key terms 'curcumin', turmeric yellow, 'photoaging', photodamage, skin aging, ultraviolet, radiation, and UV irradiation. Primary research studies included for comparison involve only animal experimental.

Selection Criteria

PICO ptotocol was used to clarify the eligibility criteria for 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 ultraviolet 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 ultraviolet 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

Firstly, we searched the article in the databases using the following keywords in the title: curcumin, turmeric yellow, photoaging, photodamage, skin aging, ultraviolet, 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. Secondly, we screened the titles and the abstracts of the articles using several keywords (curcu, turmeric,

UV, ultraviolet, photo, and aging) and only the related 112 articles that contained the keywords were included. Thirdly, 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 subjected to UV irradiation. From 9 studies, 8 studies used mice and only 1 study used rats as animal models for photoaging. The most common strain of mice used were hairless SKH-1 mice.[11–13] The other hairless mice used were hairless Hos,[14] BALB/c derived Uncovered (*Uncv*) hairless mice,[15] and nude mice.[16] The rest of the animals were hairy and their dorsal back were shaved before intervention/treatment which were Laca mice,[17] IRC rats,[18] and BALB/C mice.[19]

Ultraviolet Treatment

Ultraviolet type used in the studies investigating the effect of curcumin on photoaging mostly was ultraviolet B (UVB) with wavelength 290-320 nm , although there was a study using broad spectrum ultraviolet (UVA and UVB) with wavelength 260-400 nm. The ultraviolet 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 were 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 to 2 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 fibre), the expression of pro-inflammation cytokines and matrix metalloproteinase, the existence of apoptosis, tumour suppressor activity, lipid peroxidation, and many more. The most assessed outcome was skin/epidermal thickness.

The summary of the results is presented on Table 1.

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. Additionally, in 2014, the Nude mouse was also identified as a suitable model for studying the progression of photoaging.[20]

Curcumin is the main biologically active polyphenol constituent in Curcuma genus.[21] Over the past century, curcumin has been reported to have anti-inflammatory, antioxidant, antimicrobial, wound-healing, and antineoplastic activities.[22] 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,[23] poor water solubility,[24] and low oral bioavailability,[25] and Data regarding the application of turmeric extract under the photoaging concept is still scarce.

Sumiyoshi and Kimura (2009) investigated the protective effects of *Curcuma longa* against chronic ultraviolet B (UVB)-induced skin damage. They studied a *Curcuma 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. Additionally, 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 matrix metalloproteinase-2 (MMP-2) expression induced by chronic UVB exposure.[14]

Agrawal and Kaur (2010) 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 seconds, 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 significantly faster healing time with the highest dose of curcumin EVs. Histopathological examinations further supported the protective properties of curcumin in elastic vehicles. The highest dose of curcumin in the elastic vehicle 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.[26]

Li et al. (2018) 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/cm2 for 3 consecutive days). Moreover, curcumin effectively promoted nuclear accumulation of NF-E2-related factor 2 (Nrf2) in the skin of hairless mice. The study suggests that curcumin has potential as an agent for preventing and/or treating acute inflammation and photoaging induced by UV radiation.[15]

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 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.[11]

In their study, Kusumawati et al. (2018) explored the anti-aging potential of C. 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 (TLC) 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 anti-aging effects of *Curcuma heyneana*. These findings underscore the presence of antioxidant compounds in *Curcuma heyneana*, highlighting its robust anti-aging properties and suggesting its potential application as a candidate for developing anti-aging drugs or as a phyto-cosmeceutical.[18]

Cho and colleagues (2018) explored the ethanolic extracts of Curcuma 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. Curcuma 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 DLE/CLE being on par with the standard drug. This investigation underscores the synergistic protective potential of the combination against UVB-triggered photodamage.[12]

Zheng and colleagues (2020) assessed the effectiveness of Curcuma longa rhizome-derived essential oil (CL-EO) in combating skin aging caused by ultraviolet B (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 anti-aging 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-1β 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 skincare products and cosmetics.[27]

Adusumilli and colleagues (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. Analysis also indicated decreased levels of p53 protein in the skin treated with curc-np. Furthermore, the study demonstrated lower levels of the IL-6 as inflammatory cytokine and higher levels of the 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.[19]

Hur and colleagues (2022) examined the effectiveness of a chlorin e6–curcumin conjugate, a photosensitizer made up of chlorin e6 (Ce6) and curcumin connected by 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&E staining and Masson's trichrome staining indicated a decrease in skin thickness and an increase in collagen fiber density. Overall, this treatment shows potential in delaying and enhancing the effects of skin aging induced by UV radiation..[13]

Conclusion

Curcumin, given orally or topically, was found to have photoprotective effect on UV-exposed skin. From this review, Curcumin is reported to attenuate the photoaging effect of UV irradiation especially in animal model. Curcumin can act as anti-oxidant, anti-inflammation, and anti-aging caused by UV exposure. Besides, Curcumin also can reduce epidermal thickness, wrinkles, inflammatory cytokines, and increase 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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Figure 1. PRISMA Diagram flow

Table 1. Reported outcomes of turmeric/curcumin application after UV irradiation

Authors	Country	Population	Methods	Outcomes
Sumiyoshi and Kimura[14]	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[26]	India	Laca mice	Topical curcumin elastic vesicles	• Macroscopic changes and lesion formation prevention • Recovery time reduction • Normal MDA levels restoration • The reduction of increased catalase activity
Li H., et al.[15]	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 H. S., et al.[11]	South Korea	SKH-1 hairless mice	Topical *C. zedoaria* extract	• Inhibition of wrinkle formation • Inhibition of COX-2 and MMP-13 expression
Kusumawati et al.[18]	Indonesia	IRC rats	Topical *C. heyneana* ethanolic extract	• Reduction of the epidermal thickness • Decreased sunburn cell (SBC) • Distance reduction between collagen • Increased fibroblast and elastic fibers

Cho BO, et al.[12]	South Korea	SHK-1 mice	Topical *Curcuma longa* extract	• Reversal of increased epidermal thickness • Reduced oxidative stress • Increased SOD activities and decreased MDA • Upregulate of Akt and Nrf2 activities. • Prevention of skin damage, collagen degradation and mast cells infiltration
Zheng Y., et al.[27]	China	Nude mice	Topical *Curcuma longa* essential oil (CL-EO)	• Decreased epidermal skin thickness • Reduced wrinkles • Better symptoms (rough skin, erythema, and edema) • Decreased IL-1β and TNF-α levels
Adusumilli NC. Et al.,[19]	USA	Balb/c mice	Topical curcumin nanoparticles (curcnp)	• Less erythema • Fewer sunburn cells and less dermal inflammatory infiltrate • Less p53 tumor suppressor • Lower expression of pro-inflammatory interleukin (IL)-6 • Higher expression of anti-inflammatory IL-10
Hur G-H, et al.[13]	Korea	SKH-1 mice	Chlorin e6–curcumin conjugate	• Reduced skin roughness • Attenuation of increased epidermal thickness

	• Attenuation of collagen loss

PROSPERO registry number: CRD42023391685.

Reporting guidelines:

This study has been reported as per the PRISMA reporting guidelines

Patient declaration of consent statement: None

Fill the PRISMA checklist given below:

Reporting guidelines for Review Articles (Systemic and Narrative review articles): PRISMA (2009)

A. Systematic Review and Meta-Analysis

Section/topic		**Checklist item**	**Yes/ No**
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes
ABSTRACT			
Structured summary	2	Provide a structured summary (IMRAD) including, as applicable: **Introduction**(objectives); **Methods**; (study eligibility criteria, participants, and interventions; study	No

		appraisal and synthesis methods); **results**; **Discussion** (limitations, conclusions and implications of key findings) **systematic review registration number (PROSPERO)**	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Yes
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Yes
METHODS			
Protocol and registration	5a	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number	Yes
	5b	Registration on PROSPERO (preferable)	Yes
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Yes
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Yes
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Yes
Study selection	9	State the process for selecting studies (i.e., screening, eligibility –inclusion/exclusion criteria, included in systematic review, and, if applicable, included in the meta-analysis).	Yes

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Yes
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Yes
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Yes
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Yes
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. (only for meta-analysis study)	No
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	No
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. (only for meta-analysis study)	No
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Yes

Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Yes
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). (only for meta-analysis study)	No
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. (only for meta-analysis study)	No
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency. (only for meta-analysis study)	No
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15). (only if meta-analysis was performed)	No
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). (only for meta-analysis study)	No
DISCUSSION			
Summary of evidence	24a	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Yes
	24b	Reporting the conflicting findings (from literature) and putting forth new ideas and/or new research directions	Yes

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Yes
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Yes
Citations	27	To cite from recent literature in the articles	Yes
FUNDING			
Funding	28	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review and the Grant number	No

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PRIMARY SOURCES

1	coek.info Internet	32 words — 1%
2	Byoung Ok Cho, Denis Nchang Che, Jae Young Shin, Hyun Ju Kang, Sang Jun Kim, Jiwon Choi, Sung Zoo Kim, Seon Il Jang. " Photoprotective properties of combined extracts from leaves and rhizomes against chronic UVB-induced photodamage ", Journal of Food Biochemistry, 2018 Crossref	31 words — 1%
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