Hindawi
Journal of Food Biochemistry
Volume 2023, Article ID 5915769, 26 pages
https://doi.org/10.1155/2023/5915769

Review Article

Potential of Mushrooms Bioactive for the Treatment of Skin Diseases and Disorders

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Received 30 August 2023; Revised 6 November 2023; Accepted 25 November 2023; Published 12 December 2023

Academic Editor: Seyed Mohammad Taghi Gharibzahedi

Mushrooms have long been revered not only as a staple food source but also for their potential medicinal properties. Their role as a natural repository of bioactive compounds positions them uniquely in the pharmaceutical domain, with particular relevance to cosmeceuticals and nutricosmetics. The global ethnobotanical and ethnopharmacological chronicles highlight the traditional application of mushrooms against many diseases, with many even finding their way into cosmetic formulations. This review aims to consolidate the existing knowledge regarding the efficaciousness of mushroom-derived bioactives in the realm of skin disorders and diseases. In addition, it sheds light on the instances where certain mushroom species have been implicated in causing dermatological reactions, underscoring the dual nature of these fungal entities. A comprehensive assessment was undertaken involving ethnobotanical databases and relevant scientific literature to identify mushrooms used traditionally for treating skin conditions. In addition, contemporary research elucidating the biological activities of these mushrooms, specifically their antioxidant, anti-inflammatory, antimicrobial, and wound-healing capabilities, was scrutinized. Special attention was accorded to instances of contact dermatitis induced by mushrooms, notably the shiitake fungus. Preliminary findings reinforce the therapeutic potential of certain mushrooms in managing skin ailments, attributed primarily to their antioxidant, anti-inflammatory, and antimicrobial properties. Conversely, some species, prominently shiitake, emerged as potent dermatitis triggers. Mushrooms

undeniably harbor an array of compounds that can be instrumental in treating various skin conditions, thereby underscoring their potential in dermatological applications. However, an understanding of their dual nature, acting both as a remedy and a trigger for certain skin reactions, is essential for their judicious application in skin care. Further research is mandated to unravel the comprehensive pharmacological spectrum of these fungal treasures.

1. Introduction

The skin is the outermost organ, covering and protecting the body from the external environment Reference [1] and its structure has three layers: epidermis, dermis, and subcutaneous fat tissues [2]. Among the several functions of the skin, layers are protected from the external environment, internal homeostasis maintenance, protection from ultraviolet light damage, and defense after microorganism entry (Figure 1). Skin diseases are shared worldwide, constituting over 30% of general disorders [3]. Skin diseases and disorders (SDDs) vary greatly in symptoms and severity. They can be temporary or permanent and may be painless or painful. Therefore, a considerable amount of research has focused on bioresources to develop novel drugs for skin diseases, where mushrooms are present as a source of valuable compounds. Mushrooms are regarded worldwide as a component of gourmet cuisine and valued by humankind as a culinary wonder for their unique flavor. Although more than 2,000 species of mushrooms exist in nature, merely 25 are widely accepted as food, and few are commercially cultivated (Supplementary File 1). In addition, mushrooms comprise a vast yet largely untapped source of powerful new potential pharmaceutical substances. Polysaccharides, notably beta-glucans, activate Langerhans cells and macrophages, modulating immune responses and inflammatory processes in skin conditions [4]. Triterpenoids play a key role in skin health by inhibiting the synthesis of proinflammatory cytokines such as TNF-alpha and IL-6 and suppressing COX-2 expression, which is pivotal in the inflammation cascade [5]. Similarly, phenolic compounds bolster skin's defenses by upregulating endogenous antioxidant enzymes while also inhibiting oxidative enzymes like xanthine oxidase, mitigating the effects of oxidative stress [4]. Lectins contribute to cancer management by inducing apoptosis in malignant cells through both intrinsic and extrinsic pathways and curbing angiogenesis, which is vital in halting the progression of melanoma and other skin tumors [6]. Furthermore, ergothioneine, a compound that accumulates in mitochondria, provides a shield against mitochondrial DNA damage, maintaining cellular integrity and skin function [7]. The active form of Vitamin D, calcitriol, has a profound influence on skin health, modulating keratinocyte growth and differentiation, which are key in conditions like psoriasis [8]. Kojic acid, a well-known inhibitor of the melanin-producing enzyme tyrosinase, alters melanogenesis, offering a lightening effect on hyperpigmented areas [9]. The essential trace element selenium is integral in protecting against UV-induced cellular damage and inhibiting apoptosis of keratinocytes, due in part to its incorporation into antioxidant selenoproteins [10]. Omega-3 fatty acids, present in some mushrooms, are potent antiinflammatory agents capable of inhibiting the NF-kB pathway, thereby reducing inflammatory mediators in skin diseases such as atopic dermatitis [11, 12]. Lastly, chitin and chitosan, components of mushroom cell walls, are shown to enhance fibroblast proliferation and collagen synthesis, speeding up wound healing and fortifying the skin barrier, underscoring the extensive therapeutic potential of mushrooms in dermatological applications [13]. On this basis, multiple biological activities have been documented related to skin disease. Mushrooms like *Trametes versicolor* (Turkey Tail) contain polysaccharides, which are believed to have immunomodulatory effects; these can potentially help in conditions like psoriasis, where the immune response is misdirected towards skin cells [14]. *Ganoderma lucidum* contains triterpenoids, which might have anti-inflammatory and antihistamine properties, beneficial for skin conditions exacerbated by inflammation and allergic reactions [15]. The antioxidant activity of polysaccharides from several species such as *Pleurotus* spp. and *Agaricus* spp. [16–18], the potential of mushroom extract to decrease the secretion of proinflammatory mediators [19, 20], the antimicrobial activity of phytochemicals coming from mushroom extracts against bacteria and fungi activity [21], and the wound healing of mushroom species as adjuvants in new forms of treatment of skin damage, in different diseases, such as diabetes [22, 23], have been documented. However, some mushrooms also cause dermatitis, and one of the most common is that generated by the shiitake fungus, this being the best known and used. Thus, this review aimed to investigate the ethnobotanical data regarding the use of mushrooms for the potential treatment of SDDs, the biological activity in both *in vivo* and *in vitro* studies, and some contact dermatitis caused by mushrooms.

2. Methodology

The primary objective of this comprehensive review was to collate and assess the ethnobotanical evidence surrounding the utilization of mushrooms in the treatment of skin diseases and disorders (SDDs), to explore their biological activity in *in vivo* and *in vitro* studies, and to catalog any reported cases of contact dermatitis associated with mushroom exposure. To achieve a comprehensive literature search, multiple databases were scoured, including ethnobotanical databases, PubMed/MEDLINE, ScienceDirect, Web of Science, Google Scholar, Embase, and the Cochrane Library; a combination of keywords and MeSH (Medical Subject Headings) terms were employed to maximize search

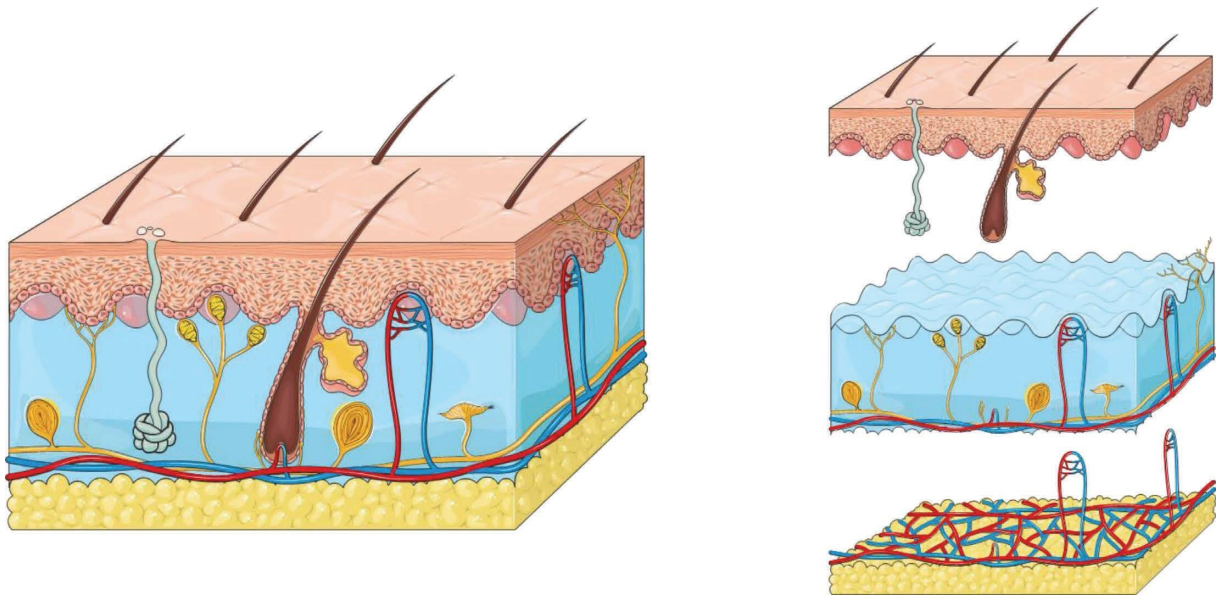

Figure 1: The structures of the skin. The epidermis, the outermost layer of the skin, is mainly composed of keratinocytes which undergo a process of maturation and eventually form a protective layer. The epidermis contains four to five sublayers, including the stratum basale, stratum spinosum, stratum granulosum, stratum lucidum (only in thick skin like palms and soles), and stratum corneum. Dermis, situated below the epidermis, the dermis consists of two sublayers: the papillary dermis and reticular dermis; it provides strength and elasticity to the skin due to the presence of collagen and elastin fibers. Hypodermis (subcutaneous layer) is the deepest layer of the skin, primarily made up of adipose tissue (fat cells). Accessory structures include hair follicles, sweat and sebaceous glands, and nails. Hair follicles give rise to hair which offers protection and plays a role in sensory functions. Sweat glands help in thermoregulation through perspiration, while sebaceous glands produce sebum, an oily secretion that moisturizes the skin and hair.

precision: "Mushrooms," "Ethnobotany," "Skin diseases," "Dermatology," "Fungal extracts," "Contact dermatitis," "*In vivo*," "*In vitro*." Boolean operators (AND, OR) were used to further refine the search, e.g., "Mushrooms" AND "Ethnobotany" OR "Bioactive compounds" AND "Dermatology."

2.1. Inclusion Criteria. Ethnobotanical records specifying the use of mushrooms for SDDs; studies focusing on the biological efficacy of mushroom extracts or compounds in both *in vivo* and *in vitro* setups; reports of contact dermatitis due to mushroom exposure; experimental, clinical trials, observational studies, and case studies; full-text articles available in English; articles published within the last 10 years.

2.2. Exclusion Criteria. Articles not directly related to the therapeutic or adverse effects of mushrooms on skin conditions; studies lacking direct ethnobotanical relevance or those not emphasizing *in vivo* or *in vitro* activity; articles unavailable in full text or not in English; non-peer-reviewed publications, such as literature reviews, opinion pieces, and editorials; studies deemed to have insufficient data or ambiguous methodologies.

For each article that met the inclusion criteria, a structured data extraction form was used to capture: authors, year of publication, article title, and source; traditional uses, regions, and cultural practices linked with mushroom use; design, mushroom type under study, targeted skin condition, main findings, and conclusions drawn; specific compounds identified, their quantities, and their roles (therapeutic or harmful); occurrences, symptomatic presentations, the mushroom species responsible, and resulting outcomes. The most representative data were methodically organized, summarized, and reported to present a holistic understanding of the current knowledge on the topic.

3. Ethnobotanical Data regarding the Use of Mushrooms in the Treatment of SDDs

Skin diseases constitute over 30% of general disorders [3] worldwide. A large amount of research has focused on bioresources to develop novel drugs for skin diseases, where mushrooms are a source of valuable compounds. On the other hand, the ethnobotanical and ethnopharmacological use of mushrooms against various skin diseases has been documented in different countries, and a number of species have been used as cosmetic ingredients [24] (Table 1). Mushroom species *Ganoderma lucidum* (Reishi) have been a part of traditional Chinese medicine formulations to treat various skin conditions, including rashes, wounds, and even more severe conditions like eczema and psoriasis; also, the native American tribes have been known to use certain mushrooms in poultices to treat skin infections and minor burns [41, 42]. Traditionally used in Siberian folk medicine, Chaga has been applied topically to treat various skin conditions [37, 43]; recent studies suggest that its high content of antioxidants might play a role in reducing skin inflammation and improving overall skin health [41]. Apart

Table 1: Ethnopharmacological use of mushroom species relevant to SDDs.

Mushroom species	Country used	Ethnobotanical use	References
Agaricus arvensis Schaeff.	India	For treating scalds and burns	[25]
Agaricus campestris L.: Fr.	Pakistan	Against wounds	[26]
Agrocybe dura (Bolton) Singer	Pakistan	Against wounds and as a skin tonic Used as a skin tonic	[26]
Antrodia camphorata (M. Zang and C.H. Su) Sheng H. Wu, Ryvarden, and T.T. Chang (formerly known as *Taiwanofungus camphoratus* (M. Zang and C.H. Su) Sheng H. Wu, Z.H. Yu, Y.C. Dai, and C.H. Su) (syn. *Antrodia cinnamomea* T.T. Chang and W.N. Chou)	Taiwan	Against itchy skin	[27]
	China	Against itchy skin	[28]
Astraeus hygrometricus (Pers.) Morgan	Pakistan	Against wounds	[26]
	India	Its spores against skin burns as ointment prepared with mustard seed oil	[25]
Auricularia auricula-judae (Bull.) Quél. (syn. *Hirneola auricula-judae* (Bull.) Berk.)	Europe	Astringent	[29]
Bovista sp. Pers.	India	Its spores for treating bruised skin infections	[25]
Bovista nigrescens Pers.		Against broken skin or wounds	[30]
Bovista plumbea Pers.		Against skin infections	[25]
Calvatia cyathiformis (Bosc) Morgan	India	Against wounds by powdering fruitbodies	[25]
	Mexico	Against burns in dried and minced form	[31]
Calvatia gigantea (Batsch) Lloy (syn. *Langermannia gigantea* (Batsch) Rostk.)	Italy	Against burns	[32]
	Europe	For dressing wounds	[29]
Calvatia utriformis (Bull.: Pers.) Jaap	Italy	Against burns	[32]
Chlorophyllum brunneum (Farl. and Burt) Vellinga	Pakistan	Against wounds	[26]
Clavulina rugosa (Fr.) Schroet.	India	Against skin diseases	[30]
Coprinellus disseminatus (Pers.) J.E. Lange	Pakistan	Used as a skin tonic	[26]
Coprinus comatus (O.F.Mull.: Fr.) Pers.	India	Against wounds, skin infections, and bruises	[25]
Coprinus micaceus (Bull.: Fr.) Fr.		For curing skin infections	[25]
Cordyceps sinensis (Berk.) Sacc.	China	For curing night sweating	[33]

Table 1: Continued.

Mushroom species	Country used	Ethnobotanical use	References
Coriolopsis polyzona (Pers.) Ryvarden	Tanzania		[34]
Daedaleopsis confragosa (Bolton) J.	India	Against skin diseases	[30]
	Nigeria		[35]
Daldinia concentrica (Bolton) Ces. and De Not	India	Against itching and healing minor skin infections, applied by mixing with coconut oil	
Entoloma bloxami (Berk. and Broome) Sacc		For curing skin diseases	[25]
Flammulina velutipes (Curt.) Singer	India	Against skin diseases by mixing its ashes with vegetable oil	
Fomes fomentarius (L.) Fr. (syn. *Agaricus fomentarius* (L.) Lam., *Polyporus fomentarius* (L.: Fr.) Fr.)	Korea	Against wounds Against alopecia	[36]
	Europe	For wound cauterization	
Fomitopsis betulina (Bull.) B.K. Cui, M.L. Han and Y.C. Dai (syn. *Piptoporus betulinus* (Bull.) P. Karst., or *Polyporus betulina* (Bull.) Fr.)	Russia, Poland, and other Baltic countries	Against wound bleeding	[29]
Fomitopsis officinalis (Vill.) Bondartsev., Singer., (syn. *Laricifomes officinalis* (Vill.) Kotl., and Pouzar, syn. *Fomes officinalis* (Vill.) Bres.)	Ancient Greeks	For inhibiting sweat secretion	
Ganoderma applanatum (Pers.) Pat.	Tanzania	For cleaning wounds	[34]
Ganoderma boninense Pat.		Against skin diseases and wounds	
Ganoderma lucidum (Curtis) P. Karst.		For cleaning wounds	
Ganoderma tsugae Murrill			
Geastrum fimbriatum Fr.	Mexico	For softening baby's skin	[31]
Geastrum saccatum Fr.			
Geastrum sessile Fr.	Pakistan	Used as a skin tonic	[26]
Geastrum triplex Jungh.	India	Its spores for curing skin diseases	[25]
	Pakistan	Against wounds	[26]
	Mexico	For softening baby's skin	[31]
Gomphus floccosus (Schwn.) Singer	India	For eczema and athlete's foot disease	[25]
Hericium erinaceus (Bull.) Persoon	China, Japan	Against wounds	[29]
Humaria hemisphaerica (Wigg.) Fuckel	India	For treating blisters on the skin	[25]
Hygrocybe sp. (Schaeff.) P.		Against skin diseases	[30]
Hypsizygus tessellates (Bull.) Singer			
Inonotus hispidus (Bull.) P. Karst.		As a topical disinfectant and for curing boils	[25]
Inonotus obliquus (Fr.) Pilát. (syn. *Fuscoporia obliqua* (Fr.) Aoshima)	Russia, Poland, and other Baltic countries	As a topical disinfectant used as soap	[29]
	Ancient Greeks	For washing wounds	[37]
Langermannia gigantea (Batsch.: Fr.) Rostk.	Pakistan	Against wounds	[26]
Lycoperdon candidum Pers.	Mexico	Against burns	[31]
Lycoperdon echinatum Pers.	India	Against wounds	[30]

Table 1: Continued.

Mushroom species	Country used	Ethnobotanical use	References
Lycoperdon perlatum Pers	Mexico	Against burns	[31]
	India	Its spores against wounds and for curing skin	[25]
Lycoperdon pyriforme Schaeff.		Its spores against wounds	
	Mexico	Against burns	[31]
Macrolepiota procera (Scoop.) Singer	Tanzania	Against wounds	[38]
Melanoleuca grammopodia Bull.	India	Against skin diseases	[30]
Morchella vulgaris (Pers.) Boud.		Against wounds	[25]
Mycena galericulata (Scop.) Gray.		Against skin diseases	[30]
Peziza repanda Pers.		For curing eczema	[25]
Phallus sp. Junius ex Linnaeus		Against wounds, skin infections, boils, or lesions	
Phallus impudicus L.	China	As a balm	[29]
	India	Against wounds	[25]
Phellinus rimosus (Berk.) Pilát	Tanzania	For cleaning wounds	[34]
	Cambodia	Against wounds by chewing and spitting the whole fruitbody on wounds	[39]
Pholiota nameka (T.Itô) S.Ito and S.Imai *Piptoporus betulinus* (Bosc) Fr.	Pakistan	Against wounds	[26]
Pisolithus arhizus (Scop.) Rauschert	India	Its spores against wounds and for curing skin to relieve burning, itching, and minor healing infections	[25]
		Against skin diseases and wounds	[30]
Pleurotus sp. (Fr.) P. Kumm.	India	For curing eczema in paste form by mixing its powdered fruitbody with water	[25]
Pleurotus dryinus (Pers.) P. Kumm.	Pakistan	Against wounds	[26]
Pleurotus ostreatus (Jacq.: Fr.) P. Kumm.	India	Its spores against wounds	[25]
Pleurotus sapidus Schulzer and Kalchbr.		Against skin diseases and wounds	[30]
Pleurotus tuber-regium (Rumph. ex Fr.) Singer	Tanzania	Against skin diseases	[34]
Podaxis pistillaris (L.) Fr.	India	Against skin diseases and burns	[25]
	Pakistan	Against wounds	[26]
Polyporus sp. P.Micheli ex Adans.	Tanzania	Against skin diseases	[34]
Ramaria stricta (Pers.) Quél.	India	To enhance skin color in powdered form	[25]
Russula delica (Pers.) Fr.	India	Against skin diseases and wounds	[30]
Scleroderma sp. Pers.	India	Against wounds	[25]
	Pakistan	Used as a skin tonic	[26]
Scleroderma citrinum Pers.	India	Against skin diseases and wounds	[30]
Scleroderma bovista Fr.	Turkey	Against skin wounds	[40]
Sparassis spathulata (Schwein.) Fr.	India	Against skin diseases, e.g., rashes, itching, dryness, and healing of wounds through mixing with butter or oil	[25]
Termitomyces heimii Natarajan	India	Wounds healing	[30]
Termitomyces marcocarpus Z.F. Zhang and X.Y. Ruan	Pakistan		[26]
Termitomyces microcarpus (Berk. and Broome) R.	India		[30]

Table 1: Continued.

Mushroom species	Country used	Ethnobotanical use	References
Trametes versicolor (L.) Lloyd. H	India	Against dermatitis	[25]
Ustilago maydis (DC.) Corda *Vascellum pratense* (Pers.: Quél.) Kreisel. *Vascellum qudenii* (Bottomley) P. Ponce de León	Mexico	For softening baby's skin Against burns	[31]
Volvariella bombycina (Schaeff.) Singer	Pakistan	Against wounds	[26]
Xylaria sp. Hill ex Schrank	India	For curing eczema	[25]

from its culinary uses, shiitake (*Lentinula edodes*) has been employed in traditional East Asian practices for its skin-healing properties; it was believed to rejuvenate the skin and reduce signs of aging [44]. Looking over the ethnobotanical/ethnopharmacological data related to mushrooms may keep light on the medical/pharmaceutical research relevant to skin diseases. For this purpose, our survey through literature using PubMed/MEDLINE and Scopus databases indicated the use of a limited number of mushroom species in ethnobotany/ethnopharmacology against skin-related diseases.

Given the increasing interest in natural and botanical ingredients in skincare, many modern cosmetic and therapeutic formulations now integrate mushroom extracts for their potential benefits; for instance, Reishi and Cordyceps extracts are commonly found in creams and serums aiming to provide antiaging and skin rejuvenating benefits [45]. While traditional evidence supports the benefits of mushrooms for skin health, rigorous clinical trials and scientific validations are essential; the precise mechanisms, safety profiles, and dosage regimens need to be established. Mushrooms, with their rich ethnobotanical history and a plethora of bioactive compounds, present promising potential for the treatment of various skin diseases; bridging the gap between traditional practices and modern medicine requires a comprehensive understanding and validation of their pharmacological actions.

4. Mushrooms-Derived Biological Effects: Therapeutic Potential for Managing SDDs

4.1. Antioxidant and Anti-Inflammatory Activity. Oxidative stress plays a pivotal role in the pathophysiology of skin inflammation, acting as both a trigger and a consequence of inflammatory processes. Various studies recognize mushrooms 'therapeutic activity and nutritional value [46–48]. These fungi have shown antioxidant activity highlighting polysaccharides as their primary metabolites [49, 50], which is essential in several species such as *Pleurotus* spp. and *Agaricus* spp. [16, 17]. In addition, studies indicate that polysaccharides, phenols, flavonoids, fatty acids, and tocopherols, among other compounds, are responsible for antioxidant activity [51]. For example, phenolic compounds might stimulate the endogenous production of antioxidant molecules in cells [52], inhibiting free radicals, sequestering oxygen, decomposing peroxide, and chelating metal ion [53]. A comprehensive review carried out by Sanchez [54] found that the active components in mycelia extracts, sporocarps, and cultures of these structures were responsible for the antioxidant effect. The first report on the antioxidant activity of aqueous and methanolic extracts of *Pleurotus ostreatus* in distinct growth stages was conducted by González-Palma et al. [55]. In the study, flavonoids and undetermined metabolites were responsible for antioxidant activity, showing greater reduction power in the case of aqueous extracts. In addition, Boonsong et al. [56] studied the antioxidant activity of the edible mushroom species *Lentinus edodes*, *Volvariella volvacea*, *Pleurotus eous*, *Pleurotus sajor-caju*, and *Auricularia auricular* from extracts rich in phenols and flavonoids. *L. edodes* ethanolic extract showed the highest antioxidant, chelating, and superoxide radical scavenging activity, positively correlated with total flavonoid and phenol content [56]. In an investigation carried out by Gebreyohannes et al. [57], the antioxidant potential of the *Auricularia* spp. and *Termitomyces* spp. was evaluated using the DPPH free radical method and expressed by the inhibitory concentration value (IC_{50}). Extracts of both species revealed suitable antioxidant activities in the range of IC_{50} 40–70 μg/mL. The antioxidant capacity extracts from four species of wild edible mushrooms (*Pleurotus cystidiosus*, *P. flabellatus.*, *P. florida*, and *P. ostreatus*) were evaluated in a study conducted by Vishwakarma [58]. All species exhibited significant antioxidant properties; however, *P. ostreatus* showed the highest antioxidant activity using the DPPH, β-carotene and H_2O_2 elimination assays. Chen et al. [59] evaluated the antioxidant activity of melanin, extracted from *Auricularia auricula-judae* in terms of its capacity to eliminate free radicals and its antioxidant effects in *C. elegans*. It was observed that at a concentration of 1 mg/mL, the free radical scavenging capacity exceeded 85%, influencing the half-life and locomotion of *C. elegans* [59]. On the basis of the fact that the production of reactive oxygen species significantly impacts the destruction of collagen in the skin, Choi et al. studied the antioxidant activity of *Auricularia auricula-judae* (Bull.) and its relationship with collagen production in human keratinocytes. The extract obtained from this mushroom species showed a positive effect in eliminating DPPH free radicals and superoxide anions, with potential use in the skincare industry [60]. An *in vivo* study by Son et al. revealed the antiinflammatory effect of mushroom extracts on ear thickness, ear epidermal thickness, and eosinophil infiltration in the skin tissues of mice. Their antiinflammatory effect improved more significantly with the aqueous fractions produced by solid fermentation of *Ganoderma lucidum* on *Artemisia capillaris* leaves than with aqueous samples of *Artemisia capillaris* leaves or *Ganoderma lucidum* [61]. According to another study by Ramya et al. [62] focusing on the preventive effect on inflammation of the bioactive extract of the mushroom *Morchella elata*, skin thickness, level of lipid peroxidation, and histopathological alterations of mice were reduced, indicating the antiinflammatory effect of *Morchella elata* extracts [62].

4.2. Antimicrobial and Antifungal Activity. Mushrooms contain bioactive compounds with potent antimicrobial and antifungal properties in an era where *Staphylococcus aureus* colonization and antimicrobial resistance are on the rise. These natural agents could be particularly beneficial in combating severe infections, such as fusariosis in immunocompromised patients, providing alternative therapeutic strategies in the context of hospital-acquired infections and the challenge of invasive diseases following procedures like allogeneic transplants [63]. Mushrooms need antibacterial components to survive in their natural environment; they have phytochemicals with antimicrobial action, positioning them as potential pharmacological resources to control

resistant pathogens effectively. A study evaluated 35 wild mushrooms from Kenyan forests. *Trametes* spp. (Arabuko-Sokoke forest), *Trametes* spp., and *Microporus* spp. (Kakamega forest) exhibited antimicrobial activities against a wide variety of bacterial strains [57]. Another *in vitro* study evaluated the extract from five edible mushrooms against Gram-positive bacteria (*Bacillus cereus* and *Staphylococcus aureus*) and Gram-negative bacteria (*Salmonella enteritidis* and *Escherichia coli*). Of the five mushroom species, *A. brasiliensis* presented the highest responses for antioxidant and antibacterial activity [64]. There is growing evidence of the antimicrobial effect of volatile compounds produced by *P. spadiceum* against plant fungi and bacteria [65]. In fruit growing, the activity of the hydroalcoholic extract obtained from the mushroom *Lactarius deliciosus* against *Monilinia fructicola*, a pathogenic fungus that infects stone fruits such as peach, nectarine, and plum in Brazil, was evaluated [66]. The antimicrobial activity of mushroom extracts and the production of phytochemicals known for their action against bacteria and fungi depend on genetic factors, culture conditions, pH, and the substrate composition influencing the metabolic pathway that allows the production of these phytochemicals of biological interest [21]. Worldwide, more studies are needed to clarify the role of these microbial communities in both human health and pathology [67].

Table 2 shows examples of mushroom species with antimicrobial and antifungal activity in SDDs.

5. Healing Activity

The wound healing process consists of four main phases: homeostasis, inflammation, proliferation, and remodeling [76, 77]. Fibroblasts play a fundamental role in the process by participating in the extracellular matrix generation. Several investigations describe the wound healing role of mushrooms, as potential adjuvants in skin damage treatment for different diseases, such as diabetes [22]. Polysaccharides found abundantly in various mushroom species play a crucial role in enhancing skin hydration, improving its barrier function; they also possess antiinflammatory properties, aiding in reducing skin redness and irritation [78]. Exhibiting antiinflammatory and antioxidant properties, triterpenoids derived from mushrooms like *Ganoderma lucidum* (Reishi) help soothe skin irritations and protect against oxidative damage. Phenolic compounds present in mushrooms such as *Agaricus bisporus* also act as powerful antioxidants, combating free radicals that accelerate skin aging [78]. Commonly found in mushrooms, ergosterol, when exposed to UV light, converts to provitamin D2, which is beneficial for skin health [78]; the presence of essential amino acids and antioxidants in mushrooms accelerates the wound healing process by promoting collagen synthesis and reducing oxidative stress at the wound site [78]. A review by Jones et al. [13] summarized the role of chitin, chitosan, and other polysaccharides in the cell walls of wound healing by mushrooms (Figure 2). These polysaccharides can accelerate proliferation in cells (such as fibroblasts and keratinocytes), acting as a support matrix for cell expansion and regeneration of damaged tissue [13]. A study conducted by Wen et al. [79] revealed that the polysaccharides extracted from *Tremella fuciformis* increased collagen production, thus contributing to the wound healing process [79]. *Ganoderma lucidum* is a mushroom species studied for the healing activity of its extracts, rich in polyphenols and flavonoids [80], as for its interaction with the skin microbiota and its relationship with the inflammatory processes associated with wound healing [81]. In addition, *G. lucidum*, studied by Abate et al. [82], showed the ethanolic potential of its extract, rich in ganoderic acid, in increasing cell migration patterns and accelerating the healing process, mainly re-epithelialization [82]. One study showed *that Auricularia auricula-judae* extract promoted the proliferation, migration, and invasion of fibroblasts and keratinocytes, as well as increasing the wound-healing process by raising collagen synthesis and decreasing E-cadherin expression [83]. In the same way, *Metacordyceps neogunnii* extract, another type of edible mushroom, slightly improved the fibroblast cells (BJ-1) migration after 24 hours of exposure to the extract [84]. Another study evaluated silver nanoparticles using extracts from *Boletus edulis* and *Coriolus versicolor* showing improvements in the migration of murine L929 fibroblast cells at low extract concentrations [75]. Research conducted on extracts of immature bamboo mushrooms (*Dictyophora indusiate*) improved the healing process by reducing metalloproteinase 2 (MMP-2) in fibroblasts. These mushrooms are highlighted as essential natural ingredients for skin-healing pharmaceutical products [85]. A study that evaluated the effect of ethanolic extracts from 4 mushroom species (*Pisolithus tinctorius*, *Russula capensis*, *Imleria badia*, and *Pleurotus ostreatus*) on *in vitro* models (characteristic of the diabetic state), showed positive effects on wound healing [86]. Mapoung et al. [83] investigated the nutrient-rich macrofungi *Auricularia auricula-judae* in terms of its wound-healing effects from the high amount of water-soluble polysaccharide-rich extracts (AAP). The BALB/c mice, six to eight weeks old males, were employed to observe the wound closure in their skin by examination of three groups, in which the wounds were sterilized with 0.9% of normal saline, 1.0% w/v of AAP, and 2.5% w/v of AAP. The results revealed that the group receiving 2.5% w/v of AAP showed an observable wound contraction on day 9. In addition, the 2.5 and 1 w/v of AAP showed a strong wound contraction on day 12, thus supporting the significant potential for accelerating the wound healing of polysaccharides obtained from *Auricularia auricula-judae* [83]. In another *in vivo* study by Krupodorova et al. [87]; the wound healing activity of the aqueous extracts obtained from mushrooms *Ganoderma lucidum* 1900 (Curtis) P. Karst and *Crinipellis schevczenkovi* 31 Buchalo was investigated. The three months old white albino male mice line FVB/Cg, were separated into three groups, and treated with 20 μL *G. lucidum* mycelium extract and 20 μL *C. schevczenkovi* mycelium extract for six days, and the control group was treated with sterile distilled water. The results demonstrated that the wound healing process was more active on day 3 in mice treated with a *C. schevczenkovi* extract than the treated group with a *G. lucidum* extract. In contrast, the healing process was similar on day 5 for both groups treated with mushroom extracts. Therefore, the wound-healing process in both groups

Table 2: Overview of mushroom-derived compounds with antimicrobial and antifungal properties for skin disease management.

Mushroom source and activity	Extract and active molecules	Pathogens targeted	Mechanism/Beneficial role in SDDs	Reference
Pleurotus ostreatus (*Antimicrobial*)	Methanol and aqueous (Tannins, terpenoids, alkaloids, flavonoids, saponins, glycosides, steroids)	*Shigella* sp., *Staphylococcus* sp., *Vibrio* sp., *E. coli*, *Penicillium* sp., *Yeast and Moulds*	Disrupts pathogen cell walls, prevents skin infections, and supports wound healing	[68]
Pleurotus ostreatus (*Antimicrobial*)	Water and ethanol	*E. coli*, *B. cereus*, *P. aeruginosa*, *B. subtilis*, *S. typhi*, *S. aureus*	Enhances skin integrity by preventing pathogenic bacterial infections	[21]
Trametes spp. (*Arabuko-Sokoke forest*), *Trametes*, *Microporus* spp. (*Kakamega forest*) *Antimicrobial*)	Chloroform, 70% ethanol, and hot water	*S. aureus*, *MRSA*, *K. pneumoniae*, *P. aeruginosa*, *E. coli* (*clinical isolate*)	Inhibits bacterial biofilm formation, useful in treating resistant skin infections	[69]
Agaricus bisporus, et al. (*Antimicrobial*)	Ethanol (Gallic acid)	*B. cereus, S. aureus*, *E. coli*, *S. enteritidis*	Reduces inflammation and microbial growth on the skin	[64]
Porostereum spadiceum (*Antibacterial*, *Antifungal*)	N-hexane (4-dichloro-4-methoxybenzaldehyde)	*C. michiganensis*, *R. solanacearum*, *A. brassicicola*, *C. orbiculare*	May be used for topical treatment against skin-affecting plant pathogens	[65]
Lentinus arcularius (*Antibacterial*, *Antifungal*)	Ethyl acetate	*E. coli*, *P. aeruginosa*, *S. aureus/C. albicans*, *S. cerevisiae*, *A. niger*	Protects against both bacterial and fungal skin infections	[70]
Lactarius deliciosus (*Antifungal*)	Hydroalcoholic extract	*M. fructicola*	Potential application in antifungal treatments for skin affected by fruit pathogen infections	[66]
Omphalotus japonicus (*Antibacterial*)	Methanol (Omphalotols A and B)	*H. pylori*	Possible applications in treating H. pylori-associated dermatological conditions	[71]
Cordyceps sinesis, et al. (*Antibacterial*)	Ethanol	*K. pneumoniae*, *E. aerogenes*, *S. aureus* sub sp., *B. thuringiensis*	Can aid in the management of bacterial infections of the skin	[72]
Lentinula edodes (*Antibacterial*)	Water and methanol	*S. aureus*, *K. pneumonia*	Could be useful in the topical treatment of bacterial skin infections	[73]
Sarcodon squamosus (*Antibacterial*, *Antifungal*)	Methanol	*M. luteus*, *S. aureus*, *B. subtilis*, *P. vulgaris*, *E. coli*, *Y. enterocolitica/C. albicans*	May offer a dual-action approach to treating skin infections caused by bacteria and fungi	[74]
Coriolus versicolor Boletus edulis (*Antibacterial*, *Antifungal*)	Distilled water	*P. aeruginosa*, *K. pneumonia*, *S. aureus*, *E. faecalis/C. albicans*, *C. utilis*	Supports the treatment of infections and enhances skin microbiota balance	[75]

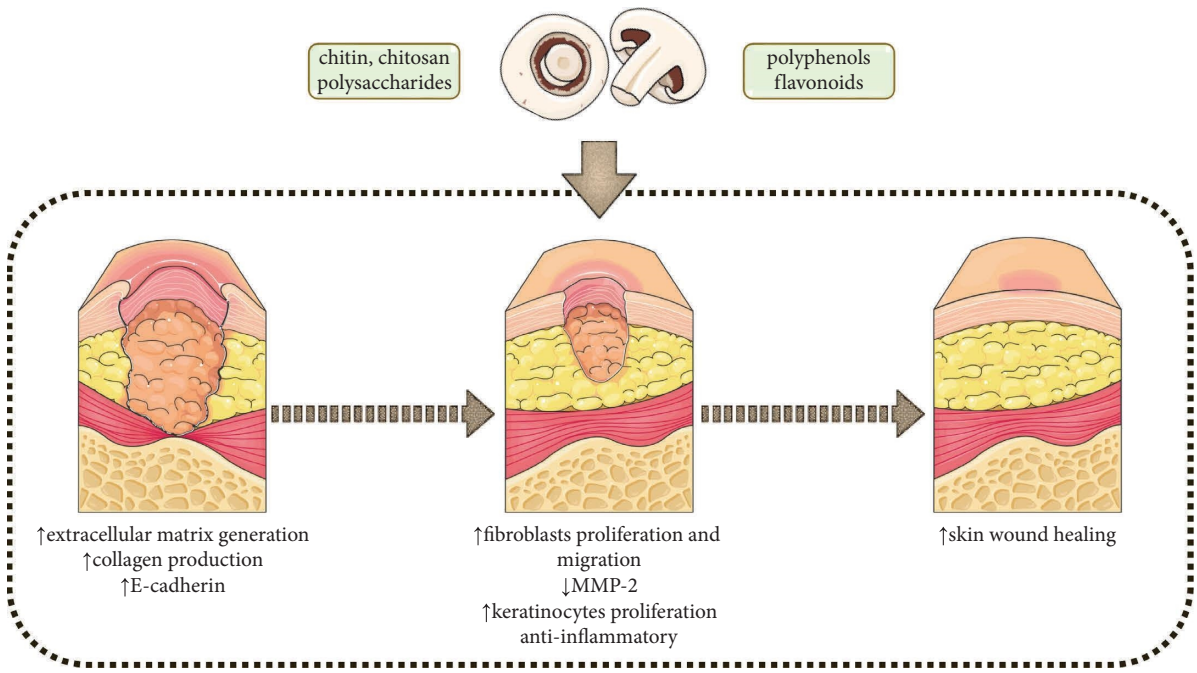

Figure 2: Illustrative scheme regarding the role of bioactive mushrooms in wound healing. Abbreviations and symbols: ↑increase, ↓decrease, MMP-9 (matrix metalloproteinase 9).

was better compared to the control group, indicating the high wound-healing activity of the mushroom extracts [87].

5.1. Effects on Skin Melanoma. Skin melanoma, while comprising only 5% of skin cancers, is notoriously aggressive and often resistant to conventional therapies, driving the exploration of novel anticancer agents [88]. Recent studies have focused on the effective anticancer agents such as bioactive compounds found in mushrooms [89]. Beta-glucans, predominantly found in mushrooms such as shiitake and Maitake have been shown to modulate the immune system and inhibit the growth and proliferation of melanoma cells [90, 91]. Lectins as protein molecules, abundant found in certain mushroom species can recognize and bind specifically to cancer cells, leading to their apoptosis (programmed cell death), thus curbing melanoma progression [92]. Mushrooms like *Ganoderma lucidum* (Reishi) contain triterpenoids that exhibit antiinflammatory and antioxidant activities, targeting melanoma cells and preventing metastasis [92]. Potential mechanisms of mushrooms bioactives against melanoma [91, 92]:

(i) Inhibition of cell proliferation by mushroom extracts, particularly from species like *Agaricus blazei*, have demonstrated an ability to halt the proliferation of melanoma cells, inducing cell cycle arrest [91, 92]

(ii) Induction of apoptosis, mushroom-derived bioactives can activate the intrinsic apoptotic pathways in melanoma cells, leading to cell death and preventing tumor progression [91, 92]

(iii) Antimetastatic activity; certain mushrooms have compounds that inhibit melanoma cell migration and invasion, thereby curbing the metastasis, which is a significant challenge in melanoma management [91, 92]

(iv) Immunomodulation; beta-glucans bolster the body's immune response against melanoma, enhancing the activity of macrophages and natural killer cells, which play a role in targeting and destroying cancer cells [91]

Liu et al. [93] investigated the *in vivo* antitumor and antimetastatic activities of chloroform extract from *Cordyceps taii* (CFCT). Male mice aged between 5 and 7 weeks, average weight of 18.0 ± 2.0 g, were injected with melanoma B16F10. After the tumor growth, the mice were divided into three groups for CFCT treatment according to the applied dose of CFCT, which were 20, 50, and 100 mg/kg. A model group was treated only with saline, and a combined administration group was treated with 20 mg/kg CFCT and 20 mg/kg cyclophosphamide (CTX). The results showed that the tumor growth of melanoma B16F10 in the mice group treated with 100 mg/kg CFCT and the combined administration was significantly inhibited with CFCT treatment. The antimetastatic activity of CFCT for melanoma B16F10 in mice was observed by considering the common metastasis of melanoma to lung tissue in mice. According to the results, only the model group and the group treated with 20 mg/kg CFCT showed a metastatic focus of melanoma B16F10, indicating that CFCT was influential in the inhibition of melanoma metastasis in mice [93].

In a similar *in vivo* study by Harhaji Trajković et al. [94], the tumor growth inhibition in inoculated C57BL/6 mice with syngeneic B16 tumor cells was observed as a result of treatment with methanol extract from *Cariolus versicolor* (50 mg/kg) for 14 days. The direct focus on skin melanoma in these studies substantiates the specific impact of mushroom-derived bioactives on this form of skin cancer; as research progresses, the translation of these findings to clinical applications could improve the treatment landscape for skin melanoma. Figure 3 shows the antimelanoma effect of mushrooms bioactive compounds.

5.2. Effects on Atopic Dermatitis. Atopic dermatitis (AD), often referred to as eczema, is a chronic inflammatory skin disorder characterized by itchiness, redness, and a rash. AD is induced by a combination of genetic, psychologic, pharmacologic, environmental, and immunological factors. Though its etiology is multifactorial, involving genetic, environmental, and immunological factors, there's been a growing interest in alternative therapeutic agents, including mushroom-derived bioactives, for its treatment and management [95, 96]. Many mushrooms exhibit antiinflammatory activities, which are critical in managing atopic dermatitis since inflammation is a significant contributor to its pathogenesis [97]. For instance, polysaccharides extracted from *Ganoderma lucidum* (Reishi mushroom) have demonstrated the ability to suppress the expression of proinflammatory cytokines, potentially mitigating the inflammatory response associated with AD [97]. Skin barrier dysfunction is also a hallmarking feature of atopic dermatitis, and certain mushroom derivatives have been shown to bolster the skin barrier. Chitin, a component present in the cell walls of mushrooms, can be transformed into chitosan, which is known for its moisturizing effect on the skin, potentially helping to restore the skin barrier [98]. Itching associated with AD can significantly reduce the quality of life for patients; mushrooms like *Pleurotus ostreatus* (oyster mushroom) possess compounds that exhibit antipruritic (antiitching) effects, offering potential symptomatic relief [99]. An imbalance in immune responses is a critical aspect of AD pathophysiology; many mushroom species are renowned for their immunomodulatory effects. β-glucans, which are abundant in mushrooms like shiitake (*Lentinula edodes*), may modulate immune responses, thus potentially offering therapeutic advantages for AD patients [99]. Oxidative stress plays a pivotal role in the aggravation of atopic dermatitis, and many mushrooms, such as the Cordyceps species, are rich in antioxidants, which can counteract oxidative stress, further aiding in the alleviation of AD symptoms [100]. Secondary bacterial infections are common in AD lesions due to compromised skin integrity; mushroom extracts like those from *Agaricus bisporus* (white button mushroom) have shown antimicrobial properties, potentially preventing or treating these secondary infections [101]. Watanabe et al. [96] examined the effects of hot water extract of the mushroom Basidiomycetes-X (BDM-X) on atopic dermatitis (AD) skin lesions in NC/Nga mice, which can develop AD clinically very similar to humans. A cream is used to cause AD-like skin lesions in mice; one-third was kept untreated with the cream as the control group. The reminder with skin lesions were divided into two groups, one of which was treated with the BDM-X extracts. The results showed that AD skin lesions in BDM-X-treated mice were rapidly decreased, whereas the other group with AD still had the skin lesions. This significant result revealed the high potential of BDM-X extracts in AD treatment [96]. Another study focusing on the treatment of AD, conducted by Choi et al. [102], analyzed the ethanolic extract efficiency of *Lentinula edodes*, including polyphenols, flavonoids, β-carotene, and lycopene. The eight weeks old female BALB/c mice were employed to investigate various effects of AD. The AD lesion in mice ears was induced through exposure to *Dermatophagoides farinae* extract (DFE) and 4-dinitrochlorobenzene (DNCB). Mice were divided into four groups: one with only AD lesions, another with AD receiving 250 mg/kg *L. edodes* extract, a group with AD receiving 500 mg/kg *L. edodes* extract, and the control group. Two groups with AD receiving 500 mg/kg and 250 mg/kg *L. edodes* extract showed considerably better results than other groups within 28 days after the induction of AD. Overall results indicated that *L. edodes* extract effectively decreased several AD symptoms by reducing the severity of AD lesions, cervical lymph nodes, and inflammatory cytokines in the ears of mice [102].

5.3. Effects on Hyperpigmentation. Hyperpigmentation, one of the common skin disorders observed in all skin conditions, including acne or atopic dermatitis, with various symptoms such as dark spots, darker skin, and irregular grey patches, can be treated with depigmentation agents [103, 104]. The therapeutic potential of mushroom bioactives in addressing hyperpigmentation has been a subject of growing research interest; certain mushroom extracts have demonstrated inhibitory effects on tyrosinase, the key enzyme responsible for melanin synthesis. For instance, *Agaricus bisporus* (white button mushroom) contains compounds that have been found to inhibit tyrosinase activity, thus potentially reducing melanin production and aiding in the treatment of hyperpigmentation [105]. Oxidative stress is one of the factors that can trigger or exacerbate hyperpigmentation. Many mushrooms, such as *Ganoderma lucidum* (Reishi mushroom), are rich in antioxidants that can combat oxidative stress, offering a two-pronged approach to addressing both melanin production and the underlying triggers [92]. Inflammation-induced hyperpigmentation, or postinflammatory hyperpigmentation (PIH), is a common concern following acne, skin injuries, or inflammatory skin conditions. Mushrooms like Cordyceps and shiitake (*Lentinula edodes*) exhibit anti-inflammatory properties, which might help in reducing the occurrence or severity of PIH [45]. Some mushroom extracts can promote an even skin tone and improve overall skin radiance. A healthy skin barrier is crucial for preventing external triggers, like UV radiation and

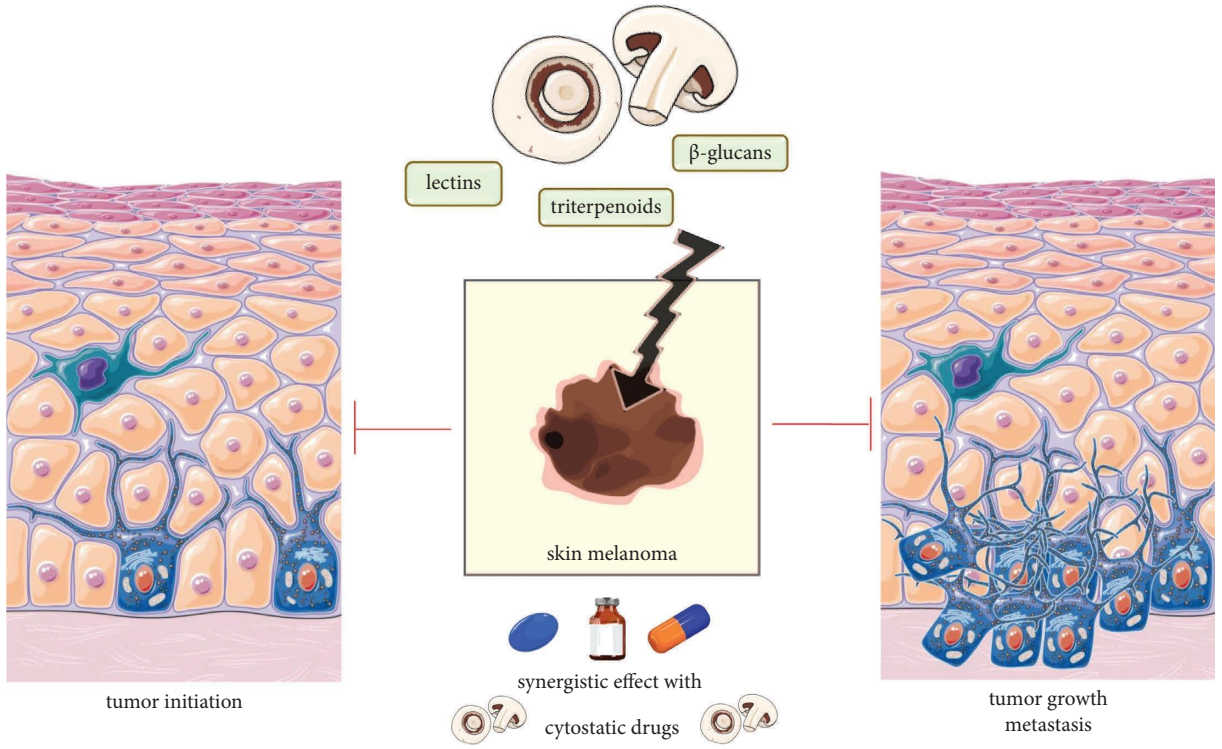

Figure 3: Antimelanoma effect of mushrooms bioactive compounds. Symbol: ⊥ inhibition.

environmental pollutants, from inducing hyperpigmentation; components like beta-glucans, present in several mushrooms, can bolster the skin's barrier function [106]. *Trametes versicolor*, also known as the Turkey tail mushroom, has been incorporated into skincare products for its potential skin-brightening effects [106]. Given their multifaceted action on skin health, mushroom bioactives might enhance the efficacy of other depigmenting agents or treatments; they could be incorporated into comprehensive treatment regimens for hyperpigmentation, ensuring more holistic care [106]. An *in vivo* study conducted by Pavic et al. [107], explored the toxicity of antimelanogenic compounds found in mushrooms to inhibit excessive skin pigmentation. The zebrafish was preferred as the preclinical experimental model to evaluate the toxicity by carrying six different doses of ethanol extracts of each of the five mushrooms for five days. The results revealed the toxicity of five selected mushroom extracts subjected to application doses. The greatest toxicity profiles have been achieved for *Laetiporus sulphureus* (LSE) and *Agaricus silvaticus* (ASE), which were not toxic at high doses of up to 400–500 mg/mL. In contrast, the remaining three extracts were detected as possibly toxic and unsafe for humans. This study showed that the tyrosinase activity and melanin synthesis in zebrafish were inhibited by LSE and ASE extracts without inflammatory, immunosuppressive, or toxic effects, indicating their safety for possible usage in cosmetics and other applications [107]. Generally, mushroom-derived bioactives have exhibited a favorable safety profile when compared to some chemicals often used to treat hyperpigmentation, and this makes them attractive alternatives, especially for individuals with sensitive skin. The most representative pharmacological studies on the therapeutic potential of mushrooms against different skin diseases and/or skin disorders are summarized in Table 3.

6. Clinical Studies Related to Bioactive Compounds of Mushrooms and SDDs

Several investigations on the effects of different mushroom extracts and/or their bioactive compounds on skin conditions and aging processes are found in the literature. Yamamoto and Kimura [23] investigated the mushroom *Sparasis crispa* (SC) in terms of its therapeutic effects on skin conditions in humans. To understand the effects of SC on skin conditions in humans, 26 healthy volunteers, between the ages of 20 and 60 years, were divided into two groups: orally SC-administered and placebo. According to the results obtained after four weeks, the cheek transepidermal water loss was considerably lower in the SC-administered group than in the placebo group. Thus, it supported the positive effect of SC administration on improving human skin conditions [23]. Another recent clinical study was conducted by Lee et al. [123] to investigate the antioxidant, anti-inflammatory, antiallergic, antidiabetic, and anti-angiogenic effects of veratric acid derived from the mushroom *Sparassis crispa* and demonstrate its clinical effects. A cream including veratric acid isolated from *Sparassis crispa* and the control was applied for 12 weeks on the right and left periorbital areas of 20 women, average of 47.7 ± 4.8 years old. The results showed that the veratric acid extract improved facial wrinkle formation from *Sparassis crispa* by increasing

Table 3: Summary of preclinical studies on animal models about the therapeutic potential of mushrooms on SDDs.

Mushroom species and their extracts	Types of skin diseases and/or disorders	Effect	Results	References
Mannogalactan from *Pleurotus eryngii* (cold aqueous extraction)	Melanoma (skin cancer)	Anticancer	60% reduction of the tumor volume in melanoma-bearing C57BL/6 mice with the treatment of mannogalactan (50 mg/kg) compared to the control group	[108]
Choloroform extract of *Cordyceps taii* (methanol extraction)			Considerable *in vivo* potential of antitumor and antimetastatic activities probably due to its antiproliferation, antioxidant, and immunoregulatory effects	[93]
Extract of bioactive compounds from *Pleurotus ferulae* (ethanol extraction)			↓tumor formation, ↓growth, size, and final weight of tumor *in vivo* with prevention of tumor cell proliferation ↓cell migration, ↑apoptosis	[109]
CARI III (dietary supplement) is composed of *Phellinus linteus*, *Inonotus obliquus*, *Antrodia camphorata*, and *Ganoderma lucidum* (CARI, Inc., Seoul, South Korea)			↓tumor weight with the treatment of 300 mg CARI III/kg/day compared to the treatment of doxorubicin (Dox) ↑life span (50.88%) in the CARI III-administered animal group comprising the tumor control animal group	[110]
Methanol extract including total terpenoids and purified methanol extract including mainly acidic terpenoids from *Ganoderma lucidum* (methanol extraction)			↓tumor growth *in vivo* with the treatment of both extract types obtaining a more potent effect with methanol extract including total terpenoids than purified methanol extract including mainly acidic terpenoids	[94]
Extracts of *Cordyceps sinensis* (extraction with petroleum ether, ethyl acetate, ethanol and hot water)		Anticancer/Antitumor	14 times lower tumor volume in the group of B16-melanoma-bearing mice with the treatment of methanol extract, including total terpenoids, compared to control tumor-bearing mice ↓B16-induced melanoma in C57BL/6 mice and approximately 60% reduction of tumor size more than 27 days with ethyl acetate extraction	[111]
Acidic polysaccharide from *Phellinus linteus*		Antimetastatic	↓melanoma cell metastasis in mice ↓adhesion, ↓invasion of cancer cells through the extracellular matrix not directly influential on the growth of cancer cell	[112]

Table 3: Continued.

Mushroom species and their extracts	Types of skin diseases and/or disorders	Effect	Results	References
Hot water extract of *Ganoderma lucidum*	Skin wounds	Wound healing/Antioxidant	The highest wound closure in streptozotocin-induced diabetic rats with the treatment of 10% (w/w) aqueous extract cream compared to treated groups with Intrasite gel (positive control) and aqueous cream (negative control) The shortest reepithelization period with the treatment of 10% (w/w) aqueous extract cream Considerable higher *in vivo* antioxidant activity with 15% (w/w) aqueous extract compared to negative and positive control groups Lower oxidative protein products and lipid damage in treated diabetic rats with aqueous extract compared to negative and positive control groups	[113]
Extract of *Cantharellus cibarius*	Skin wounds (circular excision and linear incision wound models)	Wound healing/ Antiinflammatory	↑healing activity for treated rats with extract of *C. cibarius*, and Madecassol (reference drug) compared to nontreated and vehicle-treated rats completely repairing the epidermal layer, increasing collagen production, considerable neovascularization and epithelization degree in the treated rats with the extract ↓COX-2 in treated rats with extract than in nontreated and vehicle-treated rats	[114]
Extract of *Antrodia camphorate* (ethanol extraction)	Skin wounds (excision model)	Wound healing/ Anti-inflammatory	↑wound healing closure in treated rats with extract (for both doses of 100 mg/kg and 200 mg/kg) and Intrasite gel (reference drug) compared to treated rats with vehicle Considerably less scar width at wound closure and less inflammatory cells, more collagen, and more fibroblast in granulation tissue with extract treatment than vehicle treatment	[115]

Table 3: Continued.

Mushroom species and their extracts	Types of skin diseases and/or disorders	Effect	Results	References
Aqueous lyophilized extract of *Ganoderma lucidum*	Skin wounds	Wound healing	↑healing activity with an increase in wound contraction, accumulation of collagen, hexosamine, and total protein content for treated rats with extract	[80]
Sparassis crispa			↑wound closure in streptozotocin-induced diabetic rats with oral administration of *S. crispa* ↑migration of macrophage and fibroblast, ↑regeneration of collagen, and epithelialization with *S. crispa* treatment compared to the control group (nontreated with *S. crispa*)	[116]
Aqueous extract of *Hericium erinaceus*		Wound healing	Higher and quick wound healing in rats treated with the extract and Intrasite gel than in rats treated with sterilized distilled water Considerably less scar width in healed wound area and lower macrophages and higher collagen in the healed wound for treated rats with extract than treated rats with sterilized distilled water	[117]

Table 3: Continued.

Mushroom species and their extracts	Types of skin diseases and/or disorders	Effect	Results	References
Extract of *Hypsizigus marmoreus* (ethanol extraction)	Atopic dermatitis	Antiatopic dermatitis/ Antiinflammatory	↓severity score of dermatitis and the epidermis thickness in treated BALB/c mice group with extract for five weeks compared to another treated group with PCL ↓IL-1β, ↓IFN-γ production levels in concanavalin A-stimulated and lipopolysaccharide-stimulated mouse splenocytes and macrophages with extract treatment ↑IL-4 with administration of extract to splenocytes of mouse	[95]
Aqueous extract of *Cordyceps militaris*		Antiatopic dermatitis/ Antiinflammatory	↓epidermal and dermal thickness and infiltration of mast cell in ears of DFE/DNCB-induced BALB/c mice group with oral administration of the extract ↓immunoglobulin levels and gene expression of T helper (Th)1/Th2 cytokines in the tissue of mouse ear with extract	[118]
Extract of *Lyophyllum decastes*		Antiatopic dermatitis/ Antiallergic	↓AD-like skin lesions development according to low scores of total skin severity and levels of immunoglobulin E in NC/Nga mice with oral administration of the extract ↓IL-4, no inhibition of IFN-γ production with extract treatment Exertion of antiallergic action due to suppression of serum IgE and Th2-type immune responses with extract treatment	[119]
Aqueous extract of *Grifola frondosa*		Antiatopic dermatitis/ Anti-inflammatory	↓score of dorsal skin dermatitis with extract treatment ↓AD-like skin lesion, ↓Th-1/Th-2 response in NC/Nga mice with extract treatment Synergistic effect in AD-like skin lesions by reduction of serum IgE, mast cells infiltration, and cytokines expression with combined treatment of extract and dexamethanose	[89]

Table 3: Continued.

Mushroom species and their extracts	Types of skin diseases and/or disorders	Effect	Results	References
Extracts of *Pleurotus eryngii*		Antiatopic dermatitis/ Antiinflammatory/Antiallergic	↓AD-like skin lesions in DNCB-induced NC/Nga mice with continuous extract treatment ↓severity of dermatitis, ↓IgE and thymus and activation-regulated chemokine (TARC), and mRNA expression of TNF-α, INF-γ, IL-4, IL-5, and IL-13 in mice with extract treatment ↓dermis and dermal infiltration thickness of inflammatory cells and mast cells with extract treatment ↓allergic contact dermatitis due to modulation of T helper Th1 and Th2 responses and decrease of the inflammatory cells and mast cells infiltration in the skin lesions in NC/Nga mice	[120]
Extract of *Ganoderm A formosanum* (ethanol extraction)	Abnormality of skin pigmentation	Antityrosinase/ Antimelanogenesis	↓surface pigmentation level on the body of zebrafish with extract treatment after 48 h due to considerable reduction of tyrosinase activity and melanin content No significant differentiation in terms of morphology and mortality of treated zebrafish with extract compared to the control group Less toxicity and similar efficiency for depigmentation with extract treatment in lower dosages than kojic acid treatment ↓hyperpigmentation, ↓tyrosinase activity ↓melanin formation activity for treated zebrafish with extract	[121]
Extract of *Antrodia cinnamomea* (ethanol extraction)		Antityrosinase/ Antimelanogenesis	Less toxic effect and similarly effective depigmentation of zebrafish with extract treatment at a lower dosage (50 ppm) compared to kojic acid (1400 ppm)	[122]

Note: ↑increase, ↓decrease, AD (atopic dermatitis), IL (interleukin), Interferon-gamma (IFN-γ), TARC (thymus and activation-regulated chemokine), TNF-α (tumor necrosis α).

cell proliferation, inhibiting the collagen decrease in the dermis, increasing tissue inhibitors of metalloproteinases, and increasing filaggrin against UV radiation [123]. Although several studies indicated that mushrooms have therapeutic potential on several skin diseases, more *in vivo* and clinical studies should be performed to understand the working mechanisms of the mushroom extracts in both animal and human body and their effects on the whole-body system.

7. Allergic Contact Dermatitis Caused by Mushrooms

Among allergic dermatitis as skin side effects caused by mushrooms, the most common and well-known is that caused by the shiitake. Dermatitis produced by the shiitake fungus is characterized by skin eruptions due to a toxic reaction to lentinan, a thermolabile polysaccharide. Nakamura first described shiitake dermatitis in 1977, when he reported 23 cases of people who consumed the fungus and presented erythematous lesions, reminiscent of self-flagellation from the Middle Ages [124]. In Japan, shiitake dermatitis is traditionally associated with the consumption of shiitake mushrooms. Although shiitake mushroom generates this dermatitis because lentinan is thermolabile, its toxicity can be avoided if the mushroom is consumed cooked [125]. Shiitake dermatitis is a rare skin reaction to lentinan, a polysaccharide component in the cell walls of shiitake mushrooms (*Lentinula edodes*). Lentinan is a β-(1 $\longrightarrow$ 3)-d-glucan. Lentinus edodes corresponds to a biologically active macromolecule with remarkable anticancer activity, which is given through the activation of the human immune system [126]. It has been shown that the chemical structure of lentinan is β-(1 $\longrightarrow$ 3)-d-glucan which has 2 (1 $\longrightarrow$ 6)-glucopyranoside branches for every five linear (1 $\longrightarrow$ 3)-β-glucopyranoside linkages, which can be characterized instrumentally by techniques such as high-performance liquid chromatography (HPLC), FITT, and nuclear magnetic resonance (NMR). Additional cases of hypersensitivity reactions to mushrooms have been documented. For instance, contact dermatitis has also been reported after handling or ingesting other mushroom species, such as the common button mushroom (*Agaricus bisporus*) and other edible varieties [13, 127]. These reactions are typically characterized by pruritic and eczematous eruptions, which are histologically similar to shiitake dermatitis, suggesting a common immunological pathway in the hypersensitivity response to different mushroom species [128]. Other instances include reports of airborne contact dermatitis from spores of various mushroom types, which can occur in both occupational settings, such as mushroom farming, and in environments with high spore concentrations [127]. These reactions can be more complex, involving respiratory symptoms alongside dermatological manifestations, illustrating the diverse immunological challenges posed by mushroom bioactives [127]. To address these adverse reactions comprehensively, it is crucial to investigate the full spectrum of immunogenic components in mushrooms, their potential cross-reactivity with other allergens, and the conditions under which they become pathogenic. Further research into the identification of specific allergenic proteins and polysaccharides, as well as their mechanisms of action, will be vital in developing preventive strategies and therapeutic interventions for mushroom-related hypersensitivity reactions [129].

8. Therapeutic Perspectives, Limitations, and Challenges

8.1. Insights into Mushroom-Derived Compounds for SDDs Management/Prevention. The nuanced roles of mushroom-derived compounds in skin health are increasingly evident, with several key mechanisms offering therapeutic avenues for SDD management and prevention:

Beta-glucans and immune modulation: beta-glucans, prevalent in varieties like shiitake and maitake, have been shown to enhance the skin's immune defense by activating dendritic cells and macrophages, leading to a more robust response to pathogenic challenges and potentially reducing the incidence and severity of inflammatory skin conditions [128]. Triterpenoids and inflammatory pathways: the triterpenoids present in Reishi mushrooms exhibit an ability to modulate inflammation through the suppression of NF-kB activation, which could play a role in mitigating chronic inflammatory states associated with conditions such as psoriasis and atopic dermatitis [130, 131]. Antioxidant phenolics and skin integrity: the antioxidant properties of phenolic compounds in mushrooms like Chaga may protect dermal fibroblasts from oxidative stress, thus preserving skin integrity and preventing the premature aging associated with oxidative damage [17]. Lectins and tumor inhibition: certain mushroom lectins demonstrate specificity in binding to aberrant cell membranes, initiating apoptosis, and potentially offering a targeted approach to managing melanoma and nonmelanoma skin cancers [6]. Ergothioneine and mitochondrial protection: ergothioneine has shown promise in protecting skin cells from mitochondrial DNA damage induced by UV radiation, suggesting a role for this compound in the prevention of photoaging and photocarcinogenesis [7]. These detailed mechanistic pathways highlight the potential of mushroom bioactives as adjunctive or alternative therapies in the management and prevention of various SDDs. Continued research in these areas may yield significant advancements in dermatological treatments.

8.2. Cytotoxicity and Allergenicity Effects of Mushroom Bioactives. The therapeutic benefits of mushrooms are balanced by a need to understand their potential cytotoxic and allergenic effects [48]. Research into various mushroom species has revealed a spectrum of bioactive compounds with diverse biological activities, some of which may exhibit cytotoxicity and allergenicity under certain conditions [48]. For example, compounds such as hydrazine derivatives found in certain edible mushrooms have shown cytotoxic properties, which could pose a risk if consumed in large quantities or if the mushrooms are not properly processed [132]. Similarly, the potential allergenicity of mushrooms is

an area of ongoing research, with instances of hypersensitivity reactions documented in susceptible individuals upon exposure to specific mushroom species [132]. The cytotoxic effects of mushrooms are often a result of their defense mechanisms, producing compounds that can be harmful to cells. While these properties can be leveraged in fighting cancer cells, as with the antitumor effects of polysaccharide-K (PSK) extracted from *Trametes versicolor* [14], they may also cause adverse effects in nontarget cells. It is, therefore, crucial to characterize these effects fully to mitigate risks associated with mushroom consumption or therapeutic use. Allergenicity, on the other hand, may manifest as hypersensitivity reactions, such as contact dermatitis or respiratory allergies, particularly in occupational settings or among mushroom cultivators [13, 127]. For instance, shiitake mushroom dermatitis is a well-documented condition caused by lentinan, a polysaccharide that can trigger an inflammatory response upon skin contact [128]. Recent investigations into these effects have emphasized the importance of identifying the molecular mechanisms underlying these responses. Techniques such as proteomics and immunoblotting have been employed to pinpoint the specific mushroom proteins that elicit immune reactions [133]. Furthermore, understanding the role of mushroom-derived compounds in modulating the immune system can provide insights into mitigating allergenic responses while preserving their health benefits [15]. Overall, while mushrooms are a rich source of bioactives with significant health benefits, it is imperative to balance their therapeutic potential with safety considerations. Ongoing research and rigorous clinical trials are necessary to elucidate the full scope of cytotoxic and allergenic effects posed by mushroom bioactives and to establish guidelines for safe consumption and therapeutic application.

8.3. Limitations, Challenges, and Clinical Pitfalls. The potential therapeutic properties of mushroom bioactives have stirred considerable interest in the dermatological community. However, like all emerging treatments, there are limitations, challenges, and potential pitfalls that need to be acknowledged. Much of the evidence supporting the efficacy of mushroom bioactives in skin therapy comes from *in vitro* studies or *in vivo* animal models, but the number of randomized controlled trials in humans is still limited, necessitating further research to confirm efficacy, safety, and optimal dosing. Variability in mushroom composition depend on factors such as growth conditions, harvesting time, and postharvest processing, the bioactive compound profile of a given mushroom species can vary significantly and this poses challenges in ensuring consistent therapeutic effects. Other species of mushrooms can cause allergic contact dermatitis or other hypersensitivity reactions; identifying and categorizing allergenic mushrooms are crucial, especially when recommending topicals containing mushroom extracts. Some mushroom bioactives might interact with other medications, either enhancing or inhibiting their effects; this can be particularly concerning for patients on multiple medications or those with underlying health conditions. The method used to extract bioactives from mushrooms can significantly influence their potency and therapeutic value; standardizing these methods is crucial for ensuring consistent results and safety profiles. While many mushroom bioactives have been deemed safe for short-term use, long-term safety data is often lacking; potential cumulative effects or long-term side effects must be assessed through extended clinical trials. The surge in interest surrounding "natural" treatments might lead some individuals to self-prescribe mushroom-based remedies without proper guidance, risking incorrect dosages, potential side effects, or suboptimal outcomes. Also, challenges persist in the utilization of mushroom extracts and their associated metabolites as ingredients in cosmeceutical and nutricosmetic products; these challenges range from optimizing extraction processes, validating efficacy and safety claims, using microcarriers and nanocarriers for controlled release, and weighing the advantages and disadvantages of using extracts versus individual compounds [103]. Despite these clinical challenges, the diverse biomolecules contained in mushrooms offer a sustainable option for developing cosmeceutical and nutricosmetic formulations, although more research is needed to address concerns regarding stability, compatibility, safety assessments, and toxicological studies [103]. Given the vast number of mushroom species and their bioactives, regulatory agencies might find it challenging to evaluate and categorize each one; this can lead to delays in approvals or inconsistencies in quality control. Researching, developing, and standardizing mushroom-based treatments can be expensive; these costs might be passed on to patients, limiting access to these treatments, especially in regions where insurance does not cover alternative therapies. Careful and rigorous scientific evaluation is vital to harness their potential while ensuring patient safety and optimal therapeutic outcomes.

9. Overall Conclusions and Future Prospects

Different biologically active compounds, including polysaccharides, proteins, peptides, vitamins, minerals, dietary fibers, alcohols, terpenoids, and phenolics, are present in mushrooms. These compounds exhibit antidiabetic, antiobesity, anticancerous, antitumor, anti-inflammatory, antimicrobial, antiviral, antiallergic, antiaging, antiwrinkle, antioxidant, immunomodulating, hepatoprotective, hypoglycemic, and skin whitening activities. Different skin problems-induced by inflammation and the high activity of free radicals can be treated with mushroom extracts with antioxidant and anti-inflammatory activities. In addition, extracts of bioactive compounds from mushrooms with anti-inflammatory, antioxidant, photoprotective, antityrosinase, antielastase, and anticollagenase activities can reduce the severe effects of inflammatory skin diseases, providing photoprotection and correcting skin hyperpigmentation. Therefore, mushrooms are considered essential and original ingredients for developing new pharmaceutical products due to their health benefits and protective activities against different SDDs. After exploring their therapeutic and/or healing potentials against different types of diseases across

different *in vitro*, *in vivo*, and clinical studies, it has been observed that mushrooms have attracted significant attention from researchers in recent years. Fungal compounds from large mushrooms Basidiomycetes species present several biological activities such as antioxidant, antiinflammatory, and antimicrobial, some associated with pharmaceutical, cosmeceutical, and nutricosmetic potential, in *in vitro* and *in vivo* studies. However, ethnobotanical/ethnopharmacological data shows a limited number of mushroom species related to the treatment of skin diseases. Mainly polysaccharides, followed by phenols, flavonoids, fatty acids, and tocopherols, from fungal species *Agaricus* spp., *Auricularia* spp., *Lentinus* spp., and *Pleorotus* spp. (among other mushroom species), showed antioxidant activity. The metabolisms of several mushroom species present antimicrobial activity against a wide variety of fungi, Gram-positive, and Gram-negative bacteria including *Staphylococcus aure*us, *Salmonella enteritidis,* and *Escherichia coli*. The results obtained from scientific studies revealed the potential antiageing effects of the enzyme-assisted extract mushroom *Agaricus bisporus* and their purified forms with reduction of the lipid peroxidation, increasing the antioxidant enzymes, improving the organ functions, and enabling the lipid metabolism. The antimicrobial activity of fungal extract depends upon genetic factors and environmental conditions that can influence the metabolic pathway that allows the production of these phytochemicals. Mushroom chitin and chitosan play a key role in the treatment of wounds by accelerating the proliferation of fibroblast, keratinocytes, and polysaccharides. Some fungi species can cause dermatitis or superficial mycosis. Many scientific studies have demonstrated the natural antioxidant potential of mushrooms. Their extracts rich in a wide variety of metabolites, could be incorporated, for example, as dietary supplements to complement the natural production of antioxidants at a cellular level. In summary, different mushroom compounds as polysaccharides, proteins, peptides, vitamins, minerals, dietary fibers, alcohols, terpenoids, and phenolics present *in vitro* and *in vivo* biological activities for potential use on several skin diseases. However, greater biomedical and clinical studies are necessary to prove these preliminary data.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest that could have appeared to influence the work reported in this paper.

Authors' Contributions

All authors contributed and made significant contributions to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas—that is, revising or critically reviewing the article; giving final approval of the version to be published; agreeing on the journal to which the article has been submitted; and confirming to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript.

Acknowledgments

The authors would like to express their gratitude to Dr. Irina Zamfir, MD, RCP London, Basildon University Hospital, UK, for providing professional English editing of this manuscript and for editorial support.

Supplementary Materials

Details of phytochemicals in mushrooms are provided in the supplementary file. (*Supplementary Materials*)

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