# Mushroom based Cosmeceuticals: An Upcoming Biotechnology Sector

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http://dx.doi.org/10.13005/bbra/3097

(Received: 24 March 2023; accepted: 03 May 2023)

Mushrooms have been an established source of nutrition for hundreds of years. They are recently being exploited for their potential applications in other sectors as well. One of their emerging applications has been in the cosmetic industry where their bioactive properties are being used either as cosmeceutical for topical administration or as nutricosmetics for oral administration. Certain genera of mushrooms which are being used in cosmetic industries are Lentinula, Ganoderma, Pleurotus, Cordyceps, Inonotus, Tremella, Grifola, Schizophyllum, Pleurotus, Coriolus, Ganoderma, Euphorbia, Pistacia, Trametes, Agaricus, Phellinus, Antrodia. The mushroom extracts and their bioactive metabolites show excellent anti-oxidant, antiwrinkle, anti-aging, moisturizing and skin whitening effects making them ideal and multifunctional cosmetic components. The mounting benefits of various mushroom extracts in skin and hair care products have also fast-tracked the commercial production of mushrooms which is worth mass attention. The present review discusses about the role, diversity, properties and commercial status of mushrooms that are being exploited by the cosmetic industry.

Keywords: Bioactive metabolites; Cosmetics; Cosmeceuticals; Mushroom.

Cosmetics are personal care products that are applied topically or ingested orally to replenish, protect and enhance the physical features of an individual. They contain a combination of chemical compounds which are either synthetic or natural that have a positive effect on the skin or other areas they are applied to. The cosmetic industry has seen a lot of growth in recent years <sup>1</sup>. With increasing awareness about the side-effects of chemical products and the benefits of natural ones, there has been a gradual shift in the demands by the young generation consumers for more 'green' products<sup>1,2</sup>. The change in buying pattern of the consumers drew attention of the cosmetic brands towards various botanical extracts <sup>2</sup>. Mushrooms were also looked at with renewed interest. They possess abundant amounts of proteins, lipids, essential amino acids, glycogens, riboflavin, nicotinic acid, and valuable minerals. The mycelia and fruiting bodies of some wild mushrooms contain several biologically active compounds such as polysaccharides, phenolics, terpenoids, lectins, ergosterols, and volatile organic chemicals that perform several biological functions such as

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anti-oxidant, anti-microbial, anti-inflammatory, anti-tyrosinase, and anti-hyaluronidase activities <sup>3,4</sup>. Owing to this, they have become an important component of various cosmetic formulations for skin and hair <sup>5</sup>. The present study elaborates on the scope of mushrooms in the cosmetic industry with focus on their diversity, bioactive properties and commercial status.

#### **Cosmetics, Cosmeceuticals and Nutricosmetics**

The word 'cosmetic' is often considered to be makeup and perfumes which are meant to be women-oriented but in the current time, many other products are included in it and the target of these companies include not only women but also men and babies <sup>6,7</sup>.

Restorative products are designed to fulfil several demands including utility and preferences of the consumers. For illustration, numerous cosmetic products are manufactured to supply cleaning and protection against some harmful environmental factors such as UV radiations in daylight <sup>8</sup>.

One of the most fascinating aspect of cosmetics is their interaction with the skin. The top layer of skin is the stratum corneum which secures the body from chemical and natural harm. Some of the cosmetic formulations include microemulsions, liposomes, multiple emulsions, with the common aim of interaction with stratum corneum and maintaining its liquid crystalline structure <sup>9</sup>. To enhance these properties further, cosmetics arena has broadened to include cosmeceuticals and nutricosmetics.

Cosmeceutical is an amalgamation of cosmetics and pharmaceuticals, that improve appearance through its cosmetic property and biologically activates the skin through its pharmaceutical property <sup>10</sup>. They are applied topically and provide the skin with additional nutrients needed to revitalize it. These include lotions, creams, serum, face masks, etc. Because of their less side effects and added benefit of multifunctionality, cosmeceuticals are increasingly being used in cosmetic products <sup>11</sup>.

Nutricosmetics are similar to cosmeceuticals except that they are ingested orally like a supplement in the form of pills or tablets <sup>12,13</sup>. Nutricosmetics are typically made up of the ingredients such as mushroom extracts , PUFA, amino acids, carotenoids, polyphenols, vitamins, and other mushroom-derived elements. Skin beneficial effects of fruiting body extracts of *Grifola frondose* and oral supplements of *Sparassis crispa* with healing effects on Diabetic wounds, type I collagen synthesis, and epithelialization are examples of nutricosmetics <sup>14,15,16</sup>.

## **Bioactive properties of mushrooms**

Mushrooms are a reservoir of biological compounds that provide various therapeutic effects. These biological compounds are important nutritional constituents that have various health benefits. They perform biological functions some of which have been depicted in Fig. 1 <sup>51</sup>.

#### Anti-oxidative activity

Oxygen is vital for sustenance of living beings, especially human life. Ironically, it has been linked with cell death and tissue damage leading to a fast-paced aging process and various ailments such as diabetes, cardiovascular diseases, neurodegenerative diseases, and cancer <sup>17</sup>. The process of oxidation releases free radicals like oxygen or various reactive oxygen species (ROS) in small concentrations that are unstable and tend to pair with surrounding chemical compounds for stability. In such cases, the body has an internal anti-oxidant defense system that includes glutathione peroxidase, catalase, and superoxide dismutase to combat these harmful compounds and neutralize their harmful effects. However, if they are produced in high concentration, the endogenous antioxidant defense system can sometimes be overwhelmed by stress that leads to an imbalance in oxidative homeostasis.

The free radicals are very reactive and can attack surrounding chemical compounds to pair up their electrons. This can have destructive consequences such as cell senescence or apoptosis. Therefore, there is a need for an external antioxidant defense system. Mushrooms being a preferable natural source of anti-oxidants play an important role in this respect. Intensive study of the scavenging property of ROS of mushrooms has been carried out <sup>18,19</sup> and potential anti-oxidative properties of *Pleurotus citrinopileatus* <sup>3</sup>, *Coriolus versicolor*, and *Ganoderma applanatum* <sup>20</sup> have been documented. These mushrooms contain bioactive compounds such as polyphenols, polysaccharides, vitamins, carotenoids, and minerals that have excellent anti-oxidative properties. Owing to these properties, their extracts have become an essential part of the cosmeceutical formulations like antiaging and anti-wrinkle creams <sup>21</sup>. Generally, prolonged exposure to ultraviolet radiations in sunlight produces ROS leading to skin sunburn, wrinkle and aging. Cosmetic products loaded with such natural anti-oxidants scavenge ROS and provide photo-protective effects.

# Anti-tyrosinase activity

An important pigment responsible for providing skin color is melanin. It protects skin from UV-induced dermal irritation by absorbing UV light and scavenging ROS. It is produced in melanocytes within specialized organelles called melanosomes located in the epidermis of the skin through a process known as melanogenesis <sup>18</sup>. Its biosynthesis pathway is regulated by the rate-limiting enzyme tyrosinase 22 . Tyrosinase is a multifunctional, glycosylated, coppercontaining enzyme that catalyzes two important steps in the mammalian melanin biosynthetic pathway. The first step is conversion of tyrosine to dihydroxyphenylalanine (DOPA) and the second step is conversion of DOPA to DOPA quinone. This can be converted either to a brown black colored pigment ie.. eumelanin or a yellow red colored pigment ie. pheomelanin depending on the physiological conditions 52.

Overproduction or abnormal distribution of melanin can be caused due to auto-immune conditions, exposure to UV radiation, hormonal therapy, genetic factors and drug reaction. This can lead to several skin disorders such as skin hyperpigmentation, freckles, age spots, melasma, lentigines, etc<sup>24</sup>.

The inhibition of tyrosinase activity is a key factor to skin whitening agents in the cosmetics industry. Bioactive compounds such as flavonoids, terpenoids, polysaccharides, and coumarin derivatives, are being used by the cosmetic industry because of their ability to regulate melanin synthesis by either blocking the expression of tyrosinase in one or more steps or by regulating the distribution of melanosomes whilst also providing additional benefits such as skin hydration, anti-oxidant, anti-inflammatory and, anti-aging effect thereby preserving the skin health. <sup>18,22</sup>. Mushrooms such as *Ganoderma lucidum*<sup>4</sup>, *Euphorbia characias*<sup>23</sup>, and *Pistacia atlantica*  subsp. *mutica* <sup>24</sup>show strong anti-tyrosinase activity and are being researched extensively for applications in skin whitening products.

# Anti-hyaluronidase activity

Human skin aging is a complex biological process regulated by two key factors- one of which is intrinsic aging or innate aging controlled by hormonal changes of the aging body and is ultimately inevitable and the other is extrinsic aging otherwise also known as photoaging which depends on outside factors such as the UV irradiation. Skin aging has been associated with degradation of the extracellular matrix (ECM)- reduced collagen synthesis, increasing collagen degradation and loss of skin moisture, or decreasing hyaluronic acid levels <sup>14</sup>.

Hyaluronan or Hyaluronic acid (HA) is an important compound playing a vital role in skin moisturizing. It is also the predominant component of the ECM (Extracellular Matrix). It is present throughout the body including the umbilical cord, vitreous of the eye, synovial fluid, heart valves, the lung, the aorta, skeletal tissues, and more than 50% of it is found in the skin. It is a glycosaminoglycan (GAG) that has the unique capacity to bind and retain water molecules thereby increasing viscosity, reducing extracellular fluid permeability, and revitalizing the skin. It helps the skin to hold moisture and in doing so makes it look turgid, young, pliable, and hydrated. However, HA metabolism is complicated with multiple sites controlling its synthesis, deposition, association with cellular proteins and degradation. Also, with aging, HA concentration diminishes in the body, resulting in skin aging and the inability of the skin to heal itself. On top of that, hyaluronidase, an endoglycosidase degrades HA by randomly cleaving its internal â-N-acetyl-hexosamine glucosidic linkages in the molecule <sup>53</sup>

Anti-aging skin cosmetics have been providing HA fortopical applications but due to the inflammatory reactions caused by them, cosmetic industry is switching to the application of bioactive compounds that exhibit excellent antihyaluronidase activity<sup>25</sup>. In this regard, mushroom extracts are being looked upon. Mushrooms such as *Pleurotus citrinopileatus* <sup>3</sup> and *Trametes lactinea* <sup>26</sup> possess anti-hyaluronidase activity in their extracts and are thus being used in cosmetic formulations.

#### Anti- inflammatory activity

Inflammatory diseases can occur due to increased production of inflammatory mediators such as interleukins, tumor necrosis factor, intercellular adhesion molecule-1, inducible cyclooxygenase-2-type, nuclear factor-PB, prostaglandin E2<sup>27</sup>

Several studies have demonstrated that mushrooms have anti-inflammatory potential as they can aid in reducing the production of inflammatory mediator <sup>28</sup>. The anti-inflammatory activity of mushrooms and their extracts has been reviewed by Taofiq et al<sup>29</sup>. Agaricus bisporus, Phellinus linteus, Cordyceps species, Antrodia camphorate and Pleurotus species were the most studied species. Strong anti-inflammatory activity of polysaccharides, terpenes, and phenolic derivatives have been reported. Reduced levels of inflammatory mediators such as nitric oxide (NO) and other inflammatory mediators such as interleukins (IL 1, IL-6, IL-8), tumor necrosis factor (TNF), and Prostaglandin E2 (PGE2) from inflammatory cells have been ascribed to the mechanism of anti-inflammation.

Further, these metabolites from mushrooms can also find applications in cosmeceutical formulations as they are natural and safe substances with no undesirable side effects or adverse consequences <sup>28</sup>Linoleic acid, found in Bobbi Brown Brightening Intensive Cream and True Cosmetics Youth Revealing Complex, for example, is an anti-inflammatory compound that promotes healthy skin growth <sup>14</sup>Linoleic acid has been obtained from *Agaricus subrufescens*,<sup>30</sup>and it is also found in *Astraeus* spp. <sup>31</sup>, *Cordyceps* <sup>32</sup>, and *Pleurotus sajor-caj* <sup>33,14</sup>.

## Anti-microbial activity

Fungi, *Staphylococcus aureus*, *Streptococcus* species, and other non-pathogenic organisms colonise the skin on a regular basis. The age of an individual, as well as environmental factors like sebum production, temperature, and humidity, influence the distribution and density of the skin's microflora <sup>34</sup>. Given their opportunistic nature and strong resistance profiles, these bacteria pose a concern when skin lesions arise, producing serious localised infections even with systemic invasion <sup>35</sup>Skin diseases such as cellulitis, atopic

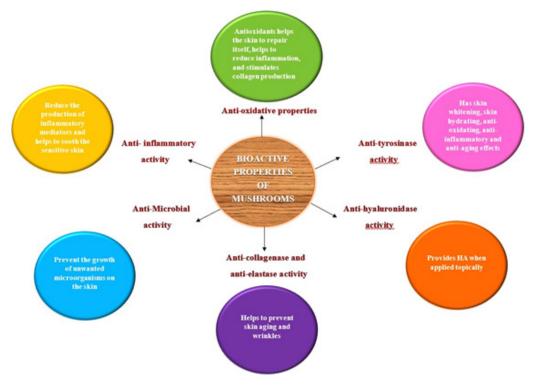


Fig. 1. Bioactive properties of mushrooms being utilized in the cosmetic products

dermatiti, erysipelas, folliculitis, impetigo, furuncle and psoriasis have been linked to the presence of these bacteria <sup>36</sup> The cosmetic industry is constantly looking for intriguing natural compounds to substitute synthetic antimicrobials, especially since these bacteria have developed resistance to traditional topical antimicrobials <sup>37</sup>Numerous research investigations have found that mushrooms

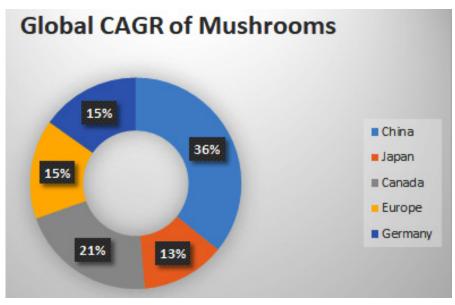


Fig. 2. Global compound annual growth rate (CAGR) of mushrooms

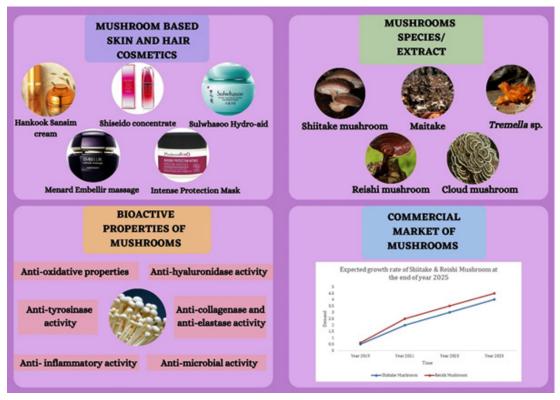
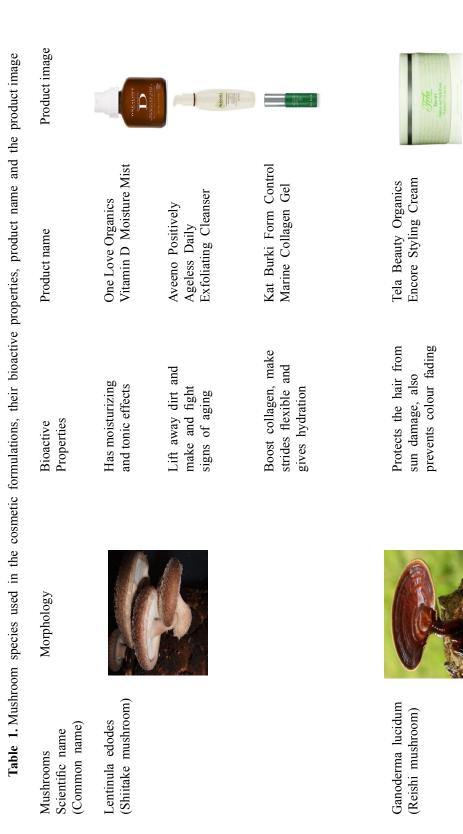


Fig. 3. Role of mushrooms in cosmetic industry



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Menard Embellir Refresh massage	The Face Shop Real Nature Lingzhi Face Mask	Shiseido Ultimune Power Infusing Concentrate	Dr. Andrew Weil for Origins Mega-Mushroom Skin Relief Face Mask	Hankook Sansim Firming cream	Kose Sekkisei Cream
Prevents anti-aging	Slows down the pre-mature aging and has anti-inflammatory properties	Reduces signs of aging and has skin moisturizing properties	Has anti-inflammatory and skin reliefing properties	Has skin tightening and Anti- hyperlipidemia activity	Has moisturizing effect, suppress melanin production

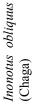
Ganoderma lingzhi (Lingzhi mushroom)

Ganoderma lucidum and *Lentinula edodes* (Reishi and Shiitake ) mushroom

and Pleurotus ostreatus Cordyceps sinensis (Caterpillar mushroom) Ganoderma lucidum (Reishi and Oyster mushroom)



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(Snow fungus) rmis



(Almond mushroom) subrufescens Agaricus

Phellinus linteus (Sang Hwang mushroom)













effect, revitalizes and Has moisturizing hydrates the skin skin

Moisturizing gel

Antioxidant, keeps the skin hydrated

Has anti-inflammatory Has skin revitalizing and anti-oxidant properties

properties. Also beneficial for eczema

Grow Hyal B5 Toner

Root Science RS Reborn Organic Face Mask

properties, also helps to soothes the irritated Has anti-inflammatory

La Prairie Advanced Marine Biology Night Solution

Circulation Hydrating BeautyDiy Aqua Gel

Surkran Grape Seed Lift Eye Mask

Moisturizing Mask Vitamega Facial



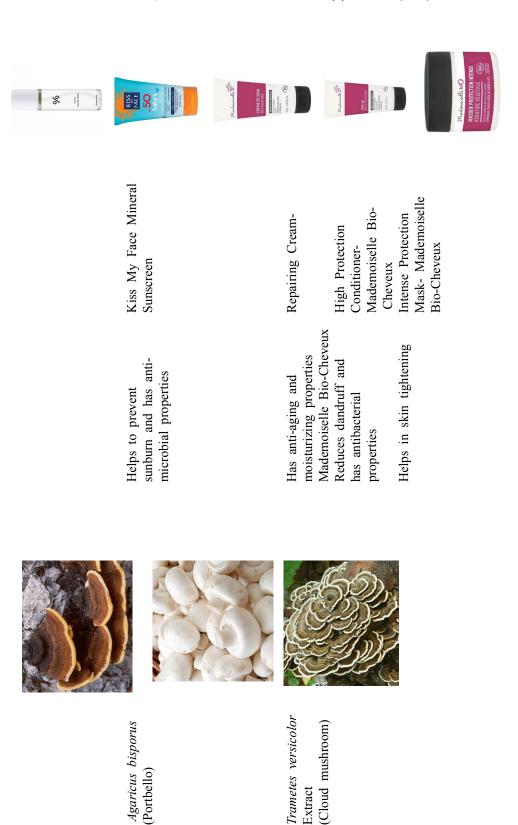








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contain anti-microbial properties. It was discovered by Alves et al. (2012) <sup>38</sup> that both edible and non-edible mushrooms have anti-pathogenic microorganism activity. Lentinula edodes was documented to be the most potential against majority of bacteria, followed by other mushrooms like Boletus, Ganoderma, and Lepista. Phenolic compounds that are present in mushrooms exhibit anti-bacterial activity by interfering with the cell envelope of the pathogens, resulting in their lysis<sup>37</sup>. Phenolic acids such as vanillic, protocatechuic, 2,4-dihydroxybenzoic, and p-coumaric acids had greater anti-bacterial activity against various bacterial pathogens, while caffeic, ferulic, ellagic, syringic and chlorogenic acids also demonstrated promising findings 39

## Anti-elastase and anti-collagenase activity

Epidermis of skin is securely connected and sustained by connective tissue to the underlying dermis. Two important structural protein ie. collagen and elastin, which are required for a variety of protective functions in the skin are produced by dermal fibroblasts in the extracellular matrix <sup>40</sup>. Elastin gives elasticity to the connective tissues. It has been observed that with age there is an increase in elastase activity. Elastase is an elastin-degrading metalloproteinase that reduces elastic fibers leading to decrease in skin resilience and eventually wrinkle formation. Thus, interest in screening for cosmetic compounds from natural sources like plants, algae and mushrooms has increased immensely <sup>41</sup>Another vital component of the extracellular matrix of skin is collagen. It is responsible for maintaining the skin's flexibility, strength and elasticity. UV irradiation induced collagen breakdown is one of the cause for the aging process 42

Overexposure to UV rays causes a high production of ROS, which causes skin aging. These ROS activate protein kinases, which in turn activate another activator protein factor 1 ie. AP-1 and cause unregulated production of MMPs (Matrix metalloproteinases), which cause collagen breakdown and skin wrinkling. As a result, research is now focused on searching for inhibitors of AP-1 that can be used as a cosmeceutical ingredient to inhibit MMP expression<sup>43</sup>Bae et al. (2005) <sup>44,45</sup> identified an exopolysaccharide from *Grifola frondosa*'s submerged mycelial culture. The capacity of exopolysaccharide (EXP) to suppress the production of MMP-1 protein in dermal fibroblasts following exposure to UVA was studied. At 250 g/mL concentration of exopolysaccharide, there was a substantial reduction in MMP-1 mRNA expression of up to 61.1%. From this, it can be inferred that the exopolysaccharide is playing an essential role in the photo-aging potential of mushroom's extract. A sulfur-containing derivative of histidine is l-Ergothioneine (EGT). EGT's potential to suppress MMP-1 protein production in dermal fibroblasts was examined by Obayashi et al. (2005) 46. After exposing dermal fibroblasts to UVA, 2 mg/mL of EGT reduced production of MMP-1 protein by 52%, demonstrating strong scavenging capacity against ROS and suppression of TNF  $- \dot{a}$ . These results suggest that EGT can be an essential ingredient for developing anti-aging cosmetic formulations.

#### **Commercial status**

Mushroom and their products have a substantial demand in the global market. Mushroom based skin and hair care products, though in their infancy, have already marked their place in the market with a number of commercial products being launched by global cosmetic brands such as Bio Botanica Inc. (U.S.), Bristol Botanicals Limited (U.K.), Qirines Brand (Korea), Menard Brand (Japan) etc. Table 1 lists various commercial mushroom based cosmetic products <sup>1,45,54</sup>.

The increasing demand of mushrooms is also reflected from their significantly high compound annual growth rate (CAGR) in global market. Even amid the COVID-19 crisis, the global market for mushrooms estimated at US\$45.3 Billion in 2020, is projected to reach a revised size of US\$72.5 Billion by 2027, growing at a compound annual growth rate (CAGR) of 7% over the analysis period 2020-2027<sup>47</sup>. According to the projected CAGR of different countries, China shows the maximum CAGR of 36% followed by 21% for Canada and 15% for Europe and Germany for mushrooms (Fig. 2).

As far as the types of mushrooms are concerned, the demand in the global market is divided. Button mushrooms have the largest segment with a volume share of 61.8% and are widely cultivated across the globe. Oyster Mushrooms with the highest CAGR of 11.2% are mostly popular in Chinese, Japanese and Korean cooking as they have delicate texture and mild savory flavour. Shiitake Mushrooms are mostly consumed in Japan, China and South Korea due to their high health & skincare benefits <sup>48</sup>. Reishi Mushroom market is dominated by the Asia Pacific region.

Overall, after button and oyster (black/ yellow/pink and others) mushroom, shiitake mushroom is the third most demanding category of mushroom with the global market size of USD 362.7 million in 2020 which is projected to reach USD 447.7 million by 2026, with healthy growth rate of more than 3.6% due to its high demand in cosmetics and pharmaceutical sector. Shiitake mushroom is widely used in hair cosmetics as it helps to maintain the hygiene of the scalp and manipulate the structural properties of hair 49. In addition, the extract market Size of Reishi mushroom is also forecast to reach \$ 560.78 million by 2025 growing at a CAGR of 4.68% during the forecast period 2020-2025. The extract of organic Reishi mushroom held the largest share in the mushroom extract market in 2019 50. Therefore, we can say that Reishi and Shiitake are ruling the cosmetic market of mushrooms as both of them contain a lot of health & skincare benefits.

#### CONCLUSIONS

Mushrooms and their extracts have bioactive properties such as anti-oxidant, anti-tyrosinase, and anti-hyaluronidase that neutralize free oxygen radicals, control skin hyperpigmentation, and prevent the breakdown of hyaluronic acid, respectively. They also have antiinflammatory potential, anti-pathogenic activity, anti-collagenase, and anti-elastase properties. These properties have led to a surge in demand for mushroom-based skin and hair products due to consumer awareness and preference for organic and natural extract-based products (Fig. 3).

However, several difficulties have impeded the growth of the mushroom business, like inadequacy of scientific research, inadequate technology, insufficient investment, unstable farmgate prices, poor supply, poor quality, disease, pest attacks, lack of trained labour, inappropriate timing, and inadequate storage facilities. Appropriate efforts are needed to overcome these obstacles faced during mushroom cultivation and marketing.

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