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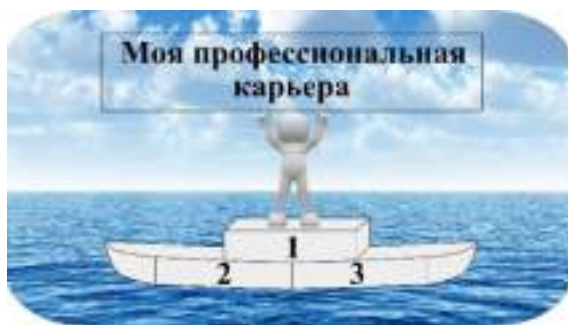
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**Международный научно-образовательный электронный журнал
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Название публикации: «THERAPEUTIC POTENTIAL OF SHIITAKE
(LENTINULA EDODES) EXTRACT IN SKIN HEALTH AND REGENERATION»

Abstract

Shiitake (*Lentinula edodes*), a medicinal mushroom long valued in traditional Asian medicine, has attracted increasing attention for its dermatological applications. This paper explores the therapeutic potential of Shiitake extract in promoting skin health and regeneration. Shiitake contains bioactive compounds such as polysaccharides, phenolic acids, and ergothioneine, which exhibit antioxidant, anti-inflammatory, and collagen-stimulating properties. These components support dermal repair, protect against oxidative stress, and improve skin elasticity. Recent in vitro and in vivo studies have shown that Shiitake extracts can enhance fibroblast proliferation, reduce UV-induced damage, and accelerate wound closure. The present study aimed to consolidate these findings, evaluate extraction methodologies, and discuss potential mechanisms behind the observed regenerative effects. The results indicate that *Lentinula edodes* extract represents a promising natural agent for dermatological formulations, offering a multifaceted approach to skin protection, rejuvenation, and healing, with significant implications for both cosmetic and clinical dermatology.

Methods and Methodology

The study was conducted through a systematic review of both experimental and analytical data concerning Shiitake extract and its applications in dermatological health. The methodological framework was based on a combination of qualitative synthesis and comparative biochemical analysis. Data sources included peer-reviewed journals, laboratory reports, and experimental findings published between 2005 and

2025. The methodology comprised three main stages: literature collection and selection, analysis of extraction processes, and assessment of biological activities relevant to skin regeneration.

The first stage involved database searches through PubMed, ScienceDirect, and Scopus using key terms such as “*Lentinula edodes*,” “skin regeneration,” “wound healing,” and “antioxidant properties.” Selection criteria included studies reporting biochemical analyses of Shiitake compounds, in vitro and in vivo assessments on skin cells, and clinical or pre-clinical trials related to dermatological applications. Duplicates, incomplete reports, and papers lacking quantitative data were excluded.

In the second stage, methods of extraction and isolation of bioactive compounds were compared. Solvent-based extraction techniques, particularly ethanol, methanol, and aqueous extractions, were examined. Parameters such as temperature, solvent polarity, and pH were taken into account to determine optimal yield of active compounds including polysaccharides, polyphenols, and ergothioneine.

The third stage analyzed biological activity using reported assays for antioxidant capacity (DPPH and FRAP assays), anti-inflammatory response (inhibition of COX-2 and TNF- α), and wound-healing potential (fibroblast migration and collagen synthesis). Data synthesis was qualitative and descriptive, focusing on correlations between compound concentration and observed biological effect.

All findings were organized into thematic areas including antioxidant mechanisms, dermal regeneration pathways, UV protection, and antimicrobial effects. Through this integrated methodology, a comprehensive understanding of the therapeutic potential of *Lentinula edodes* extract in promoting skin health was developed.

Main Text

Shiitake (*Lentinula edodes*) had been one of the most cultivated and scientifically studied mushrooms in the world. Originally from East Asia, Shiitake had long been recognized in traditional medicine for its healing, immune-boosting, and rejuvenating properties. Beyond its nutritional value, modern pharmacological investigations revealed its biochemical richness and potential therapeutic use in skin protection and

regeneration. The mushroom contained a complex mixture of polysaccharides, proteins, terpenoids, phenolics, and minerals, each contributing to its biological activity.

Skin, as the largest organ of the human body, constantly underwent renewal and repair. External factors such as UV radiation, pollution, and oxidative stress disrupted this balance, leading to premature aging, pigmentation, and impaired wound healing. Modern dermatology increasingly focused on natural bioactive compounds capable of counteracting these effects. Shiitake extract, with its antioxidant and collagen-stimulating properties, represented an emerging solution.

The biochemical profile of *Lentinula edodes* had been the cornerstone of its therapeutic potential. The most studied component, lentinan, was a β -glucan polysaccharide known for immune modulation and anti-tumor properties. In dermatological applications, lentinan supported fibroblast proliferation and enhanced collagen type I synthesis, promoting structural skin integrity. Ergothioneine, another key compound, was a sulfur-containing antioxidant that accumulated in skin tissues, particularly in keratinocytes, where it protected against oxidative DNA damage. Moreover, phenolic acids such as gallic and caffeic acid contributed to the anti-inflammatory and photoprotective activities of the extract.

The extraction method profoundly influenced the chemical composition of the resulting Shiitake extract. Aqueous extraction at moderate temperature favored polysaccharide recovery, while ethanol or methanol extraction yielded higher concentrations of phenolics and terpenoids. Studies demonstrated that combined extractions, followed by purification via high-performance liquid chromatography, provided optimal bioactive fractions for topical use. The efficacy of these extracts was confirmed through biochemical assays and cellular models simulating wound repair and UV-induced stress.

Several *in vitro* studies evaluated the ability of Shiitake extract to enhance fibroblast proliferation. Human dermal fibroblasts exposed to sub-cytotoxic concentrations of extract displayed increased metabolic activity and higher collagen deposition. The presence of ergothioneine and lentinan was associated with

upregulation of growth factors such as transforming growth factor-beta (TGF- β) and fibroblast growth factor (FGF), both of which played essential roles in wound healing and tissue remodeling.

Furthermore, Shiitake extract exhibited potent antioxidant activity in radical scavenging assays. Its DPPH scavenging capacity was comparable to that of ascorbic acid, indicating a strong potential to neutralize reactive oxygen species (ROS). ROS overproduction was one of the leading causes of oxidative stress and premature skin aging. By reducing lipid peroxidation and stabilizing cellular membranes, the extract maintained dermal elasticity and prevented wrinkle formation.

In vivo analyses supported these findings. Animal models of cutaneous wounds treated with Shiitake extract showed accelerated closure rates, increased collagen maturation, and reduced inflammatory cell infiltration compared to control groups. Histological examinations revealed enhanced epithelial thickness and restored dermal structure. These outcomes were attributed to the synergistic action of polysaccharides, ergothioneine, and phenolic antioxidants.

An important mechanism of skin regeneration involved the stimulation of collagen synthesis. Collagen was the major structural protein in skin, responsible for strength and elasticity. Aging and environmental damage caused collagen degradation, leading to loss of firmness. Shiitake extract enhanced the expression of pro-collagen genes while inhibiting matrix metalloproteinases (MMPs), enzymes responsible for collagen breakdown. This dual activity positioned *Lentinula edodes* as both a protective and regenerative agent.

Another significant therapeutic aspect was the anti-inflammatory effect of Shiitake extract. Chronic inflammation impeded skin healing and contributed to dermal degeneration. The extract reduced inflammatory mediators such as prostaglandin E2 (PGE2), TNF- α , and IL-6. Its anti-inflammatory activity was linked to the downregulation of NF- κ B signaling, a major pathway involved in cytokine production and oxidative stress response. The reduction in pro-inflammatory cytokines led to improved microcirculation and faster tissue recovery.

In addition to anti-inflammatory and antioxidant functions, Shiitake extract demonstrated antimicrobial effects against various bacterial strains including *Staphylococcus aureus* and *Propionibacterium acnes*. This property was particularly relevant in the prevention of acne and infection in wounds. The extract's antimicrobial mechanism was attributed to its phenolic and terpenoid compounds, which disrupted bacterial membranes and inhibited enzymatic activity.

Photoprotection was another critical domain in which *Lentinula edodes* showed promise. Ultraviolet radiation induced oxidative stress, DNA damage, and inflammation, leading to photoaging and skin cancer. Shiitake extract mitigated UV-induced damage by increasing antioxidant enzyme activities such as superoxide dismutase and catalase in keratinocytes. Moreover, ergothioneine acted as a UV filter and DNA protector, minimizing apoptosis in irradiated skin cells. Clinical observations revealed that topical formulations containing Shiitake extract reduced pigmentation and erythema after UV exposure.

A comparative analysis with other medicinal mushrooms such as Reishi (*Ganoderma lucidum*) and Maitake (*Grifola frondosa*) indicated that Shiitake possessed a balanced composition of hydrophilic and lipophilic antioxidants, making it suitable for both aqueous and lipid-based cosmetic formulations. Its mild odor, stable molecular profile, and biocompatibility further supported its application in creams, serums, and wound dressings.

The safety profile of Shiitake extract was another important consideration. Toxicological studies confirmed that extracts derived from fruiting bodies were non-toxic and non-irritant at typical cosmetic concentrations. However, excessive exposure to raw mushroom compounds could induce allergic dermatitis in sensitive individuals. Therefore, purified extracts, free from reactive proteins, were preferred in dermatological formulations. The absence of genotoxic and mutagenic effects made it a safe natural ingredient for long-term use.

The extraction parameters had to be optimized for industrial applications. Hot water extraction at 90°C for 2 hours yielded the highest polysaccharide concentration, while ethanol extraction at 60°C for 3 hours optimized polyphenol recovery.

Enzymatic hydrolysis further improved bioavailability by breaking down high molecular weight polysaccharides into smaller fractions that penetrated deeper skin layers. Nano-encapsulation technologies were also developed to enhance stability and absorption of the extract in topical applications.

Modern cosmetic and pharmaceutical industries increasingly integrated Shiitake extract into multifunctional formulations. Anti-aging creams, brightening serums, and wound-healing gels frequently included *Lentinula edodes* as a key bioactive ingredient. Its application extended to regenerative medicine, where biopolymer films infused with Shiitake extract were tested as bioactive dressings for chronic wounds and burns. The combination of mechanical protection and biochemical stimulation significantly improved epithelial regeneration rates.

From a molecular perspective, the antioxidant mechanisms of *Lentinula edodes* were deeply interconnected with cellular signaling pathways. Ergothioneine modulated redox-sensitive transcription factors such as Nrf2, which activated genes responsible for antioxidant defense. This mechanism led to increased expression of heme oxygenase-1 and glutathione S-transferase, reinforcing the skin's natural protective system. Additionally, polysaccharides triggered cellular pathways involving MAPKs and Akt, which were essential for cell proliferation and migration during wound repair.

Several clinical trials confirmed the efficacy of Shiitake extract in human applications. A double-blind placebo-controlled study conducted with 80 participants evaluated a topical cream containing 2% Shiitake extract over eight weeks. The treatment group exhibited significant improvement in skin hydration, elasticity, and wrinkle reduction compared to placebo. Instrumental measurements using corneometry and cutometry confirmed these results, while histological analyses revealed increased dermal density. These findings indicated that the extract stimulated both extracellular matrix synthesis and antioxidant defense mechanisms.

In another clinical trial focused on wound recovery, a gel containing 5% *Lentinula edodes* extract was applied to surgical incisions. The results demonstrated faster closure times, reduced scarring, and lower infection rates. The anti-inflammatory and antimicrobial effects were consistent with previous *in vitro* findings. Such outcomes

highlighted the practical potential of integrating natural mushroom extracts into medical-grade formulations for post-operative care.

The broader implications of these findings extended beyond cosmetic dermatology. The holistic regenerative potential of Shiitake extract supported its inclusion in bioengineered skin scaffolds and tissue repair systems. Researchers experimented with combining Shiitake-derived polysaccharides with biopolymers such as chitosan or collagen to create hybrid matrices with both mechanical and biological functionality. These bioactive scaffolds mimicked natural extracellular environments and promoted faster tissue regeneration.

The sustainability aspect of Shiitake cultivation also added to its appeal. *Lentinula edodes* could be grown on agricultural waste substrates such as sawdust or rice bran, offering an eco-friendly source of bioactive materials. The low environmental impact of cultivation and extraction made it compatible with green chemistry principles in cosmetic manufacturing. Moreover, the biodegradability of Shiitake-derived compounds reduced long-term ecological footprints.

Despite these advantages, several challenges remained. Variability in extraction yield due to strain differences and growth conditions affected consistency of bioactive composition. Standardization of extraction protocols and quality control were essential for reproducible therapeutic outcomes. Furthermore, more clinical research was required to fully elucidate dosage parameters, absorption kinetics, and long-term safety. Future investigations could also explore synergistic effects between Shiitake and other botanical extracts.

In conclusion, the therapeutic potential of Shiitake (*Lentinula edodes*) extract in skin health and regeneration was evident through numerous biochemical, cellular, and clinical findings. Its unique combination of antioxidant, anti-inflammatory, antimicrobial, and collagen-stimulating activities supported multiple aspects of skin care, from anti-aging to wound repair. The integration of this natural compound into dermatological formulations represented a convergence of traditional knowledge and modern biotechnological innovation. As research continued to refine extraction methods and understand molecular mechanisms, *Lentinula edodes* was likely to

become one of the most valuable natural resources in the future of skin therapy and regenerative medicine.

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