Review Article

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

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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 Basidiomycetes 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 [23,24].

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 in 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
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 cholesterol-lowering 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

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**Figure 2:** Chemical structures of the β-glucans (β-(1,3-1,6)-D-glucan) found in the fruiting bodies of *Agaricus brasiliensis*. 

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Dietary fiber may decrease intestinal fermentation rates by human microbiota. Certain mechanisms associated with reduced adiposity.

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 metabolism by interfering with VLDL production [55]. Soluble fibers also promote the increase of micellar emulsification, solubilization, and hydrolysis [59,60]. Phenolic compounds inhibit intestinal absorption of dietary 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 Agaricus 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. Yurkiv, 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 3: Preclinical and Clinical Studies Done with *Agaricus brasiliensis* in Different Forms.

<table>
<thead>
<tr>
<th>Trials (Pre-clinical / Clinical)</th>
<th>Study sample (animal model characteristics/ sample size, gender and age)</th>
<th>Study Duration</th>
<th>Study design and Treatment Mode</th>
<th>Primary findings</th>
<th>Adverse events</th>
<th>References</th>
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<td>PRE-CLINICAL</td>
<td>Swiss mice, male (7–8 weeks old) (n = 6/group)</td>
<td>According to the treatment: 12 days, 12 hours or 24 hours.</td>
<td>Aqueous Extract / Treatment schedule: saline (saline 0.9% + oecal 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 in 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. In this study, 18 mice (6/group) were euthanized 12 h after CLP to analyze oxidative stress parameters and 18 mice (6/group) were euthanized 24 h after CLP to analyze pro-inflammatory cytokines. Pretreatment with Ab aqueous extract was able to increase the survival of septic animals by a mechanism involving immunomodulatory and antioxidant protective effect.</td>
<td>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 <em>A. brasiliensis</em> extract, as revealed by preservation of the reduced glutathione and protein thiol 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 <em>A. brasiliensis</em> can inhibit the initiation of structural events that can lead to hepatocyte necrosis.</td>
<td>None reported</td>
<td>[78]</td>
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<td>Holtzman rats, male (60 days old), 180 – 210 g. (n = 5-8/group)</td>
<td>23 days</td>
<td>Aqueous extract / 400 mg · kg⁻¹/d in adjuvant-induced arthritic rats.</td>
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<td>None reported</td>
<td>[66]</td>
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<td>Wistar rats, male (150–180 g) (n = 6-8/group)</td>
<td>14 days</td>
<td>Mycelia powder / orally administered at a dose of 1 g/kg in control and diabetic animals.</td>
<td>Protective effect on the antioxidant 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.</td>
<td>None reported</td>
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<td>Fischer rats, female (90 days old), 205 g (n = 6/group)</td>
<td>6 weeks</td>
<td>Dehydrated mushroom powder in hypercholesterolemic diet.</td>
<td>Diet supplementation with <em>A. brasiliensis</em> significantly improved serum lipid profiles, comparable to the effect observed for simvastatin. In addition, <em>A. brasiliensis</em> dietary supplementation markedly promoted fecal cholesterol excretion. Increased expression of CYP7A1, ABCG5/G8 and LDLR was observed following <em>A. brasiliensis</em> administration.</td>
<td>None reported</td>
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<td>BALB/c mice, male (8 weeks old) (n = 4/group)</td>
<td>7 days</td>
<td>Hot Water Extracts /Saline, <em>A. brasiliensis</em> extract at 25 mg/kg weight, or <em>A. brasiliensis</em> extract at 250 mg/kg weight were given to animals every day for 7 days.</td>
<td>Hot water extracts of <em>A. brasiliensis</em> 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 <em>A. brasiliensis</em> water extract prolongs tail bleeding in mice.</td>
<td>None reported</td>
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<td>Wistar rats, male (150–160 g) (n = 6-8/group)</td>
<td>14 days</td>
<td>Mushroom preparations (powder) were orally administered at a dose of 1 g/kg in control and diabetic animals.</td>
<td>Positive corrective influence on the structural and quantitative changes of the carbohydrate determinants of surface glycoconjugates and leads to a reorganization 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.</td>
<td>None reported</td>
<td>Vitak, et al. 2015. [81]</td>
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<td>Table</td>
<td>Description</td>
<td>Treatment</td>
<td>Duration</td>
<td>Outcome</td>
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<td><strong>Agaricus brasiliensis</strong> (Sun mushroom) and its therapeutic potential: A review</td>
<td>Administration of ABE dose-dependently reduced the elevated bilirubin level induced by phenylhydrazine. ABE treatment also reduced the total antioxidant status, cascade O2−/SOD, level of NF-κB protein, and adrenomedullin (AM).</td>
<td>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.</td>
<td>14 days</td>
<td>None reported [82]</td>
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<td>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.</td>
<td>Mushroom powder (1 g/kg body weight and administered orally)</td>
<td>14 days</td>
<td>None reported [64]</td>
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<td>Hypoglycemic effects of <em>A. brasiliensis</em> and <em>G. lucidum</em> occurred in the diabetic rats, as evidenced by decreased blood glucose and glycated 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.</td>
<td>Mycelia powder / were orally administered at a dose of 1 g/kg in control and diabetic animals.</td>
<td>14 days</td>
<td>None reported [84]</td>
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<td>The medicinal mushrooms' administration is accompanied by an increase in antioxidant enzyme activity to control values and is even higher in the case of <em>A. brasiliensis</em> administration when compared with the diabetic group. As for the indicators of lipid peroxidation under mushroom administration of <em>A. brasiliensis</em> and <em>G. lucidum</em>, we observed a significant decrease of TBARS levels compared with the diabetic group.</td>
<td>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.</td>
<td>14 days</td>
<td>None reported [83]</td>
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<td><em>A. brasiliensis</em> 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.</td>
<td>According to the treatment: 7 days before or 5 days after the pathogenic challenge. Aqueous extract / Group 1: received only water; (2) received water and SEST; (3) received only <em>A. brasiliensis</em> aqueous extract; (4) received <em>A. brasiliensis</em> aqueous extract and SEST. In experimental groups 3 and 4, mice received 0.6 mL extract per day per animal, by intragastric gavages.</td>
<td>According to the treatment:</td>
<td>None reported [85]</td>
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<td>The bioactive compounds in <em>A. brasiliensis</em> revealed the potential to improve conditions of muscle fatigue without altering other parameters.</td>
<td>Male volunteers (n = 6/group)</td>
<td>24 days</td>
<td>None reported [86]</td>
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<td>Percentage body fat, percentage visceral fat, blood cholesterol level and blood glucose level were decreased, and natural killer cell activity was increased.</td>
<td>According to the treatment: 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 <em>A. brasiliensis</em> (each tablet contained 300 mg of <em>A. brasiliensis</em>).</td>
<td>24 days</td>
<td>None reported [87]</td>
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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.

**References**


49. Carmelini.


