

(REVIEW ARTICLE)



Antidepressant potential of *Agaricus Bisporus*: A comprehensive study

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World Journal of Biology Pharmacy and Health Sciences, 2025, 21(01), 604-615

Publication history: Received on 09 December 2024; revised on 21 January 2025; accepted on 24 January 2025

Article DOI: <https://doi.org/10.30574/wjbphs.2025.21.1.0076>

Abstract

Many important nutrients and medicinal bioactive chemicals are thought to be possible to be found in mushrooms. *Agaricus Bisporus* is the most significant commercially grown mushroom worldwide and a member of the Basidiomycetes family. Rich in minerals, vitamins, lipids, fiber, proteins, and carbohydrates, this mushroom is a well-known nutritious food. Mirtazapine is a commonly prescribed antidepressant medication that is a member of the BCS Class II drug class and has high permeability and low solubility. Goal: The formulation of the gastroretentive floating tablets of mirtazapine was statistically optimized using the Box Behnken design. Materials and Procedures: Using design expert software, a polynomial model was created after the responses were examined using the three components of the three design levels. A comparison was made between three distinct independent components. Reviewing contemporary research on the nutritional and therapeutic qualities of *Agaricus Bisporus* is the primary aim of this research. Only findings released after 2006 have been taken into consideration due to the acceleration of mushroom research during the past 10 years. The maintenance of human health has relied heavily on the use of therapeutic substances derived from plants and fungi from ancient times. Natural products are the source of more than half of all contemporary clinical medications and are crucial to pharmaceutical industry drug research initiatives. A significant natural food and medicinal source is mushrooms. The significance of edible and wild mushrooms was recognized by traditional Aboriginal people, and these are currently being examined for their bioactivity in treating a range of illnesses. This review's objective is to provide a concise scientific explanation of the pharmacognosy, chemistry, and pharmacology of button mushrooms.

Keywords: *Agaricus Bisporus*; Antidepressant; Nutrition; Mushroom; Button Mushroom

1. Introduction

Globally, mushrooms are already a significant component of human diets as non-animal sources of protein, but less is known about their environmental impact and value chain. A controlled drug delivery system is utilized to improve a medicine's therapeutic efficacy and get around some issues with traditional therapy (1). A member of the kingdom's Agaricaceae family, division Basidiomycota of fungi, *Agaricus Bisporus* Imbach is one of the most widely grown mushrooms around the world. Champignon, button, and white mushrooms are some of the common names for this species. In this essay, the word "mushroom" will be used instead. Apart from its medicinal and cosmetic uses, this fungus is primarily consumed by humans. It is extremely nutritious because it is a source of (2). The agent must be delivered to the target tissue in the ideal quantity at the ideal timing in order to achieve optimum therapeutic efficacy, resulting in low toxicity and few adverse effects. Delivering a medicinal ingredient to the target site in a prolonged controlled release form can be accomplished in a number of ways. Microspheres are tiny spherical particles that usually have dimensions between 1 μm and 1000 μm , which is in the micrometer range. Microspheres can also be called microparticles. A variety of synthetic and natural materials are used to make it. Commercially available microspheres come in three varieties: glass, polymer, and ceramic (3). In order to create microspheres using a variety of natural and artificial materials. Commercially available microspheres come in three varieties: glass, polymer, and ceramic.

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Polyethylene microspheres are frequently utilized as either temporary or permanent fillers (4). Polyethylene microspheres can form porous structures in ceramics and other materials because of their lower melting temperature. Many important nutrients and medicinal bioactive chemicals are thought to be possible to be found in mushrooms. *Agaricus Bisporus* is the most significant commercially grown mushroom worldwide and a member of the Basidiomycetes family. This mushroom is a well-known, healthful food because of its abundance of minerals, vitamins, fiber, lipids, proteins, and carbohydrates (5). These mushrooms are known being hepatoprotective, antioxidant, antimicrobial, anticancer, antidiabetic, antihypercholesterolemic, and antihypertensive properties. They contain a number of active ingredients, including essential amino acids, peptides, glycoproteins, polysaccharides, lipopolysaccharides, triterpenoids, nucleosides, lectins, fatty acids, and their derivatives. Reviewing contemporary research on the nutritional and therapeutic qualities of *Agaricus Bisporus* is the main goal of this study (6).

Material – *Agaricus Bisporus* collect from local market, Methanol

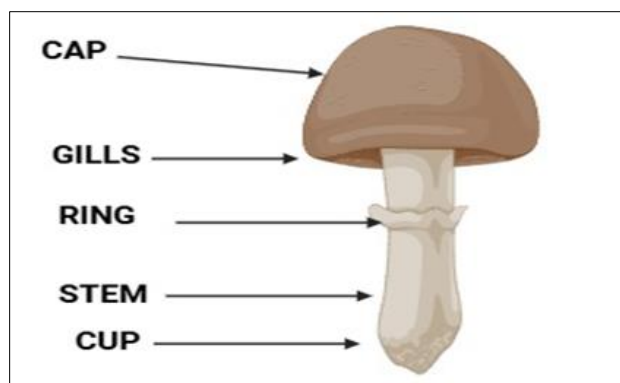


Figure 1 *Agaricus Bisporus*

1.1. Plant profile

Table 1 Botanical Discription

Botanical name	<i>Agaricus Bisporus</i> (Lange) Imbach
Kingdom	Fungi
Divison	Basidiomycota
Class	Agaricomycetes
Order	Agaricales
Family	Agaricaceae
Genus	<i>Agaricus</i>
Species	<i>Agaricus Bisporus</i>

1.1.1. History and ethnopharmacology

The basidiomycete fungus that can be eaten *A. Bisporus* is indigenous to North American and European grasslands. Often referred to as WBM, or white button mushroom it is extensively grown in the majority of nations and makes up the majority of every mushroom eaten in Australia and The United States. It was first grown in France, according to historical records, and cultivar strains came from Western Europe(7). Only the pharaohs were considered deserving of eating perhaps even touching mushrooms, as the ancient Egyptians thought They may grant immortality. They were able They were able to provide immortality mushrooms. frequently known as "food for the gods" in the ancient Rome. Folklore in Mexico, China, Russia, and other nations claimed that mushrooms gave people supernatural power (8).

1.1.2. Historical review of medicinal plant

The most prevalent species in the fungus kingdom, which includes edible mushrooms, is *Agaricus*. Up to 38% of the world's mushroom production comes from the genus *Agaricus*, which includes both species *A. bisporus* (such as button, Swiss brown with portobello variations) and species *Agaricus campestris* (such as field mushroom).One *Flammulina*

filiformis, or enoki), oysters (*Ostreatus Pleurotus*), shiitake (*Lentinus edulis*), *Tricholoma murrillianum*, or matsutake, and porcini (*Boletus edulis*) are further edible mushrooms (9). Face and neck erythema was recorded. She experienced tightness in her chest, tongue angioedema, and urticaria. This led to more intramuscular adrenaline (500 mg), which improved her condition. A chest radiograph was normal, and an ECG revealed atrial fibrillation without ischemic alterations.

Four hours after experiencing acute symptoms, The tryptase level of the patient was increased at 24.8 mg/L(reference range < 11.5 mg/L). After being admitted to the ward for the night, she was discharged the next day after being weaked off of oxygen (10).

1.1.3. Historical sources relevant for study of medicinal plants

The edible basidiomycete mushroom *A. bisporus* is indigenous to North American and European grasslands. Often referred to as white button mushroom (WBM), it is extensively grown in the majority of nations and makes up the majority of all mushrooms consumed in Australia and the US. It was first grown in France, according to historical records, and cultivar strains came from Western Europe. The pharaohs were the only ones considered deserving of eating perhaps even touching mushrooms, as the ancient Egyptians thought They may grant immortality. Mushrooms were frequently Known as "food for the gods" in classical Rome (11).The free form of iron in mushrooms makes up one-third of their content. Their polysaccharide content successfully fights HIV and is utilized as an anticancer medication. The mushrooms' biologically active chemicals have been utilized as insecticides and nematodes and have antifungal, antibacterial, antioxidant, and antiviral qualities.Studies have shown that women who regularly consume these button mushrooms are less likely to get breast cancer (12).

1.1.4. Phytoconstituent

Given that *A. bisporus* is classified as a dish that is good for people health and contains high levels of dietary fiber, antioxidants, and vitamins like thiamine, vitamin and ascorbic acid D2, in addition to minerals like folates, ergothioneine (ET), as well as polyphenol that could be beneficial for cardiovascular and diabetic conditions, it is possible that The anti-inflammatory properties of the mushroom, hypoglycemic, as well as low cholesterol properties . Together with ergosterol, tocopherols, linoleic acid, and lectins, β -glucans make up around half of the bulk of the fungal cell wall (13). The primary aromatic component of mushrooms is agaritine and its derivatives, which are chemically classified as hydrazines. Certain types of mushrooms, such as *A. bisporus*, contain hydrazines. Agaritine has been shown to contribute to the creation of damaging aryl diazonium ions. In mushrooms, gamma-glutaminy-4-hydroxybenzene is the main phenolic component(14).

Table 2 The components of *Agaricus Bisporus*

CONSTITUENT	(UNIT/100 G)	REFERENCES
PROXIMATE H2O	92.45 Gram	(15)
ENERGY	22 KCAL	(16)
PROTEIN	93 KJ	(17)
ADJUSTED PROTEIN	3.09 G	(18)
TOTAL LIPID	2.18 G	(19)
ASH	0.34 G	(20)
CARBOHYDRATE	0.85 G	(21)
FIBER	3.26 G	(22)
SUGAR	1.98 G	(23)
GLUCOSE	1.48 G	(24)
FRUCTOSE	0.17 G	(25)
FIBER	1 G	(26)

Table 3 The microelements that *Agaricus Bisporus* contains

MICROELEMENT	VALUE/(UNIT/100 G)	REFERENCES
Calcium (Ca)	3 mg	(27)
Iron (Fe)	0.5 mg	(28)
Magnesium (Mg)	9 mg	(29)
Phosphorus (P)	86 mg	(30)
Potassium (K)	318 mg	(31)
Sodium (Na)	5 mg	(32)
Zinc (Zn)	0.52 mg	(33)
Copper (Cu)	0.318 mg	(27)
Manganese (Mn)	0.047 mg	(28)
Selenium (Se)	9.3 µg	(25)

Table 4 *Agaricus Bisporus* contains vitamins.

Vitamins	Value/(unit/100 g)	Refereces
Vitamin C,total ascorbic acid	2.1 mg	(34)
Thiamin	0.081 mg	(20)
Riboflavin	0.402 mg	(23)
Niacin	3.607 mg	(21)
Pantothenic acid	1.497 mg	(35)
Vitamin B6	0.104 mg	(36)
Folate	17 µg	(37)
Choline	b17.3 mg	(38)
Betaine	9.4 mg	(39)
Vitamin B12	0.04 µg	(22)
Tocopherol, beta	0.01 mg	(26)
Tocopherol, gamma	0.01 mg	(40)
Tocopherol, delta	0.01 mg	(41)
Vitamin D (D2 + D3)	0.2 µg	(42)
Vitamin D2 (ergocalciferol)	0.2 µg	(43)

2. Medicinal importance of *Agaricus Bisporus*

In order to create functional foods, there is growing interest in removing the bioactive components from mushrooms. The use of *A. bisporus* in numerous traditional medicines has a long history. Extracts from *A. bisporus* and/or the bioactive substances it contains are being used more and more globally as anti-cancer agents, antioxidants, and anti-inflammatory substances to treat a range of human diseases, such as cancer, diabetes, fungal and bacterial infections, immune system problems, and coronary heart disease (44).

2.1. Anti cancer

One of the most deadly illnesses in the world is cancer. Polysaccharides and other natural active components from mushrooms have recently been isolated and shown to have strong anti-cancer effects against a variety of cancer cell

lines. The glucan and other polysaccharides found in basidiomycota are thought to have therapeutic properties. The beta-glucan family of chemicals includes the polysaccharides, which seem to have anti-tumorigenic properties through boosting cellular immunity (45). α -glucan, β -glucan, and galactomannan are the three primary polysaccharides found in *A. bisporus* with galactomannan accounting for 55.8% of the total. According to, (1 \rightarrow 3) and (1 \rightarrow 6)-d-glucans are the most frequently extracted glucans from *A. bisporus* 69% more tumor necrosis factor (TNF α) was produced when Juice from fruits enhanced with *A. bisporus* α -glucans (5 g glucans/day) ingested lipopolysaccharide (42).

2.2. Antidiabetic

The three main polysaccharides present in *A. bisporus* are Galactomannan, α -glucan, and β -glucan, with galactomannan making up 55.8% of the total. The most often isolated glucans from *A. bisporus* are (1 \rightarrow 3) and Consuming fruit juice supplemented with α -glucans from *A. bisporus* (5 g glucans/day) and (1 \rightarrow 6)-d-glucans Lipopolysaccharide resulted in a 69% increase in tumor necrosis factor (TNF α) (46). Adults at risk for type 2 diabetes may benefit from frequent use of *A. bisporus* over time due to its many components, which have possible health benefits of antioxidants and anti-inflammatory.

indicated that consuming *Agaricus Bisporus* could be a useful method for postmenopausal women to prevent nonalcoholic fatty liver disease's stage of liver steatosis that can be reversed early (47).

2.3. Antioxidant

Numerous writers have documented *A. bisporus*'s total phenolics and antioxidant qualities. In comparison to *Lentinula edodes*, *Pleurotus Grifola frondosa*, *Pleurotus eryngii*, and *Ostreatus*, *A. bisporus* mushrooms, particularly port abellas (*A. bisporus* brown), had a greater capacity for antioxidants (48). Phenolic chemicals are said to be the primary antioxidant components present in mushrooms. There is a strong correlation between phenolic contents and antioxidant activity, indicating that phenolic compounds may be the main source of antioxidant activity in edible. On the other hand, although having a low level of antioxidant activity, *A. bisporus* exhibits significant levels of phenolics compound (40).

“One of the main risk factors for the development of atherosclerosis” one of the most dangerous diseases in humans, and subsequent cardiovascular illness is hyperlipidemia, which is distinguished by high triglyceride levels or cholesterol (Esmailzadeh or Azatbakth, 2008). Because phytosterols inhibit the absorption of cholesterol, they can lower LDL and plasma cholesterol (49).

2.4. Antihyperlipidemic

Increased triglyceride or cholesterol levels, or hyperlipidemia, are a major risk factor for the the beginning and development of atherosclerosis, one of the most dangerous illnesses in humans, and consequent cardiovascular disease (50). As a hypolipidemic agent, lovastatin lowers cholesterol in people with hypercholesterolemia, lowering their risk of cardiovascular disease. shown that the triple-negative breast cancer cell line MDA-MB-231 responds to lovastatin's anti-cancer actio The cell line for triple-negative breast cancer MDA-MB-231 reacts to the anti-cancer effects of lovastatin. asserted that 565.4 mg/kg of *Agaricus Bisporus* of lovastatin and proposed that *A. bisporus*, the white button mushroom, lowers serum and/or liver cholesterol levels (46).

2.5. Antimicrobial

According to certain earlier research, *A. bisporus* extracts made with methyl alcohol demonstrated antibacterial properties against a variety of bacteria, yeasts, and dermatophytes. Extracts from *A. bisporus* have been shown to exhibit microbial inhibition (51). As seen in Figure 1, AgNPs, or silver nanoparticles are among most widely employed Nanoparticles of metal and have strong antibacterial and antifungal properties. It is believed that *Agaricus Bisporus* plays a significant Role in the creation of AgNPs, or silver nanoparticles; it was shown that *A. bisporus* ranked second (by roughly 11%) in the synthesis of significant nanoparticles, behind the oyster mushroom *Pleurotus sp* (52).

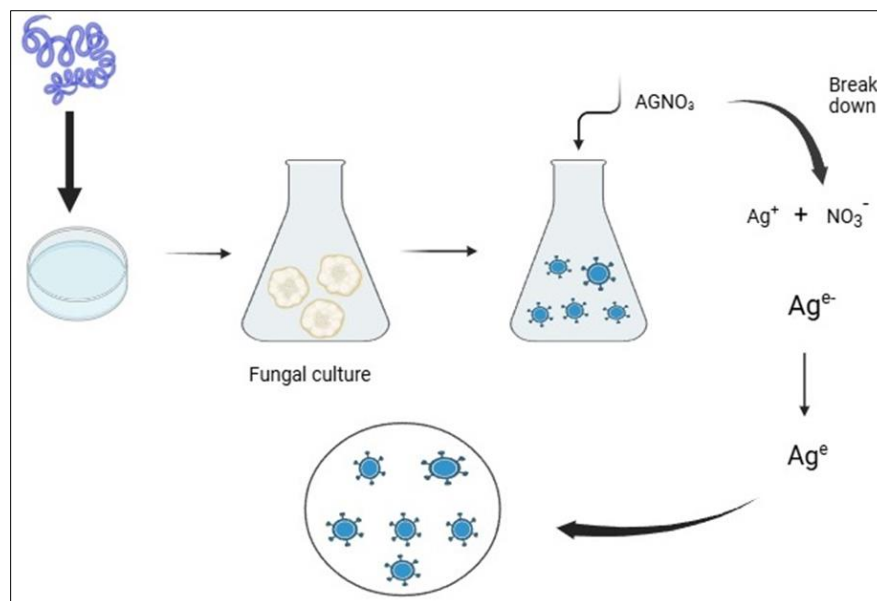


Figure 2 Biosynthesis silver Nanoparticles Using Mushroom *Agaricus Bisporus*

2.6. Anticholesterlomic and antiglycemic

Examining the theory that consumption of WBM fruiting bodies controls antiglycemic reactions was the aim of this investigation. Rats were given a hypercholesterolemic diet for these investigations, and streptozotocin injections caused type 2 diabetes in the rats for three weeks (25). Oral administration of ABP for four weeks significantly reduced plasma TC and LDL in hypercholesterolemic rats, leading to the conclusion that *A. bisporus* exhibited both hypoglycemic and hypolipidemic effects on rats (53).

2.7. Anti inflammatory activity

The anti-inflammatory qualities were tested using activated macrophages. of *A. bisporus* methanolic excerpts , and it was discovered that certain edible mushroom species may have anti-inflammatory properties in vitro (54).

3. Improved dendritic cell maturation from bone marrow

This study investigated how *A. bisporus* supplementation affected the maturation of bone marrow-derived dendritic cells in C57BL mice in vitro (BMDC) and discovered that the manifestation of maturation indicators CD40, CD80, CD86, and major histocompatibility complex-II increased dose-dependently (49).

3.1. Skin disorders

This study's objective was to investigate how isolated *A. bisporus* tyrosinase affected B16F10 melanocytes' ability to produce melanin by inhibiting pigment cell machinery. It was demonstrated using B16F10 melanocytes that pure tyrosinase stimulates melanogenesis because it increases tyrosinase absorption. Purified tyrosinase enhanced melanin concentration and cellular tyrosinase activity in B16F10 melanocytes in a way that is depending on dosage. Based on the results, pure tyrosinase may be utilized as a potential therapy for vitiligious skin conditions (55).

3.2. Antinociceptive properties

Komura et al. demonstrated the anti-inflammatory and antinociceptive properties of mannogalactans, fucogalactans, and fucomannogalactans that were separated from *A. bisporus* var. *hortensis* and *Agaricus brasiliensis* (56).

3.3. *Agaricus Bisporus* as nanoparicles

The methanolic nanoparticles of *A. bisporus* have various advantages to treat cancer, viral, bacterial, fungal diseases, etc, Because there are so many fruiting bodies generated worldwide, this kind of nanoparticle synthesis by edible and medicinal mushrooms is both economical and appropriate for use in nanomedicine (37). As a saprotrophic decomposer of leaf litter, the basidiomycete *A. bisporus* naturally influences the carbon cycle in terrestrial habitats (57).

3.4. Future prospect

Based on a variety of components found in *A. bisporus*, emerging data from fascinating new research indicates that mushrooms may also help to increase energy, reduce fatigue and balance the effects of stress, support healthy skin and hair, cleanse the liver and flush out toxins, enhance brain cell function, and promote memory and concentration (58).

4. Mechanism of action

- **Neurotransmitter modulation** Neurotransmitters implicated in mood regulation, including serotonin, dopamine, and norepinephrine, may be affected by L-lysine in terms of their levels and activity (59).
- **Stress reduction** by modifying the hypothalamic-pituitary-adrenal (HPA) axis, L-lysine may help lower anxiety and stress (60).
- **Antioxidant activity** Due to its antioxidant qualities, L-lysine may help shield the brain from inflammation and oxidative damage (61).

5. Biochemical pathway

- **SEROTONIN PATHWAY** The production of serotonin, a neurotransmitter that controls mood, hunger, and sleep, involves L-lysine (62)
- **Dopamine and Norepinephrine Regulation** Dopamine and norepinephrine are neurotransmitters that are essential for motivation and mood management, and L-lysine may have an impact on their function (63).
- **GABA and Glutamate Regulation** L-lysine may also affect the activity of two neurotransmitters involved in mood regulation: glutamate (an excitatory neurotransmitter) and GABA (an inhibitory neurotransmitter) (64).

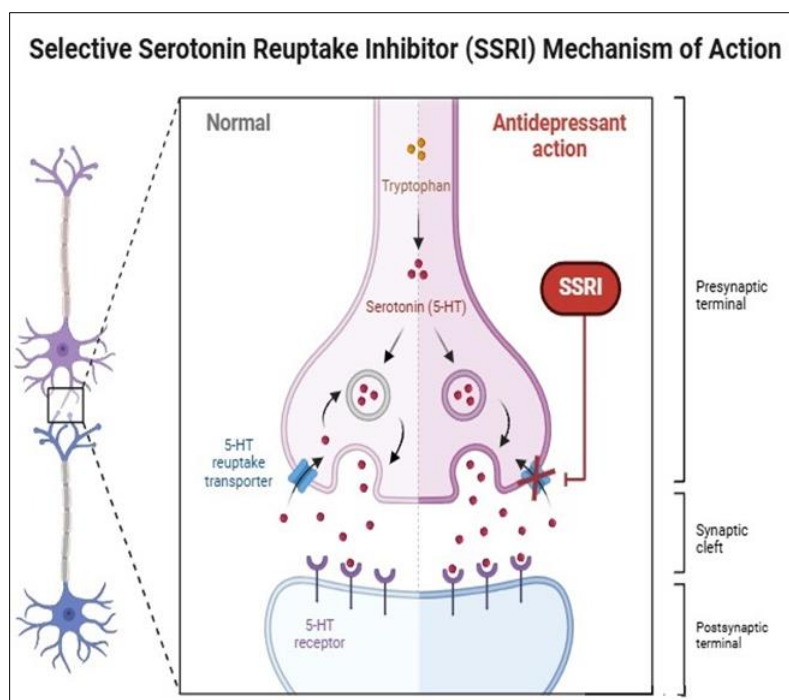


Figure 3 Biochemical Pathway

6. Clinical evidence

- **Reduced Symptoms of Depression:** L-lysine supplementation has been demonstrated to lessen depressive symptoms, such as elevated mood, decreased anxiety, and improved cognitive performance (65).
- **Anxiolytic Effects:** In both human and animal research, L-lysine has been shown to have anxiolytic (anti-anxiety) properties (66).
- **Antidepressant Effects:** Studies on animals have demonstrated that L-lysine has antidepressant properties, and some human research indicates that it might also have antidepressant properties (67).

7. Animal studies

- Decreased stress and anxiety: Studies on mice and rats have demonstrated that L-lysine supplementation reduces stress and anxiety behaviors (68).
- Better mood: In animal models, L-lysine has been shown to elevate mood and lessen Depressive model (69).

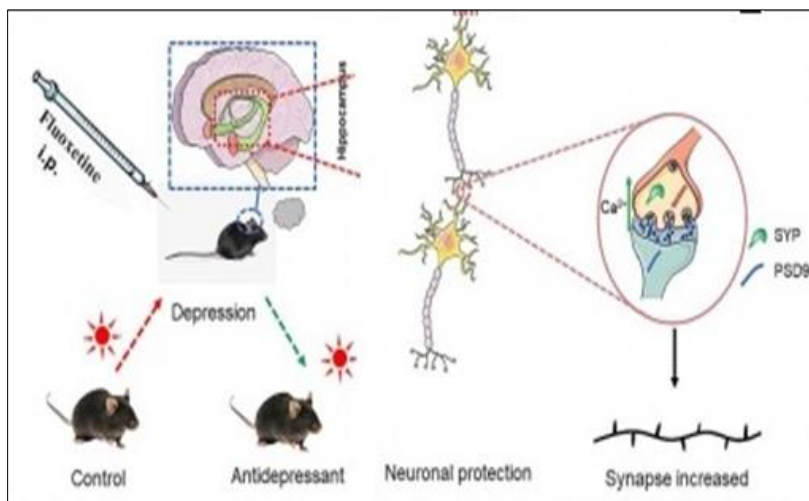


Figure 4 Rat on Antidepressant

7.1. Safety and interaction

- Safety: Although large dosages of L-lysine may result in gastrointestinal adverse effects, it is usually regarded as safe for intake (70).
- Interactions: Blood thinners, diabetic drugs, and immunosuppressants are among the drugs that L-lysine may interact with (71).

7.1.1. Future prospect

Based on a number of components found in *A. bisporus*, it appears that mushrooms may also help to: increase energy, reduce fatigue and balance the effects of stress, support healthy skin and hair, cleanse the liver and flush out toxins, enhance brain cell function, and improve memory and concentration.

Table 5 Patent on *Agaricus Bisporus*

S no.	Patent Number	Title	Description	Assignee	Filing Date
1	US10893921B2	Pharmaceutical composition containing <i>Agaricus Bisporus</i> extract	Treating cancer and immune-related disorders	MycoMed Technologies Inc.	2020-01-17
2	EP3647797A1	Medicinal mushroom extract and uses thereof	Treating various diseases, including cancer, diabetes, and neurodegenerative disorders	Agaricus Biosciences LLC	2020-07-22
3	WO2020121015A1	<i>Agaricus Bisporus</i> -based composition for treating inflammatory diseases	Treating inflammatory diseases, such as arthritis and asthma	Korea University Research and Business Foundation	2020-04-23
4	CN112345191B	<i>Agaricus Bisporus</i> polysaccharide and its	Antitumor therapy	Sichuan University	2020-05-19

		application in antitumor therapy			
5	JP2020515111A	<i>Agaricus Bisporus</i> extract and its use in treating dementia	Treating dementia	Hokkaido University	2020-02-20
6	JP2021522121A	<i>Agaricus Bisporus</i> extract and its use in treating skin diseases	Treating skin diseases, such as acne and psoriasis	Hokkaido University	2021-01-28
7	CN113456921B	<i>Agaricus Bisporus</i> polysaccharide and its application in immunotherapy	Immunotherapy	Sichuan University	2020-12-15

8. Conclusion

Because of its high nutritional content, a bisporus may offer substantial protection against malnutrition, particularly in developing and underdeveloped nations. Although *A. bisporus* has medicinal properties, especially as an antioxidant, antibacterial, anticancer, and anti-cardiovascular disease agent, however it is not good for your diet. In recent decades, edible mushrooms have gained popularity as a source of medication or as an addition to health foods. This adage is appropriate for mushrooms because of their amazing therapeutic food, medicine, and mineral properties. They are therefore a great advantage for human welfare. In the future, *A. bisporus* may be employed to treat a variety of illnesses and serve as a vital component or backbone of research.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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