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REVIEW

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Emerging therapeutic potential of curcumin in the management of dermatological diseases: an extensive review of drug and pharmacological activities

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Abstract

Background Curcumin is a bright colored polyphenolic moiety which is derived from the rhizomes of *Curcuma longa* of family *Zingiberaceae*. Its simple molecular structure, high efficacy, variable therapeutic effects and multidimensional use make it ideal for various treatment regimens.

Main body It has been used for centuries for its antioxidant, anti-inflammatory and antibacterial characteristics which makes it ideal in the determent and treatment of skin inflammation, psoriasis, acne, premature skin aging and skin cancers. It also exhibits antiviral, antiulcer, anticarcinogenic, antimutagenic, antibacterial, hypocholesteremia and antifungal, benefits making it a perfect multifunctional moiety for treating numerous disorders. Curcumin offers protection against skin damage induced by persistent UVB exposure. Curcumin has substantial therapeutic potentials against various skin conditions like anti-inflammatory, antioxidant effects, wound healing efficiency any many more. It illustrates a multiplicity of important medicinal properties which has a great potential in treating various dermatological diseases.

Conclusion The study seeks to provide a comprehensive update on curcumin and its exceptional medicinal profile, which can be efficaciously and appropriately utilized in treating skin conditions like psoriasis, acne, dermatitis, scleroderma, skin cancers, skin aging, fungal infections and wounds.

Keywords Skin, Curcumin, Psoriasis, Wound healing, Fungal infection, Cancers

Background

Turmeric (*Curcuma longa*) is a rhizomatous herbaceous perennial plant which belongs to the family *Zingiberaceae* and is known for its medicinal properties since ancient times. In India, it is extensively used as a home cure for a variety of ailments in Siddha, Ayurveda and Unani. In South East Asian nations, it is used as a coloring agent, spice, preservative and culinary ingredient.

Turmeric is being actively used for multiple conditions like liver disorders, jaundice, dyspepsia, flatulence, biliary disorders, urinary tract infections, burns and several other skin problems [1]. It is composed of around 300 different chemical components which includes terpenoids and phenolic constituents [2]. Diferuloylmethane or curcumin (75%), demethoxycurcumin (20%) and bisdemethoxycurcumin (5%) [3] are the naturally occurring curcuminoids present in turmeric. Curcumin is responsible for turmeric's vivid yellow color, and it is made up of curcumin I (94%), curcumin II (6%) and curcumin III (0.3%) [4].

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Curcumin (1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is a natural polyphenol which is lipophilic in nature (Fig. 1). Its simple molecular structure, high efficacy, variable therapeutic effects and multidimensional use make it ideal for various treatment regimens [5]. Curcumin interacts to several proteins and suppresses the action of kinases. It modulates the expression of several cytokines, enzymes and cell survival proteins by influencing the activation of different transcription factors [6].

It is well known for its wide range of therapeutic effects like antioxidant, anti-inflammatory, anticarcinogenic, antidiabetic, antibacterial, antifungal, antiprotozoal, antiviral, antiulcer and anticoagulant activities to name a few [7, 8]. The literature suggests that oral and topical use of turmeric helps in preventing and treating various skin diseases like premature aging, dermatitis, wounds, inflammation and psoriasis [9].

The human skin spreads over an area of about 20 square feet and is composed of tissue layer which safeguards the muscles and organs beneath. It protects, separates and shields the body from its surroundings, regulates body temperature and performs sensory tasks. Researches show that curcumin has substantial therapeutic potentials against various skin conditions like anti-inflammatory, antioxidant effects, wound healing efficiency any many more as shown in Figs. 2 and 3.

Table 1 shows some of the products of curcumin available in the market for the treatment of skin disorders. The study seeks to provide a comprehensive update on curcumin and its exceptional therapeutic activities which can be efficaciously and appropriately utilized in treating skin conditions.

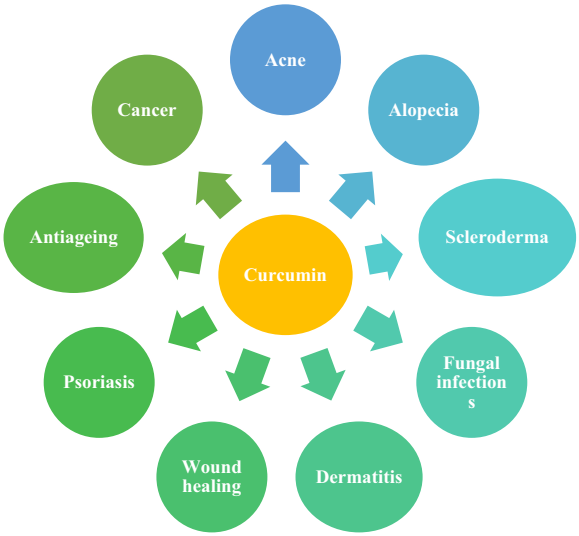

Fig. 2 Potential of curcumin in disorders of skin

Main text

Curcumin as an active antioxidant

The phenol and diketone moieties are potent free radical quenchers which are highly responsible for the antioxidant properties of curcumin [10]. The free radicals are generated when human skin is exposed to solar radiations, mechanical stress or chemical pollutants. These free radicals lead to skin damage, inflammation and in severe cases skin cancer. Researches shows that curcumin can improvise the systemic markers of oxidative stress markers [11] and can enhance the serum activities of various antioxidants like superoxide dismutase [12–14]. Curcumin acts on the harmful free radicals through various mechanisms It can regulate the activity of antioxidant enzymes like glutathione peroxidase, superoxide dismutase and catalase which actively neutralizes the free radicals [15, 16]. It can actively prohibit ROS generating enzymes like as lipoxygenase/cyclooxygenase and

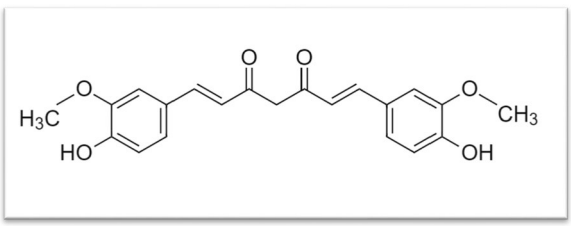

Fig. 1 Chemical structure of curcumin

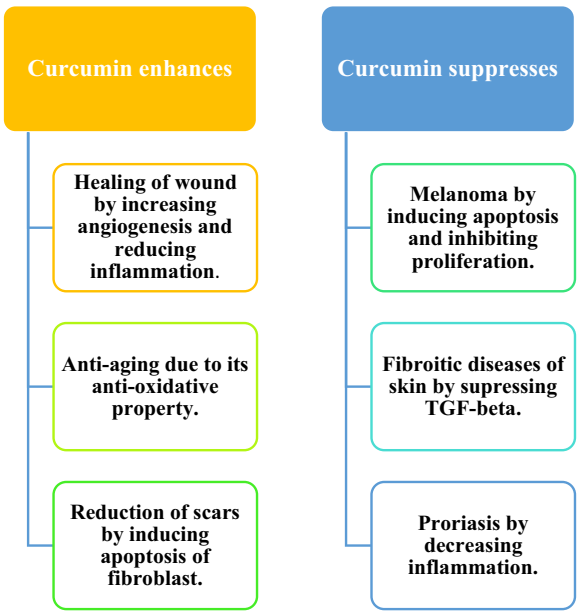

Fig. 3 Mechanism of actions of curcumin in skin disorders

Table 1 Commercial products of turmeric used for skin diseases

Brand name	Company	Benefits of the product
Turmeric extract	Ambe NS Agro	Antistress, skin whitening and replenishing
Bionatural turmeric root	Bioorganic concepts	Antioxidant and whitening agent
HerbEx extract	Biospectrum	Anti-inflammatory
Turmeric spot treatment	Cocokind	Acne and pimples
Vicco turmeric cream	Vicco	Blemishes, pimples and acne
Turmeric capsules	Naturemade	Antioxidant
Actiphyte turmeric	Lipotec	Antimicrobial
Turmeric oil	Gfn-selco	Antioxidant and soothing action
Turmeric capsules	Naturevibe botanicals	Immunity booster
Tegosoft OS	Evonik	Anti-aging
Dermalab extract	Dermalab	Anti-inflammatory

xanthine hydrogenase/oxidase [15]. Additionally, being lipophilic in nature, it is a chain breaking antioxidant as it can scavenge peroxyl radicals [17]. The literature-based evidences reveal that curcumin has a strong protective action against hydrogen peroxide-induced skin damage to the keratinocytes and fibroblasts [18].

Treatment for psoriasis

Psoriasis is a severe, persistent and multifactorial autoimmune disease which affects about 3% population of the world. It is caused by hereditary and immunological causes, and it has a significant impact on the skin and joints [19]. The T cell-mediated immunity leads to excessive hyperproliferation of the keratinocytes which results in inflammation, causing excessive cell buildup on the skin surface which rapidly forms inflamed and painful red patches and scales. The normal growth cycle of the skin cell takes approximately 28 to 30 days, but in a psoriasis the skin cells get matured and replaced in every 3–5 days, which results in scaling on the surface of the skin.

The beneficial effect of curcumin in psoriasis is due to its anti-inflammatory, immunomodulating and antioxidant activities. A study was conducted by taking different skin samples of untreated psoriatic patients, patients undergoing topical therapy and non-psoriatic subjects.

Reduced phosphorylase kinase level was found in the patients who were being given topical 1% curcumin alcoholic gel. It revealed that curcumin can suppress the activity of phosphorylase kinase which is responsible for the activation of NF-kB (NF-kB-nuclear factor kappa light chain enhancer of activated B cells) and thus constrain human psoriasis [20, 21]. Curcumin can suppress the exorbitant production of TNF-α (tumor necrotic factor alpha) through activated macrophages [22] and can block the TNF dependent activation of NF-κB by binding to the receptor-binding sites of TNF-α through covalent and non-covalent interactions [22, 23].

Jun Sun et al. demonstrated that daily dose of 1% curcumin gel can diminish imiquimod-induced skin psoriasis-like inflammation by blocking potassium channels expressed in T cells and lowering IL17A, IL17F, IL22 (interleukins) and other pro-inflammatory cytokines in mouse ear samples [24]. Kang et al. in research showed that oral administration of curcumin for 20 days in mice like psoriasis model can reduce generation of T cell inflammatory factors like IL-17, IL-22, IFN-γ, IL-2, IL-8 and TNF-α by 30–60% [25].

Bahraini et al. did a study with forty patients who had scalp psoriasis, and it was inferred that in comparison with the placebo, daily administration of turmeric tonic reduced cutaneous symptoms like scaling, erythema, lesions and also enhanced the patients' quality of life [26].

Antiga et al. in a clinical trial reported that (oral curcumin) Meriva which was a novel lecithin-based delivery system of curcumin was effective as an adjuvant therapy in treating psoriasis vulgaris and was also found to reduce the serum levels of IL-22 [27].

Sun et al. (2017) investigated the effects of curcumin (dose: 0.25 mg/day) and tacrolimus formulations (dose: 0.1 mg/day) on the psoriasis-like mouse model. Their findings revealed that tacrolimus and 50 nm Curcumin nanoparticles gel reduced the thickness of white scales and the pink coloration in inflamed skin [28].

A clinical study confirmed that administration of oral curcumin is efficacious in plaque psoriasis and has an exceptional safety profile [29].

Bilia et al. in a randomized, placebo controlled, double-blind clinical trial affirmed that curcumin-loaded nanoparticles along with oral acitretin are effective in

treating moderate-to-severe psoriasis and improve the lipid serum profile of the psoriatic patients [30].

A study suggested that administration of nanostructured lipid carriers of curcumin and caffeine topically can significantly treat psoriasis and the combination has a great potential in treating psoriasis locally [31]. In a recent study, Jin et al. used smart pearls technology in combination with glycyrrhizic acid to enhance the permeation and anti-psoriatic activity of curcumin in an imiquimod-induced psoriasiform mice. Smart Pearls are a dermal delivery system for poorly soluble active agents, containing nanoporous silica particles loaded with amorphous active agents to increase bioavailability [32].

Curcumin in acne

The cutaneous and long-term disease of skin is acne which occurs when oil and dead cells of the skin clog the follicles of hair which results in abnormal production of sebum. There are several factors that play a prominent role in the generation and pathophysiology of acne, but the major factors are genetics, inflammation, hyperproliferation of follicles, infection by *Propionibacterium acnes* and sebaceous glands producing sebum in excess amount [31, 33]. Genes such as CYP1A1, interleukins (IL-1α) and tumor necrosis factor (TNF-α) when varied contribute to the development of acne. Lesions formed due to acne can be classified as inflammatory or non-inflammatory, and these lesions affect parts of chest and back but the major area of infection is face. For the treatment of acne, mostly antibiotics are prescribed but they are associated with adverse effects and sometimes also develops resistance. The resistance of *Propionibacterium acnes* to therapies of antibiotics has steadily increased in recent years, with increasing resistance to clindamycin and erythromycin [34, 35]. Thus, there is a need of developing novel herbal therapies to treat this infection that are devoid of these drawbacks. Due to its wide safety profile and uses, curcumin's antimicrobial activity has been extensively being studied even at high doses in the clinical trials [36].

The antimicrobial and anti-inflammatory properties of curcumin make it a good candidate for treating acne. In a study, microemulsion of curcumin containing myristic acid was formulated which delivered curcumin in less duration and was able to inhibit bacteria (*S. epidermidis*) responsible for acne [37]. In another study, lauric acid-based emulsion incorporating curcumin was developed which was able to inhibit *Propionibacterium acnes. Also,* the smaller size of the emulsion increased its contact and penetration into the membrane of cells [38].

Rajanikant and Jagetia developed a formulation containing curcumin (100 mg/kg) and used mouse skin as a model for in vivo studies for 20 days. Curcumin antioxidant properties reduced the peroxidation of lipids, increased the concentration of glutathione and enhanced the activity of the enzyme superoxide dismutase and glutathione peroxidase in the skin. Thus, improving the condition of acne [39].

A dose-dependent, in vitro microbicide activity against both *Propionibacterium acnes* and *Staphylococcus aureus* was obtained with curcumin activated by blue light. This may be due to the action of vanillin (product obtained by photolytic degradation of curcumin) which disrupted the membrane of the bacterial cell [40].

Potential against scleroderma

The disease of connective tissue which results in fibrosis and vasculopathy of organs and skin is called scleroderma [41]. Scleroderma may be due to increased production of extracellular matrix (ECM) vascular abnormalities and fibrosis [42]. It has been discovered that the oxidative stress has significant role in disease development [43]. Many studies have confirmed that scleroderma patients have increased free radical content, such as peroxynitrite and hydroxyl radicals, and the 8-isoprostane levels in serum increases [44]. In addition, mice treated with free radical release agents demonstrate cutaneous fibrosis [45]. Thus, many diseases of skin can be related to oxidative stress, leading to inflammatory diseases. Scleroderma features include immune system activation and inflammatory cells perivascular infiltration, and thus, for treatment, immune-suppression can be taken into consideration [46]. Scleroderma hallmark is ECM accumulation in excessive amount which induces inflammation [47, 48]. When ECM of the tissues is disrupted, it can initiate and propagate the inflammation which liberate ECM molecules like sulfated proteoglycans, tenascins and hyaluronan fragments. These molecules result in triggering and amplification of inflammation and acts as 'alarmins' [45].

Curcumin has the anti-fibrosis effect, characterized by formation of keloid, production of ECM in fibrosis and reduced deposition of collagen [49]. In scleroderma, significant role is played by isoforms of protein kinase C (PKC), i.e., ε and δ. A study with the administration of curcumin, done in vitro and in vivo, found that fibrosis and accumulation of ECM reduced due to decline in the PKC δ levels [50]. Nuclear factor κ-light-chain-enhancer of activated B cells (NF-κB) and cytokines responsible for fibrosis and angiogenesis are abnormally regulated [21]. In scleroderma lung fibroblasts (SLF), curcumin induces HO-1 and GST P1 which inhibits protein kinase C epsilon (PKCε), thus inducing apoptosis. Curcumin was also able to modulate cascade of TGF-β by inhibiting decline of TGIF (TGF-β induced factor) [51]. Another research indicated that curcumin may have a beneficial impact in scleroderma care as it may provide protection to rats

from lung fibrosis caused due to numerous agents [52]. This shows that curcumin has a potential role in the scleroderma treatment, but ample work is also required.

Anti-inflammatory and wound healing effect of curcumin

Stimuli like irritants and pathogens make the defense mechanism of the body to act and involve molecular mediators, blood vessels and immune cells, resulting in inflammation (acute and chronic). Inflammation signs include heat, swelling, immobility, redness and pain. The immunoregulatory responses and inflammation of skin are due to several factors like mitogen-activated protein kinase (MAPK), c-Jun NH2-terminal kinase, NF-κB activation, IL-1, IL-6, IL-8, IL-10 and IL-21 induced by TNF-α and cytokines. Cytokine receptors alteration, cytokines dysregulation and cytokines overproduction are associated with disorders of skin inflammation.

The anti-inflammatory properties of curcumin have been unambiguously identified in various organs, such as the skin and liver, by modulating autoimmune disease and preventing damage to the tissues of the organs [53, 54]. Curcumin reduces the expression of the two principal cytokines—TNF-α and IL-1 produced by macrophages and monocytes, and thus helps in modulating inflammation [3, 25]. NF-κB (transcriptional pro-inflammatory factor) is also inhibited by curcumin. This regulates genes responsible for response of inflammation. The anti-inflammatory activities of curcumin may be used to regulate skin inflammation caused by various skin diseases. In a study conducted ex vivo and in vitro, to avoid bovine serum albumin denaturation, the anti-inflammatory activities of curcumin nanospheres and curcumin were investigated and compared with diclofenac sodium. Curcumin nanospheres showed highest anti-inflammatory activity in the in vitro test [55].

Skin is an important, environmental-protective organ for the body. Chronic skin injuries allow the body to begin a complex and multistep healing process to restore the integrity of the tissue. These processes include remodeling, proliferation, inflammation and homeostasis [56, 57]. After injury, clot is formed due to platelet aggregation. Inflammation starts at the site of injury due to migration of macrophages and neutrophils at wound location. They promote the migration of fibroblast at the wound site which starts blood vessels generation and re-epithelialization. This phase is called proliferation, and collagen plays a major role in that [58, 59]. Wound healing final step is scar tissue formation and remodeling of collagen. Neutrophils is attracted to the site of injury which releases IL-1 and TNF-α [55]. The phase of inflammation is prolonged due to increased level of reactive oxygen species and destructive proteases associated with neutrophils in the area of wound, and this delays the healing of wound [60, 61].

The anti-infective, anti-inflammatory and antioxidant properties of curcumin play a significant role in healing of wound [3, 58]. In order to improve the rate of healing of wound, curcumin topical application showed facilitation of re-epithelialization in areas of burn wound [59, 62]. Various clinical trials showed that curcumin improved the healing of wound, increased cuticular layer thickness and epidermal growth rate in comparison with the subjects untreated [63–66].

Another study on rat skin showed that curcumin when applied topically improved the healing of burn wound, enhanced epithelialization, formation of granulation tissue, angiogenesis in comparison with control group [59]. In research, nanovesicles of curcumin were prepared and studied in both in vitro and in vivo which helped in the prevention of skin lesions formation and damage of epithelia by inhibiting the biochemical process [63]. The nanovesicles also increased the penetration of curcumin into the skin.

Active antifungal agent

In general, fungal infections occurring in humans in mostly tropical and subtropical areas are more conducive to the growth and spread of fungi [67]. They posed a persistent and real danger to the lives of humans at this period. Healthy people are helpless against numerous systemic infections, subcutaneous, cutaneous and superficial infections that can change from specific conditions to serious dangerous diseases threatening to life [64, 65]. Dermatophytes are majorly responsible for fungal infections of nails, hair and skin. Candida species are also responsible for infections that further persuade to deep tissues and may be threatening to life [68]. Continuous improvement is made in treating skin-related fungal infections with treatment, but they remain difficult to manage. In general, traditional formulations (shampoo, spray, cream) do not cause any adverse effects, although sometimes causes little redness, burning or itching, while oral medications may lead to several side effects. Researchers have been investigating the use of many herbs that can be used effectively as potent antifungal agents.

It is stated from studies that curcumin has significant antimicrobial activity against parasites, viruses, fungi and bacteria. The fungal inhibitory activity of curcumin (0.8 g/L) was shown in a study of plant tissue culture [69]. Curcumin antifungal activity is shown by its action against C-5 sterol desaturase and ergosterol inhibiting activity by producing reactive oxygen species and thus shows prominent activity toward *Paracoccidioides brasiliensis* [70, 71]. Curcumin also modifies the ATPase

movement properties and decreases proteinase emission, contributing its antifungal activity [72]. It was found responsible for the inhibition of the candida species, as it inhibits H + extrusion and provides acidic environment [73]. Curcumin's anti-inflammatory effects have rendered it the most effective agent for candidiasis treatment. It was able to inhibit fungi growth in mice more than that of dexamethasone administered orally [74]. Curcumin with photodynamic treatment was confirmed as a viable technique for antifungal activity against the yeasts' planktonic form [75]. The problem of development of resistance is occurring with already available antifungals, and thus, combined treatment is the medical endeavor to remedy the current condition and eradicate the fungal infection altogether. It provides synergistic action, fewer resistance, low toxicity and broad spectrum [76]. Curcumin when used along with miconazole, fluconazole, ketoconazole, voriconazole and itraconazole showed higher potency against fungi. Similar affect was observed with nystatin and amphotericin. The minimum inhibitory concentration against candida was reduced when curcumin was used with ascorbic acid [77]. Table 2 shows the efficacy of Curcumin as an active antifungal agent.

Protection against skin cancer

Skin cancer is a condition in which the skin outer layers show cells malignant in nature. Skin cancer is classified into two types, i.e., melanoma and non-melanoma. In melanoma cancer, melanocytes are involved, whereas in case of non-melanoma, squamous or basal cells are involved. Majority of skin cancers are categorized as non-melanoma [78]. The interaction between the environment and genes is responsible for skin cancer. The main cause of the cancer in skin is sun exposure but genetic factor also plays a crucial role in the occurrence of the cancer. Some other factors which contribute to the skin cancer are arsenic exposure, trauma and X-rays [79].

Studies have shown that expression of cytokine can promote melanoma cell metastasis and growth. It is reported in a study that more than 80 percent of cell lines of human melanoma contain osteopontin, growth factor AA derived from platelet, vascular endothelial growth factor, interleukins—1α,6,8, transforming growth factor β and cytokines in excessive amount that stimulates angiogenesis, invasion and tumor development [80].

A study conducted in vitro with curcumin (dose ranging from 5-50 μm) on the cell lines of fibroblast of lungs (MRC-5) and cell lines of melanoma (M14, MV3, A375) showed that as the curcumin concentration increased, melanoma cells viability decreased. Curcumin was found responsible for triggering of melanocytes apoptosis as it suppressed NF-κB activation and proliferation. It also suppressed expression of myeloid cell leukemia-1 and protein of B cell lymphoma (Bcl-2). The induction of apoptosis by curcumin was confirmed by the increase in ratio of t-bax to Bcl-2. Thus, curcumin was able to provide relief in the antitumor activity by inducing apoptosis [81]

Jose et al. [82] formulated liposomes of 1,2-dioleoyl-3-trimethylammonium-propane in which curcumin was encapsulated along with small interfering RNA transcription 3 activators and signal transducers. This combination was able to inhibit the weight of tumor and progress in its volume in melanoma-based animal model in comparison with alone small interfering RNA transcription 3 activators and curcumin liposome.

Tsai et al. [83] demonstrated in his study that curcumin can provide protection against UVB radiation-induced skin cancer growth in a mouse model. Li et al. [84] illustrated that curcumin has a chemoprotective potential against skin carcinogenesis in vivo and in vitro.

Table 2 Curcumin efficacy as an antifungal

S. no	Findings of study	Fungal agents used in the study	References
1	Curcumin showed 250–2000 μg/mL range of MIC along with fungicidal action toward species of *candida*	Ten clinical isolates, four strains of ATCC and 14 *candida* strains	[72]
2	Photodynamic therapy along with curcumin (40 μM) was utilized in the study. It was able to inhibit 85 percent of the *candida species* activity and also led to reduction of biomass of the biofilm of all the three fungal agents	*C. tropicalis, C. glabrata, C. albicans*	[75]
3	Curcumin was administered orally in BALB/c mice in a study done in vivo. It was found more effective in the reduction of fungal infection in comparison with dexamethasone	Oropharyngeal candidiasis	[74]
4	Curcumin was able to show high efficacy and inhibitory action toward these agents	Clinical isolate, fluconazole-resistant strains and 38 strains of *Candida*	[72]
5	Curcumin was used along with fluconazole which was able to produce a synergistic action and in vitro studies found that it was highly active against *C. albicans*	*C. albicans* (Clinically-resistant Isolate)	[100]
6	Cell wall inhibitory agents and curcumin was used which produced a high synergistic action against the cell wall of the fungi leading to its disruption	*C. albicans*	[65]

In carcinogenesis of skin, crucial role is played by oxidative stress. Oxidative cell stress is generated by free radicals produced by activation of oxygen. These free radicals are produced mainly by chemicals and UV light. Thus, curcumin which has an antioxidant property may be used as an important chemo-preventive agent for carcinogenesis of the skin of the mouse [85]. The ability of curcumin to inhibit cancer of skin can be justified by this data and thus can be used as an adjuvant therapy in its treatment.

Anti-aging property

Continuous exposure of the skin to ultraviolet radiations, i.e., UV either from sunlight or any other artificial source, can lead to premature aging of the skin which is called as 'photoaging' and can alter the normal skin structure.

The antioxidant and anti-inflammatory action of curcumin helps it in averting the premature aging of the skin. It can protect the skin partially against UV deterioration which reduces the chance of skin tumors development thereby preventing premature aging. [86].

A clinical study evaluated the usefulness and efficiency of an herbal gel (Tricutan®) which was a combination of gotu kola, rosemary and turmeric on 28 women who were in there 30's. The study revealed that using the herbal gel for four weeks can significantly ameliorate the signs of photoaging and skin firmness [9].

A molecular-based biology study illustrated inhibitory effects of curcumin on UVB-induced generation of reactive oxygen species (ROS) and in vitro expression of matrix metalloproteinase (MMP) by inhibiting the activation UVB-induce of nuclear factor-κB (NF-κB), mitogen-activated protein kinase and AP-1 transcription factor signal pathways [87]. Thus, curcumin can be helpful in treating photoaging.

Curcumin in atopic dermatitis

Atopic dermatitis is a chronic disease of skin with a still unclear etiology and stems from a complex combination of factors like immunity, environment and genetics [88]. Infants are likely to be affected along which it is highly prevalent in adults as well [89]. Pathogenesis of atopic dermatitis critically includes an imbalance in the subsets of T cell. Cytokines such as IL-31,13,5,3 are abnormally reduced by Th2 in the initial stage, whereas this response switches over to Th1 type-immune response in the later stages, along with an intense increase in IL-18,12,6,1 and TNF α by monocytes [90]. Curcumin has historically been used in the countries of Asia to treat symptoms of atopic dermatitis [91].

Curcuma longa is used to isolate *p*-hydroxycinnamic acid (a phytocomponent) which inhibits the activation of T cell by modulating the pathway of PKCθ (protein kinase C theta) [20]. When *p*-hydroxycinnamic acid was administered in a model study of animals, it was observed that the keratinocytes produced reduced number of cytokines both in vitro and tissues of ear. This led to improvement in inflammation and thickening of epidermal layer [93].

In patients 150 patients of eczema, Herbavate® (an herbal cream) along with *C. longa* when used daily shows significant alleviation of itching, thickening, scaling and erythema assessed by a 4-point score weekly ($p < 0.001$). Safety profile was also good, as only 5 patients reported side effects, there was no local intolerance and no patient showed adverse events [94].

Some reports showed contact urticaria and dermatitis after the application of cream containing curcumin topically [95–97]. Thus, there is a need to establish more trial study to investigate the curcumin role in the management of atopic dermatitis.

Potential activity in iatrogenic dermatitis

Iatrogenic dermatitis includes a number of conditions of skin inflammation which can be directly linked to medical procedures and the administration of drugs. For instance, radiation-induced dermatitis and allergic contact dermatitis fall under this category. Various studies demonstrate the efficacy of curcumin for the prophylaxis of iatrogenic dermatitis. In a model, curcumin when applied topically shows significant improvement in recovery of epithelial cell and irradiated skin, due to its anti-inflammatory activity [98].

A randomized study that assessed curcumin (administered orally 6 g/day) in patients of breast cancer ($n = 30$) while undergoing sessions of radiotherapy shows a significant reduction in the severity of dermatitis induced by radiations [49, 99]. When 4 g/day of curcumin was administered in the patients of cancer ($n = 40$) undergoing under capecitabine treatment, curcumin was found to prevent the syndrome of hand–foot induced by capecitabine. However, the mechanism for this action of curcumin was not elucidated fully [82, 91, 92].

In another study, 1 g of curcumin when administered orally daily along with piperine for the period of four weeks in 46 patients, symptoms of chronic pruritus induced by sulfur mustard was improved. Due to the curcumin antioxidant properties, the levels and activities of catalase, glutathione, superoxide dismutase in serum along with levels of markers of inflammation were reduced [9].

Conclusion

Curcumin illustrates a multiplicity of important medicinal properties which has a great potential in treating various dermatological diseases. The clinical studies cited in the article reveal that curcumin has an exceptional

anti-inflammatory, antioxidant and antibacterial activities, which can be efficaciously and appropriately utilized in treating skin conditions like psoriasis, acne, dermatitis, scleroderma, skin cancers, skin aging, fungal infections and wounds.

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Author contributions
BK contributed to conceptualization, methodology, writing—original draft, writing—review and editing, and visualization; RA was involved in writing—original draft, and writing—review and editing. UP contributed to writing—original draft, and writing—review and editing. PKS was involved in supervision and review. All authors gave their individual critical revision and final approval of the version to be submitted.

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Availability of data and materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
The authors declare no conflict of interest.

Competing interests
The authors declare that they have no competing interests.

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