

Review

Fungal Bioactives in Modern Cosmetic Formulations—A Review

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Abstract

Fungal-derived compounds are attracting increasing interest in cosmetic science because of their chemical diversity, multifunctional biological activity, and suitability for controlled biotechnological production. Macrofungi produce a wide range of bioactive metabolites, including polysaccharides, phenolic compounds, terpenoids, sterols, and pigments, many of which exhibit antioxidant, anti-inflammatory, moisturizing, photoprotective, and barrier-supporting properties relevant to skin health. However, current research is largely limited to isolated metabolites and simplified in vitro models, whereas comparatively little attention has been paid to the performance of fungal-derived compounds in finished cosmetic formulations. In practice, cosmetic efficacy depends not only on biological activity but also on extraction methods, physicochemical stability, formulation compatibility, and delivery efficiency. This review examines fungal-derived bioactive compounds from the perspective of cosmetic formulation and industrial applicability. It discusses how cultivation conditions, extraction procedures, and formulation design influence stability, bioavailability, and cosmetic performance, and critically evaluates extraction technologies, fermentation systems, encapsulation strategies, lipid carriers, hydrogels, and nanoscale delivery platforms. The review also addresses major limitations, including oxidative instability, variability in metabolite composition, limited penetration of high-molecular-weight compounds, and insufficient standardization and clinical validation. Although fungal-derived compounds show considerable promise for multifunctional cosmetic formulations, their broader industrial application will require improved standardization, optimized formulation strategies, and robust clinical evaluation of efficacy and safety.



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1. Introduction

Biotechnologically derived ingredients are receiving increasing attention in cosmetic research because controlled production systems offer greater reproducibility and reduced dependence on environmental variability than many conventional botanical raw materials. Even minor differences in raw material composition may influence formulation stability, sensory properties, and biological performance. Controlled microbial cultivation

also enables the optimization of production processes and large-scale production under standardized conditions [1–3].

Among microbial systems, fungi represent one of the most chemically diverse sources of bioactive metabolites [4–6]. Macrofungi produce polysaccharides, phenolic compounds, terpenoids, sterols, pigments, and peptides with potential relevance to skin physiology [5–7]. Reported activities include antioxidant effects, modulation of inflammatory pathways, support of epidermal barrier function, regulation of melanogenesis, and protection against extracellular matrix degradation [7–9]. These properties have led to increasing interest in fungal-derived compounds as cosmetic ingredients, particularly in moisturizing, anti-aging, regenerative, and photoprotective formulations [6,7].

Despite the growing interest in their biological activity, the incorporation of fungal metabolites into finished cosmetic products remains relatively limited [3,5,6]. Most available studies focus on isolated compounds or simplified *in vitro* models under controlled experimental conditions [5,6,10]. Much less attention has been paid to formulation-dependent behavior, storage stability, compatibility with cosmetic matrices, or skin delivery. Consequently, promising mechanistic findings often fail to translate into consistent cosmetic performance [3,5].

Research in this area also remains fragmented. Studies on fungal bioactive compounds are commonly divided among natural product chemistry, fermentation technology, extraction methods, biological evaluation, and formulation design [5,11,12]. The relationships between these stages are discussed less frequently, although they directly affect stability, bioavailability, release behavior, and skin interaction [13].

Several technological limitations continue to limit the broader industrial application of fungal-derived cosmetic ingredients [3,5]. Variability associated with strain selection, cultivation conditions, and extraction procedures compromises reproducibility and standardization [6,14–16]. In addition, high-molecular-weight polysaccharides show limited penetration through the stratum corneum, whereas lipophilic metabolites often require carrier systems to improve dispersion and delivery [17–19]. Oxidative instability during processing and storage presents another important challenge [20].

This review focuses on fungal-derived bioactive compounds in cosmetic formulations, with particular emphasis on extraction strategies, physicochemical properties, formulation architecture, delivery systems, and industrial applicability. Current limitations related to standardization, stability, delivery efficiency, and clinically relevant efficacy assessment are also critically evaluated [3]. Unlike previous reviews, which have mainly emphasized the biological activities and cosmetic potential of fungal-derived compounds, the present review adopts a translational perspective. It integrates fungal biotechnology, extraction technologies, formulation science, safety assessment, regulatory considerations, and the current level of clinical evidence. This integrated approach provides a comprehensive framework for understanding the factors governing the successful incorporation of fungal-derived bioactive compounds into modern cosmetic formulations. It also identifies key scientific and technological challenges, current knowledge gaps, and future research directions [21,22]. The relationships between fungal bioactive compounds, production technologies, delivery systems, mechanisms of action, and their cosmetic functions are summarized in Figure 1.

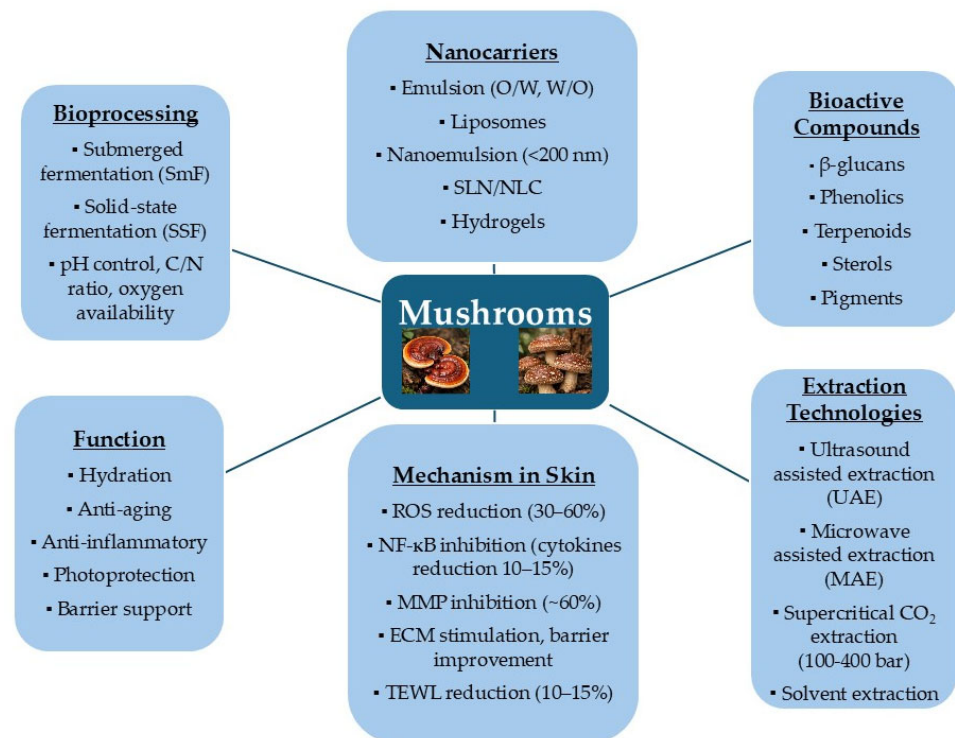


Figure 1. Overview of fungal-derived bioactive compounds, extraction technologies, biotechnological production systems, delivery platforms, mechanisms of action in skin, and their potential cosmetic functions.

2. Methods

This review was conducted as a structured narrative review aimed at critically evaluating fungal-derived bioactive compounds and their applications in cosmetic formulations. Particular emphasis was placed on extraction technologies, formulation strategies, biological activity, delivery systems, safety assessment, regulatory considerations, and industrial applicability. To improve the transparency and reproducibility of the literature identification and selection process, the review methodology was guided, where applicable, by the principles of the PRISMA 2020 Statement [23]. However, owing to the substantial methodological heterogeneity of the available evidence, including differences in fungal species, extraction procedures, analytical techniques, formulation strategies, experimental models, and reported outcome measures, the review was not designed as a full systematic review. Therefore, no quantitative meta-analysis was performed.

A comprehensive literature search was conducted between 10 April and 25 May 2025 using four electronic databases: Scopus, Web of Science, PubMed, and Google Scholar. No restrictions regarding the year of publication were applied during the initial search to capture both historical and contemporary studies relevant to fungal-derived cosmetic ingredients. Nevertheless, priority was given to recent peer-reviewed publications reflecting current advances in cosmetic science, fungal biotechnology, formulation engineering, and skin biology. Earlier publications were included only when they represented seminal studies or provided essential information on biological mechanisms, extraction methodologies, formulation technologies, or analytical approaches. The search strategy combined controlled vocabulary with free-text keywords related to fungal bioactive compounds, cosmetic science, and formulation technologies. Representative search terms included “fungal bioactives”, “macrofungi”, “fungal metabolites”, “mushroom extracts”, “cosmetic formulations”, “cosmeceuticals”, “skin delivery”, “encapsulation”, “nanoformulations”, “liposomes”, “solid lipid nanoparticles”, “hydrogels”, “ β -glucans”, “triterpenoids”, “phenolic compounds”, “ergosterol”,

“antioxidant activity”, “anti-inflammatory activity”, “photoprotection”, “skin barrier”, “fungal biotechnology”, and “fermentation”. Boolean operators (AND, OR) were used, where appropriate, to refine and optimize the search strategy for each database. The eligibility criteria were established prior to the literature screening process. Publications were considered eligible if they investigated fungal-derived compounds with potential cosmetic relevance, including studies addressing extraction technologies, cultivation, biotechnological production, physicochemical characterization, formulation development, encapsulation strategies, skin delivery systems, biological activity, safety evaluation, regulatory aspects, or industrial applications. Both original research articles and review papers published in peer-reviewed journals were considered.

Studies were excluded if they were unrelated to cosmetic or topical applications, lacked sufficient methodological or analytical information, focused exclusively on pharmacological applications without relevance to cosmetic science, or did not provide information relevant to the objectives of the present review. Conference abstracts, editorials, and duplicate publications were also excluded. The initial identification of potentially relevant publications was performed by one author through database searches and manual screening of the reference lists of eligible articles. Subsequently, the retrieved studies were independently evaluated by three authors for their scientific relevance, methodological quality, and consistency with the scope of the review. Any uncertainties regarding study eligibility were resolved through discussion until consensus was achieved.

The selected literature was critically evaluated with particular emphasis on methodological quality, analytical characterization of fungal-derived compounds, extraction procedures, formulation-related properties, physicochemical stability, bioavailability, biological evidence, safety considerations, regulatory aspects, and industrial applicability. to the considerable heterogeneity of study designs, fungal species, extraction methods, formulation approaches, experimental models, and reported outcome measures, the available evidence was synthesized qualitatively rather than quantitatively. The literature identification and study selection process is summarized in the workflow presented in Figure 2.

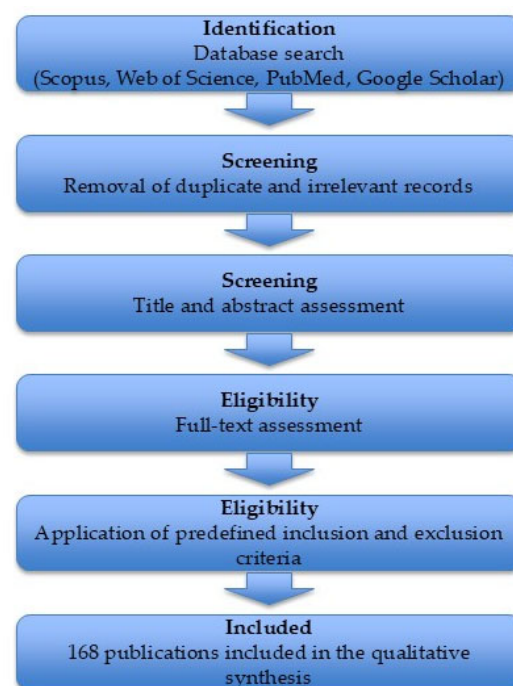


Figure 2. Workflow summarizing the literature identification and study selection process used in the present review.

3. Fungi as a Source of Cosmetic Raw Materials

Fungi are among the most chemically diverse sources of bioactive compounds explored for cosmetic applications [24,25]. Unlike many plant-derived raw materials, fungal biomass can be produced under controlled fermentation conditions, thereby improving the reproducibility of metabolite production while reducing dependence on environmental variability [24,26,27]. Even relatively small differences in chemical composition may influence formulation stability, sensory properties, and biological performance in cosmetic systems [20,28]. Interest in fungal metabolites continues to expand, with more than 900 new compounds being reported in 2024 alone [29].

Macrofungi produce a broad spectrum of primary and secondary metabolites, including polysaccharides, phenolic compounds, terpenoids, sterols, pigments, proteins, and peptide fractions [30–32]. In cosmetic systems, their functionality is determined not only by their biological activity but also by physicochemical properties, such as molecular weight, polarity, rheological behavior, and oxidative stability [33]. These characteristics affect formulation compatibility, bioavailability, and interactions at the skin surface [17].

Polysaccharides are among the most extensively studied fungal metabolites in cosmetic and skin-related research [34,35]. Particular attention has been given to β -glucans composed mainly of β -(1 $\rightarrow$ 3) and β -(1 $\rightarrow$ 6)-linked glucose units [36]. Their molecular weight typically ranges from 10^5 to 10^6 Da, although the molecular weight distribution may be broader depending on the fungal species, extraction conditions, and fractionation procedures [34]. In extracts obtained from *Lentinula edodes*, β -glucans accounted for $13.86 \pm 0.79\%$ of total glucans, which reached $16.94 \pm 0.66\%$ [37].

Due to their hydrophilic and film-forming properties, fungal polysaccharides are widely used in formulations intended to improve skin hydration and barrier function [7,34]. Reductions in transepidermal water loss (TEWL) of approximately 10–15% are commonly reported in formulation studies [38]. Formulations containing *Tremella fuciformis* polysaccharides have been reported to improve skin hydration and reduce transepidermal water loss (TEWL) [39]. However, their high molecular weight limits penetration through the stratum corneum, restricting their activity largely to the skin surface unless penetration-enhancing systems are used [18].

Extracellular polysaccharides (EPS) produced during fungal fermentation differ from intracellular polysaccharide fractions in rheological behavior and may affect the texture and sensory properties of cosmetic formulations [40,41]. EPS isolated from *Grifola frondosa* reduced the expression of MMP-1 mRNA by approximately 61.1% at a concentration of 250 $\mu\text{g/mL}$ in UVA-irradiated human dermal fibroblasts [42]. EPS production varies substantially among fungal strains and cultivation conditions, and optimization of submerged culture parameters may markedly increase polysaccharide yields [43]. Comparisons between studies are complicated by differences in cultivation protocols, extraction procedures, and analytical methodologies, which are often insufficiently standardized [44].

Fungal phenolic compounds, including phenolic acids and hispidin-related derivatives, are widely investigated because of their antioxidant and anti-inflammatory properties [45,46]. Their antioxidant activity is largely related to ROS scavenging and electron-donating capacity [47]. Both phenolic content and antioxidant potential vary substantially among fungal species and extraction protocols [48,49]. Total phenolic content may range from approximately 5–15 mg GAE/g in lower-yield extracts to more than 80 mg GAE/g extract in highly active systems such as *Inonotus obliquus* [50]. Reported DPPH IC_{50} values range from approximately 15–40 $\mu\text{g/mL}$ in highly active extracts to over 100–300 $\mu\text{g/mL}$ in lower-potency preparations, including some *Pleurotus ostreatus* extracts [51].

Antioxidant activity data should be interpreted with caution, since the extraction solvent, fractionation strategy, assay conditions, and normalization methods can substantially

influence the reported results [47,51]. In some studies, DPPH IC₅₀ values for mushroom extracts varied by approximately fourfold, depending on the extraction solvent and analytical methodology, ranging from 21.7 to 96.3 µg/mL [51]. Due to their relatively low molecular weight and their polarity, fungal phenolic compounds are generally compatible with aqueous cosmetic formulations [14]. However, their use in topical systems may be complicated by oxidative instability during processing and storage [52].

Terpenoids, especially lanostane-type triterpenes, represent another major class of fungal metabolites relevant to cosmetic applications. In *Ganoderma lucidum*, ganoderic acids may constitute the major triterpenoid fraction, with ganoderic acid T and ganoderic acid S reported among the predominant compounds in some extract [53]. Lower total triterpenoid levels have been observed in species such as *Antrodia camphorata*, although their concentrations vary substantially depending on cultivation and extraction conditions [54]. These compounds are widely studied for their antioxidant and anti-inflammatory effects, including the modulation of nitric oxide (NO), TNF-α, IL-6, and matrix metalloproteinase-related pathways [55]. Application of fungal triterpenoids in cosmetic systems is complicated by poor aqueous solubility and high lipophilicity. For this reason, lipid carriers, nanoformulations, and encapsulation strategies are frequently explored to improve dispersion and bioavailability [17]. Another challenge is oxidative degradation during processing and storage, which may compromise both formulation stability and biological activity [52].

Compared to polysaccharides and triterpenoids, fungal sterols have received less attention in cosmetic research. Ergosterol, the predominant fungal sterol, is usually present at concentrations below 1% of dry biomass and is highly sensitive to UV exposure and oxidation. Although present at relatively low levels, ergosterol may contribute to membrane stability and the organization of the skin barrier because of its structural similarity to other biologically relevant sterols [56,57]. Their compatibility with lipid-based cosmetic systems and their potential interactions with stratum corneum lipids may further support their application in barrier-oriented formulations [58].

Fungal pigments, including carotenoids and melanin-like compounds, represent another group of fungal-derived bioactive compounds with potential cosmetic relevance, although they remain relatively poorly characterized [59,60]. In *Cordyceps militaris*, β-carotene and lycopene contents reached approximately 0.328 ± 0.045 mg/g and 0.277 ± 0.004 mg/g, respectively [61]. Pigment concentrations vary widely among fungal species and under different cultivation conditions, ranging from µg/g to mg/g [62]. Antioxidant and photoprotective activities have been described in several experimental models, with ROS reduction estimated at approximately 30–60%, depending on the assay methodology and experimental conditions [63].

Results obtained in chemical antioxidant assays do not always reflect performance in complex cosmetic formulations. Carotenoids are highly sensitive to oxidation and light exposure, whereas melanin-like pigments present additional formulation challenges related to coloration, limited solubility, and insufficient standardization [59].

Proteins and peptide fractions derived from fungi have received less attention than polysaccharides, phenolic compounds, or terpenoids. Existing studies indicate moisturizing and skin-conditioning effects, although mechanistic evidence and quantitative data remain limited. Their application in cosmetic systems may be complicated by structural instability and susceptibility to enzymatic degradation [6].

The activity of fungal-derived cosmetic ingredients usually results from multicomponent extracts rather than isolated compounds alone. Interactions between hydrophilic and lipophilic fractions may influence viscosity, oxidative stability, rheological behavior, release profile, and bioavailability in cosmetic formulations. High-molecular-weight polysaccharides are primarily associated with film formation and water retention, whereas lipophilic

metabolites, such as triterpenoids, often require carrier systems to improve distribution and interaction with the skin surface [34,64].

Although fungal-derived bioactive compounds show considerable cosmetic potential, several factors still limit their broader industrial application [65]. Variability in metabolite production among strains and cultivation systems compromises reproducibility and standardization. The chemical complexity of fungal extracts also makes it difficult to attribute biological effects to individual compounds. Another major challenge is the limited number of robust clinical studies evaluating the long-term efficacy and safety of fungal-derived cosmetic ingredients under realistic conditions of cosmetic use [24,65]. Table 1 summarizes the principal fungal-derived bioactive compounds relevant to cosmetic applications, together with their biological functions, technological advantages, and formulation challenges. Table 1. Major classes of fungal bioactive compounds relevant to cosmetic applications.

Table 1. Major classes of fungal bioactive compounds relevant to cosmetic applications.

Bioactive Class	Representative Compounds	Main Biological Activities	Potential Cosmetic Applications	Major Limitations	Industrial Consideration	References
Polysaccharides	β -glucans, heteropolysaccharides, exopolysaccharides	Moisturizing, antioxidant, immunomodulatory, wound-healing, barrier-supporting	Hydrating products, anti-aging formulations, post-treatment care, barrier repair cosmetics	High molecular weight, limited skin penetration, viscosity-related formulation challenges	Require delivery systems or formulation strategies to enhance skin penetration while preserving hydration and film-forming properties.	[7,34,39,44]
Phenolic compounds	Gallic acid, protocatechuic acid, <i>p</i> -hydroxybenzoic acid, hispidin derivatives	Antioxidant, anti-inflammatory, photoprotective, anti-aging	Protective formulations, antioxidant serums, anti-pollution cosmetics	Oxidative instability, sensitivity to processing and storage conditions	Require stabilization against oxidation and careful control of processing and storage conditions.	[14,45,46,48]
Triterpenoids	Ganoderic acids, lucidenic acids, lanostane derivatives	Anti-inflammatory, anti-melanogenic, anti-aging, regenerative	Anti-aging products, skin-soothing formulations, multifunctional dermocosmetics	Poor aqueous solubility, limited bioavailability	Need solubility-enhancing formulation approaches and advanced carrier systems to improve bioavailability.	[8,53–55]
Sterols	Ergosterol and derivatives	Barrier-supporting, antioxidant, membrane-stabilizing	Barrier-repair formulations, protective skincare products	Sensitivity to UV radiation and oxidation	Require protection against oxidative degradation during formulation and storage.	[11,56–58]
Pigments	Carotenoids, melanin-like compounds	Antioxidant, photoprotective, free-radical scavenging	Photoprotective cosmetics, protective skincare products	Color stability, formulation compatibility, oxidation susceptibility	Limited formulation versatility due to color stability and oxidative degradation.	[59]
Proteins and peptides	Bioactive peptides, protein fractions	Conditioning, moisturizing, regenerative effects	Skin-conditioning and moisturizing formulations	Limited stability, enzymatic degradation	Require stabilization strategies to preserve biological activity during formulation and storage.	[10,22]
Complex extracts	Multi-component fungal extracts	Multifunctional biological activity resulting from synergistic interactions	Multifunctional cosmetic formulations	Difficult standardization and batch-to-batch variability		[5,6,22,66]

4. Extraction and Biotechnological Production Technologies

Successful incorporation of fungal-derived compounds into cosmetic formulations depends not only on their biological activity but also on the way these metabolites are

produced, isolated, purified, and stabilized before formulation [66]. Extraction strategies and downstream processing strongly influence whether fungal metabolites can be effectively applied as a cosmetic ingredient. Parameters such as extraction temperature, solvent polarity, purification intensity, and drying conditions directly affect chemical composition, molecular integrity, oxidative stability, and formulation compatibility [67].

A major challenge in the extraction and formulation of fungal-derived bioactive compounds is their remarkable chemical diversity. Hydrophilic macromolecules, particularly polysaccharides, differ substantially from low-molecular-weight phenolic compounds and highly lipophilic triterpenoids or sterols in terms of their physicochemical properties, extraction behavior, and solvent affinity. Consequently, extraction procedures should be tailored to specific classes of fungal metabolites rather than used as a universal approach. Polysaccharides are typically isolated using aqueous extraction systems, especially hot water extraction performed at temperatures of approximately 80–100 °C [34]. Elevated temperatures improve β -glucan solubilization and facilitate disruption of the fungal cell walls, generally increasing the extraction yield. However, prolonged thermal exposure may partially depolymerize polysaccharide fractions and alter their rheological properties [38,68]. In cosmetic formulations, these structural modifications are important because viscosity, film-forming properties, hydration capacity, and sensory characteristics are closely related to the molecular structure [69].

Hydroalcoholic extraction systems are commonly used for the extraction of medium-polar metabolites, including many fungal phenolic compounds. Ethanol–water mixtures remain particularly attractive because they combine relatively high extraction efficiency with compatibility with cosmetic applications. However, a major limitation is their low extraction selectivity. Hydroalcoholic solvents often co-extract proteins, pigments, and polymeric fractions which can affect formulation stability, odor, color, and oxidative resistance [67,70,71].

Lipophilic metabolites, such as lanostane-type triterpenoids and sterols require extraction conditions that differ from those used for hydrophilic fungal fractions. Conventional organic solvents often provide high recovery of these compounds. However, their use raises concerns related to residual solvents, environmental impact, and downstream purification. Alternative extraction technologies are therefore being increasingly explored to improve selectivity while reducing solvent consumption [72].

Among advanced extraction methods, ultrasound-assisted extraction (UAE) is one of the most widely studied techniques for fungal metabolites. Acoustic cavitation enhances solvent penetration into fungal matrices and accelerates mass transfer, often reducing extraction time by 30–70% compared to conventional procedures. UAE can also reduce solvent consumption and improve recovery of phenolic compounds and selected triterpenoids. However, excessive sonication intensity may promote the oxidation and degradation of sensitive compounds, particularly during prolonged extraction or at high power settings [72,73].

Microwave-assisted extraction (MAE) is another extraction technique used to enhance extraction efficiency [74]. Rapid heating of the solvent–matrix system shortens processing time and can improve the recovery of intracellular metabolites. A major limitation is localized overheating, which may be difficult to control in extracts containing thermolabile compounds. Despite their clear advantages at the laboratory scale, the industrial application of UAE and MAE in cosmetic manufacturing remains limited because reproducibility, process scalability, and uniform energy distribution continue to pose technical challenges [75,76].

Supercritical fluid extraction (SFE), particularly when using supercritical CO₂, is widely used for the isolation of lipophilic fungal metabolites [77]. Performed at moderate

temperatures and elevated pressures, SFE enables the selective extraction of triterpenoids, sterols, and other non-polar fractions while reducing residual organic solvents levels in the final extract. High-purity extracts obtained by SFE often exhibit improved oxidative stability and greater compatibility with cosmetic formulations [78]. The main challenges associated with SFE include high equipment costs, process complexity, and the need for careful optimization of pressure conditions and co-solvent composition [79,80].

Alongside extraction technologies, fungal biotechnology plays a key role in determining metabolite composition and production efficiency. Submerged fermentation (SmF) is currently the dominant cultivation strategy because it enables precise control of parameters such as pH, oxygen availability, nutrient composition, and temperature [81,82]. Controlled cultivation conditions improve the reproducibility of fungal biomass production and facilitate process standardization for cosmetic applications [83].

Solid-state fermentation (SSF) is an alternative cultivation strategy that more closely resembles natural fungal growth conditions. In some fungal species, SSF enhances the production of enzymes, phenolic compounds, and secondary metabolites in comparison with liquid cultivation systems. The process may also reduce water and energy consumption, improving overall sustainability. However, industrial scale-up remains challenging because oxygen transfer, heat dissipation, and process monitoring are more difficult to control than those in submerged cultivation systems [84,85].

Metabolite production is strongly dependent on cultivation conditions. Carbon and nitrogen sources, the C/N ratio, oxygen concentration, agitation rate, and environmental stress influence fungal secondary metabolism. High glucose concentrations may suppress the biosynthesis of selected metabolites through catabolite repression, whereas nitrogen limitation often stimulates the production of phenolic compounds and triterpenoids. Relatively small modifications in cultivation strategy can substantially alter the final metabolite profile [86,87].

Downstream processing further adds to the technological complexity. Filtration, centrifugation, concentration, membrane separation, and chromatographic purification are frequently used to remove biomass residues and improve the purity of the extracts. Although these procedures improve standardization and physicochemical consistency, extensive purification may also reduce synergistic interactions naturally present in complex fungal extracts [88].

Extraction and purification procedures influence not only the composition of fungal extracts but also their physicochemical behavior in cosmetic systems. Harsh processing conditions can reduce the molecular weight of polysaccharides, alter viscosity, and decrease hydration-related properties. Oxidative degradation during extraction may also reduce the antioxidant activity of phenolic fractions and destabilize pigments and triterpenoids [52].

The polarity-dependent distribution of fungal-derived compounds influences their behavior in emulsion systems. In oil-in-water emulsions, hydrophilic fractions are primarily localized near the skin surface, where they support hydration-related functions. Formulations containing *Tremella fuciformis* extracts reduced transepidermal water loss (TEWL) by approximately 12.4% and produced moderate increases in viscosity and density compared to control formulations. No erythema or edema was observed after 48 or 72 h of application, suggesting good skin compatibility under the tested conditions [89]. Lipophilic metabolites dispersed within oil droplets can interact more readily with epidermal lipids and may penetrate into deeper skin layers [17]. Emulsion systems allow simultaneous incorporation of hydrophilic and lipophilic fungal fractions within a single formulation. The long-term stability of these systems may still be affected by oxidation, coalescence, and phase separation [17,89].

Encapsulation and nanoscale delivery systems are increasingly explored to address poor solubility, oxidative instability, and the limited penetration of fungal-derived compounds. Liposomes are widely used because their phospholipid bilayers allow the simultaneous incorporation of hydrophilic and lipophilic metabolites. Nanoemulsions with droplet diameters below 200 nm improve the dispersion of poorly soluble compounds and increase the interfacial surface area, potentially improving bioavailability [17].

Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are widely explored as delivery systems capable of improving the controlled release and limiting the oxidative degradation of sensitive metabolites. These platforms are particularly suitable for the delivery of triterpenoids, carotenoids, and oxidation-sensitive phenolic fractions [90].

Encapsulation strategies can improve the storage stability of fungal extracts. Ethanolic extracts of *Agaricus bisporus* and *Pleurotus ostreatus* encapsulated in alginate microspheres, achieved encapsulation efficiencies of 72.81% and 99.63%, respectively. Encapsulation also delayed degradation and modified release kinetics during long-term storage [91]. Hydrogels represent an important formulation platform for fungal-derived ingredients, particularly polysaccharides and exopolysaccharides. Their high water content and viscoelastic properties promote prolonged hydration and the sustained release of incorporated compounds. However, excessive polymer concentration can reduce spreadability and negatively affect sensory acceptance, highlighting the need for careful formulation optimization [52].

Lipid-based nanosystems are considered particularly useful for the delivery of lipophilic fungal metabolites [92]. Nanogels containing *Ganoderma lucidum* triterpenoids showed high drug loading, favorable spreadability, and enhanced epidermal accumulation compared with conventional gel formulations. Encapsulation of fungal triterpenoids in nanoscale delivery systems has been reported to improve the release characteristics, storage stability, and formulation performance [93].

Despite substantial technological progress, formulation stability remains a major limitation for broader industrial application of fungal-derived cosmetic ingredients. Phenolic compounds readily undergo oxidation, carotenoids are highly sensitive to oxygen and light exposure, and triterpenoids may also gradually degrade during storage. Surfactants, preservatives, pH, and rheology modifiers can further affect physicochemical stability and biological activity [52,62].

Economic and technological limitations also remain significant. The production of highly purified fungal metabolites is relatively expensive, whereas large-scale manufacturing of advanced delivery systems requires specialized equipment and highly standardized process conditions [72,94]. Standardized methodologies for the evaluation of release kinetics, long-term stability, penetration efficiency, and formulation-dependent bioavailability remain limited [70].

Further progress in this field will require the closer integration of fungal biotechnology, extraction science, formulation engineering, physicochemical characterization, and clinically relevant evaluation strategies. Without such integration, many fungal-derived bioactive compounds may remain difficult to implement in commercially viable cosmetic systems. A better understanding of the biological mechanisms underlying these effects is equally important for the rational design of effective cosmetic formulations [6]. From an industrial perspective, no single extraction or production technology is universally optimal for all fungal-derived cosmetic ingredients. Conventional solvent extraction remains economically attractive and technically simple, although it often requires large volumes of solvent and may provide lower selectivity. Ultrasound- and microwave-assisted extraction offer shorter processing times and improved extraction efficiency but may be less suitable for thermolabile compounds when operated under inappropriate conditions [72,95]. Su-

percritical fluid extraction provides high-purity extracts without organic solvent residues and is particularly attractive for lipophilic metabolites. However, its widespread industrial application is currently limited by high equipment costs and process complexity [79]. In contrast, controlled submerged fermentation and biotechnological production systems offer excellent batch-to-batch reproducibility, scalability, and independence from seasonal variability, making them particularly promising for the sustainable production of standardized cosmetic ingredients [83]. Therefore, the selection of the most appropriate technology should be based not only on extraction efficiency but also on scalability, production costs, environmental sustainability, regulatory requirements, and compatibility with the intended cosmetic application [72].

5. Mechanisms of Action of Fungal-Derived Bioactive Compounds in Skin

Fungal-derived bioactive compounds exert their effects through multiple interconnected biochemical and cellular pathways rather than through single-target mechanisms [96]. Their effects include the modulation of oxidative stress, inflammatory signaling, extracellular matrix (ECM) remodeling, cellular responses, and skin barrier function [97]. Such multi-target activity is well suited for cosmetic formulations, where simultaneous antioxidant, regenerative, and barrier-supporting effects are often desirable [98]. A recent systematic review covering 52 studies identified *Trametes versicolor*, *Schizophyllum commune*, *Tremella fuciformis*, *Pleurotus ostreatus*, *Ganoderma lucidum*, *Lentinula edodes*, and *Inonotus obliquus* among the macrofungi most commonly investigated in skin-related applications [22,99].

Oxidative stress is one of the major factors contributing to skin aging due to the accumulation of reactive oxygen species (ROS) generated endogenously and in response to environmental stressors such as UV radiation and pollution [100,101]. Elevated ROS levels promote lipid peroxidation, protein oxidation, and DNA damage, thereby leading to impaired cellular function [102].

Phenolic compounds, carotenoids, triterpenoids, and polysaccharides reduce oxidative stress through direct radical scavenging and the activation of endogenous antioxidant defense systems [47]. Polysaccharides isolated from *Tremella fuciformis* showed strong antioxidant activity in H₂O₂-induced oxidative stress models using cultured human fibroblasts. At a concentration of 200 µg/mL, intracellular ROS levels were significantly reduced compared to those in oxidatively stressed controls [103]. In UVA-induced photoaging models, *Tremella fuciformis* polysaccharides applied at concentrations ranging from 3.13 to 12.5 mg/mL reduced ROS and malondialdehyde levels while increasing the activities of catalase, superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px) [104]. In keratinocyte models, concentrations between 1 and 5 mg/mL were non-cytotoxic and promoted cell viability [105].

Several fungal metabolites also activate Nrf2-mediated antioxidant signaling pathways, which may provide longer-lasting protection against oxidative injury. Carotenoids further contribute through singlet oxygen quenching and protection against UV-induced oxidative damage [63].

Chronic low-grade inflammation (inflammaging) is closely associated with skin aging and functional the deterioration [106]. Fungal metabolites regulate inflammatory responses largely through the inhibition of NF-κB signaling and the modulation of pro-inflammatory mediators such as TNF-α, IL-1β, and IL-6. Effects on mitogen-activated protein kinase (MAPK) signaling pathways, including ERK, JNK, and p38, have likewise been described [107].

β-glucans exhibit immunomodulatory activity through receptors including Dectin-1, thereby promoting balanced immune responses without complete immunosuppres-

sion [108]. This property may be beneficial in formulations intended for sensitive or compromised skin [109].

The structural integrity of the skin is strongly associated with extracellular matrix (ECM), particularly its major components, collagen and elastin. Their degradation is mediated by matrix metalloproteinases (MMPs), which become activated under oxidative and inflammatory conditions [110].

Several experimental studies suggest that fungal extracts exert protective effects against ECM degradation. In UVB-induced photoaging models using human dermal fibroblasts (HDFn), *Ganoderma lucidum* extract reduced collagen degradation following irradiation with UVB dose of 30 mJ/cm². In reconstructed 3D skin models exposed to 40 mJ/cm² UVB, treatment with *Ganoderma lucidum* extract at 100 µg/mL for 48 h reduced markers of photoaging and modulated the expression of MMP-1 and procollagen type I [111].

Some fungal metabolites can stimulate collagen synthesis through mechanisms associated with transforming growth factor-β (TGF-β) signaling pathways. Polysaccharide-rich extracts from *Auricularia auricula-judae*, containing 349.83 ± 5.00 mg of polysaccharides/g extract and characterized by a molecular weight of approximately 158 kDa, enhanced the proliferation, migration, and invasion of fibroblasts and keratinocytes. A significant increase in collagen synthesis was also observed ($p < 0.05$) [112].

Polysaccharides, particularly β-glucans, contribute to skin hydration and barrier function through both physical and biological mechanisms. High-molecular-weight polymers form hydrophilic films on the skin surface, thereby improving water retention and epidermal hydration. In a randomized, double-blind, placebo-controlled clinical trial involving 30 healthy adults, oral administration of 3 g/day of *Flammulina velutipes* powder for 4 weeks increased cheek skin hydration from 58.2 to 64.2 arbitrary units (a.u.), compared to an increase from 53.5 to 56.3 a.u. in the placebo group ($p = 0.033$). More pronounced effects were observed among female participants ($p = 0.007$). No statistically significant differences in transepidermal water loss (TEWL) were detected between the groups ($p = 0.161$) [113].

Several fungal-derived compounds influence the expression of proteins associated with epidermal differentiation and barrier formation, including filaggrin and involucrin, although detailed quantitative data remain limited [114]. Sterols may support the organization of stratum corneum lipids and improve barrier cohesion [115].

Fungal metabolites influence cell proliferation, differentiation, melanogenesis, and tissue repair. Experimental studies have demonstrated the anti-melanogenic activity of *Ganoderma lucidum* extracts in B16 melanoma cells. However, these findings are currently based predominantly on preclinical models and require further validation in clinically relevant settings. At a concentration of 40 µg/mL, melanin production decreased by 29.34%, whereas intracellular tyrosinase activity was reduced by 21.93% [116]. The extract exhibited an IC₅₀ value for tyrosinase inhibition of 0.32 mg/mL. At a concentration of 1 mg/mL, tyrosinase inhibition reached approximately 80% [117]. Polysaccharides isolated from *Ganoderma lucidum* also downregulated UVB-induced melanogenesis-related genes in B16F10 and PIG1 cells, whereas concentrations below 160 µg/mL showed no significant cytotoxicity [118].

In vitro studies have shown that polysaccharides isolated from *Tremella fuciformis* promote wound-healing responses in keratinocytes and fibroblasts, further in vivo and clinical studies are required to confirm their therapeutic relevance in cosmetic applications. Concentrations between 100 and 200 µg/mL enhanced migration and repair processes, whereas concentrations between 100 and 300 µg/mL significantly reduced melanin accumulation [119].

A characteristic feature of fungal-derived ingredients is their multi-target activity which is associated with complex mixtures of bioactive compounds. Synergistic interactions between antioxidant, anti-inflammatory, regenerative, and barrier-supporting fractions may improve overall efficacy compared to isolated molecules [88].

The biological activity of fungal metabolites depends on formulation design and bioavailability. High-molecular-weight polysaccharides mainly remain on the skin surface, whereas lower-molecular-weight phenolic compounds, terpenoids, and sterols may penetrate deeper epidermal layers. Delivery systems, including encapsulation platforms, nanoemulsions, liposomes, and lipid carriers are being explored to improve stability, penetration, and functional performance [120,121].

Despite promising biological activity, most available evidence still derives from *in vitro* and *ex vivo* models, whereas robust clinical studies remain limited. Differences in fungal species, extraction procedures, purification protocols, and experimental methodologies further complicate direct comparisons between studies. Future progress will require the closer integration of mechanistic studies, formulation science, and clinically relevant efficacy evaluation [6,24]. Therefore, many of the reported biological effects should currently be considered preliminary until confirmed in well-designed clinical studies.

6. Formulation Strategies in Innovative Cosmetic Systems

Successful incorporation of fungal-derived compounds into cosmetic formulations depends not only on biological activity but also on physicochemical compatibility with the formulation system [64]. Stability, solubility, partitioning behavior, and resistance to degradation strongly influence the performance of cosmetic formulations after topical application [18]. The behavior of fungal metabolites in cosmetic matrices is determined largely by molecular weight, polarity, oxidative susceptibility, and interactions with other formulation components [122].

A major formulation challenge arises from the heterogeneous composition of fungal extracts. Hydrophilic polysaccharides and exopolysaccharides coexist with lipophilic sterols, terpenoids, and other low-polarity metabolites, although these fractions exhibit markedly different behavior in topical systems [34]. High-molecular-weight β -glucans are generally retained within aqueous phases, contributing to viscosity, film formation, and water-binding properties. Lipophilic compounds require incorporation into oil phases or carrier systems to improve dispersion and reduce precipitation [123].

Differences between hydrophilic and lipophilic fungal fractions become particularly evident in emulsion-based systems. In oil-in-water formulations, hydrophilic compounds remain mainly near the skin surface and are associated primarily with hydration effects [124]. Several studies report reductions in transepidermal water loss of 10–15% after application of polysaccharide-rich formulations [89]. Lipophilic metabolites dispersed within the internal oil phase may penetrate more effectively into superficial epidermal layers. Penetration efficiency depends strongly on droplet size, surfactant composition, and physicochemical properties of the active compound [120].

Emulsions remain practical systems for combining chemically distinct fungal fractions within a single formulation. Their stability may be affected by phase separation, oxidative degradation, coalescence, and interactions between surfactants and extract components [125]. Fungal polysaccharides can also modify rheological behavior, often requiring empirical optimization of emulsifiers and stabilizing agents for individual extract compositions [126].

Advanced delivery systems are primarily employed to improve the stability, bioavailability, and controlled release of fungal-derived bioactive compounds [127]. Liposomes facilitate the simultaneous incorporation of hydrophilic and lipophilic metabolites, whereas

nanoemulsions improve the dispersion of poorly water-soluble compounds and enhance kinetic stability [128]. Solid lipid nanoparticles and nanostructured lipid carriers have also been investigated as protective systems for oxidation-sensitive fungal metabolites, improving storage stability and enabling controlled release [129]. Nevertheless, the performance of these systems remains strongly dependent on lipid composition, particle size distribution, surfactant concentration, and storage conditions. Aggregation and physicochemical instability during long-term storage continue to represent important technological limitations [130]. Hydrogels are more suitable for hydrophilic fungal fractions, particularly polysaccharides and extracellular polymers [131]. Their high water content and viscoelastic properties support prolonged hydration and slower release of incorporated compounds [132]. Hydrogels may also serve as platforms for combining fungal-derived ingredients with vitamins, peptides, or plant extracts [133]. At higher polymer concentrations, increased viscosity can impair spreadability and an undesirable sticky feel on the skin. In practice, sensory acceptability often limits polymer concentration before biological performance does [134].

Stability remains a major technological challenge in fungal-derived cosmetic systems [91]. Phenolic compounds readily oxidize, carotenoids are sensitive to light and oxygen exposure, and some triterpenoids gradually degrade during storage [52]. These processes are affected by temperature, pH, surfactants, preservatives, metal ions, and rheology modifiers [33]. Extraction procedures may further influence formulation performance by altering molecular structure or removing stabilizing components present in crude extracts. Preservation systems represent an additional factor influencing the behavior of fungal-derived compounds in finished cosmetic formulations. Preservatives must ensure microbiological safety while remaining compatible with sensitive fungal metabolites, particularly phenolic compounds, polysaccharides, and protein-rich fractions [135]. Incompatibility between preservatives, surfactants, and fungal bioactives may affect pH, viscosity, oxidative stability, and sensory properties. Therefore, preservative selection, antioxidant protection, packaging, and storage conditions should be considered integral components of formulation development rather than mere technological requirements [1].

Sensory characteristics are equally important in cosmetic formulation design. Texture, absorption rate, residue formation, and perceived skin comfort strongly affect consumer acceptance [136,137]. High concentrations of fungal polysaccharides may improve hydration while increasing tackiness and reducing formulation elegance [134]. Lipid-based nanosystems can partially improve spreadability and reduce greasy after-feel compared with conventional oil-rich formulations [121].

From a formulation perspective, this chemical diversity may also create stability and compatibility problems, since individual fractions often differ in optimal pH range, oxidative stability, and interactions with emulsifiers or preservatives. Maintaining long-term homogeneity is particularly difficult when hydrophilic and lipophilic metabolites must remain stable within the same formulation matrix [124]. Several fungal-derived ingredients have already been incorporated into commercial cosmetic formulations. β -Glucans are widely used as moisturizing and barrier-supporting ingredients, while polysaccharides from *Tremella fuciformis* have gained attention because of their high water-retention capacity. Ergothioneine is increasingly incorporated into antioxidant and anti-aging formulations owing to its cytoprotective properties, whereas extracts from *Ganoderma lucidum* are used in products intended to soothe the skin and support the epidermal barrier function [22,138]. These examples demonstrate that successful commercialization depends not only on biological activity but also on formulation stability, quality control, regulatory compliance, and standardized production processes [135].

Despite advances in delivery technologies, broader industrial implementation remains limited by oxidative instability, poor penetration of high-molecular-weight compounds, storage difficulties, and high production costs of nanoscale carriers. The lack of standardized methodologies for the evaluation of release kinetics, skin penetration, and formulation-dependent bioavailability further complicates comparisons between studies. Future progress will require the closer integration of formulation science, fungal biotechnology, analytical chemistry, and process engineering [24,130]. The relationship between physicochemical properties of fungal-derived compounds, formulation strategies, and expected cosmetic outcomes is illustrated in Figure 3. An overview of formulation approaches and delivery systems used for the incorporation of fungal-derived bioactives into cosmetic products is presented in Table 2.

Table 2. Formulation strategies and delivery systems for fungal-derived cosmetic ingredients.

Formulation Strategy	Suitable Fungal Compounds	Main Advantages	Main Technological Limitations	Typical Cosmetic Applications	References
Conventional Emulsions	Mixed extracts, Phenolic compounds, polysaccharides	Well-established technology; low cost; industrial scalability	Oxidation, phase separation, limited protection of active compounds	Creams, lotions, emulsions	[1,122,135]
Oil-in-Water Emulsions	Hydrophilic and moderately lipophilic fractions	Pleasant sensory properties, good consumer acceptance	Limited long-term stability	Daily skincare formulations	[1,122,135]
Liposomes	Phenolic compounds, triterpenoids, sterols	Dual encapsulation; improved skin delivery	Limited storage stability	Anti-aging; regenerative formulations	[125–127]
Nanoemulsions	Lipophilic metabolites, carotenoids, triterpenoids	Enhanced dispersion; improved skin delivery	Surfactant dependence; formulation sensitivity	Serums and advanced cosmetic formulations	[128,129]
Solid Lipid Nanoparticles (SLN)	Triterpenoids, carotenoids, phenolic compounds	Controlled release, protection against oxidation, improved physicochemical stability	Manufacturing complexity, particle aggregation	Dermocosmetics anti-aging formulations	[130–132]
Nanostructured Lipid Carriers (NLC)	Lipophilic fungal metabolites	Higher loading capacity, improved stability	Optimization of lipid composition	Multifunctional formulations	[30–132]
Nanogels	Triterpenoids, mixed extracts	Enhanced skin retention; controlled release	Production complexity	Targeted skincare formulations	[133]
Electrospun Nanofibers	Encapsulated fungal bioactives	High loading capacity and controlled release	Limited industrial implementation	Advanced topical delivery	[134]
Microspheres and Microcapsules	Complex fungal extracts	Protection against environmental degradation, controlled release	Variable release characteristics	Stabilized cosmetic formulations	[123]

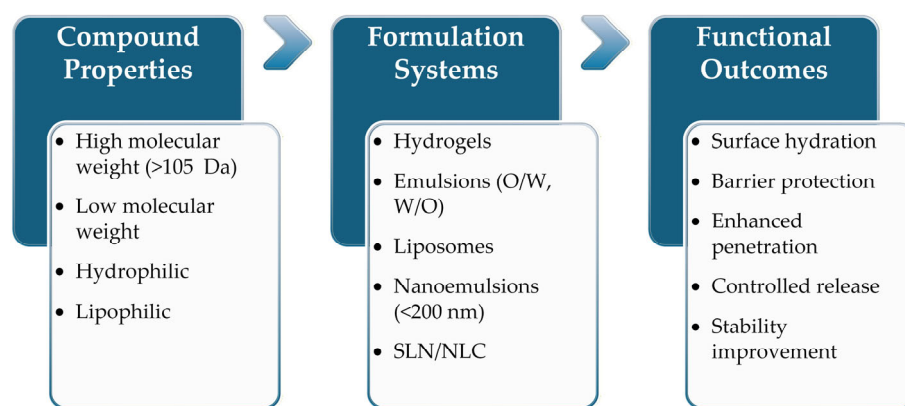


Figure 3. Relationship between physicochemical properties of fungal-derived compounds, formulation systems, and functional cosmetic outcomes influencing stability, bioavailability, and skin performance.

Despite their considerable potential, the industrial implementation of advanced delivery systems remains associated with several practical limitations. Large-scale production of liposomes, nanoemulsions, and lipid nanoparticles requires specialized equipment, strict process control, and increased manufacturing costs compared with conventional cosmetic formulations. Long-term physicochemical stability, batch-to-batch reproducibility, and regulatory evaluation of nanostructured systems continue to present major challenges [139,140]. In addition, comprehensive safety assessment is required because changes in particle size and skin penetration may influence local exposure and biological response. Although numerous laboratory studies demonstrate improved stability and delivery efficiency of fungal-derived bioactive compounds, relatively few well-designed clinical studies have confirmed that these technological advantages translate into superior cosmetic efficacy under real-use conditions. Consequently, further clinical investigations and standardized evaluation protocols are required before advanced delivery systems can be considered routine solutions for fungal-derived cosmetic ingredients [139].

7. Efficacy Evaluation and Testing Methods

Although numerous fungal-derived compounds exhibit promising antioxidant, anti-inflammatory, moisturizing, photoprotective, and anti-aging activities in chemical assays and cell-based models, these findings should generally be regarded as preliminary evidence rather than conclusive evidence of cosmetic efficacy [6,17,64]. Table 3 summarizes the levels of evidence and the experimental approaches currently used to assess the cosmetic efficacy of fungal-derived bioactive compounds, ranging from in vitro assays to clinical studies.

The biological activity of an isolated compound represents only one factor determining the performance of a finished cosmetic product. In practical applications, cosmetic efficacy is influenced by multiple additional factors, including formulation composition, physicochemical stability, skin penetration, release characteristics, interactions with other ingredients, and storage conditions [20,64]. Consequently, results obtained from chemical assays or simplified biological models should be regarded as preliminary evidence rather than conclusive evidence of cosmetic efficacy. Confirmation of cosmetic efficacy requires progressively higher levels of experimental validation, including ex vivo skin models and well-designed clinical studies in humans using standardized formulations and objective instrumental measurements [141–143].

Table 3. Levels of evidence and experimental approaches used to evaluate the cosmetic efficacy of fungal-derived bioactive compounds.

Level of Evidence	Experimental Approach	Main Purpose	Major Limitations	Strength of Evidence	References
Chemical assays	DPPH, ABTS, FRAP	Demonstrate intrinsic antioxidant capacity	No prediction of cosmetic efficacy	Low	[17,64,141]
Cell-based studies	Keratinocytes, fibroblasts	Demonstrate biological mechanisms	No skin barrier	Low–Moderate	[40,105,141]
Ex vivo studies	Human skin, Franz diffusion cells	Evaluate penetration and skin retention	Limited physiological complexity	Moderate	[142]
Animal studies	Murine models	Demonstrate biological response	Limited translation to humans	Moderate	[143]
Human clinical studies	Randomized clinical trials + instrumental evaluation	Demonstrate cosmetic efficacy	Limited number of studies	High	[144,145]

Evaluation of fungal-derived compounds in cosmetic systems requires multiple experimental approaches because no single model fully reproduces the complexity of skin physiology and formulation-dependent responses. Biological activity observed under simplified laboratory conditions does not always translate into measurable cosmetic effects after incorporation into finished cosmetic formulations [144]. Penetration efficiency, physicochemical stability, release profile, and interactions with formulation components strongly influence final performance at the skin surface [17,64].

7.1. Cell-Based Studies

Cell-based *in vitro* models using keratinocytes and dermal fibroblasts are widely used to investigate the antioxidant, anti-inflammatory, regenerative, and extracellular matrix-related effects of fungal-derived compounds. Many studies report reduced oxidative stress, inhibition of inflammatory mediators, and modulation of matrix metalloproteinase activity following treatment with fungal extracts or isolated metabolites. These systems provide good reproducibility and allow mechanistic investigation under controlled conditions [145]. Their predictive value for cosmetic efficacy remains limited because they do not fully reproduce the barrier properties and structural complexity of intact skin. Strong activity observed in cell-based assays may therefore overestimate their practical effectiveness, particularly for compounds with poor skin penetration or limited formulation stability [146].

7.2. Skin Permeation Studies and Ex Vivo Models

Ex vivo models preserve the structural organization of skin tissue and better reflect physiological conditions than conventional cell-based systems [147]. These models play a key role in evaluating skin permeation, penetration, and distribution of bioactive compounds within different skin layers. Franz diffusion cells systems are commonly used to evaluate penetration, permeation, and distribution of fungal-derived compounds within skin layers [147]. These studies demonstrate the influence of molecular weight and formulation strategy on delivery efficiency. High-molecular-weight polysaccharides generally remain localized near the skin surface, whereas lower-molecular-weight lipophilic compounds penetrate more effectively into deeper epidermal regions. *Ex vivo* systems

are also used to evaluate hydration-related parameters and transepidermal water loss (TEWL), thereby linking the physicochemical properties of fungal-derived compounds with formulation-dependent behavior [18].

7.3. Clinical and Instrumental Efficacy Assessment

In vivo studies performed on human volunteers remain essential for the evaluation of cosmetic efficacy under realistic application conditions [136,137]. Commonly assessed parameters include skin hydration, TEWL, elasticity, wrinkle depth, pigmentation, and sensory properties [148]. To ensure objective and reproducible efficacy assessment, non-invasive instrumental techniques are widely employed in cosmetic research [149]. Corneometry is commonly used to evaluate skin hydration. TEWL measurements provide information on epidermal barrier function, cutometry assesses skin elasticity and firmness, whereas mexametry and high-resolution skin imaging systems are applied to assess skin pigmentation, erythema, and wrinkle-related parameters [141]. These instrumental methods complement clinical observations by providing quantitative data and improving the reliability of efficacy assessment [141]. Compared with cell-based systems, effects observed in vivo are often less pronounced because the biological response depends not only on the activity of fungal-derived compounds but also on formulation stability, penetration efficiency, dosing regimen, and interindividual variability [142,143].

Despite the growing number of mechanistic and formulation-oriented studies, robust clinical evidence supporting fungal-derived cosmetic ingredients remains limited [6]. Many published studies involve small sample sizes, short treatment periods, or insufficiently standardized formulations and analytical methodologies [63]. Interpretation of efficacy data is further complicated by variability in extraction procedures, fungal species, cultivation conditions, assay protocols, and formulation composition [32].

Future clinical studies should prioritize randomized controlled study designs, adequately powered sample sizes, standardized formulations, and sufficiently long treatment periods to generate robust and clinically meaningful evidence. The application of objective instrumental techniques, including corneometry, TEWL measurements, cutometry, mexametry, and high-resolution skin imaging, will further improve the reliability and comparability of efficacy assessments across independent studies [142,143].

Current evidence indicates considerable biological potential of fungal-derived compounds in cosmetic applications. Reproducible clinical efficacy, however, remains highly dependent on formulation design, delivery strategy, and methodological standardization. Further progress in this field will require the closer integration of mechanistic studies, formulation science, and clinically relevant efficacy evaluation [6,62].

8. Safety, Toxicological, and Regulatory Considerations

8.1. Toxicological Considerations

The incorporation of fungal-derived compounds into cosmetic formulations requires evaluation extending beyond biological activity alone [3]. The toxicological profile, formulation-dependent exposure, physicochemical stability, and regulatory classification all influence whether fungal-derived ingredients can be safely used in topical products [150]. Although many macrofungi have a long history of use in food and traditional medicine, their dermal application raises additional concerns associated with skin penetration, repeated exposure, and formulation-dependent interactions [151]. Extraction and purification procedures may further modify metabolite composition, meaning that safety cannot be inferred solely from the source organism [34].

Contamination originating from cultivation and downstream processing remains a important issue [152]. Fungal materials may also contain contaminants or chemically

altered metabolites associated with cultivation, extraction, fermentation, or storage conditions [153]. Even species generally regarded as safe may produce undesirable compounds when cultivation conditions deviate from controlled parameters. Analytical control based on chromatographic and spectrometric methods is therefore required to verify the compositional consistency and the absence of toxic impurities [154].

The potential for skin irritation and sensitization differs between classes of fungal metabolites [155]. High-molecular-weight polysaccharides, such as β -glucans, generally show low irritation potential because penetration through the stratum corneum is limited [18]. Smaller phenolic compounds, terpenoids, and sterol-like metabolites may penetrate more effectively into viable epidermal layers, depending on concentration and formulation type [17]. Toxicological assessment commonly includes reconstructed epidermis models, in vitro cytotoxicity assays, and human patch testing. However, none of these methods fully reflect long-term exposure conditions. Long-term and repeated exposure studies are particularly important for cosmetic ingredients intended for chronic daily application, as cumulative effects cannot always be predicted from short-term toxicity assays.

Formulation architecture may substantially influence the toxicological behavior of fungal-derived compounds [156]. Liposomes, nanoemulsions, and lipid nanoparticles are used to improve stability and penetration efficiency, but these same properties may alter tissue exposure [157]. Enhanced penetration is not always advantageous from a toxicological perspective, particularly in nanoscale systems where dermal transport mechanisms remain incompletely characterized [158]. Storage stability is equally important because oxidation and degradation products may differ toxicologically properties that differ from those of the original compounds [20].

8.2. Microbiological Stability

Microbiological stability represents another key aspect of safety evaluation in fermentation-derived cosmetic systems [159]. Formulations containing polysaccharides or protein-rich fractions may support microbial growth if preservation systems are insufficient [160]. Preservatives must therefore maintain microbiological safety without destabilizing formulations or altering sensitive fungal metabolites [161]. In addition to toxicological and microbiological aspects, the successful implementation of fungal-derived cosmetic ingredients also requires compliance with the applicable regulatory framework governing cosmetic products.

8.3. Regulatory Considerations

Regulatory classification further complicates implementation of fungal-derived cosmetic ingredients [3]. Within the European Union, cosmetic products are regulated under Regulation (EC) No 1223/2009, which requires the preparation of a Cosmetic Product Safety Report including exposure assessment and toxicological evaluation of the finished formulation [162]. Regulatory interpretation may become less clear for ingredients obtained through fermentation engineering, metabolic modification, or advanced extraction technologies [163]. Regulatory requirements are not fully harmonized across major cosmetic markets. Differences in safety assessment procedures, documentation requirements, and ingredient classification may complicate the global commercialization of fungal-derived cosmetic ingredients. These challenges are particularly relevant for ingredients obtained through fermentation or other biotechnological processes, for which regulatory interpretation may vary between jurisdictions [164].

The wording of formulation claims also remains important. Products promoted primarily for moisturizing, protective, or conditioning effects are regulated differently from those products suggesting therapeutic or anti-inflammatory activity [137]. Distinctions

between cosmetic and medicinal positioning may become blurred when fungal-derived ingredients are associated with regenerative or pharmacologically active effects, particularly in products positioned between dermocosmetics and topical therapeutics [65].

Standardization continues to represent a major barrier to broader industrial implementation. Cultivation conditions, extraction procedures, drying methods, and purification strategies may substantially alter chemical composition, oxidative stability, and formulation behavior [34]. Quality control based on selected marker compounds may improve reproducibility. However, multifunctional fungal extracts often contain chemically interacting fractions that are difficult to characterize using only a limited number of analytical marker [154].

8.4. Current Challenges and Future Perspectives

Commercial interest in biotechnology-derived cosmetic ingredients continues to increase, although fungal-derived bioactive compounds remain less common than plant-derived materials in large-scale cosmetic products. Production costs, limited clinical validation, formulation instability, and regulatory uncertainty still restrict wider implementation. Some fungal metabolites additionally require specialized delivery systems because of poor water solubility or limited storage stability [165].

Despite these limitations, fungal-derived compounds remain a promising group of multifunctional cosmetic ingredients with potential applications in hydrating, antioxidant, and barrier-oriented formulations [166]. Further progress in this field will depend on the closer integration of cultivation technology, analytical characterization, formulation engineering, toxicological evaluation, and regulatory standardization [24]. In addition to demonstrating efficacy, fungal-derived cosmetic ingredients must also meet rigorous safety and regulatory requirements before their successful commercial application.

9. Challenges and Limitations

Despite the considerable progress achieved in the characterization of fungal-derived bioactive compounds, several scientific and technological challenges continue to limit their broader application in cosmetic formulations. One of the major obstacles is the lack of standardization across fungal species, cultivation conditions, extraction procedures, and purification protocols, which substantially affects metabolite composition, biological activity, and the reproducibility of research findings [34]. In addition, formulation stability remains a critical issue, as many fungal-derived compounds are susceptible to oxidation, degradation, or poor compatibility with complex cosmetic matrices during processing and storage [20]. Although numerous studies have demonstrated promising biological activities under experimental conditions, robust clinical evidence supporting the efficacy and safety of fungal-derived cosmetic ingredients remains limited [6]. Furthermore, regulatory uncertainty and differences in safety assessment requirements continue to complicate the industrial implementation of novel fungal-derived ingredients, particularly those produced using advanced biotechnological approaches [65].

Future research should therefore focus on improving the reproducibility, standardization, and translational potential of fungal-derived cosmetic ingredients. The development of harmonized cultivation and extraction protocols, together with metabolomic profiling, chemical fingerprinting, the identification of characteristic marker compounds, standardized analytical methodologies, and comprehensive quality control procedures, will be essential for ensuring batch-to-batch consistency and improving reproducibility. These measures will also facilitate comparisons between independent studies and support the regulatory acceptance of fungal-derived cosmetic ingredients [167,168]. Standardized cultivation protocols controlling fungal strain selection, fermentation parameters, nutrient

composition, harvesting time, and downstream processing are equally important to minimize variability in metabolite composition and ensure consistent biological activity [82,83]. At the same time, greater emphasis should be placed on optimizing formulation strategies and advanced delivery systems capable of improving the stability, bioavailability, and controlled release of fungal bioactive compounds [64]. Equally important will be the design of well-controlled clinical studies using standardized formulations and validated efficacy assessment methods to provide robust evidence to support cosmetic claims [65].

From an industrial perspective, successful commercialization of fungal-derived cosmetic ingredients will require the closer integration of fungal biotechnology, analytical chemistry, formulation science, toxicological evaluation, and regulatory standardization [24]. The implementation of sustainable production technologies, combined with rigorous quality control and harmonized regulatory frameworks, may significantly facilitate the translation of promising laboratory findings into safe, effective, and commercially viable cosmetic products [34].

Overall, fungal-derived bioactive compounds represent a promising source of multi-functional cosmetic ingredients. Future advances in this field will depend not only on the discovery of new bioactive metabolites but also on the successful integration of biotechnology, formulation engineering, clinical validation, and regulatory science. Such integration will enable their broader implementation in next-generation cosmetic formulations [6].

The major scientific, technological, and regulatory challenges affecting the development of fungal-derived cosmetic ingredients, together with potential future research directions, are summarized in Table 4.

Table 4. Current challenges and future perspectives for the development of fungal-derived cosmetic ingredients.

Current Challenge	Scientific and Technological Consequences	Impact on Industrial Application	Potential Solutions and Future Directions	References
Variability in metabolite composition among species, strains, and cultivation systems	Inconsistent biological activity and difficulties in reproducibility	Reduced standardization and quality control	Optimization and standardization of cultivation protocols, implementation of quality management systems	[34,82,83]
Lack of harmonized extraction procedures	Significant variability in extract composition and biological activity	Difficult comparison between studies and commercial products	Development of validated extraction and analytical methodologies	[32,34,167,168]
Poor aqueous solubility of lipophilic metabolites	Limited bioavailability and formulation compatibility	Reduced formulation efficiency	Encapsulation technologies, lipid-based carriers, nanoformulations	[64,130–132]
Oxidative instability of phenolic compounds, carotenoids, and selected triterpenoids	Loss of biological activity during storage	Reduced product shelf life	Stabilization strategies and protective delivery systems	[59,124,130]
Limited penetration of high-molecular-weight polysaccharides	Restricted delivery to deeper skin layers	Reduced efficacy in certain applications	Controlled depolymerization and advanced carrier systems	[34,39,64]
Complex composition of fungal extracts	Difficult identification of active compounds and mechanisms of action	Regulatory and standardization challenges	Integrated metabolomic and bioactivity-guided studies	[6,24,34]

Table 4. Cont.

Current Challenge	Scientific and Technological Consequences	Impact on Industrial Application	Potential Solutions and Future Directions	References
Insufficient clinical evidence	Limited support for efficacy claims	Slower commercialization and reduced consumer confidence	Randomized clinical trials and long-term safety studies	[65,144,145]
Regulatory uncertainty	Variability in classification and approval requirements	Delayed market introduction	Development of dedicated regulatory frameworks	[24,63,65]
High production and formulation costs	Limited economic feasibility	Restricted large-scale implementation	Process optimization and industrial scale-up	[130,135]
Limited knowledge regarding long-term safety and repeated exposure	Uncertainty concerning chronic use	Challenges in risk assessment	Comprehensive toxicological and dermatological evaluation	[65,143–145]
Lack of standardized methods for evaluating skin penetration and bioavailability	Difficult comparison of efficacy data	Reduced translational value of laboratory studies	Harmonized testing protocols and validated in vitro/in vivo models	[64,141–143]
Growing consumer demand for sustainable and natural ingredients	Increased pressure for environmentally responsible production	Opportunity for industrial growth	Integration of fungal biotechnology with green extraction and sustainable manufacturing technologies	[24,34,66]

10. Conclusions

Fungal-derived compounds represent a promising source of bioactive ingredients for modern cosmetic formulations owing to their chemical diversity, multifunctional biological activity, and compatibility with controlled biotechnological production. Polysaccharides, phenolic compounds, triterpenoids, sterols, pigments, and peptide fractions exhibit considerable potential for applications related to skin hydration, antioxidant protection, barrier support, anti-inflammatory activity, and protection against photoaging. However, successful cosmetic performance depends not only on the intrinsic biological activity of these compounds but also on appropriate extraction strategies, formulation design, physicochemical stability, and efficient delivery systems.

Although significant progress has been achieved in fungal biotechnology and formulation development, broader industrial implementation still requires better standardization of cultivation and extraction procedures, robust clinical validation, and harmonized quality and regulatory frameworks.

Future advances will depend on the successful integration of fungal biotechnology, formulation science, analytical characterization, toxicological evaluation, and clinically relevant efficacy assessment. Such an interdisciplinary approach will facilitate the translation of promising laboratory findings into safe, effective, and scientifically validated next-generation cosmetic formulations.

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Abbreviations

The following abbreviations are used in this manuscript:

DPPH	2,2-Diphenyl-1-picrylhydrazyl
ECM	Extracellular Matrix
EPS	Extracellular Polysaccharides
ERK	Extracellular Signal-Regulated Kinase
GAE	Gallic Acid Equivalents
GSH-Px	Glutathione Peroxidase
HDFn	Human Dermal Fibroblasts (normal)
IL	Interleukin
MAE	Microwave-Assisted Extraction
MAPK	Mitogen-Activated Protein Kinase
MMP	Matrix Metalloproteinase
NF-κB	Nuclear Factor Kappa B
NLC	Nanostructured Lipid Carriers
NO	Nitric Oxide
Nrf2	Nuclear Factor Erythroid 2–Related Factor 2
ROS	Reactive Oxygen Species
SFE	Supercritical Fluid Extraction
SLN	Solid Lipid Nanoparticles
SmF	Submerged Fermentation
SOD	Superoxide Dismutase
SSF	Solid-State Fermentation
TEWL	Transepidermal Water Loss
TGF-β	Transforming Growth Factor Beta
TNF-α	Tumor Necrosis Factor Alpha
UAE	Ultrasound-Assisted Extraction
UVA	Ultraviolet A Radiation
UVB	Ultraviolet B Radiation

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