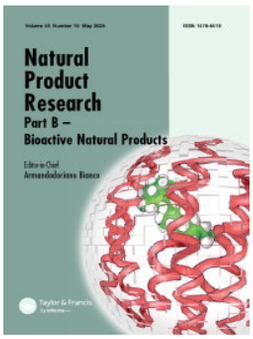

Natural Product Research

Formerly Natural Product Letters

ISSN: 1478-6419 (Print) 1478-6427 (Online) Journal homepage: www.tandfonline.com/journals/gnpl20

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To cite this article: Rajesh Sreedharan Nair , Nashiru Billa , Ajay Babu Pazhayattil , Sarath Chandran C. , Mohammed Tahir Ansari , Kai Bin Liew & Andrew P. Morris (10 May 2026): Enhancing the therapeutic efficacy of curcumin in topical applications through nanoformulations, Natural Product Research, DOI: 10.1080/14786419.2026.2669679

To link to this article: https://doi.org/10.1080/14786419.2026.2669679

Published online: 10 May 2026.

NATURAL PRODUCT RESEARCH
https://doi.org/10.1080/14786419.2026.2669679

Enhancing the therapeutic efficacy of curcumin in topical applications through nanoformulations

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ABSTRACT

Curcumin, one of the prominent curcuminoids present in turmeric, possesses significant value in the pharmaceutical industry owing to its diverse array of pharmacological activities, including antimicrobial, anti-inflammatory, antiviral, antioxidant, and anti-cancer properties. Traditionally used for mild skin conditions, curcumin has recently shown significant potential in treating dermatological cancers and promoting wound healing. However, it has poor dermal absorption due to low solubility and limited skin permeation. Applying appropriate formulation strategies appears to be gaining traction as a means to harness its full therapeutic value. In this regard, nano formulations of curcumin have proven useful in managing certain skin conditions. This review focuses on the topical applications of various curcumin nanoformulations, with a particular emphasis on wound healing and anti-skin cancer effects. We analyze the reported in vitro and in vivo studies of commonly used curcumin nanoformulations in this area and comprehensively discuss various formulation approaches to achieve optimum therapeutic efficacy.

ARTICLE HISTORY
Received 9 October 2025
Accepted 1 May 2026

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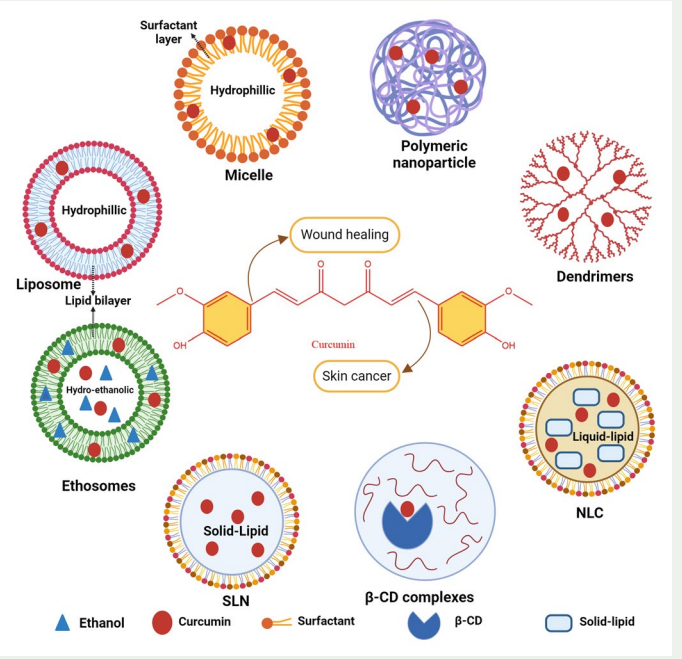

1. Introduction

1.1. Curcumin chemistry and pharmacology

Curcumin is a yellow phenolic compound present in the rhizome of turmeric (*Curcuma longa* Linn) used for centuries in Indian and Chinese cuisines (Naksuriya et al. 2014). The main chemical constituents termed 'curcuminoids', are curcumin [(1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-dione)], desmethoxycurcumin and bis-desmethoxycurcumin. The content of curcumin in turmeric varies between 2% to 5% of the total turmeric mass and constitutes approximately 77% of the curcuminoid content. Curcumin exhibits medicinal properties, including anti-inflammatory, anti-microbial, antioxidant, anti-cancer, and antidiabetic effects (Hewlings and Kalman 2017). Furthermore, curcumin has also been found to possess cardioprotective, neuroprotective, nephroprotective, hepatoprotective and wound healing activities (Akbik et al. 2014). Several preclinical and clinical studies have shown that curcumin is safe even at high doses and a Phase -I trial report that a dose of 12 g/day is very well tolerated (Shoba et al. 1998). Despite having an extensive spectrum of pharmacological actives curcumin suffers from poor systemic availability, necessitating some formulation intervention for optimal activity (Yallapu et al. 2012).

1.2. Wound healing properties

A typical healing agent protects would against invading microorganisms, reduces inflammation at the wound site, induces cell proliferation and helps regain tissue structure. The anti-inflammatory, anti-infectious, and anti-oxidant properties of

curcumin are thought to be responsible for its wound healing capacity (Sun et al. 2012). The activation of fibroblasts at the wound surface is essential in the remodelling process, and studies report the movement of fibroblasts to the wound site following treatment with curcumin (Mohanty et al. 2012). Curcumin regulates the production and alignment of collagen fibres, ensuring balanced scar formation (Figure 1). The collagen content of wounds in rats treated with curcumin loaded chitosan-alginate sponge increased and was compact compared to controls (Dai et al. 2009).

1.3. Curcumin as anti-skin cancer agent

Curcumin has shown significant success in the prevention and the treatment of various types of skin cancers (Esmaeli and Dehabadi 2026). The three prevalent types of skin cancer are melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) (Figure 2). Curcumin hinders cell multiplication, metastasis and promotes apoptosis on cancer cells (Kah et al. 2023). Its anticancer effect may be achieved through different pathways by regulating inflammatory modulators (interleukins), tumour necrosis factors (TNF- α), epidermal growth factors (EGF), and transcription factors (STAT 3) (Bar-Sela et al. 2010). A key indication of curcumin against melanoma is based on its arrest of cell cycle at G2/M phase and induction of apoptosis by downregulating the nuclear factor-kB (NF-kB). Studies further support curcumin's anti-melanoma activity at concentrations about 6.1–7.7 mM (Nabavi et al. 2018).

2. Pharmacokinetics of curcumin

Pharmacokinetic studies of curcumin have revealed that poor absorption and rapid elimination contribute to its low bioavailability. Curcumin has poor aqueous solubility and it is sensitive to a high pH and light. Curcumin degrades rapidly in alkaline media with reports showing a pH-dependent degradation which occurs quickly at

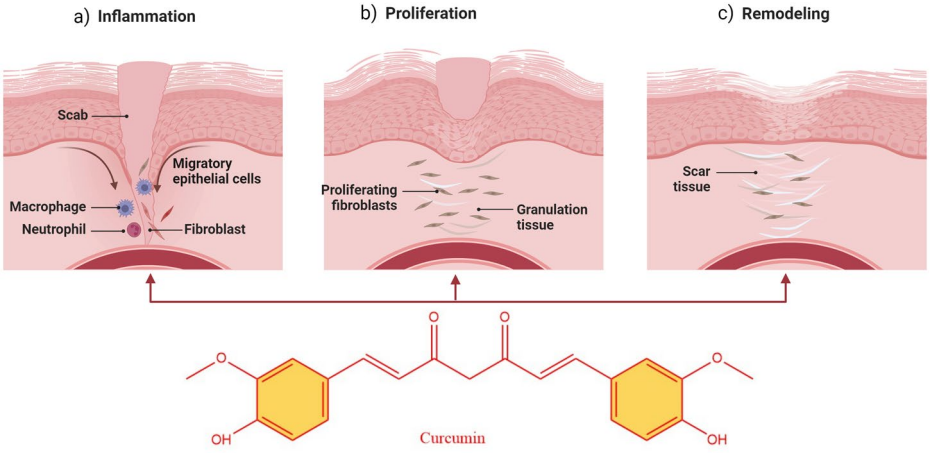

Figure 1. The effect of curcumin on the inflammation (a), proliferation (b), and remodelling stages of the wound healing process, produced using biorender.com.

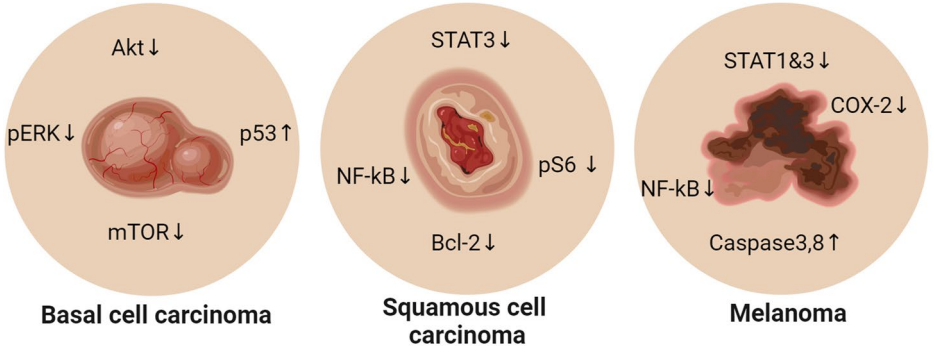

Figure 2. Regulation of multiple signalling pathways by curcumin against most common skin cancers (↑: upregulation; ↓: downregulation), produced using biorender.com.

neutral to alkaline conditions (Wang et al. 1997). The conjugated diene structure of curcumin may be responsible of its greater stability in acidic conditions. However, in alkaline condition, deprotonation from the phenolic group destabilises its structure leading to degradation [trans-6-(4'-hydroxy-3'-methoxyphenyl)-2,4-dioxo-5-hexanal, ferulic acid, vanillin and feruloylmethane] (Sharma et al. 2005). Curcumin is predominantly metabolised by conjugation and reduction. Upon oral administration, it is conjugated to glucuronides and sulphates, however systemic administration causes reduction to tetrahydrocurcumin, hexahydrocurcumin and octahydrocurcumin (Shen and Ji 2012). The majority of the dose was excreted in the faeces, and only a small amount was recovered in the urine. Blood plasma analysis revealed low plasma concentrations, a finding that was further supported by other studies. 400 mg oral dose of curcumin to rats resulted in non-detectable levels in the heart blood, and traces detected in portal blood. Up to 38% of administered dose was recovered in the gut after 24 h (Ravindranath and Chandrasekhara 1980).

2.1. Bioavailability enhancement techniques for curcumin

On co-administering curcumin with piperine (20 mg/kg), its bioavailability increased by more than 150% in rats. Similar observations were made in humans, with undetectable serum levels when curcumin was administered alone, but considerably higher bioavailability (>2000%) when co-administered with piperine (Shoba, et al. 1998). Patients with adenomatous polyposis receiving 480 mg oral dose of curcumin with 20 mg of quercetin registered a 50% decrease in polyp size (Cruz–Correa et al. 2006). The extensive angiogenesis in cancer tissues may form imperfect vascular structures and impair lymphatic drainage with the increased production of many permeability mediators. All of these abnormal changes can enhance the macromolecular or fluid transport to tissues, known as the 'enhanced permeability and retention effect (EPR) (Maeda et al. 2000). Nano-drug delivery systems can prolong retention of encapsulated therapeutic agent in systemic circulation and concentrate in tumour *via* the EPR effect, thus applicable for enhancing the bioavailability of curcumin and reducing rapid metabolism (Sreedharan Nair et al. 2025).

3. Curcumin nanoformulations for enhanced anti-skin cancer and wound healing activity

Nanoparticulate delivery systems are typically about 100 nm, although larger particles may still be categorised as nanoparticles (De Jong and Borm 2008). The carriers are typically made of biocompatible materials such as lipids or polymers, can encapsulate various active ingredients, including vitamins, antioxidants, and drugs (Fairuz et al. 2022). On application to the skin, nanocarriers enhance the skin penetration, allowing

Table 1. Formulation techniques, composition and the key charateristics of commonly used curcumin nanoformulations developed for topical applications.

Delivey system	Method of preparation & composition	Size	ZP	References
Deformable liposomes	Hydration of lipid film: DPPC,chloroform,methanol.	110–130 nm	−6 to −16mV	(Campani et al. 2020)
Ethosomes	Modified thin-film hydration: SPC,cholesterol,tween 80.	67 nm	−87.3 mV	(Nair et al. 2022)
Transferosomes	Thin film hydration and extrusion: Phosphatidylcholine, Sodium cholate, Tween 80, Labrasol, Transcutol, limonene and oleic acid.	150 to 342 nm	−5 to −28Mv	(Abdel-Hafez et al. 2018)
Transethosomes	Thin film hydration followed by sonication: Soybean phosphatidylcholine, Tween 80	109 to 115 nm	−5 to −7 mV	(Rezigue, et al. 2025)
Chitosan NPs	Ionic gelation technique: Chitosan,TPP, dilute acetic acid solution.	167–252 nm	+18.0 to + 20.0 mV	(Nair et al. 2019)
Nano-invasomal gel	Mechanical dispersion followed by sonication: Nerolidol, SPC, Carbopol 934.	98 – 335 nm	_	(Kumar et al. 2022)
Nanoemulsion loaded hydrogel	Low-energy emulsification: Eucalyptus oil, Tea tree oil, Labrafac PG, Capryol 90, Transcutol HP, Tween 80, Cremophor EL, carbopol 934.	11 nm	−19 mV	(Algahtani et al. 2020)
Hyaluronic Acid Micelles	Amide reaction technique: Hyaluronic acid, Octadecylamine, N-hydroxysuccinimide, dimethylformamide	165 nm	−27 mV	(Niu et al. 2022)
Nanosuspensions	Solvent-antisolvent precipitation technique: Acetone, HPMC	147 – 734 nm	−24 to −29 mV	(Shi et al. 2020)
Niosomes	Thin-film hydration technique: Span 20, Tween 20, cholesterol	384–444 nm	−9.3 mV	(Akbari, et al. 2020)
Invasomes	Dispersion technique: Phospholipid, ethanol, terpene	302 ± 1.5 nm	−12.5 mV	(Kumar and Sahoo 2023)
SLN	Emulsion-solvent evaporation technique: Ceramide 2, Glyceryl monostearate, stearic acid, palmitic acid and Tween 80	102–156 nm	− 20 to − 38 mV	(Gaur et al. 2016)
NLC	Colloidal dispersion of oil and water phase followed by high shear homogenisation. Solid lipid (Compritol® 888ATO and Precirol® ATO 5), liquid lipid (Labrasol®), Pluronic® F-127, Tween® 80).	112–214 nm	− 4 to − 38 mV	(Espinosa-Olivares et al. 2020)
Microemulsion	Acid hydrolysis of the bleached fibres: Cetyltrimethylammonium bromide, Oleic acid, limonene, Cremophor RH 40, Transcutol P.	150 nm	−60 mV	(Zainuddin et al. 2021)
Dendrimeric micelles	Conjugation of PAMAM dendrimers with histidine-arginine dipeptides and cholesterol	372–386 nm	+29 to +31 mV	(Thuy, et al. 2022)

DPPC: 1,2-dipalmitoyl-sn-glycero-3-phosphocholine; HPMC: Hydroxypropyl methylcellulose; NPs: Nanoparticles; PAMAM: Polyamidoamine; PEG: Polyethylene glycol; SPC: Soya Phosphatidylcholine; TPP: Sodium tripolyphosphate.

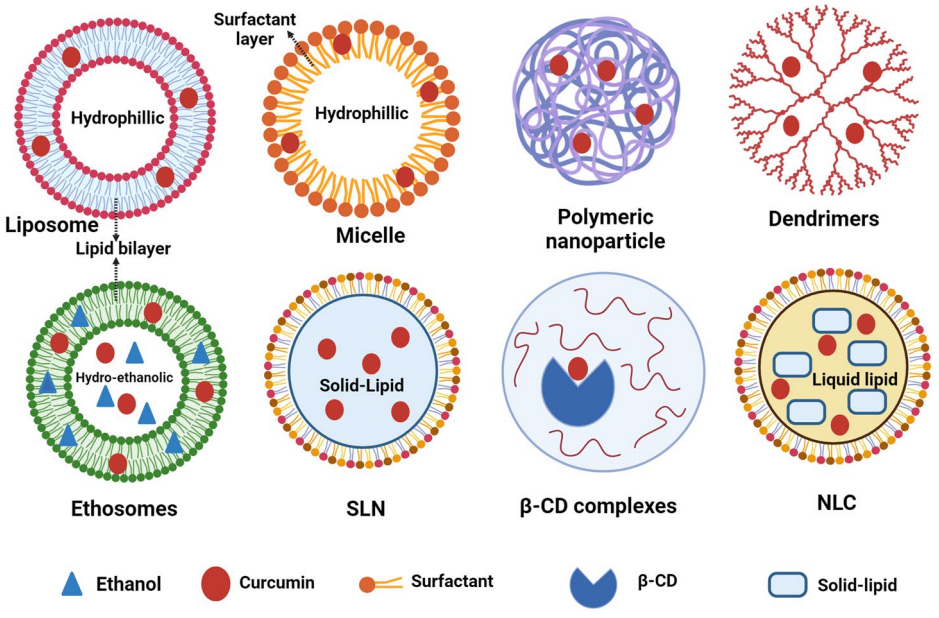

Figure 3. Curcumin encapsulated nanocarriers for superior bioavailabilty and targeted drug delivery (created using biorender.com).

for targeted and controlled release at the affected region. Due to their tiny size, nanocarriers enables them to traverse the skin's barrier more efficiently, ensuring deeper and more effective delivery of therapeutic agents (Manickam et al. 2019). Curcumin nanoformulations show considerable promise for promoting health in both humans and animals, demonstrating strong safety profiles and minimal toxicity even with repeated administration. Topical nanoformulations enable targeted delivery of curcumin to wound sites, thereby enhancing its therapeutic efficacy and antimicrobial activity (Salehi et al. 2021). Nanocarriers commonly employed in skin applications include polymeric nanoparticles, liposomes, ethosomes, transferosomes, transethosomes, niosomes, micelles dendrimers, solid-lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) (Figure 3).

3.1. Liposomes

Liposomes are spherical vesicles containing phospholipids and cholesterol as the major ingredients (Liakopoulou et al. 2025). On application to the skin, liposomes may exert their local or systemic actions. Liposomes can be used for targeted drug delivery to the skin appendages, particularly the pilosebaceous structures in treating hair follicle-associated disorders (El Maghraby et al. 2008). The anti-neoplastic effect of curcumin-containing liposomes made from soybean and egg-yolk phospholipids in rats showed a 2-fold increase in cumulative permeation than curcumin solution, with superior anti-inflammatory effects compared to pure curcumin (Basnet et al. 2012). Kianwash et al. developed liposomes containing curcumin and propylene glycol (Cu-PG) and evaluated their wound healing efficacy in rats with burn injuries. A

concentration of 0.3% Cu-PG liposome (Cu-PGL) was found to be effective in treating burns without causing any adverse effects. Application of Cu-PGL on burned rat skin resulted in significant improvement in wound healing, with a notable reduction in wound size after 18 days, compared to control. The Cu-PGL also exhibited antibacterial activity comparable to that of standard silver sulfadiazine cream (Kianvash et al. 2017). A nanocomposite hydrogel system incorporating curcumin nanosuspensions (CUR-Ns) and curcumin liposomes (CUR-Lip) has been developed to enhance localised and non-invasive delivery of curcumin for skin cancer treatment. The formulations demonstrated significantly improved anticancer activity against A431 skin cancer cells compared with free curcumin while maintaining good biocompatibility. Notably, the two nanocarriers exhibited distinct therapeutic profiles: CUR-Ns enabled faster initial skin permeation, whereas CUR-Lip provided sustained release and higher skin deposition. These findings highlight the potential of nanocarrier-loaded hydrogels as versatile platforms for tailored topical delivery of curcumin in skin cancer therapy (Aye et al. 2026).

3.2. Transferosomes

Transferosomes contain additional bilayer softening agents known as edge-activators; including surfactants such as polysorbates or sodium cholate. These vesicles possess higher deforming capacity than the conventional liposomes (Cevc and Blume 2001). Being ultradeformable, transferosomes can easily pass through the transappendageal or intercellular pathway. Hema et al. developed a transferosome containing curcumin and diclofenac diethylamine for transdermal delivery and evaluated *in vitro* (Chaudhary et al. 2013). The lipid-surfactant ratio, lipid-suractant weight and the sonication time were the independent variables. Whereas, the particle size, entrapment efficacy and the transdermal flux were the dependent variables. The study revealed the importance of formulation optimisation to be ideal for transdermal delivery with high flexibility and flux. The application of flexible liposomes for delivering curcumin and STAT3 siRNA utilising iontophoresis was reported as a viable treatment approach for skin cancer. Curcumin was complexed with STAT3 siRNA after its incorporation in cationic liposomes. Furthermore, the penetration of the nanocomplex in excised pig skin suggests a clathrin-mediated endocytotic route for curcumin-loaded siRNA complex. Compared to treatments with unformulated curcumin or free STAT3 siRNA, co-delivey of curcumin and STAT3 siRNA *via* flexible liposomes resulted in a significant reduction of cancer cell proliferation and induction of apoptosis. This study suggests the application of iontophoresis for enhanced penetration of the nanocomplex into the viable epidermis for effective skin cancer treatment (Jose et al. 2017).

Sharma et al. reported a comparative evaluation of curcumin ointment and curcumin transferosomes for wound healing activity. An elevation in hydroxyproline levels indicates a rise in the production of collagen, which subsequently promotes improved healing of wounds. The findings revealed a 2.5-fold increase in hydroxyproline content and a 2-fold increase in tensile strength compared to the curcumin ointment. These results suggest the superior wound healing potential of curcumin transferosomes (Sharma et al. 2015).

3.3. Ethosomes

A similar concept to producing liposomes with the exception of a high (20–45%) ethanol content and these called ethosomes (Momekova et al. 2024). The high ethanol content may soften the SC lipids, thereby increasing the skin permeability of drugs. Ethosomes can carry both hydrophilic or hydrophobic compounds across the SC (Touitou et al. 2000). Ethosomal formulations carry drug molecules inside a soft malleable vehicle comprising of phospholipids, ethanol and water. The therapeutic agent is released when the vesicle fuses with cell membranes in the deeper layers of the skin (Raj et al. 2023). Transethosomes are advanced lipid-based nanovesicular carriers composed of phospholipids, ethanol, and an edge activator (surfactant), which combine the advantages of both ethosomes and transferosomes (Rezigue et al. 2025).

Pathan et al. synthesised ethosomes for transdermal application using the Box Behnken model by varying concentrations of lipid, ethanol, and cholesterol as independent variables, whereas encapsulation efficiency, flux, and ethosome size were the dependent variables. The particle size was 300 nm, which is ideal for skin permeation, with an 80% encapsulation of curcumin. Permeation across human cadaver skin showed an enhanced flux compared to pure drug solutions, and the anti-inflammatory activity demonstrated a 58% reduction in inflammation compared to the control (Pathan et al. 2018). The ethanol and phospholipids synergistically promotes skin permeation. Ethanol can disrupt the lipid packing of SC, and the deformable ethosomes are capable of permeating through the narrow channels created. Additionally, interactions between the phospholipids of ethosomes and stratum corneum (SC) lipids may have lowered the lipid transition temperature, thereby facilitating skin permeation (Alfehaid et al. 2024).

3.4. Niosomes

Niosomes are another spherical vesicles containing non-ionic surfactants in cholesterol, and can encapsulate both hydrophilic and lipophilic drugs (Carter et al. 2019). They are highly flexible, biocompatible and non-immunogenic. Although they have structural resemblance to liposomes, niosomes have high stability and low production cost than liposomes. Curcumin loaded niosomes can be employed as for controlled transdermal delivery of drugs in chronic skin conditions. Akbari et al. prepared curcumin niosomes by film-hydration technique and investigated the influence of key formulation components on particle size and zeta potential (Akbari et al. 2020). On increasing the cholesterol concentration from 0 to 1.8%, particle size decreased from 444 nm to 384 nm and the zetal potential found to increase from −0.7 to −9.0. The *ex-vivo* skin permeation of curcumin niosomes revealed a significant drug deposition in skin layers than pure curcumin. The results of the formalin and the tail-flick tests indicated that the curcumin niosome formulation possessed higher anti-inflammatory as well as antinociceptive activities compared to the drug-free gel or curcumin gel. Based on their findings, it appears that curcumin nisomes can improve drug transport to the targeted site, thereby enhancing therapeutic effect. There is synergistic antibacterial effect against *Staphylococcus aureus* and *Pseudomonas aeruginosa* when curcumin niosomes are combined with silver/copper nanoparticles (Targhi et al. 2021). The

optimised niosomal nanoparticles exhibited good entrapment efficiencies and sustained release profiles. Compared to unformulated curcumin, the niosomal formulations demonstrated enhanced antibacterial activity. Additionally, a chitosan gel-based niosomal formulations demonstrated enhanced antibacterial effects and biofilm eradication compared to the niosomal formulations alone. These findings suggest that curcumin niosomes-metal NPs incorporated chitosan hydrogel have great potential for wound healing applications.

3.5. Inclusion complexes

The solubility and stability of curcumin can be improved by forming cyclodextrin complexes by grinding. Sun and co-workers designed *in situ* hydrogels with curcumin-β-cyclodextrin (HP-β-C) inclusion complexes for treating melanoma (Sun et al. 2014). *In situ* hydrogels were prepared with curcumin alone and also with inclusion complexes using poloxamers 407 and 188 as the matrix. *In-vitro* drug release and drug permeation were found to be higher with curcumin inclusion complexes. The *in-vitro* cytotoxicity in mouse melanoma cell was much higher with HP-β-C. The cell cycle analysis revealed that the cytotoxicity effect was mediated by blocking the cellular proliferation in the G2/M stage of the cell cycle followed by apoptosis. The study concludes that *in situ* gel of curcumin in HP-β-C inclusion complex would be a promising delivery for melanoma treatment.

3.6. Micelles

Micelles are nanoscale colloidal structures formed by the self-assembly of amphiphilic molecules in aqueous media, consisting of a hydrophobic core and a hydrophilic shell. This unique structure enables micelles to encapsulate poorly water-soluble drugs within their hydrophobic core (Deng et al. 2025). Gong et al. formulated a biodegradable *in situ* gel containing curcumin loaded micelles prepared using a solid dispersion, where the drug and polymer (PEG–PCL copolymer) were co-dissolved in ethanol followed by evaporation (Gong et al. 2013). This resulted a uniform mixture in which curcumin was homogeneously dispersed within the polymer mix. The coevaporated product was then dispersed in saline to form curcumin-micelles, and this was incorporated in to a hydrogel (Cur-HG). *In- vitro* release studies suggest that the formulation exhibit an excellent adhesion on application and provide extended release of curcumin. The excision wound model treated with the formulation exhibited an enhancement in wound closure. However, in both the incision and excision models, the Cur-HG-treated groups showed higher collagen content, better granulation, and higher wound maturity. Histopathological examinations further confirm that Cur-HG enhances the repair of cutaneous wounds. In another study, curcumin-loaded nanomicelles based on a binary surfactant system (Vitamin E-TPGS and Kolliphor ELP) were developed for topical melanoma treatment. The optimised formulation demonstrated enhanced anticancer activity in melanoma cells and promoted apoptosis indicating a potentially safer and more effective topical delivery system. These studies suggest that curcumin-loaded micelles show significant potential for promoting wound healing and improving topical melanoma treatment (Paganini et al. 2025).

3.7. Polymeric nanoparticles

Polymeric nanoparticles are extensively used in topical and transdermal drug delivery. In recent years, naturally-derived polymers such as chitosan have garnered considerable interest because they are biocompatible with toxicity. Polylactic acid co-glycolate (PLGA) is widely utilised in drug delivery (Sharma et al. 2016) and synergistic effects of PLGA and curcumin nanoparticles have been reported for wound healing (Chereddy et al. 2013). The exogenous lactate released from the PLGA polymer can speed-up healing, and the PLGA–curcumin nanoparticles exhibit superior wound healing effects in a mouse model compared to either the drug or polymer alone. Histology and RT-PCR results further support the enhanced wound healing of PLGA–curcumin nanoparticles. The formulation offers improved water solubility of curcumin and suggests that a nanoparticulate system can sustain the release of curcumin over several days.

Chitosan, derived from chitin present in crustaceans, possesses biocompatibility and affinity to bind to various compounds (Elgadir et al. 2015). Sabitha et al. report the evaluation of a curcumin chitin nanogel (CCNGs), for the treatment of melanoma (Mangalathillam et al. 2012). Cytotoxicity studies on human dermal fibroblast cells and human melanoma cells revealed that the curcumin nanogel exhibited specific cytotoxicity towards melanoma cells and that it was less toxic to dermal fibroblasts. Although CCNG showed excellent anticancer effect, the *in vitro* permeation studies using porcine skin showed low cumulative permeation (4 µg/cm^2 at 24 h), suggesting that further formulation enhancement is required (Nair et al. 2013).

The antimicrobial and wound healing activity of curcumin nanoparticles synthesised using tetramethyl orthosilicate and chitosan showed effective suppression of methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* and demonstrated superior wound healing in a murine model (Krausz et al. 2015). Similarly, Mirza et al. developed curcumin–chitosan–TPP nanoparticles *via* ionotropic gelation, with a mean particle size of 160 nm, a zeta potential of +7 mV, and 75% encapsulation efficiency. Upon topical application to anaesthetised mice, the formulation suppressed *S. aureus* and *P. aeruginosa* growth over a 3-day period (Mirnejad et al. 2014). Similar studies have further confirmed the enhanced antimicrobial and wound healing efficacy of curcumin nanoparticles prepared using tetramethyl orthosilicate and chitosan, compared to unformulated curcumin (Krausz, et al. 2015). These studies indicate enhanced antibacterial activity and wound healing efficacy of curcumin when chitosan nanocarriers were used compared to unformulated curcumin.

3.8. Solid-lipid nanoparticles (SLN) and nanostructured lipid carriers (NLCs)

Because of their solid lipid composition, SLNs serve as reservoirs for drugs, enabling controlled release (Aydin et al. 2024). Sandhu et al. developed curcumin loaded solid lipid nanoparticles (Cu-SLNs) for wound healing purpose, 60 with a polydispersity index (PDI) of 0.14, and size less than 200 nm. The Cu-SLNs showed excellent photostability over one year and exhibited a zero-order release pattern over 5 days, with potent activity against Staphylococcus aureus (MIC 64 µg/mL) (Sandhu et al. 2021). On the otherhand, the curcumin dispersion was found ineffective. Wound healing of

Cu-SLN was faster compared to controls, suggesting a promising wound therapy option particularly for infected wounds.

Due to specific limitations of SLNs, such as drug leakage during storage and low drug encapsulation efficiency, a newer generation of lipid carrier called NLCs was developed,(Elmowafy and Al-Sanea 2021) where a portion of the solid lipids is substituted with liquid lipids in the matrix with drug. Due to their enhanced properties and biocompatibility NLCs, are efficient drug carriers able to encapsulate hydrophilic and lipophilic drugs (Liakopoulou, et al. 2025). NLC encapsulated epidermal growth factor (EGF) and curcumin (EGF-Cu-NLC) for wound healing activities by double-emulsification process produced a size of 332 nm and encapsulation efficiency of 81.0% and 99.0% for EGF and curcumin, respectively (Lee et al. 2020). *In vitro* cell culture on fibroblasts and keratinocytes demonstrated that the bioactivity of EGF was preserved in NLC. Moreover, enhanced cell migration and simulation of wound healing was observed in chronic wound model on diabetic rats. Overall, these outcomes indicate that the NLCs incorporated curcumin and EGF have promising potential in facilitating the healing of chronic wounds.

3.9. Nano and microemulsions

Studies suggest that micro or nano-emulsions present promising features for transdermal delivery of lipophilic drugs (Raju Y et al. 2017) wherein, microemulsions comprised of eucalyptol and Tween 80 in an ethanol-water system demonstrated enhanced transdermal permeability of curcumin (15-fold) compared to curcumin solution containing eucalyptol (Liu and Chang 2011). Similarly, terpene microemulsions containing permeation enhancers such as limonene, 1,8-cineole, and alpha-terpineol were evaluated for the transdermal delivery of curcumin using neonatal pig skin, with demonstrably higher permeation of curcumin from limonene microemulsions than from 1,8-cineole and alpha-terpineol microemulsions (Liu et al. 2011). Curcumin-containing nano-emulsion comprised of clove oil, Tween-80 and PEG-400 prepared by ultrasonication (Cur-NE) with hydrodynamic diameter of 94 nm, zeta potential of −12.0, and a PDI of 0.26 showed an enhanced skin permeation through excised rat skin compared to curcumin solution (Cu-S) (Ahmad et al. 2019). Clove oil and Tween-80 are permeation enhancers and promotes skin permeation of curcumin. Further Cu-NE exhibited significant enhancements in wound healing in comparison to pure clove oil, Cu-S, and control nano-emulsion in excised wound model similar to those produced with fusidic acid cream. Histopathological examination revealed no signs of inflammation with Cu-NE, indicating safety and non-toxicity.

3.10. Dendrimers

Dendrimers are nanoscale monodispersed systems with a high degree of structural complexity. They are primarily composed of an inner core and a branching chain referred to as dendrons. The inner core encapsulate drug compounds, whereas the dendrons helps in targeting to specific tissues (Yiyun et al. 2007). Iontophoresis significantly enhances the skin penetration of peptide dendrimers. While passive diffusion

showed dendrimer stability in dermal and epidermal extracts for up to 6 h, no detectable drug amount was observed in the receptor phase. In contrast, iontophoresis markedly improved dendrimer permeation (Mutalik et al. 2013). Studies also highlight the importance of sonophoresis in enhancing the efficacy of ketoprofen-encapsulated arginine dendrimers. Permeation studies using mouse skin showed a 3-fold increase in ketoprofen delivery with dendrimers compared to pure drug solutions. The bioavailability was comparable between the transdermal and oral routes (Manikkath et al. 2017). Dendrimeric micelles co-encapsulating paclitaxel and curcumin have been developed for the treatment of bacterial infections and melanoma, with curcumin-loaded micelles showing superior antibacterial activity against *E. coli* compared to pure curcumin (Thuy et al. 2022). Furthermore, the anti-skin cancer efficacy was tested against mouse melanoma cells (B16F10), and the results indicated that curcumin-loaded dendrimeric micelles exhibited higher anticancer properties than free curcumin. Moreover, when administered alone to B16F10 cells, these dendrimers were non-toxic, supporting their safety as nanocarriers. Considering all factors, dendrimeric micelles hold great promise as a safe and effective delivery system for curcumin in the treatment of skin cancer and bacterial wound infections.

3.11. Electrospun nanofibers

Electrospun nanofibers have gained considerable attention as advanced biomaterials for wound healing and skin-related therapeutic applications due to their unique structural and functional properties (Cheng et al. 2024). Electrospinning employs a high-voltage electric field to generate ultrafine fibres from polymer solutions, forming nanofibrous membranes with a high surface area-to-volume ratio and interconnected porosity (Xue et al. 2019). These structures closely mimic the architecture of the natural extracellular matrix (ECM), thereby supporting cell adhesion, proliferation, and migration, which are essential for tissue regeneration and wound repair. In addition, electrospun scaffolds can absorb wound exudates, maintain a moist microenvironment, and enable the controlled or sustained release of therapeutic agents. Antibacterial membranes for wound-healing applications were developed by coating curcumin onto electrospun PVA/kappa-carrageenan (PVA/KC) membranes using electrospraying. The prepared membranes exhibited low cytotoxicity, good cell adhesion, and supported collagen production, along with a suitable degradation profile for wound healing. Antibacterial studies further demonstrated that curcumin-loaded membranes showed enhanced activity against *Escherichia coli* and *Staphylococcus aureus* compared with PVA and PVA/KC membranes. Overall, these findings highlight the potential of electrosprayed curcumin-coated membranes as promising bioactive dressings for improved wound management (Petrai et al. 2025).

4. Conclusion and future perspectives

Various skin condition remains a challenge in managing, especially chronic infections and melanomas. This is compounded by multidrug resistance, meaning more effective strategies must implement in managing chronic skin conditions. Plant-derived

phytochemicals have recently drawn significant research attention as potential therapeutic agents for chronic illnesses. From the foregoing review, it is apparent that curcumin holds potential for treating various skin conditions, but also suffers from poor delivery. Application of novel drug delivery planforms suggest that we can harness the full potential of curcumin, whilst toxicity to the skin is also addressed. It is suggested that formulation scientists, dermatologist and the pharmaceutical industry work hand-in-hand in addressing chronic skin condition using curcumin in novel drug delivery platforms.

Acknowledgements

During the preparation of this manuscript, the authors used AI tools, such as ChatGPT, to improve sentence clarity and correct grammatical errors. All content was thoroughly reviewed and edited by the authors, who take full responsibility for the final version. The authors also gratefully acknowledge Swansea University for supporting the publication of this review through its publishing agreements.

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CRediT: **Rajesh Sreedharan Nair**: Conceptualization, Writing – original draft, Writing – review & editing; **Nashiru Billa**: Conceptualization, Writing – review & editing; **Ajay Babu Pazhayattil**: Writing – original draft, Writing – review & editing; **Sarath Chandran C.**: Conceptualization, Writing – original draft, Writing – review & editing; **Mohammed Tahir Ansari**: Writing – original draft, Writing – review & editing; **Kai Bin Liew**: Writing – original draft, Writing – review & editing; **Andrew P. Morris**: Conceptualization, Writing – review & editing.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

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