Agaricus brasiliensis (Sun mushroom) and its therapeutic potential: A review

Aline Mayrink de Miranda*

Department of Pharmaceutical Sciences, Pharmacognosy Laboratory, University of São Paulo, Ribeirão Preto, Brazil

Abstract

In recent decades, the chemical, nutritional, and functional properties of edible mushrooms have attracted considerable attention, resulting in numerous reports on their health-associated benefits. One among such edible mushrooms, Agaricus brasiliensis, is native to Brazil and is an important food supplement. This review discusses the therapeutic potential of Agaricus brasiliensis and summarizes the current studies on this edible mushroom.

Agaricus brasiliensis

To date, more than 10,000 species of mushrooms have been reported, from which only 2,000, belonging to 30 genera, are edible. There are four classes of fungi namely Ascomycota, Basidiomycota, Zygomycota and Chytridiomycota [1]. Edible mushrooms belong to the classes of Basiodiomycetes and Ascomycetes. These edible fungi represent 50% of macrofungi and the poisonous 10% [2]. Mushrooms have numerous therapeutic properties including antiviral, antibacterial, hypoglycemic, antihypertensive, anti-tumor and immunomodulatory [3-5]. The anti-inflammatory and antioxidant effects of several species of mushrooms, such as Agaricus bisporus, Boletus edulis, Agaricus blazei, Agrocybe cylindracea, and Ganoderma lucidum have been previously studied. Different antioxidants have been reported in these species including polysaccharides, ergosterol, nicotinic acid, triterpenes, and phenolic compounds [6-8]. Certain polysaccharides extracted from mushrooms can act as scavengers of superoxide and hydroxyl radicals [9].

Agaricus brasiliensis (Wasser, 2002) is also known as Agaricus blazei Murrill [10] or A. subrufescens Peck [11]. It is indigenous to Brazil where it is referred to as sun mushroom, godliness mushroom, or champignon of Brazil. The sun mushroom is a filamentous fungus classified under the Agaricaceae family, Basidiomycota division, Fungi kingdom. The cultivation of this mushroom considerably increased during the 1960s in Piedade, southwest São Paulo. Due to favorable climatic conditions, Brazil has excelled in A. brasiliensis cultivation in the states of São Paulo, Paraná, and Minas Gerais [12,13].

The origin and scientific name of A. brasiliensis remains controversial [11,14], and disagreements over nomenclature remain unresolved [15-17]. Thus, herein, we opted for the name Agaricus brasiliensis [14], which is presently used by most researchers. Nevertheless, the name Agaricus blazei will be maintained when referring to studies containing this taxonomic designation.

Unlike other species, A. brasiliensis grows outdoors in temperate regions with ambient temperatures ranging from 23 – 28°C. Its height varies ranging from 10 to 15 cm (Figure 1). It develops in open, sunny fields and its fruiting bodies require light to mature.
Hence it is often referred to as the sun mushroom [18]. Medicinal mushrooms are an inexhaustible source of compounds with promising pharmacological activities [19,20]. The therapeutic potential of Agaricus brasiliensis has been reported by several studies which are reviewed here.

**Pharmacological activities and therapeutic potential**

In certain Asian countries, this mushroom has been widely used as a functional food or as medicine. In 2005, a study by Zhong, Tai, and Yamamoto [21] showed that its antitumor mechanism is mediated by innate and/or adaptive immunity. However, the cellular responses to this stimulus remain unclear. Rubel, et al. [22] evaluated the immunomodulatory and antitumor effects on mice fed a diet supplemented with mycelia obtained from solid-state fermentation. The Sarcoma 180 tumor growth was inhibited by consuming A. brasiliensis supplemented diet. The authors observed that the pattern of immune response had shifted thereby increasing CD4+ and CD8+ and decreasing CD19+ cell populations. Their results suggested that polysaccharides, such as β-glucans and other mushroom metabolites, possibly promote T-cell dominance that is imperative to restrain tumor growth. Restoring a suitable balance between cellular and humoral immunity is an essential process for restraining tumor growth [18,22].

β-glucans, polysaccharides produced by various organisms, consist of a backbone formed by linear β (1→3)-, β (1→4)-, or β (1→6)-linked glucose molecules, which may also contain branches. The type of linkages differs among different β-glucans. β-glucans from yeast and fungi consist of β (1→3)-linked glucopyranosyl units with β (1→6)-linked side chains, whereas those from oat and barley are composed of unbranched β (1→3) and β (1→4) linkages. The activity of β-glucans may be influenced by their structural properties, such as polymer length, degree of branching, tertiary structure, and molecular weight. Besides the structure, the method of isolation can also affect both yield and the activity of β-glucans [23,34].

In 2005, Bernardshaw, Johnson, and Hetland [25] reported that oral administration of ABM extracts (Agaricus blazei Murrill) provided protection against systemic Streptococcus pneumoniae infection. Thus, ABM extracts could also be prophylactic and therapeutic against certain bacterial infections in humans. Original aqueous extracts of Agaricus brasiliensis did not stimulate natural killer (NK) cells. Lin, et al. [26] investigated the immunomodulatory potential of aqueous extracts of Agaricus blazei in mice with WEHI-3 leukemia.

Administration of this extract promoted NK cells and increased cancer cell phagocytosis by macrophages and monocytes.

Recently, it has been suggested that mushroom extracts could have prophylactic/therapeutic effects against pneumonic superinfection and severe lung inflammation that complicates SARS-CoV-2 infection. Several compounds have been identified in Basidiomycetes mushrooms have various therapeutic effects, including highly diversified anti-inflammatory compounds, such as polysaccharides, terpenoids, phenolic compounds, glycerides and other low molecular weight molecules [7,27]. Therapeutic benefits from administering mushroom to patients infected with SARS-CoV-2 is associated with mitigating inflammation, often referred to as "cytokine storm", observed in these patients. In addition, when mixed with two different mushroom species from Hericium and Grifola genera (H. erinaceus and G. frondosa), the sun mushroom has been shown to significantly reduce bacteremia and improve symptoms and quality of life of patients affected by other inflammatory diseases such as inflammatory bowel disease (IBD) patients [24,28].

Di Naso, et al. [29] found that mushroom treatment reduced oxidative stress in the lungs of diabetic rats and allowed for lung tissue recovery in these animals. Niwa, et al. [30] observed that administration of Agaricus blazei extract to diabetic rats significantly suppressed spikes in fasting blood glucose and hemoglobin A1c levels. It also significantly

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**Figure 1:** Agaricus brasiliensis fruiting bodies. A and B: Different stages of maturation. C: Cultivation in plastic bag. D: Protected cultivation. E: Unprotected cultivation.
mitigated the loss of body weight commonly observed in untreated diabetes. Some mushroom metabolites have efficacy against the causative protozoan of leishmaniasis and may, therefore, be therapeutic for this disease [31,32].

Several studies have demonstrated that certain mushroom species lower serum cholesterol including *Grifola frondosa* (Maitake), *Lentinula edodes* (Shiitake), *Flammulina velutipes* (Enokitake), *Pleurotus ostreatus* (Oyster mushroom), *Polyporus confluens*, *Ganoderma lucidum* (Reishi Mushroom), *Auricularia auricular*, *Tremella fuciformis* and *Volvariella volvacea* (straw mushroom) [20,33-38].

Most mushrooms are known to produce certain bioactive substances such as lovastatin and eritadenine. These substances were investigated as potential treatment strategies against cardiovascular diseases [39]; however, the mechanism of action of fungi extracts remains to be fully elucidated. Possible mechanisms include the reduction in serum lipid profile, increase in bile acid excretion and LDL receptor expression, change in phospholipid metabolism, and hepatic HMG-CoA reductase inhibition [40-42]. Few studies have demonstrated the cholesterollowering potential of *Agaricus brasiliensis*, however, the results of these reports are conflicting. In 2003, Lee and Koh evaluated the effects of liquid culture supplementation on the lipid levels in male Sprague-Dawley rats maintained on a high-fat diet. Compared to the untreated controls, animals administered *A. blazei* presented significant dose-dependent reductions in serum total cholesterol, LDL-C, and triglycerides and concomitant increases in HDL-C. Braga, et al. [43] evaluated the effects of water-based mushroom extracts on blood lipids and observed significant relative reductions only in the triglyceride and VLDL levels but not the LDL or HDL levels. Gonçalves, et al. [44] assessed the effects of ABM (5%) extract supplementation on atherogenesis in apo-E knockout mice. This supplementation paradoxically increased the numbers and sizes of atherosclerotic lesions possibly by inducing inflammation. Meanwhile, a significant increase in the level of SR-BI receptor which participates in reverse cholesterol transport was observed in rats receiving a hypercholesterolemic diet plus 1% *Agaricus brasiliensis*. These results suggest that *Agaricus brasiliensis* consumption improves the serum lipid profile in hypercholesterolemic rats by modulating the expression of the genes and transcription factors implicated in hepatic cholesterol metabolism [45]. These controversial results might stem from the methodological differences in route, dose, and time of administration.

Nakamura, et al. [46] used a mouse model of non-alcoholic steatohepatitis (NASH) in which pathogenesis was promoted by dietary induction. Supplementation with *Agaricus brasiliensis* attenuated the development of hepatic fibrosis, which is a characteristic feature of late-stage NASH. This effect appeared to be mechanistically linked to an AGA-promoted reduction in hepatic oxidative stress. These results demonstrate a novel role for *A. brasiliensis* in NASH prevention.

Functional effects of the chemical components of *Agaricus brasiliensis*

β-D-glucans are a (1→3)-linked glucose polymer with (1→6)-linked side chains and a major component of fungal cell walls. In addition, β-glucans are widely used as adjuvant in food and pharmaceutical industries due to their physical and chemical properties [47]. The β-glucans (Figure 2) are the key chemical components of *A. brasiliensis* responsible for its cholesterol-lowering effects. According to Kim, et al. [48], since β-glucans are soluble fibers, they reduce blood cholesterol levels and glucose absorption in diabetics. The biological effects of glucans are influenced by their molecular structure. Table 1 [49] presents the chemical structures and modes of action of the various glucans, including β-glucans.

Chitin, one of the two major components with β-glucan in the fungi cell walls, has an excellent affinity for bile acids, once converted to chitosan. Neyrinck, et al. [50] demonstrated that the administration of 5% fungal chitosan from *A. bisporus* to obese mice on high-fat diets modulated lipid absorption and
reduced serum adipocytokine secretion. The latter may be associated with reduced adiposity.

Dietary fibers are classified according to their relative water solubilities, viscosities, gel formation abilities, and fermentation rates by human microbiota. Certain mechanisms have been proposed to explain the cholesterol-lowering activity of dietary fiber. Dietary fiber may decrease intestinal absorption of dietary cholesterol and lower its release via the hepatic LDL receptors (LDLR) which, in turn, reduce ath erosclerotic serum lipoprotein concentration. Fukushima, et al. [40] supplemented the diets of rats with *Agaricus bisporus* fibers and reported that it reduced serum total cholesterol, non-HDL cholesterol, and triglycerides and increased the mRNA levels of the hepatic LDL receptors [35,53].

Soluble fiber may undergo fermentation by bacteria in the human colon. This process generates short-chain fatty acids (SCFA) such as butyrate, propionate, and acetate which are also hypocholesterolemic [54]. Butyrate is a signaling molecule that regulates intestinal function and cholesterol metabolism by interfering with VLDL production [55]. Changes in the propionate/acetate ratio may inhibit hepatic lipogenesis [56]. Soluble fibers also promote the increase of free cholesterol concentration in the bile by activating the ABCG5 and ABCG8 carriers which belong to the ATP-binding cassette subfamily G transporters [57]. Indeed, an increased expression of 7α-hydroxylase (CYP7A1), ATP-binding cassette subfamily G-transporters (ABCG5/G8), and low-density lipoprotein receptor (LDLR) was observed following diet supplementation with *A. brasiliensis* [45].

Mushrooms form and accumulate various secondary metabolites such as phenolic compounds, terpenes, and steroids (Table 2) [58]. Previous studies have reported that phenolic compounds inhibit intestinal absorption of dietary lipids by forming complexes with them and interfering with micellar emulsiﬁcation, solubilization, and hydrolysis [59,60]. Phenolic compounds may reduce the risk of developing cardiovascular diseases by preventing hypercholesterolemia, which is the initial stage of atheromatous plaques [61,62].

The sterols in *A. brasiliensis* structurally resemble cholesterol and can, therefore, reduce its absorption by competitive inhibition. According to Mizuno, et al. [12], this mushroom has a large amount of ergosterol.

Over the past three decades, studies on natural compounds with an antioxidant potential have substantially increased [63]. The Table 3 summarizes the main ﬁndings about the therapeutic potential of *Agaricus brasiliensis*, both for studies involving animals and humans. The search for the works considered the name *A. brasiliensis*, following the classiﬁcation by Wasser, et al. [14], currently, the most used by researchers. Yurków, et al. [64], for example, investigated the effects of the medicinal mushrooms *Agaricus brasiliensis* and *Ganoderma lucidum* on antioxidant enzyme activity in rat leukocytes.

### Table 1: Glucans in the fruiting bodies of *A. brasiliensis* and their respective biological activity.

| Chemical structure | Activity reported | Mode of action | References |
|--------------------|-------------------|----------------|------------|
| (1-6)β-glucans-protein | - | Antitumor Sarcoma 180 | [67-69] Mizuno et al. |
| (1-6)(1-3)β-glucans | - | Antitumor Sarcoma 180 | [68] |
| (1-6)β-glucans-protein | - | Antitumor Meth A | [70] |
| (1-4)α-glucans (1-6)β-glucans-protein | - | Antimetastatic Meth A (intratumoral) | Immunostimulation with selective cytotoxicity | [71] |
| (1-4)α-glucans (1-6)β-glucans-protein | Tumorcidal in Meth A tumor cells | Antitumor and Antimetastatic Meth A | Selective cytotoxicity, increased apoptosis and NK cells | [72] |
| (1-6)(1-3)β-glucans and (1-6)(1-3)-glucans-protein | - | Antitumor Sarcoma 180 | Immunostimulation | Ohno et al. (2001) |
| (1-6) (1-3)-glucans | Proliferation of T lymphocytes and B | - | - | [73] |

### Table 2: Bioactive compounds in the fruiting bodies of *Agaricus brasiliensis* with their associated pharmacological activities.

| Mushroom | Pharmacological activities | Study | Extract/Compound | References |
|----------|---------------------------|-------|------------------|------------|
| Apoptosis in leukemia cells and inhibit tumor-induced angiogenesis. | In vitro | Water extracts (agaritine and ergosterol) | [74] |
| Apoptosis and Antitumor properties | In vitro | Ethanol and Hot water extracts / Phenolic compounds, terpenes and steroids | [8] |
| Antibacterial and Antiparasitic | In vivo | Water extract (nd compounds) | [75] |
| *Agaricus brasiliensis* or *Agaricus blazei* Murill | Anti-inflammatory | In vivo | Extract (?) / β-glucan (?) | Johnson et al. (2009) |
| Anti-tumor | In vivo | β-glucan, polyphenols, vitamins | [46] |
| Cytotoxic Effect on Human Myeloma Cells and Leukemic Cells | In vitro | Extract Andosan (*Agaricus blazei* Murill (mycelium) (82.4%), Hericium erinaceus (14.7%), and Grifola frondosa (2.9%)) / Proteoglycans and ergosterol | [76] |
| Inhibition HSV-1 infection | In vitro | Extracted β-glucan | [77] |
| Trials (Pre-clinical / Clinical) | Study sample (animal model characteristics/ sample size, gender and age) | Study Duration | Study design and Treatment Mode | Primary findings | Adverse events | References |
|-------------------------------|-------------------------------------------------|----------------|--------------------------------|------------------|---------------|------------|
| PRE-CLINICAL                  | Swiss mice, male (7–8 weeks old) (n = 6/group)  | According to the treatment: 12 days, 12 hours or 24 hours. | Aqueous Extract / Treatment schedule: saline (saline 0.9% + oesal ligation and puncture –CLP/ n = 18 animals), Ceftriaxone (Cef −20 mg/kg + CLP/ n = 6 animals), aqueous extract of Ab (Ab −135 mg/kg + CLP, n = 18 animals) and sham (surgery control, n = 18 animals). All treatments were administered i.v. at a volume of 100 μL orally by gavage, 24 h before and immediately before CLP induction (time 0). In the first set of experiments, 24 animals were used to monitor the survival rate during 12 days. In the next set of experiments 36 animals were used, septic mice were euthanized at specific time points to evaluate the therapeutic potential and immunomodulatory/antioxidant activities of Ab. | Pretreatment with Ab aqueous extract was able to increase the survival of septic animals by a mechanism involving immunomodulatory and antioxidant protectiv activity. | None reported | [78] |
|                               | Holtzman rats, male (60 days old), 180 – 210 g. (n = 5-8/group) | 23 days | Aqueous extract / 400 mg · kg-1/d in adjuvant-induced articr rats. | The treatment produced significant diminutions in protein carbonylation and lipid damage in the liver, brain, and plasma. It also diminished the tissue reactive oxygen species and increased the antioxidant capacity of the plasma. Antioxidant defenses, which are diminished by arthritis, were improved by treatment with the A. brasiliensis extract, as revealed by preservation of the reduced glutathione and protein thiols levels and by the tendency of the activities of some antioxidant enzymes to normalize. The increased glucose-6-phosphate dehydrogenase activity was also almost normalized by the treatment. In addition, there were indications that A. brasiliensis can inhibit the initiation of structural events that can lead to hepatocyte neerosis. | None reported | [96] |
|                               | Wistar rats, male (150-180g) (n = 6-8/group) | 14 days | Mycelia powder / orally administered at a dose of 1 g/kg in control and diabetic animals. | Protective effect on the antioxidation system of RBCs in diabetes. The effect consists of reducing the amount of LPO products and restoring the activity of enzymes in the antioxidant defense system (SOD, Cat, and GPx) to control values. | None reported | [79] |
|                               | Fischer rats, female (90 days old), 205 g (n = 6/group) | 6 weeks | Dehydrated mushroom powder in hypercholesterolemic diet. | Diet supplementation with A. brasiliensis significantly improved serum lipid profiles, comparable to the effect observed for simvastatin. In addition, A. brasiliensis dietary supplementation markedly promoted fecal cholesterol excretion. Increased expression of CYP7A1, ABCG5/G8 and LDLR was observed following A. brasiliensis administration. | None reported | [45] |
|                               | BALB/c mice, male (8 weeks old) (n = 4/group) | 7 days | Hot Water Extracts /Saline, A. brasiliensis extract at 25 mg/kg weight, or A. brasiliensis extract at 250 mg/kg weight were given to animals every day for 7 days. | Hot water extracts of A. brasiliensis inhibit platelet function, in terms of platelet shape change, aggregation, and intracellular calcium mobilization, by way of P2Y1 receptor inhibition. While the specific substance(s) that has the inhibitory effect has not been identified yet, its activity is resistant to metabolism because the oral administration of the A. brasiliensis water extract prolongs tail bleeding in mice. | None reported | [80] |
|                               | Wistar rats, male (150–180 g) (n = 6-8/group) | 14 days | Mushroom preparations (powder) were orally administered at a dose of 1 g/kg in control and diabetic animals. | Positive correct influence on the structural and quantitative changes of the carbohydrate determinants of surface glyco-conjugates and leads to a renewal of membrane negative charges and a reduction of aggregation properties. The detected changes indicated an improvement in the functional state of erythrocytes and rejuvenation of their population as a result of the influence of the biologically active compounds of the studied medicinal mushrooms. | None reported | Vitak, et al. 2015, [81] |

**Table 3:** Preclinical and Clinical Studies Done with Agaricus brasiliensis in Different Forms.
| Study | Treatment | Duration | Description | Outcomes |
|-------|-----------|----------|-------------|----------|
| Wistar rats, male (1 week old) (<i>n = 10/group</i>) | Aqueous extract (ABE): ABE 20 mg/kg/d, ABE 50 mg/kg/d, ABE 100 mg/kg/d, and saline in control and induced neonatal jaundice. | 14 days | Administration of ABE dose-dependently reduced the elevated bilirubin level induced by phenylhydrazine. ABE treatment also reduced the total antioxidant status, decrease O2⁻/SOD, level of NF-κB protein, and adrenomedullin (AM). | None reported [82] |
| Rats, male (150-180 g) (<i>n = 6-8/group</i>) | Mushroom powder (1 g/kg body weight and administered orally). | 14 days | Mushrooms exert an inhibitory effect on NOS activity in leukocytes in EDM, decreasing NO overproduction. An increase in apoptotic processes in peripheral blood leukocytes in rats with EDM. | None reported [64] |
| Wistar rats, male (150-180 g) (<i>n = 6-8/group</i>) | Mycelia powder was orally administered at a dose of 1 g/kg in control and diabetic animals. | 14 days | Hypoglycemic effects of <i>A. brasiliensis</i> and <i>G. lucidum</i> occurred in the diabetic rats, as evidenced by decreased blood glucose and glycosylated hemoglobin concentrations. In STZ-diabetic animals treated with submerged culture mycelium powder, an increase in the number of erythrocytes in the bloodstream (an anemic effect), erythrocyte resistance to acid hemolysis, and the normalization of fetal hemoglobin concentrations, along with the intensification of erythropoiesis were observed. | None reported [84] |
| Wistar rats, male (150-180 g) (<i>n = 6-8/group</i>) | Control and diabetic animals were fed daily with 1 mL of suspension, which was created by mixing powdered mushrooms with saline in a ratio corresponding to a dose of 1 g/kg body weight and administered orally. | 14 days | The medicinal mushrooms’ administration is accompanied by an increase in antioxidant enzyme activity to control values and is even higher in the case of <i>A. brasiliensis</i> administration when compared with the diabetic group. As for the indicators of lipid peroxidation under mushroom administration of <i>A. brasiliensis</i> and <i>G. lucidum</i>, we observed a significant decrease of TBARS levels compared with the diabetic group. | None reported [83] |
| Swiss mice, male (6-7 weeks). (<i>n = 10/group</i>) | Aqueous extract Group 1: received only water; (2) received water and SEST; (3) received only <i>A. brasiliensis</i> aqueous extract; (4) received <i>A. brasiliensis</i> aqueous extract and SEST. In experimental groups 3 and 4, mice received 0.6 mL extract per day per animal, by intragastric gavages. | According to the treatment: 7 days before or 5 days after the pathogenic challenge. | <i>A. brasiliensis</i> aqueous extract as tested in the present study did not influence any of the variables selected to evaluate in vivo its immunomodulatory effect suggested in the literature. | None reported [85] |
| Male volunteers (n = 6/group) | Capsules Volunteers (n = 5/group) was randomly divided into 2 groups (placebo and treatment with <i>A. brasiliensis</i>). Four capsules were consumed daily in the morning (500 mg/capsule). | 24 days | The bioactive compounds in <i>A. brasiliensis</i> revealed the potential to improve conditions of muscle fatigue without altering other parameters. | None reported [86] |
| Female and Male volunteers, mean age 22 to 45 years old. (n = 31). | Hot Water Extract Subjects were divided into 3 groups: group 2 and group 3 (total 20 subjects) were administered the normal dose and group 1 (11 subjects) were administered a 3-fold higher dose (safety clinical study group) of <i>A. brasiliensis</i> (each tablet contained 300 mg of <i>A. brasiliensis</i>). | According to the treatment: Group 1: 6 months, 30 tablets/day; Group 2: 3 months, 10 tablets/day; Group 3: 3 months, 10 tablets. | Percentage body fat, percentage visceral fat, blood cholesterol level and blood glucose level were decreased, and natural killer cell activity was increased. | None reported [87] |
When administering *A. brasiliensis* the authors observed a significant decrease in TBARS levels compared with the diabetic group. Increased activity of antioxidant enzymes and reduction of TBARS level illustrated the antioxidant properties of these mushrooms. Tsai, et al. [8], had suggested that the antioxidant property of *A. blazei* may be associated with its high tocopherol content [8,65].

De Souza, et al. [66] evaluated the effects of aqueous *Agaricus brasiliensis* extract on the oxidative state of the liver, brain, and plasma in adjuvant-induced arthritic rats, a model for human rheumatoid arthritis. The authors found that *A. brasiliensis* aqueous preparations can, in principle, be potential auxiliaries in the treatment of patients with rheumatoid arthritis due to their capacity to reduce oxidative stress. Data obtained suggested that the continuous ingestion of *A. brasiliensis* as specific preparations or as a food supplement can possibly help to attenuate the systemic effects of rheumatoid arthritis and improve the quality of life of patients affected by this disease.

**Conclusion and perspectives**

Several studies have investigated the therapeutic potential of *A. brasiliensis*, which produced empirical evidence for the antidiabetic, anticancer, antitumor, hypoallergenic, and hypocholesterolemic activity of this species. Moreover, the sun mushroom is considered a major source of bioactive compounds with potential health benefits. Its β-glucan and phenolic compound content along with its high protein and low lipid content contribute to its therapeutic potential. Whether these effects are associated with a specific component or a synergistic effect remains to be determined. New studies are being conducted to elucidate the exact mechanism and the possible components involved in its therapeutic effect.

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