

## REVIEW ARTICLE

# Therapeutic Value of Medicinal Mushroom *Agaricus blazei* Murill

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## ABSTRACT

*Agaricus blazei* Murill (AbM) is a mushroom that has been utilized in alternative drug to anticipate cardiac disease, diabetes, arthritis, increased cholesterol, cancer, hepatitis and cancers. It contains  $\beta$ -glucan, which contributes to decreasing blood sugar in-vivo and acts against cancer. The extract of this mushroom exerts antioxidant action in-vivo. AbM contains agaritine that exerts antitumor effects against leukemic cells in vitro. This mushroom is also found to have immune-stimulatory function, tumor growth suppression, action against allergy, antiviral effects, antimicrobial function and immune modulatory effects. Researchers also studied its action in decreasing blood cholesterol. According to several studies, AbM containing (1 $\rightarrow$ 6)- $\beta$ -D-glucan-exerts anti angiogenesis action. The purpose of this extensive review on the medicinal value of AbM mushroom was to highlight its significance and its traditional uses by scientific evidence to determine the effectiveness of the mushroom in various evidence-based uses. Google Scholar and PubMed search engines were used to browse articles from 1994-2019 on the therapeutic value of AbM. Initially, 74 articles were found related to the therapeutic value of AbM. After reviewing the available article, 42 were selected based on the medicinal uses of AbM. It was concluded that AbM possessed various bioactive compounds that are responsible for its therapeutic effects.

**Keywords:** Mushroom; Antidiabetic; Therapeutics.

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## INTRODUCTION

*Agaricus blazei* Murrill (AbM) is a mushroom, basidiomycete brown fungus, origin to Brazil. It is extensively utilized for medicinal functions together with non-prescript as a nutritious mushroom as well as in extract form<sup>1</sup>. *Agaricus blazei* is a nutritious mushroom refer to the family Agaricaceae has been frequently utilized as a health nutriment additive to prevent arteriosclerosis, cancer, hyperlipidemia, chronic hepatitis together with diabetes<sup>2</sup>. In Japan *Agaricus blazei* Murrill (AbM) is familiar as Himematsutake, Agarikusutake or Kawarihiratake, in Brazil, it is known as *Cogumelo do sol* and in China as Ji Song Rong<sup>3</sup>. *Agaricus blazei* is thought to be a nutritious mushroom due to having nutritional value; also, the secondary metabolites of this mushroom are varied chemically and

possess an extensive range of biological functions. Including the bioactive substances are minerals, glucan peptides, vitamins, polyphenols, polysaccharides, glycoproteins, polyunsaturated fatty acids and triterpenoids<sup>4</sup>. According to the culture of Brazil, it would be effective against several conditions, for example, hepatitis, atherosclerosis, increased blood sugar, heart disease, dyslipidemia etc<sup>5</sup>. This mushroom possesses immune modulating and antimicrobial effects both in-vivo and in-vitro and as well as it has been used to treat cancer, hepatitis, dermatitis and hyperlipidemia traditionally<sup>6</sup>. The purpose of this extensive review on the medicinal value of AbM mushroom was to highlight its significance and to build upon the existing work in its traditional uses by synthesizing the available information to determine the effectiveness of the mushroom in various

evidence-based uses. This will also support the growing focus on the medicinal value of mushrooms in general and AbM in particular.

## DISCUSSION

*Agaricus blazei* Murill (AbM) is a nutritive mushroom origin in Brazil. It is cultivated in countries like Indonesia, Taiwan, China, Japan and Korea<sup>7</sup>. It is a basidiomycete generally familiar as sun mushroom. It is marketed as a natural form for utilization and to use in capsules, solutions, and syrups in Brazil. Several pieces of research have been revealed that the mushroom *Agaricus blazei* Murill contains polysaccharides, which are produced by mycelial fermentation, are the reason for its anti-tumor together with immune-modulating effects, and possess biological functions as discussed later in this review<sup>8</sup>.

### Diabetes Mellitus

*Agaricus brasiliensis* is the origin of Brazil. It is developed extensively in Japan. It is utilized for the healing of hepatitis, cancer, cardiac disease, dyslipidemia, dermatitis as well as polysaccharides,  $\beta$ -glucan also  $\alpha$ -glucan have been found to exert antimutagenic also immunomodulating actions both in vitro as well as in vivo. The probable system of natural polysaccharides related to Diabetes Mellitus depends on 6 ways which include the development of plasma insulin (decrease of pancreatic glucagon), the elevation of insulin susceptibility (enhancement of insulin resistance), the control of alpha glycosidase enzymes in the bowel (decrease of carbohydrates decomposition and absorption), the elevation of hepatic glycogen (blockage of sugar dysplasia), the increment in the utilization of glucose by peripheral tissue, and the scavenging of free radicals (lipid peroxidation).

Antidiabetic also hypoglycemic effects of this mushroom have been noted. Researchers found that the extract of this mushroom exert marked antioxidant action in streptozotocin-induced diabetic rats showed reduced lipoperoxidation also iNOS expression in the lungs. It has been preferred by these findings that this mushroom markedly decreases oxidative stress also play role in tissue improvement in increased blood sugar. The clinical proofs showed that this mushroom together with antidiabetic agents could enhance insulin blockage in patients having Diabetes Mellitus type-II. One group has noted that antidiabetic action by this mushroom in diabetic rats is because of the suppression of proinflammatory cytokine generation, which leads to the betterment of pancreatic beta cells mass<sup>9</sup>.

An extract of *Agaricus blazei* Murill can reduce blood glucose levels in streptozotocin induced mice and exert an antidiabetic effect. It is composed of  $\beta$ -glucan that is an immunostimulatory

compound and enhances insulin generation. One of the researchers noted that healing by beta glucan, which is contained in *Agaricus blazei* Murill as a chemical compound helps to reduce blood sugar in streptozotocin-induced rats. The mechanism of action is to raise the secretion of insulin from islands of Langerhans also preserving and reproduction of islands of Langerhans cells of both healthy and diabetic mice. *Agaricus blazei* Murill can reduce blood glucose levels in a diabetic state while according to the current study the result indicated that intake of this mushroom by normal people showed no response on random blood sugar level<sup>10</sup>.

### Anti-inflammatory Activity

The nutritious mushroom *Agaricus blazei* Murill has been included in scientific studies due to having immunomodulatory actions. One of the studies has revealed that this mushroom suppresses inflammatory procedures caused by high fat diet in mice by lowering the generation of proinflammatory cytokines (TNF- $\alpha$ )<sup>11</sup>. *Agaricus blazei* Murill stimulates the immune system by enhancing natural killer cell action also activity of macrophage<sup>12</sup>.

The extract of polysaccharides contained in mushroom *Agaricus blazei* Murill exerts antioxidant activity and immunomodulatory function in chicken spleens<sup>13</sup>. The biological functions and several pharmacological actions, which include anti-inflammatory, antitumor, anti-diabetes, immunomodulatory, anti-hypercholesterolemia, anti-oxidant and anti-heart disease effects of *Agaricus blazei* Murill have been noted<sup>14</sup>.

### Anti-cancer Effects

AbM is a traditional remedy against cancer. The active compounds contained in it are polysaccharides have been known to exert inhibitory effects against tumor indirectly by enhancing immune function<sup>15</sup>. *Agaricus blazei* Murill is used as a traditional diet. It is utilized for its antihypertensive, anticancer, lowering blood sugar, lowering cholesterol also immunostimulant effect. This mushroom is composed of  $\beta$ - (1-6) -;  $\beta$ - (1-3) -glucan,  $\alpha$ - (1-4) -;  $\beta$ - (1-6) -glucan,  $\beta$ - (1-6) -;  $\alpha$ - (1-3) -glucan,  $\alpha$ - (1-6) -;  $\alpha$ - (1-4) -glucan, riboglucan, ergosterol, lectins, glucomannan, RNA-protein complex, blazein, sodium pyroglutamate, Agaritin, ascorbic acid, agariblaze-pirol C, total phenol and  $\alpha$ - and  $\delta$ -tocopherol. *Agaricus blazei* Murill is used as a traditional diet.

It is utilized for its antihypertensive, anticancer, lowering blood sugar, lowering cholesterol also immunostimulant effect. This mushroom is composed of  $\beta$ - (1-6) -;  $\beta$ - (1-3) -glucan,  $\alpha$ - (1-4) -;  $\beta$ - (1-6) -glucan,  $\beta$ - (1-6) -;  $\alpha$ - (1-3) -glucan,  $\alpha$ - (1-6) -;  $\alpha$ - (1-4) -glucan, riboglucan, ergosterol, lectins, glucomannan, RNA-protein complex, blazein, sodium pyroglutamate, Agaritin, ascorbic acid, agariblaze-pirol C,

total phenol and  $\alpha$ - and  $\delta$ -tocopherol. Due to the presence of this composition, this mushroom can be utilized as an anticancer agent. According to the study *Agaricus Blazei* Murill extract with solvents such as chloroform, n-hexane, ethylacetate also dichloromethane possess an action against cancer in MCF-7 cells. This extract can be established as an anticancer agent in MCF-7 cells<sup>16</sup>.

Glucan contained in *Agaricus blazei* Murill revealed anticancer effect also having a standardized quantity of beta glucans. Agaritine contained in *Agaricus blazei* Murill showed an antitumor effect against leukemic cells in vitro. It was quite different from beta glucan that inhibits the generation of tumor cells indirectly. The mechanism of action includes apoptosis. Agaritine exerts an antitumor effect directly against leukemic tumor cells in vitro. Moreover, a steroid known as blazein obtained from this mushroom was found to promote cell death also structural variation suggestive of apoptotic chromatin condensation in lung cancer cells of humans. This compound has similar activity on cancer cells of the stomach as lung cancer<sup>17</sup>.

AbM is found to induce apoptosis or programmed cell death in ovarian cancer cells of humans<sup>16</sup>. In mouse models of fibrosarcoma, myeloma, prostate cancer, ovarian as well as lung cancer AbM showed antitumor activities, also in human studies against gynecological cancer (marked Natural Killer cell activity and quality of life) and leukemia<sup>19</sup>.

### Neuroprotective Effects

Administration of extract of *Agaricus blazei* Murill protects the myenteric plexus in animals. The administration of aqueous extract of *Agaricus blazei* Murill sufficiently sustained myenteric plexus homeostasis, which certainly persuades the physiology and inhibits the death of neurons as well as glial cells<sup>18</sup>. Aging mutates morpho-functional, biometric, blood factors in the jejunum, and induce morpho-quantitative variations in enteric NS. Long-term administration of aqueous extract of *Agaricus blazei* Murill greatly sustained myenteric plexus homeostasis that helps to maintain physiology also stops the death of neuron cells<sup>21</sup>.

### Hepatitis

The affirmative outcomes revealed by *Agaricus blazei* Murill in various affected models. According to several clinical evidence, it could be raising therapy for curing various infections also hepatitis specifically for patients having a resistant illness<sup>22</sup>. It was observed that *Agaricus brasiliensis* could suppress the processing of structural processes that form liver necrosis<sup>23</sup>. *Agaricus brasiliensis* is origin in Brazil also cultivated in China as well as Japan due to its medicinal effects. This mushroom has been utilized commonly to prevent several illnesses such as hepatitis. According to some studies, the extract

of this mushroom can improve hepatic injury in rats caused by  $\text{CCl}_4$ <sup>24</sup>. *Agaricus blazei* is commonly utilized to heal numerous conditions like high blood sugar, cardiac disease, increased cholesterol, cancer, and hepatitis and skin diseases. Several clinical types of research showed the possible significance of this mushroom in the therapy of chronic hepatitis.

Some researchers concluded that the polysaccharide extract from this mushroom in a dose of 1500 mg revealed a marked decrease in hepatic enzymes in 4 patients having hepatitis B over a twelve month duration, aspartate aminotransferase decreased from 246 to 61 IU per liter, alanine transaminase from 151 to 46 IU per liter. The extract of this mushroom given to rats was found to decrease the action of plasma alanine transaminase also aspartate aminotransferase increased by  $\text{CCl}_4$ . Some researchers revealed that the extract containing active compounds work on liver cell membrane directly or indirectly to improve liver injury caused by  $\text{CCl}_4$  in rats. Oral intake of fermentation mycelia and broth of this mushroom in mice having liver injury caused by ethanol caused a marked decrease in liver fibrosis<sup>25</sup>. *Agaricus blazei* Murill is a mushroom origin to Brazil.

This mushroom has been used as nutritious food for cancer. It contains biological functions such as antiviral, antibacterial, anti genotoxic, antiparasitic and anti tumoral functions. In addition, it is useful in the therapy of high blood sugar and hepatitis in an animal model<sup>26</sup>. The study helped to guide about 2 probable ways to utilize basidiomycetes to treat hepatitis. One, different basidiomycetes containing compounds have been utilized as stimulants in vaccines. A DNA vaccine can stimulate CD8 (+) T-cell response however, this response is very less in maximum mammals. About this guidance, it was found that injection of DNA vaccine to treat hepatitis together with extract of mushroom *Agaricus blazei* Murill fortified with polysaccharides, which are used as adjuvants to mice markedly, improved humoral as well as cellular immune responses<sup>27</sup>. *Agaricus subrufescens* usually utilized for the therapy of several diseases including liver disease, cancer, increased blood sugar, cardiac disease, skin disease and increased cholesterol.

### Immune Stimulatory Effects

The clinical effects from mushroom *Agaricus subrufescens* that have been reported include immune stimulatory function, tumor growth suppression, action against allergy, anti viral effects, anti microbial function and immune modulatory effects<sup>28</sup>. The fruiting body of *Agaricus blazei* Murill is enriched with  $\beta$ -glucans that helped to stimulate the innate immune system. This compound has been known to have antitumor action in both in vitro and in vivo. For in vitro it is useful for ovarian

cancer, leukemia cells, fibrosarcoma and hepatocarcinoma. For in vivo it is useful for lung cancer, fibrosarcoma and multiple myeloma. Hence, it has been thought that the clinical action of this mushroom is because of  $\beta$ -glucans having immunostimulatory action<sup>29</sup>. The mushroom *Agaricus blazei* Murill has been utilized to cure various illnesses such as cancer as well as infection. *Agaricus blazei* Murill enriched in antitumor protein-glucan complexes as well as  $\beta$ -glucans that are strong stimulators of natural killer (NK) cells, macrophages, dendritic cells and granulocytes.

This mushroom contains stimulatory actions on the formation of proinflammatory cytokines in immune cells as if monocyte-derived dendritic cells as well as monocytic cells<sup>30</sup>. Seeing that in 1960 the Japanese scholars have identified immune modulating together with antitumor functions of *Agaricus blazei* Murill in the mouse. *Agaricus blazei* Murill based mixed basidiomycete mushroom extract was known to be the particular one that markedly decreases bacteria in blood as well as improved survival estimate of the mouse in pneumococcal sepsis. After some time it was called as Andosan™ for trading and selected for more investigations that revealed its defense against allergy also G-negative sepsis in other mouse models. These functions and the antitumor effect of the mushroom presented in Andosan™ is most likely to be because of the immuno-modulatory relative shift stimulated by the mushroom<sup>31</sup>.

#### Hypercholesterolemia

*Agaricus blazei* Murill is found to have clinical effects, is usually utilized in alternative drugs to anticipate cardiac disease, arthritis, increased cholesterol, cancer, hepatitis, and increased blood sugar<sup>32</sup>. One of the studies revealed that administration of *Agaricus brasiliensis* has enhanced the serum lipid levels in rats having high cholesterol by balancing the expression of the main gene associated with the metabolism of liver cholesterol<sup>33</sup>. In Wistar rats it is found that the supplements in *Agaricus brasiliensis* are significant modulators of lipid profile. It has been detected to decrease triglycerides, cholesterol together with lipid deposit on hepatic tissue together with enhancing excretion by faeces<sup>34</sup>.  $\beta$ -Glucan in *Agaricus blazei* Murill is found to reduce blood cholesterol however, the process associated with it is not clear. Mushroom *Agaricus blazei* Murill has been given to albino Fischer rats having hypercholesterolemia for two months. It has been revealed to reduce serum cholesterol as well as bring about marked variations in gene expression associated with cholesterol<sup>35</sup>.

Moreover, studies have been recommended that *Agaricus blazei* Murill has an advantageous role in hyperlipidemia and diabetes together with the enhancement of insulin resistance as a vaccine

adjuvant and has helped to stop tumor development as well as angiogenesis<sup>36</sup>.

#### Angiogenesis

It has been notified that the food nutrients including *Agaricus blazei*-derived ergosterol possess anti angiogenic effect. Studies reported that substance containing (1 $\rightarrow$ 6)- $\beta$ -D-glucan- could exert anti angiogenesis function. The antitumor function together with antitumor immunological effect of *Agaricus blazei* contains (1 $\rightarrow$ 6)- $\beta$ -D-glucan protein complex has been notified. One of the methods has been suggested that the process of angiogenesis can be suppressed by extraction of this mushroom's fruiting body with lesser aliphatic alcohol or lesser aliphatic alcohol having twenty percent or less than twenty percent of water<sup>37</sup>.

Some researchers notified that regular administration of extract of this mushroom for six months has markedly enhanced mental as well as physical constituents of traits of the patient's life. studies suggested that pyroglutamate also ergosterol together with their anti angiogenic effects can be derived from *Agaricus blazei* Murill also  $\beta$ -glucan<sup>38</sup>. Studies revealed that *Agaricus blazei* Murill possesses an effect against angiogenesis means it suppress the development of new blood vessels to the tumor. It also suppresses an enzyme known as aromatase related to the formation of breast cancer<sup>39</sup>.

#### Nutraceutical and Cosmeceutical

One of the research investigated possible reutilization of large-scale dump *Agaricus blazei* Murill. Hence, the constituents of vital supplements as well as chemical constituents were derived. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) tetrazolium reduction assay, also with Lactate dehydrogenase assays were utilized to examine activity as well as cell death of human colorectal adenocarcinoma cell lines HT29 and Caco-2 of *Agaricus blazei* Murill ethanolic extract. *Agaricus blazei* Murill ethanolic extract was added in a semi solid base cream used cosmetically. The cell activity, functions of extracts and finished product ingredient on a keratinocyte cell line HaCaT were analyzed. Principal supplements like carbohydrates, proteins also with a low fat compound were derived for *Agaricus blazei* Murill. Furthermore, its pH was also desirable. The cell activity of HaCaT cells in the extract existence as well as the final product was sustained by the dependence of concentration that showed the safeness of *Agaricus blazei* Murill ethanolic extract for pharmaceutical cosmetic purposes. The outcomes recommend that *Agaricus blazei* Murill remnants can be utilized as a cheap as well as a worthwhile source of pharmaceutical nutrition and pharmaceutical cosmetic components<sup>40</sup>. To the best of our knowledge we are ending the discussion by presenting the summary of the pharmacological activities of *Agaricus blazei* Murill in Table 1.

**Table 1: Summary on pharmacological activities on *Agaricus blazei* Murill.**

Pharmacological Activity	Experimental Designs	Studies
Diabetes Mellitus <sup>9,10</sup>	<i>In-vivo</i>	Vitak et al. 2017
	<i>In-vivo</i>	Misgiati and Corebima, 2015
Anti-inflammatory activity <sup>11-14</sup>	<i>In-vivo</i>	Tontowiputro et al. 2018
	<i>In-vivo</i>	Kang et al. 2015
	<i>In-vivo</i>	Xie et al. 2017
	<i>In-vitro</i>	Hahne et al. 2014
Cancer <sup>18,41-42,44</sup>	<i>In-vitro</i>	Misgiati et al. 2017
	<i>In-vitro</i>	Itoh, Ito and Hibasami, 2008
	<i>In-vivo</i>	Hsu et al. 2008
	<i>In-vivo</i>	Førland et al. 2011
Neuroprotective <sup>21</sup>	<i>In-vivo</i>	Santi-Rampazzo et al. 2015
Hepatitis <sup>23-24,43</sup>	<i>In-vivo</i>	de Souza et al. 2018
	<i>In-vivo</i>	Zhang et al. 2015
	<i>In-vivo</i>	Wang and Ma, 1994
Immune stimulatory effects <sup>29-31</sup>	<i>In-vitro and In-vivo</i>	Tangen et al. 2015
	<i>In-vitro</i>	Tangen et al. 2014
	<i>In-vivo</i>	Hetland et al. 2016
Hyperchol esterolemia <sup>33-34</sup>	<i>In-vivo</i>	de Miranda et al. 2017
	<i>In-vivo</i>	Henriques et al. 2016
Angiogenesis <sup>37-38</sup>	<i>In-vitro</i>	Ito et al. 2016
	<i>In-vivo</i>	Kimura et al. 2015
Nutraceutical and cosmeceutical applications <sup>40</sup>	<i>In-vitro</i>	Taofiq et al. 2019

### CONCLUSION

Therapeutic use of Mushroom *Agaricus blazei* Murill in diseases such as Diabetes Mellitus, Neuroprotection, Cancer, Hepatitis, Immunomodulatory agent, Hypercholesterolemia, Angogenesis and Cosmetics was highlighted which contains constituents like  $\beta$ - (1-6) and Agaritine that helps to cure various diseases. Hence, *Agaricus blazei* Murill is a promising drug for improved health. AbM also possessed various bioac-

tive compounds that are responsible for its therapeutic effects.

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### CONFLICT OF INTEREST

The authors proclaim that they have no conflict of interest.

### AUTHORS' CONTRIBUTION

All authors contributed equally to this review article and were involved in drafting the manuscript. All authors read the manuscript and approved the final version.

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