RESEARCH PAPER

Nanotechnology-Driven Polyphenol Delivery Systems For Dermatological Diseases: Therapeutic Strategies And Future Perspectives

Jithu Nambukulangara Vijayan[1*], Tapasvi Gupta[1], Arya Kadukkattil Ramanunny[2], Nila Mary Varghese[3]

[1] Jeevak Shodhshala, Gyan Vihar School Of Pharmacy, Suresh Gyan Vihar University, Jagatpura, Jaipur, Rajasthan, 302017.

[2] Chitkara College Of Pharmacy, Chitkara University, Rajpura, Punjab-140401.

[3] Elims College Of Pharmacy, Villadam Ramavarmapuram, Thrissur, Kerala- 680631.

Corresponding Author: Jithu Nambukulangara Vijayan, Jeevak Shodhshala, Gyan Vihar School Of Pharmacy, Suresh Gyan Vihar University, Jagatpura, Jaipur-302017, Rajasthan, India. Tel.: +919446312088,

Email: vijayanjithu@gmail.com

***Received:** 20th Feb, 2026; **Revised:** 4th Mar, 2026; **Accepted:** 25th Mar, 2026; **Available Online:** 10th Apr, 2026*

Abstract

Skin diseases is non-fatal condition but considered as a global burden as it affects the quality of life of patients and their companions. It is the fourth leading diseased condition that creates an impact on the physical, psychological and economic well-being of patients. Mostly conventional topical treatment options were used for skin diseases, however significant limitations such as reduction in efficacy, requirement of prolonged duration for treatment, recurrence/relapse of disease, systemic side effects, and side effects due to prolonged use of synthetic drugs has been noticed.

To overcome these limitation polyphenols has been preferred. These are biomolecules derived mostly from plants and possess antioxidant, anti-inflammatory, antimicrobial, and photoprotective properties which makes it a suitable candidate for treatment of dermatological conditions. However, significant limitations reported with these compounds are poor solubility, instability, and low skin penetration which reduces their therapeutic efficacy. To overcome these limitation, best suggested option is to encapsulate them into nanocarriers which will improve its penetration and permeation, improve its stability and bioavailability. In addition to these, surface modified nanocarriers are apt for site specific targeted drug delivery for treatment of skin diseases.

Thorough literature search has been carried out using 68 review and research articles. This review provides a comprehensive overview of polyphenol-loaded nano-formulations such as polymeric nanoparticles, lipid-based carriers, nano emulsions, and emerging nano-delivery system were discussed for skin diseases such as acne vulgaris, atopic dermatitis, psoriasis, vitiligo, and skin cancer. Moreover, the review discusses recent developments, and future perspective of polyphenol-based nano formulations in the management of skin diseases.

Keywords: Polyphenols, Nanocarriers, Dermatological diseases, Topical drug delivery, Skin cancer

How To Cite This Article: Vijayan Jn, Gupta T, Ramanunny Ak, Varghese Nm. Nanotechnology-Driven Polyphenol Delivery Systems For Dermatological Diseases: Therapeutic Strategies And Future Perspectives. Int J Drug Deliv Technol. 2026;16(27s):753-766. Doi: 10.25258/ijddt.16.27s.85

1. Introduction

Skin diseases is considered as a non-fatal condition; however, it is reported as global burden. Among the diseased condition, skin diseases ranked fourth position affecting millions of peoples across the globe irrespective of age, colour (white/black) and geographical regions (Karimkhani et al., 2017). Though skin diseases are not lethal, however, the impact of this creates psychological distress, social stigmatization, and ultimately affects quality of life (Basra & Shahrukh, 2009). In addition to the physical and psychological distress, it creates economic burden to the family and society due to higher treatment costs and comparatively higher duration of treatment (Alshamrani et al., 2019).

The severity of disease is frequently associated with degree of impairment of the skin barrier. Impairment in skin layer triggers the immune system and inflammatory responses (Fujii, 2020). Mostly skin diseases are associated with comorbidities such as asthma, cardiovascular diseases, metabolic syndrome, and depression (Lian & Chen, 2019). Furthermore, the prevalence and severity of skin diseases across the global population varies based on the various factors such as environmental, socioeconomic, genetic, and climate changes (Pezzolo & Naldi, 2020; Yakupu et al., 2023). Some of the commonly reported dermatological conditions include atopic dermatitis (AD), acne vulgaris (AV), psoriasis, urticaria, vitiligo, viral and fungal infections, and skin cancers. Among these conditions dermatitis (0.38%) has been reported to be higher in population worldwide (Ramanunny et al., 2021).

Considering the population types and skin diseases, pediatric populations have immature immune system and once they get exposure to the infectious agent they are more prone to be affected by infectious skin conditions (Kollmann et al., 2017). Contrary to this, geriatric populations are more exposed to autoimmune skin diseases as well as diseases caused due to over exposure to environmental changes such as psoriasis, urticaria, fungal infections, and pressure ulcers (Jafferany et al., 2012).

The treatment for skin diseases starts with topical followed by phototherapy, systemic or a combination of phototherapy and systemic based degree of severity (Guo & Jee, 2021). Among the treatment options, first prefers is topical application of creams, ointments, lotions, and gels These formulations are directly applied on the affected skin areas which minimizes systemic exposure. However, major challenges encountered with these conventional topical preparation is poor penetration through the stratum corneum, partial retention of drug at the site, skin irritation, and poor patient compliance due to the greasy nature of some formulations (Patil et al., 2019).

Currently considerable attention has been focused on natural bioactive compounds, particularly plant-derived polyphenols, for the prevention and treatment of dermatological diseases. Polyphenols are widely distributed in fruits, vegetables, seeds, nuts, tea, and medicinal plants. These are chemical compounds with multiple phenolic hydroxyl groups that are responsible for their diverse biological activities. On the basics of their chemical structure, polyphenols are broadly classified into phenolic acids, flavonoids, stilbenes, and lignans (Prabhu et al., 2021).

Based on the type of polyphenol, they exhibit different therapeutics activities. Some of them are antioxidant, anti-inflammatory, antimicrobial, and photoprotective properties (Działo et al., 2016). They also play a significant role in neutralizing reactive oxygen species (ROS) and thereby reducing the oxidative stress level which is one of the leading cause for the skin disease (Bolaños-Cardet et al., 2026). As stated previously, environmental factors are also considered as a reason for skin diseases. Factors such as ultraviolet radiation, pollution, and chemical exposure can stimulate excessive ROS production in the skin, that leads to oxidative damage of the cellular components in the skin which include lipids, proteins, and DNA.

Oxidative stress has been strongly associated with skin aging, inflammatory skin diseases, and carcinogenesis through activation of signaling pathways involved in inflammation, cellular proliferation, and apoptosis (Bolaños-Cardet et al., 2026). Due to their potent antioxidant properties, polyphenols protect the skin from oxidative damages and help to regulate inflammatory and cellular signaling pathways (H.-M. Liu et al., 2023). Several studies have demonstrated that polyphenols enhance the activity of endogenous antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. Apart from antioxidant activity, polyphenols also exhibit antimicrobial activity against various bacterial, viral, and fungal pathogens affecting the skin. These beneficial properties have encouraged the incorporation of polyphenols into dermatological formulation to improve skin health as well as to prevent skin diseases (De Rossi et al., 2025).

Despite the said therapeutic potential, major limitation is the clinical studies and further translation process. Few reported challenges are associated to their physicochemical and pharmacokinetic properties. Many polyphenolic compounds exhibits poor aqueous solubility, chemical instability, rapid degradation, and low bioavailability (Parisi et al., 2014). Furthermore, the outer protective layer, stratum corneum restricts the penetration of hydrophilic and high-molecular-weight compounds. Therefore, the bioactive remain at the surface layer and hence affecting the pharmacokinetic profile of the drug. This insufficiency ultimately reduces the therapeutic effectiveness of polyphenols (Schafer et al., 2023).

All the stated physicochemical, pharmacokinetic and pharmacodynamic limitations are overcome by exploring various types of nanocarriers. Nanocarriers are designed to encapsulate bioactive compounds and facilitate their transportation across various biological membrane by maintaining its size at nanometric range. These nanosized system offers several advantages such as improved solubility, enhanced stability, controlled release pattern, targeting to specific site and prolonged residence time at the site of action (Gupta et al., 2012).

This review provides a comprehensive overview of polyphenol-loaded nano-formulations such as polymeric nanoparticles, lipid-based carriers, nano emulsions, and emerging nano-delivery system were discussed for skin diseases such as AV, AD, psoriasis, vitiligo, and skin cancer (El-Zaafarany & Nasr, 2021). Thorough literature search has been carried out where 68 review and research articles were evaluated to provide sufficient idea and benefits of polyphenols loaded nanocarrier for skin diseases. Moreover, the review discusses recent developments, and future perspective of polyphenol-based nano formulations in the management of skin diseases.

2. Methods of data acquisition

The comprehensive data included in this review related to polyphenols, nanocarriers and skin are collected through thorough systematic literature search. Search engines like PubMed, Web of Science, Embase, and Google scholar are used to search studies since January 2018. The search terms included where "polyphenolic compounds|", "flavonoids", "curcumin", "quercetin," "resveratrol" "nanocarriers", "vitiligo" "psoriasis" "acne," "inflammation," "melanoma" "oxidative stress," "hyperproliferation,", "immunity," "skin barrier," "melanin," and "dermatological"etc.

3. Understanding Polyphenols and its types

Polyphenols are a diverse group of naturally occurring plant secondary metabolites characterized by the presence of one or more phenolic rings. The structure contains two benzene ring (C_6), a connect between these benzene molecule is done by oxygenated heterocyclic (C_3) Based on the changes in their chemical structure, polyphenols are generally classified into four major groups: phenolic acids, flavonoids, stilbenes, and lignans which is represented in Figure 1. These compounds exhibit significant antioxidant, anti-inflammatory, antimicrobial, and photoprotective activities, which make them highly valuable for the prevention and treatment of dermatological disorders such as psoriasis, acne, dermatitis, wound healing, and skin aging (Prabhu et al., 2021). An over view of the four major polyphenols and their subtypes with examples are mentioned in Table1 (Gaetano et al., 2025).

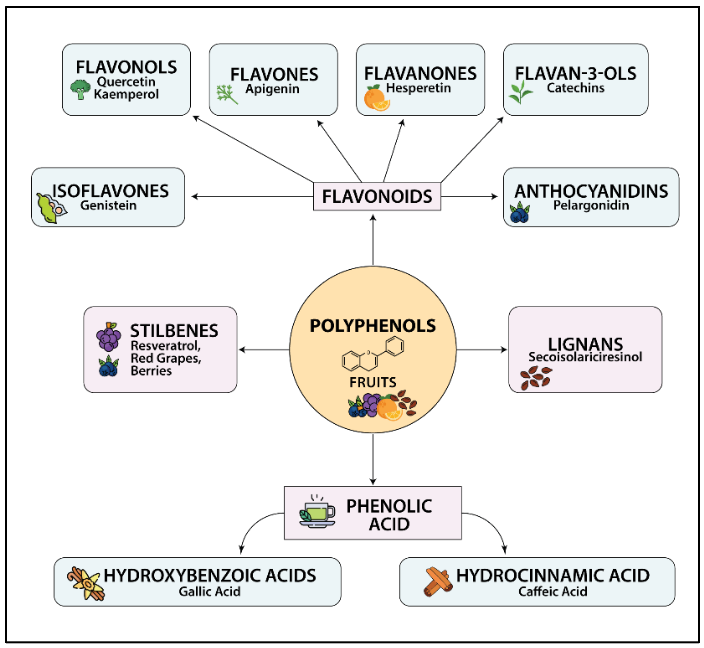

Figure 1. General classification of phenolic compounds

Table 1 provide an over view of the four major polyphenols, their subtypes, properties and common examples (Gaetano et al., 2025).

Main Class of Polyphenols	Subclasses	Structural description	Properties reported	Few examples	References
Flavonoids It is three ring structure	Flavonols	Flavonoids with a 3-hydroxyflavone structure (double bond between C2	Antioxidant, anti-inflammatory, UV protection,	Quercetin, fisetin, kaempferol, Curcumin	(Chagas et al., 2022)

containing15 carbon atoms. Ring A (C6) is connected to Ring B (C6) with a oxygen containing heterocyclic compound (C3).		and C3 and a carbonyl at C4)	antimicrobial activity		
	Flavones	Lacks 3-hydroxy group. Unsaturated 3-C chain, having a double bond between C-2 and C-3	Antioxidant, anti-inflammatory, antimicrobial activity	Apigenin, chrysin Luteolin	(Wang et al., 2022)
	Flavanones (dihydroflavones)	Absence of double bond between C2-C3, highly reactive saturated flavonoids with chiral center at C2	Antioxidant, anti-inflammatory	Naringenin, Eriodictyol, Hesperetin	(Shamsudin et al., 2022)
	Flavanols (flvan-3-ols or catechins)	Benzopyran with saturated carbon chain between C_2 and C_3 and hydroxyl groups bound to C_3	Antioxidant, antimicrobial, reduces cardiovascular risks	Catechin, Epicatechin, Epigallocatechin gallate (EGCG)	(Proteggente et al., 2002)
	Anthocyanidins (pigmented)	Glycosides containing 2-phenylchromenylium ion	Antioxidant, antidiabetics, pigment properties	Cyanidin, delphinidin, Peonidin	(Khoo et al., 2017)
	Isoflavones	Flavonoids with B-ring attached at position 3	Phytoestrogenic, antioxidant	Genistein, daidzein	{Gaetano, 2025 #391}
Phenolic Acids	Hydroxybenzoic acids	Phenolic acids with a C_6–C_1 structure	Antioxidant, anti-inflammatory	Gallic acid	(Da Silva et al., 2025)
	Hydroxycinnamic acids	Phenolic acids with a C_6–C_3 structure	Antioxidant, anti-inflammatory	Ferulic acid, caffeic acid	(López-Herrador et al., 2025)
Stilbenes	-	Compounds with two aromatic rings linked by ethylene bridge	Antioxidant, anti-inflammatory, cardioprotective	Resveratrol	(Liu et al., 2025)
Lignans	-	Dimers of phenylpropanoids	Antioxidant, estrogen-like effects	Secoisolariciresinol	(Burgberger et al., 2025)

4. Therapeutic Potential of Polyphenol-Loaded Nanocarriers in Skin Disease

Nanocarriers are designed to encapsulate various types of active ingredients which include polyphenols such as curcumin, genistein, resveratrol, quercetin. They are made into nanometric size using various components and techniques. Few of the components used in designing nanocarriers are lipids (phospholipids, lecithin, cholesterol), polymers (chitosan, poly lactic glycolic acid), surfactants (Tween, Spans), co-surfactants (Transcutol) and other ingredients such as proteins, inorganic, organic materials (Amoabediny et al., 2018). The formed nanocarriers offer significant benefits such as enhanced skin penetration through various strata of the skin, provide controlled or prolonged release pattern, protect it from degradation thereby increases its stability. In addition to these, improvement in bioavailability of poorly soluble polyphenols and its ability of targeted delivery to the deeper skin layers minimizes systemic absorption and irritation (Gupta et al., 2012).

Few nanocarriers commonly used for dermatological conditions includes vesicular types, lipid-based particular system, emulsion-based system, polymeric nanoparticles etc. Figure 2 illustrate type of the nanocarriers that are explored for skin diseases such as AV, psoriasis, AD, vitiligo and skin cancer.

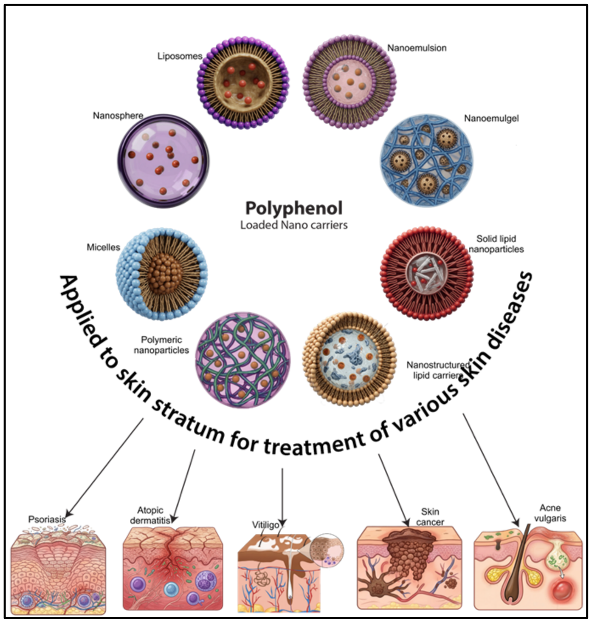

Figure 2: Types of nanocarriers explored for treatment of skin diseases

Considering the benefits of nanocarriers and its ability to transform the limitation of free polyphenols, few research studies performed are discussed in the subsections.

4.1 Acne vulgaris

AV is an inflammatory condition predominantly affects adolescents and young adults. The multifactorial pathogenesis of AV is characterized by excessive sebum production, follicular hyperkeratinization, proliferation of *Propionibacterium acnes (P.acnes)*, and activation of inflammatory pathways (Vasam et al., 2023). Among them, anyone factor can initiate the generation of ROS, disruption of antioxidant defenses, and obstruction of hair follicles, ultimately leading to the formation of comedones and inflammatory lesions (Jin et al., 2023). Few of the conventional acne treatments includes the use of antibiotics, retinoids, and hormonal treatments. Prolonged usage of these treatments is often associated with adverse effects and causes antimicrobial resistance. Consequently, increasing attention has been directed toward plant-derived polyphenols that too possess antioxidant, antibacterial, and anti-inflammatory properties. Hence, they can be considered as a safer and effective alternatives (Abubakar & Abduljalal, 2024).

For instance, curcumin-loaded solid lipid nanoparticles have shown enhanced antibacterial activity against *C. acnes* and improved dermal penetration compared with free curcumin, highlighting the ability of lipid-based nanocarriers to increase the bioavailability of poorly soluble polyphenols (Bhawana et al., 2011). Recent advancement in nanocarrier system was based on a nanoemulsion -thermogel composite system laoded with Tanshinone IIA and quercetin (TQ hydrogel) for acne treatment. *In vivo* studies of TQ hydrogel on animal model has shown significantly inhibited the inflammation on the acne tissues, suppressed androgen receptors expression and showed promising potential in reducing acne-induced scarring (Zhang et al., 2025). Still, significant innovative techniques have been utilized such as green synthesis of polyphenol-grafted lignin nanoparticles that contains gallic and tannic acid to promote sustainable application in anti-acne, antioxidant, and UV-blocking agents (Abdelmula et al., 2025)

However, it has been noticed that many polyphenolic agents such as resveratrol, quercetin and epigallocatechin gallate has been proven its anti-acne activity, but focus and more research is required to explore it into nanocarriers. Continued advancements in nanocarrier design are expected to facilitate the development of more effective and safer topical treatments for acne management.

4.2. Atopic Dermatitis

AD is a chronic, relapsing inflammatory skin disease characterized by intense itching, erythema, xerosis, and lichenified lesions. It commonly begins in childhood and it is associated with genetic susceptibility, environmental triggers, immune dysregulation and impairment of the skin barrier (Mocanu et al., 2021). A major pathological feature of AD is the defective epidermal barrier, often linked to mutations in structural proteins such as filaggrin, which increases skin permeability to allergens, microbes, and irritants. This barrier disruption triggers immune responses dominated by T helper 2 (Th2) cells, resulting in increased production of cytokines such as IL-4, IL-5, and IL-13, elevated serum IgE levels, mast cell activation, and chronic inflammation (Sroka-Tomaszewska & Trzeciak, 2021). Additionally, generation of ROS during oxidative stress can aggravate skin inflammation and tissue damage in AD.

The conventional treatments used for AD includes topical corticosteroids, calcineurin inhibitors, antihistamines, and immunosuppressive drugs. Although long-term use of these drugs cause adverse effects such as skin atrophy, systemic toxicity, and increased susceptibility to infections (Boguniewicz & Nicol, 2002). Therefore, a growing interest was generated towards natural bioactive compounds, particularly polyphenols are reported to be safer with a potential of multi-targeting towards multifactorial causes of AD.

Among the advanced research, a transdermal delivery system was developed for treatment of AD containing polyphenol mixture (PM) of quercetin, phloretin and ellagic acid {Choi, 2023 #362}. In vivo studies performed on 1-chloro-2,4-dinitrobenzene-induced mice AD model demonstrated that PM has shown more effectiveness in reducing the AD symptoms in comparison to each single polyphenol. This research clearly stated the importance of upholding the optimal concentration of each polyphenol in the mixture to obtain the benefit during treatment (Choi et al., 2023). Previously it has been observed that polyphenolic compounds specially flavonoids have been explored well for AD. A study was carried out to evaluate the efficacy of the glycosylated flavonols such as quercitrin, isoquercitrin, and rutin in similar1-chloro-2,4-dinitrobenzene induced AD mouse model. It was observed that there was an effective reduction in the overexpressed interleukin (IL)-6, chemokine (C-X-C motif) ligand (CXCL)1 and CXCL8. In vivo studies clearly demonstrated that after topical isoquercitrin treatment less erosion, scaling, and epidermal hyperplasia was observed and the results were comparable to tacrolimus ointment. Further, immunohistopathological studies exhibited reduction in epidermal hyperproliferation and immune cell infiltration after topical is quercitrin. (Yang et al., 2025). Similarly, significant number of studies has been carried out for different polyphenols such as Quercetin (flavanol), epigallocatechin gallate (catechin), chrysin (flavones), kaempferol (flavanol), Silibinin (flavonolignan) etc. for AD.

4.3 Vitiligo

Vitiligo is an autoimmune disease characterized by progressive melanocyte loss results in substantial appearance of well-defined white patches on the skin and mucous membranes. This is considered as a chronic condition which is associated with the gradual enlargement of depigmented areas over time (Sun et al., 2020). Vitiligo affects individuals globally irrespective of age, gender and ethnicity. Despite several available therapeutic approaches, a definitive cure is not possible as the etiology of vitiligo remains partly understood. Some of the extrinsic and intrinsic factors are triggered by environmental conditions and/ intrinsic cellular abnormalities that enhance oxidative stress in melanocytes, leading to elevated levels of hydrogen peroxide (H_2O_2). This accumulation disrupts cellular antioxidant defense mechanisms, including impairment of the nuclear factor erythroid-2 related factor-2 (Nrf2) signaling pathway. As a result, lipid peroxidation and ROS accumulation occur in melanocytes and keratinocytes even in clinically unaffected skin areas. Furthermore, pro-inflammatory cytokines such as IL-1, IL-6, and TNF-α stimulate the release of IL-8 in melanocytes, intensifying oxidative damage and promoting apoptosis of both melanocytes and keratinocytes (Xuan et al., 2022).

Several studies have demonstrated the beneficial effects of polyphenols in pigmentary disorders. Research studies on polyphenols has taken a step in managing vitiligo due to their antioxidant, anti-inflammatory, and melanogenesis-promoting properties. These compounds may enhance melanin synthesis, inhibit melanin degradation, scavenge free radicals, activate melanogenic signaling pathways, upregulate tyrosinase gene expression, suppress inflammatory cytokines and chemokines, and inhibit the migration of cytotoxic $CD8^+$ T lymphocytes that contribute to melanocyte destruction (J. Liu et al., 2023).

Nanocarriers loaded polyphenolic compounds can overcome the limitation of polyphenols and improve their dermal delivery. Among the therapy, phototherapy is commonly preferred using narrowband ultraviolet B (NB-UVB) The major limitations reported is phototoxicity that occur due to the interaction of ROS and UV light and insufficient melanocyte regeneration in chronic situations. More recent advancement in treatment of vitiligo is the development of bilayer microneedle for dual-release of curcumin-fructose (CF) and psoralen-loaded melanin from its nano-agent. This bilayer system was developed to enhance the efficacy and safety in vitiligo treatment through rapid antioxidant activity and sustained melanogenesis. The study has explained the design and purpose of the bi-layered nanomicelles. The upper-layer is casted with hyaluronic acid (HA) which is encapsulated with self-assembled CF to form nanomicelles (CF NMs). This nanomicelles rapidly scavengers the ROS thereby prevent photodamage and also inhibit Nuclear factor-kappa B (NF-κB) mediated inflammation. The lower layer is gelatin methacryloyl (GelMA) hydrogel which embedded with psoralen-loaded melanin which promotes melanogenesis through inhibition of JAK-STAT signaling pathway as well as through enhanced tyrosinase activity. It also decreases autophagy-induced apoptosis. Furthermore, in vivo studies on monobenzone-induced vitiligo mice were carried out using bi-layered microneedle and NB-UVB. A significant increase in pigmentation(80.55%) was observed after 14 days in groups that received treatment with bi-layered microneedle whereas only 25.90% re-pigmentation was observed in groups received NB-UVB alone (Hu et al., 2025). Similar advancement in nanocarrier systems helps to further improve their bioavailability, targeted delivery, and clinical effectiveness for vitiligo treatment. (Hu et al., 2025)

4.4. Psoriasis

Psoriasis is an autoimmune chronic, immune-mediated inflammatory skin disease characterized by plaques covered with erythema and silvery scales. Psoriasis affects approximately 2–3% of the global population and can occur at any age (Kuchekar et al., 2011). The multifactorial etiology such as genetic susceptibility, immune dysregulation, environmental triggers, and oxidative stress leads. hyperproliferation and abnormal differentiation of keratinocytes. The hallmark of this disease is the infiltration of inflammatory immune cells results in increased production of inflammatory cytokines such as tumor necrosis factor-α (TNF-α), IL-17, IL-23, and vascular endothelial growth factor (VEGF) (Lowes et al., 2014). In addition to this, oxidative stress generates excessive ROS and nitric oxide (NO), further contributes to tissue damage and inflammation (Hu et al., 2025).

Conventional treatments for psoriasis include topical agents (corticosteroids, vitamin D3 analogs, salicylic acid, coal tar, and urea), systemic therapies (methotrexate, cyclosporine, and retinoids), phototherapy, and biologic agents targeting inflammatory cytokines (Kuchekar et al., 2011). Despite their effectiveness, these therapies may cause adverse effects, limited long-term safety, and variable patient response, which has stimulated interest in alternative therapeutic approaches using polyphenols (Imran et al., 2025). A significant number of polyphenolic compounds has been reported to exhibit anti psoriasis activity such as luteolin, , delphinidin, Baicalein, quercetin and many more. Although polyphenols possess considerable therapeutic potential, their clinical application is often limited by poor water solubility, low stability, rapid metabolism, and limited skin permeation have been investigated that enhance the stability and bioavailability of polyphenols, improve skin penetration, enable controlled drug release, and increase targeted delivery to affected skin layers.

For instance, apigenin loaded ultra-deformable liposomes (APG- UDL) was developed for the management of psoriasis. In vitro permeation studies and in vivo pharmacodynamic studies of APG- UDL has reported enhancement in the permeation and treatment potential without any sign of toxicities (Urooj et al., 2025). Similar research studies were carried out to load resveratrol into soya lecithin–PLGA based hybrid nanocomposite (RSVNP) for psoriasis treatment. A spherical shape nanoparticle with an average particle size of 120 ± 8.8 nm was obtained. Further, in vivo pharmacodynamic studies on imiquimod (IMQ) induced psoriasis mice model demonstrated that treatment with RSVNP gel has shown significant reduction in the epidermal thickness as well as decrease in infiltration of inflammatory cells. The most noticed characteristic exhibited by the formulation was localized skin retention with minimal systemic effects. The histopathological studies confirmed that psoriasis severity is improvement in comparison to the diseased control and improvement in restoring skin integrity without any organ toxicity was reported with RSV nanocomposite gel (Keshari et al., 2025).

4.5 Skin Cancer

Skin cancer remains one of the most prevalent malignancies globally, with increasing incidence due to prolonged ultraviolet (UV) exposure and environmental changes. Skin cancers are classified into melanoma skin cancer (MSC) and non-melanoma skin cancer (NMSC). NMSC primarily comprises of two types- basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), which accounts about 99% of cases whereas MSC affect smaller proportion but is associated with the highest mortality and poorer prognosis (Roky et al., 2025). Conventional treatment strategies, including chemotherapy, immunotherapy, radiotherapy, and targeted therapy, which are often associated with high toxicity, elevated costs, and therapeutic resistance, particularly in metastatic stages of the disease. These limitations highlight the need for safer, cost-effective therapeutic approaches. Few of the polyphenols explored for treatment of skin cancers are fisetin, epigallocatechin-3-gallate, kaempferol, rosmarinic acid, apigenin, genistein, quercetin, luteolin, baicalein, ferulic acid, myricetin, naringenin, delphinidin etc. These polyphenols demonstrated multifaceted anticancer activities against skin cancer through modulation of oxidative stress, inflammatory cytokines, immune responses, apoptosis, metastasis-related enzymes, and angiogenic factors. Some of the targeting key pathways such as MAPK, PI3K/AKT/mTOR, NF-κB, JAK-STAT, EGFR, AKT, STAT3, p65 and vascular endothelial growth factor (VEGF) signaling, these natural compounds show significant potential as safer and cost-effective therapeutic or preventive agents for melanoma and other skin cancers.

In addition to these confirmation of activities, further studies were carried out for development of nanocarriers. A versatile photosensitizer was developed by Li et al. Photothermal therapy (PTT) was reported to induce immunogenic cell death. But major limitation is the reoccurrence of tumor which is due to existence of immunosuppressive microenvironment in tumors. Hence, an advanced nanoparticulate system was developed which contained quercetin and ferrum ion (QFN). The significance of this system is the dual action provided by QFN upon phototherapy (Li et al., 2022). Administration of QFN with near infrared light radiation induces cancer cell destruction and releases tumor antigen. The released antigen was captured by QFN and deliver it to lymph nodes which promotes dendritic cell maturation and T-cells activation. In addition to this, quercetin released improves T-cell infiltration and regulate immunosuppressive microenvironment. This mechanism was proved using in vivo studies in mice model. The treatment group (QFN-PTT) has reported significantly elongated survival time and inhibited distant tumor growth, hence tumor recurrence. This nano- photosensitizers was found to be effective and translationally feasible for photothermal therapy (Li et al., 2022).

The selection of therapy is based on the degree of severity of the carcinoma. Apart from phototherapy, dual drug therapy is preferably used. A combination of quercetin and resveratrol loaded into nanostructured lipid carrier (NLC) gel was developed for the treatment of skin cancer (Imran et al., 2020). This combination in liposomal formulation has shown already demonstrated its enhanced cellular uptake of polyphenol and exhibited better scavenging ROS in fibroblast. Further topical application onto skin lesion in mouse has reported significant reduction of oedema and leukocyte infiltration (Caddeo et al., 2016). Imran et al has carried out cytotoxicity studies of developed NLC gel and conventional gel on human epidermoid carcinoma (A431) cell line using MTT assay. The result of IC_{50} value revealed that NLC gel (IC_{50} = 86.50 μM) has the potential to delivery drugs to the deeper skin layers in comparison to conventional gel (IC_{50} = 123.64 μM) and hence proposed to be used in treatment of skin cancer (Imran et al., 2020).

Consequently, nanotechnology-based formulations offer a promising strategy to improve the therapeutic efficacy of polyphenols in various skin diseases are summarized in Table 2

Table 2: An over view of few polyphenol encapsulated nanocarriers explored for treatment of skin diseases

S. No.	Polyphenol / Active Compound	Type of Nanocarrier	Target Skin Disease	Mechanistic studies/ model used	Key Study Findings	Reference
1	Resveratrol	Solid–lipid microparticulate topical gel	Melanoma	Invitro cytotoxicity on B16F10 melanoma cell line and In vivo studies on C57 BL mice model	• Average particle size: 2.98 µm • Spherical shaped microparticles • In vitro studies confirmed sustained release profiles • *In vivo* studies on C57BL mice exhibit significant tumor reduction.	(Ravikumar et al., 2019)
2	Mangosteen (MGN) extract	Polymeric nanoparticle gel (PNP)	AV	Clinical studies on 28 patients	• After 12 weeks of clinical study on 28 patients using MGN-PNG (test) and 1% clindamycin gel(std), significant reduction of both comedone (66.86%) and inflammatory acne lesions (67.05%) was reported with test whereas 55.33% and 64.16% respectively was reported with std. • Better improvement in clinical severity • Upon treatment with both MGN-PNG and clindamycin gel, significant reduction in porphyrin levels confirmd a reduction in *P. acnes*.	(Lueangarun et al., 2019)
3	Epigallocatechin gallate (EGCG)	Microneedles (MN)	AD	In vivo studies on Nc/Nga Mouse model of AD	• Nc/Nga mouse model of AD was treatment with Once weekly administration of EGCG and L-ascorbic acid loaded poly-γ-glutamate MNs • Amelioration of skin lesion and epidermal hyperplasia observed on 4^{th} week • Reduction in serum IgE and histamine levels • Inhibition of IFN-γ and Th2-type cytokine production, in comparison to untreated AD group ($p < 0.05$). • Reduction in frequency and dose	(Chiu et al., 2021)

4	EGCG	Polymeric Nanoparticles	AD	In vivo studies on 2,4-dinitrochlorobenzene (DNCB) AD mouse model	• Topically application of PEG-PLGA-EGCG nanoparticles (EGCG-NPs) on 2,4-dinitrochlorobenzene (DNCB) AD mouse model demonstrated decreased the expression of inflammatory cytokines like TNF-α, interferon-γ (IFN-γ), IL-4, IL-6, and IL-17A in a time-dependent manner • Blocked over-expression of RIP1, RIP3, and MLKL in the entire epidermis layers and also blocks the expression of phosphorylated p38 (p-p38), extracellular signal-regulated kinase 1 (ERK1), and extracellular signal-regulated kinase 2 (ERK2)	(Han et al., 2022)
5	Gallic acid (GA)	Hyaluronic acid–modified chitosan nanoparticles (HA-CS)	Psoriasis	In vivo studies on IMQ psoriasis model	• Particle size of HACS-GA NP gel: 220.1 ± 0.18 nm. • In vivo studies on IMQ psoriasis model confirmed the targeting potential of HACS-GA NP gel to CD44 receptor that • Reduction in epidermal hyperproliferation and improved keratinocyte inhibition	(Sheikh et al., 2023)
6	Quercetin	Hydroxypropyl-β-cyclodextrin (HPCD) Liposomal gel	Psoriasis	In vivo studies on IMQ induced psoriasis model	• Improved stability, enhanced penetration and retention • Alleviated skin thickening (plaque) symptoms • Reduced skin thickening • Downregulated TNF-α, IL-17A, IL-1β.	(Zhang et al., 2023)
7	Resveratrol (RSV)	Invasome gel	Skin cancer	In vivo studies in Ehrlich-induced mice models	• RSV -Invasome particle size :208.7 ± 74 nm % entrapment efficiency 77.7 ± 6%, zeta potential (−70.4 ± 10.9 mV). • In vitro release studies: initial burst effect followed by controlled drug release for 24 h. • Smallest tumor volume with no signs of organ toxicity was observed in in vivo mice model	(Samir et al., 2024)

					• Upregulation of BAX and Caspase-3 gene levels and downregulation of NF-kB and BCL2 protein levels	
8	Eugenol (EU)	Lipid nanoparticle (NPs) embedded hydrogel	Psoriasis	In vivo studies on IMQ psoriasis model	• EU loaded in soya phosphatidylcholine NPs formulated into Carbopol 974P hydrogel (EUNPgel) reported spherical shape with a size ~200 nm, encapsulation efficiency 85%. • Inhibited keratinocyte proliferation, reduced IL-6 inflammation, superior ROS scavenging, enhanced dermal penetration. PASI score reduced from 3.75 to 0.5 within 5 days of treatment.	(Keshari et al., 2024)
9	Curcumin	Nano emulsion embedded in oligopeptide hydrogel	Psoriasis	In vivo psoriatic mice model	• Enhanced skin penetration and prolonged residue time on the skin • Oligopeptide improved cellular uptake • Reduced systemic toxicity	(Chen et al., 2025)
10	Naringenin (NR)	Nano-cochleate hydrogel	Anti-inflammatory activity	Ex vivo studies using BALB/C mice skin and lipopolysaccharide-stimulated RAW264.7 inflammation model	• Nanosized particles160–170 nm with negative zeta potential of 27 mV • Better encapsulation efficiency of 81–82% • Reduced cellular ROS levels, nitrate accumulation, and mitochondrial healing ability in a lipopolysaccharide-stimulated RAW264.7 inflammation model • Higher permeation in BALB/C mice and also reported 3.43 and 3.34-fold greater C_{max} and AUC_{0-t} in the epidermal layer, • Enhanced antioxidant and anti-inflammatory effects	(Kamble et al., 2026)
11	Quercetin	Silver Nanocomposite	Acne vulgaris	In vivo *P, acnes* and acid oil dual-induced rat model	• Three-dimensional hydrogel network • Within initial 20 min 90.2% ± 3.1% of silver ions were released whereas quercetin has shown continuous release for 24 h • Anti-microbial efficacy testing against *P. acnes* and *Staphylococcus aureus* has shown	(Ren et al., 2026)

					an inhibition zones of 33.33 ± 2.08 mm and 31.16 ± 1.28 mm respectively • Reported over 40% bacterial biofilm clearance • Antioxidant efficiency of the hydrogel was up to 73.7% ± 1.3% at 24 h with enhanced lesion resolution	

5. Conclusion and Future Perspective

Preference of patients towards safer and environmentally friendly pharmaceutical products has accelerated the shift from synthetic ingredients toward natural alternatives. Plant extracts and plant-derived compounds, particularly polyphenols, have gained significant attention in pharmaceutical, cosmeceutical and nutraceutical research due to their diverse biological activities and beneficial effects on skin health. Antioxidant, anti-inflammatory, and protective properties make them promising candidates for the development of innovative skincare formulations. However, the practical application of polyphenols is often limited by their poor physicochemical stability, low bioavailability, and limited skin penetration (Bharadvaja et al., 2023). To overcome these challenges, nanocarrier systems have emerged as promising delivery platforms capable of improving stability, enhancing skin penetration, and enabling controlled release of active compounds (Bharadvaja et al., 2023).

The findings summarized in this review indicate that polyphenol-loaded nanocarriers represent a novel and promising strategy for the treatment and management of various skin disorders. Although numerous experimental studies have demonstrated encouraging results, most investigations remain limited to in vitro experiments or animal models. Consequently, well-designed clinical studies are still required to confirm the safety, efficacy, and therapeutic potential of these nano formulations in humans.

In addition, several challenges must be addressed before these systems can be translated into commercially viable products. These include the development of standardized formulation protocols, evaluation of long-term nanoparticle stability, optimization of skin penetration and controlled drug release, and assessment of potential long-term toxicity or immunogenic effects. Furthermore, only a limited number of polyphenolic compounds have been successfully incorporated into nanocarrier systems, highlighting the need for further research to optimize formulations and fully exploit the bioactivity of these complex natural molecules.

Overall, while polyphenol-based nano-formulations show significant promise for improving skin healthcare, overcoming regulatory, technological, and large-scale production challenges will be essential for their successful clinical application and future commercialization.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for profit sectors.

Conflicts of Interest

The authors declare that there is no conflict of interest

References

Abdelmula, W. I. Y., Gorish, B. M. T., Sethupathy, S., Zijing, Z., Altayeb, H. N., & Zhu, D. Green synthesis of polyphenol-grafted lignin nanoparticles and their application as sustainable anti-acne, antioxidant, and UV-blocking agents. *Colloids and Surfaces B: Biointerfaces*, *245*, 114309. (2025).

Abubakar, A. B., & Abduljalal, A. S. The contemporary issues related to conventional treatment of acne and the way forward. *Public Health Risk Assesment Journal*, *2*(1), 17-27. (2024).

Alshamrani, H. M., Alsolami, M. A., Alshehri, A. M., Salman, A. K., Alharbi, M. W., Alzuhayri, A. J., & Mleeh, N. T. Pattern of skin diseases in a university hospital in Jeddah, Saudi Arabia: age and sex distribution. *Annals of Saudi Medicine*, *39*(1), 22-28.(2019)

Amoabediny, G., Haghiralsadat, F., Naderinezhad, S., Helder, M. N., Akhoundi Kharanaghi, E., Mohammadnejad Arough, J., & Zandieh-Doulabi, B. Overview of preparation methods of polymeric and lipid-based (niosome, solid lipid, liposome) nanoparticles: A comprehensive review. *International Journal of Polymeric Materials and Polymeric Biomaterials*, *67*(6), 383-400. (2018).

Basra, M. K., & Shahrukh, M. Burden of skin diseases. *Expert Review of Pharmacoeconomics & Outcomes Research*, *9*(3), 271-283. (2009).

Bharadvaja, N., Gautam, S., & Singh, H. Natural polyphenols: A promising bioactive compounds for skin care and cosmetics. *Molecular Biology Reports*, *50*(2), 1817-1828. (2023).

Bhawana, Basniwal, R. K., Buttar, H. S., Jain, V., & Jain, N. Curcumin nanoparticles: preparation, characterization, and antimicrobial study.

Journal of Agricultural and Food Chemistry, *59*(5), 2056-2061. (2011).

Boguniewicz, M., & Nicol, N. Conventional therapy for atopic dermatitis. *Immunology and Allergy Clinics*, *22*(1), 107-124. (2002).

Bolaños-Cardet, J., Pepió-Tárrega, B., Saiz-Poseu, J., López-Moral, A., Ullah, F., Yuste, V. J., Ruiz-Molina, D., & Suárez-García, S. The redox properties of polyphenols and their role in ROS generation for biomedical applications. *Angewandte Chemie*, *138*(3), e13698. (2026).

Burgberger, M., Mierziak, J., Augustyniak, B., Wojtasik, W., & Kulma, A. (2025). The power of lignans: plant compounds with multifaceted health-promoting effects. *Metabolites*, *15*(9), 589. (2025)

Caddeo, C., Nacher, A., Vassallo, A., Armentano, M. F., Pons, R., Fernàndez-Busquets, X., Carbone, C., Valenti, D., Fadda, A. M., & Manconi, M. (2016). Effect of quercetin and resveratrol co-incorporated in liposomes against inflammatory/oxidative response associated with skin cancer. *International Journal of Pharmaceutics*, *513*(1-2), 153-163. (2016)

Chagas, M. d. S. S., Behrens, M. D., Moragas-Tellis, C. J., Penedo, G. X., Silva, A. R., & Gonçalves-de-Albuquerque, C. F. Flavonols and flavones as potential anti-inflammatory, antioxidant, and antibacterial compounds. *Oxidative medicine and cellular longevity*, *2022*(1), 9966750. (2022)

Chen, K., Yang, H., Xu, G., Hu, Y., Tian, X., Qin, S., & Jiang, T.. Enhanced skin penetration of curcumin by a nanoemulsion-embedded oligopeptide hydrogel for psoriasis topical therapy. *RSC Medicinal Chemistry*, *16*(2), 961-969. (2025)

Chiu, Y.-H., Wu, Y.-W., Hung, J.-I., & Chen, M.-C.. Epigallocatechin gallate/L-ascorbic acid–loaded poly-γ-glutamate microneedles with antioxidant, anti-inflammatory, and immunomodulatory effects for the treatment of atopic dermatitis. *Acta biomaterialia*, *130*, 223-233. (2021)

Choi, S., Ko, J., Park, S. B., Kim, J. Y., Ha, J. H., Roh, S., An, Y. H., & Hwang, N. S. Double emulsion-mediated delivery of polyphenol mixture alleviates atopic dermatitis. *Advanced healthcare materials*, *12*(30), 2300998. (2023)

Da Silva, A. P. G., Sganzerla, W. G., John, O. D., & Marchiosi, R. A comprehensive review of the classification, sources, biosynthesis, and biological properties of hydroxybenzoic and hydroxycinnamic acids. *Phytochemistry Reviews*, *24*(2), 1061-1090. (2025)

De Rossi, L., Rocchetti, G., Lucini, L., & Rebecchi, A. (2025). Antimicrobial potential of polyphenols: Mechanisms of action and microbial responses—A narrative review. *Antioxidants*, *14*(2), 200.

Działo, M., Mierziak, J., Korzun, U., Preisner, M., Szopa, J., & Kulma, A. The potential of plant phenolics in prevention and therapy of skin disorders. *International Journal of Molecular Sciences*, *17*(2), 160. (2016)

El-Zaafarany, G. M., & Nasr, M. (2021). Insightful exploring of advanced nanocarriers for the topical/transdermal treatment of skin diseases. *Pharmaceutical Development and Technology*, *26*(10), 1136-1157. (2021)

Fujii, M. Current understanding of pathophysiological mechanisms of atopic dermatitis: interactions among skin barrier dysfunction, immune abnormalities and pruritus. *Biological and Pharmaceutical Bulletin*, *43*(1), 12-19.(2020)

Gaetano, V., Gagliardi, A., Giuliano, E., Longo, E., & Cosco, D. Chitosan Nanoparticles Loaded with Polyphenols for Cosmeceutical Applications: A State-of-the-Art Review. *Pharmaceutics*, *17*(8), 1068. (2025)

Guo, J.-W., & Jee, S.-H. Strategies to develop a suitable formulation for inflammatory skin disease treatment. *International Journal of Molecular Sciences*, *22*(11), 6078. (2021).

Gupta, M., Agrawal, U., & Vyas, S. P. Nanocarrier-based topical drug delivery for the treatment of skin diseases. *Expert opinion on drug delivery*, *9*(7), 783-804. (2012).

Han, M., Wang, X., Wang, J., Lang, D., Xia, X., Jia, Y., & Chen, Y. (2022). Ameliorative effects of epigallocatechin-3-gallate nanoparticles on 2, 4-dinitrochlorobenzene induced atopic dermatitis: a potential mechanism of inflammation-related necroptosis. *Frontiers in Nutrition*, *9*, 953646.(2022)

Hu, W., Liu, D., Gao, J., Zhang, X., Zhang, Q., & Han, L. (2025). Bioinspired polyphenols nanoparticles-assembled microneedles integrating antioxidant defense with immune-melanogenic reprogramming for precision vitiligo phototherapy. *Chinese Chemical Letters*, 111877. (2025)

Imran, M., Ali, M., Saifuddin, D., Chaudhary, A., Ahmad, A., & Mohammed, Y. Bioactive Polyphenolic Nanoformulations as Potential Therapeutic Agents Against Psoriasis. In *Emergence of Sustainable Biomaterials in Tackling Inflammatory Diseases* (pp. 431-457). Springer. (2025)

Imran, M., Iqubal, M. K., Imtiyaz, K., Saleem, S., Mittal, S., Rizvi, M. M. A., Ali, J., & Baboota, S. Topical nanostructured lipid carrier gel of quercetin and resveratrol: Formulation, optimization, in vitro and ex vivo study for the treatment of skin cancer. *International Journal of Pharmaceutics*, *587*, 119705.(2020).

Jafferany, M., Huynh, T. V., Silverman, M. A., & Zaidi, Z. Geriatric dermatoses: a clinical review of skin diseases in an aging population. *International journal of dermatology*, *51*(5), 509-522. (2012).

Jin, Z., Song, Y., & He, L. A review of skin immune processes in acne. *Frontiers in immunology*, *14*, 1324930. (2023)

Kamble, A. S., Sutar, A. D., Kaur, G., Singh, K. K., & Shukla, R. Naringenin-encapsulated nano-cochleate hydrogel for topical delivery: cellular anti-inflammatory activity and dermatokinetic profiling. *RSC Pharmaceutics*.(2026)

Karimkhani, C., Dellavalle, R. P., Coffeng, L. E., Flohr, C., Hay, R. J., Langan, S. M., Nsoesie, E. O., Ferrari, A. J., Erskine, H. E., & Silverberg, J. I. Global skin disease morbidity and mortality: an update from the global burden of disease study 2013. *JAMA dermatology*, *153*(5), 406-412. (2017).

Keshari, R., Bagale, R., Rath, S., Raut, S., Bhatt, L. K., De, A., Sen, S., & Srivastava, R. Soya lecithin–PLGA based hybrid nanocomposite enhances resveratrol delivery for psoriasis treatment and management. *Industrial Crops and Products*, *236*, 121575. (2025).

Keshari, R., Tharmatt, A., Pillai, M. M., Chitkara, D., Tayalia, P., Banerjee, R., Sen, S., & Srivastava, R. Eugenol-Loaded lipid Nanoparticles-Derived hydrogels ameliorate Psoriasis-like skin lesions by Lowering oxidative stress and modulating inflammation. *ACS Pharmacology & Translational Science*, *7*(11), 3592-3606. (2024).

Khoo, H. E., Azlan, A., Tang, S. T., & Lim, S. M. Anthocyanidins and anthocyanins: Colored pigments as food, pharmaceutical ingredients, and the potential health benefits. *Food & nutrition research*, *61*(1), 1361779. (2017).

Kollmann, T. R., Kampmann, B., Mazmanian, S. K., Marchant, A., & Levy, O. Protecting the newborn and young infant from infectious diseases: lessons from immune ontogeny. *Immunity*, *46*(3), 350-363. (2017).

Kuchekar, A. B., Pujari, R. R., Kuchekar, S. B., Dhole, S. N., Mule, P. M., Vidyapeeth, B., & Wadi, B. Psoriasis: A comprehensive review. *Int J Pharm Life Sci*, *2*(6), 857-877. (2011).

Li, L., Zhang, M., Liu, T., Li, J., Sun, S., Chen, J., Liu, Z., Zhang, Z., & Zhang, L. Quercetin-ferrum nanoparticles enhance photothermal therapy by modulating the tumor immunosuppressive microenvironment. *Acta biomaterialia*, *154*, 454-466. (2022).

Lian, N., & Chen, M. Metabolic syndrome and skin disease: potential connection and risk. *International Journal of Dermatology and Venereology*, *2*(02), 89-93. (2019).

Liu, C., Yan, Z., Chen, X., Mandal, S., Das, U., Singh, S., & Olatunji, O. J. Pharmacological insights on multifaceted therapeutic applications of stilbenoids: A comprehensive updates. *Fitoterapia*, 107034. (2025).

Liu, H.-M., Cheng, M.-Y., Xun, M.-H., Zhao, Z.-W., Zhang, Y., Tang, W., Cheng, J., Ni, J., & Wang, W. Possible mechanisms of oxidative stress-induced skin cellular senescence, inflammation, and cancer and the therapeutic potential of plant polyphenols. *International Journal of Molecular Sciences*, *24*(4), 3755. (2023).

Liu, J., Xu, X., Zhou, J., Sun, G., Li, Z., Zhai, L., Wang, J., Ma, R., Zhao, D., & Jiang, R.

Phenolic acids in Panax ginseng inhibit melanin production through bidirectional regulation of melanin synthase transcription via different signaling pathways. *Journal of ginseng research*, *47*(6), 714-725. (2023).

López-Herrador, S., Corral-Sarasa, J., González-García, P., Morillas-Morota, Y., Olivieri, E., Jiménez-Sánchez, L., & Díaz-Casado, M. E. Natural hydroxybenzoic and hydroxycinnamic acids derivatives: mechanisms of action and therapeutic applications. *Antioxidants*, *14*(6), 711. (2025).

Lowes, M. A., Suarez-Farinas, M., & Krueger, J. G. Immunology of psoriasis. *Annual review of immunology*, *32*(1), 227-255. (2014).

Lueangarun, S., Sriviriyakul, K., Tempark, T., Managit, C., & Sithisarn, P. Clinical efficacy of 0.5% topical mangosteen extract in nanoparticle loaded gel in treatment of mild-to-moderate acne vulgaris: A 12-week, split-face, double-blinded, randomized, controlled trial. *Journal of cosmetic dermatology*, *18*(5), 1395-1403. (2019).

Mocanu, M., Vâță, D., Alexa, A.-I., Trandafir, L., Patrașcu, A.-I., Hâncu, M. F., & Gheucă-Solovăstru, L. Atopic dermatitis—beyond the skin. *Diagnostics*, *11*(9), 1553. (2021).

Parisi, O. I., Puoci, F., Restuccia, D., Farina, G., Iemma, F., & Picci, N.. Polyphenols and their formulations: different strategies to overcome the drawbacks associated with their poor stability and bioavailability. In *Polyphenols in human health and disease* (pp. 29-45). Elsevier. (2014)

Patil, P., Datir, S., & Saudagar, R. A review on topical gels as drug delivery system. *Journal of Drug Delivery & Therapeutics*, *9*. (2019)

Pezzolo, E., & Naldi, L.. Epidemiology of major chronic inflammatory immune-related skin diseases in 2019. *Expert Review of Clinical Immunology*, *16*(2), 155-166. (2020)

Prabhu, S., Molath, A., Choksi, H., Kumar, S., & Mehra, R. Classifications of polyphenols and their potential application in human health and diseases. *Int. J. Physiol. Nutr. Phys. Educ*, *6*(1), 293-301.(2021).

Proteggente, A. R., Pannala, A. S., Paganga, G., Buren, L. v., Wagner, E., Wiseman, S., Put, F. v. d., Dacombe, C., & Rice-Evans, C. A. The antioxidant activity of regularly consumed fruit and vegetables reflects their phenolic and vitamin C composition. *Free radical research*, *36*(2), 217-233. (2002).

Ramanunny, A. K., Wadhwa, S., Gulati, M., Singh, S. K., Kapoor, B., Dureja, H., Chellappan, D. K., Anand, K., Dua, K., & Khursheed, R. Nanocarriers for treatment of dermatological diseases: Principle, perspective and practices. *European journal of pharmacology*, *890*, 173691. (2021).

Ravikumar, P., Katariya, M., Patil, S., Tatke, P., & Pillai, R. Skin delivery of resveratrol encapsulated lipidic formulation for melanoma chemoprevention. *Journal of microencapsulation*, *36*(6), 535-551. (2019).

Ren, J., Chen, Z., You, X., Zhao, Z., & Xu, L. Radiation Crosslinked Marine Polysaccharide Aqueous Gel Quercetin Silver Nanocomposite for Synergistic Treatment of Acne. *Journal of Applied Polymer Science*, e70360. (2026).

Roky, A. H., Islam, M. M., Ahasan, A. M. F., Mostaq, M. S., Mahmud, M. Z., Amin, M. N., & Mahmud, M. A. Overview of skin cancer types and prevalence rates across continents. *Cancer pathogenesis and therapy*, *3*(02), 89-100. (2025).

Samir, B., El-Kamel, A., Zahran, N., & Heikal, L. Resveratrol-loaded invasome gel: A promising nanoformulation for treatment of skin cancer. *Drug Delivery and Translational Research*, *14*(12), 3354-3370. (2024).

Schafer, N., Balwierz, R., Biernat, P., Ochędzan-Siodłak, W., & Lipok, J. Natural ingredients of transdermal drug delivery systems as permeation enhancers of active substances through the stratum corneum. *Molecular pharmaceutics*, *20*(7), 3278-3297. (2023).

Shamsudin, N. F., Ahmed, Q. U., Mahmood, S., Ali Shah, S. A., Khatib, A., Mukhtar, S., Alsharif, M. A., Parveen, H., & Zakaria, Z. A. Antibacterial effects of flavonoids and their structure-activity relationship study: A comparative interpretation. *Molecules*, *27*(4), 1149. (2022).

Sheikh, A., Hazari, S. A., Molugulu, N., Alshehri, S. A., Wahab, S., Sahebkar, A., & Kesharwani,

P. Hyaluronic acid engineered gallic acid embedded chitosan nanoparticle as an effective delivery system for treatment of psoriasis. *Environmental Research*, *238*, 117086. (2023).

Sroka-Tomaszewska, J., & Trzeciak, M. Molecular mechanisms of atopic dermatitis pathogenesis. *International Journal of Molecular Sciences*, *22*(8), 4130. (2021)

Sun, M.-C., Xu, X.-L., Lou, X.-F., & Du, Y.-Z.. Recent progress and future directions: the nano-drug delivery system for the treatment of vitiligo. *International journal of nanomedicine*, 3267-3279. (2020).

Urooj, S., Zahid, F., Khurshid, H., Alamri, A. H., Asiri, Z. A., Alruwaili, N. K., Amin, M., Shah, K. U., & ud Din, F. Statistically optimized, apigenin loaded ultra-deformable liposomes for the management of imiquimod induced psoriasis in mice model. *Journal of Drug Delivery Science and Technology*, 107681. (2025).

Vasam, M., Korutla, S., & Bohara, R. A. Acne vulgaris: A review of the pathophysiology, treatment, and recent nanotechnology based advances. *Biochemistry and biophysics reports*, *36*, 101578. (2023).

Wang, Y., Liu, X.-J., Chen, J.-B., Cao, J.-P., Li, X., & Sun, C.-D. Citrus flavonoids and their antioxidant evaluation. *Critical Reviews in Food Science and Nutrition*, *62*(14), 3833-3854. (2022).

Xuan, Y., Yang, Y., Xiang, L., & Zhang, C. The role of oxidative stress in the pathogenesis of vitiligo: a culprit for melanocyte death. *Oxidative medicine and cellular longevity*, (1), 8498472. (2022)

Yakupu, A., Aimaier, R., Yuan, B., Chen, B., Cheng, J., Zhao, Y., Peng, Y., Dong, J., & Lu, S. (2023). The burden of skin and subcutaneous diseases: findings from the global burden of disease study 2019. *Frontiers in public health*, *11*, 1145513. (2022)

Yang, S.-C., Chang, Z.-Y., Hsiao, C.-Y., Alshetaili, A., Wei, S.-H., Hsiao, Y.-T., & Fang, J.-Y. Topical anti-inflammatory effects of quercetin glycosides on atopic dermatitis-like lesions: Influence of the glycone type on efficacy and skin absorption. *Inflammation*, *48*(5), 2856-2873. (2025).

Zhang, H., Wang, X., Wang, Y., Zhao, Y., Chen, Y., Cui, Y., & Wang, Q. Tanshinone IIA and Quercetin Loaded Nanoemulsion-Thermogel Composite System for Enhanced Acne Management: In-vitro/In-vivo Evaluation. *Journal of Drug Delivery Science and Technology*, 107918. (2025).

Zhang, Y., Gong, S., Liu, L., Shen, H., Liu, E., Pan, L., Gao, N., Chen, R., & Huang, Y. Cyclodextrin-coordinated liposome-in-gel for transcutaneous quercetin delivery for psoriasis treatment. *ACS Applied Materials & Interfaces*, *15*(34), 40228-40240. (2023).