

## TRUTHS AND MYTHS ABOUT THE MUSHROOM *Agaricus blazei*

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**ABSTRACT:** The mushroom *Agaricus blazei* Murrill was discovered in Piedade, state of São Paulo, Brazil, and sent to Japan to be studied for its medicinal properties. Studies in guinea pigs revealed antitumor properties, triggering Japanese importation of *A. blazei* from Brazil. Because of its high price on the international market, many companies and rural growers produce *A. blazei* as alternative crop to increase income, but because interest in this mushroom occurred suddenly there has not been enough time for the scientific community to investigate it and, technology used for its cultivation is still based on empirical rules. There are also some contradicting data regarding the classification of this mushroom, and its antitumor properties still need to be confirmed in humans.

Key words: antitumor properties, cogumelo do sol, royal agaricus, sun mushroom

### VERDADES E MITOS SOBRE O COGUMELO *Agaricus blazei*

**RESUMO:** O cogumelo *Agaricus blazei* Murrill foi descoberto na cidade de Piedade, Estado de São Paulo, Brasil, e enviado para o Japão para o estudo das suas propriedades medicinais. Com a descoberta das suas propriedades antitumorais, comprovadas em cobaias, o Japão passou a importar esse cogumelo do Brasil. Devido ao seu elevado preço no mercado internacional, muitas empresas e produtores rurais passaram a buscar nesse cogumelo uma nova alternativa de renda. Diante de um interesse tão repentino, não houve tempo para que a comunidade científica pesquisasse o assunto, de maneira que a tecnologia de cultivo é ainda muito empírica. Além disso, existem informações contraditórias acerca da classificação desse cogumelo e as suas propriedades antitumorais ainda precisam ser confirmadas em seres humanos.

Palavras-chave: cogumelo do sol, propriedades anti-tumorais, royal agaricus

### INTRODUCTION

From the early days of civilization, man has used fungi for the production of fermented foods and beverages, or directly as food. In Ancient Egypt, fermentation was considered a gift from the god Osiris, while ancient Romans attributed the emergence of mushrooms and truffles to lightning bolts cast to the earth by Jupiter (Alexopoulos et al., 1996).

For centuries, Asians have attributed curative properties to some mushrooms. Reports from China since about 500 BC, on the medicinal properties of *Ganoderma lucidum* (known in China as reishi) extracts, especially its anti-cancer properties, have been passed on generation to generation (Mizuno et al., 1995a; 1995c), and since the Ming dynasty (1620 AD), there have been reports on the medicinal properties of *Lentinula edodes* (shiitake) mushrooms, considered an elixir of life and possessing the ability to enhance 'vital energy' and cure colds (Mizuno, 1995a).

In the late Twentieth Century, researchers in Japan demonstrated the antitumor effects of a Brazilian

mushroom, identified as *Agaricus blazei* Murrill, which became subject of studies by several research groups (Kawagishi et al., 1988; 1989; Osaki et al., 1994; Itoh et al., 1994; Higaki et al., 1997; Ito et al., 1997). These studies increased interest for *A. blazei* among the Japanese, and so it began to be imported from Brazil, enticing many Brazilian mushroom growers to begin cultivating *A. blazei* which became an excellent source of increased income. However, because of the reported medicinal importance of *A. blazei*, some producers registered names or brands indicating that this mushroom was their own product, making difficult the scientific identification of *A. blazei* strains. There is therefore a need to clarify several points regarding *A. blazei*, so that this important mushroom is not monopolized by only a few producers but can be freely cultivated by small farmers, who have actually been growing it for a long time in Brazil. More widespread cultivation of *A. blazei* would mean that this mushroom would be cheaper for Brazilian consumers, who cannot at present afford to buy it, and cease to be a product for export only.

### Mushrooms as a source of antitumor substances

According to Mizuno et al. (1995a), one of the pioneer studies regarding the antitumor activity of mushrooms was published by Ikegawa et al. (1968). These authors described potent antitumor activity in aqueous extracts of some mushrooms, including members of the Polyporaceae family, to which *Ganoderma lucidum* belongs. Later on, Chihara et al. (1970) reported the purification of shiitake polysaccharides with high antitumor activity. In the sequence, one of these polysaccharides, lentinan, started being commercialized by a Japanese company for the treatment of stomach cancer (Mizuno et al., 1995b). From that on, numerous reports have been published describing the isolation and study of substances with medicinal properties from a large number of mushroom species. In addition to lentinan, two other cytostatic drugs have been isolated in Japan: krestin, produced by *Coriolus versicolor* mycelium and used in the treatment of cancers of the gastrointestinal tract, lung and breast; and schizophyllan, (or Sonifilan), extracted from the culture medium of *Schizophyllum commune* and used in the treatment of cervical cancer (Mizuno et al., 1995b).

Although there is no commercial production of the purified compound responsible for the medicinal properties of *A. blazei*, several studies have been carried out to isolate and characterize *A. blazei* polysaccharides with antitumor activity (Kawagishi et al., 1989; Mizuno et al., 1990a; 1990b; Ito et al., 1997; Fujimiya et al., 1999). Based not only on indigenous or Oriental traditions, but also on experiments in which many mushrooms have been screened for substances with pharmacological properties, it is currently accepted that host edible mushrooms have some pharmacological property.

One of the great hurdles in making the medicinal properties of mushrooms more widely known is that many of the earlier studies were published in Japanese, and many of the clinical studies published in Oriental journals do not last for long (Mattila et al., 2000). Longer studies covering the entire lifespan of the test animals are then needed to assess the medicinal properties of mushrooms.

### The situation in Brazil

Contrasting to Asian, European, and North American countries, the consumption of mushrooms in Brazil has always generally been restricted to small ethnic communities or to higher economic and/or cultural status groups. The most widely consumed mushroom worldwide is *Agaricus bisporus*, which is also the most popular mushroom eaten in Brazil, although because of its relatively high price, the use of *A. bisporus* is generally limited to gourmet cuisine. Even though medicinal plants are widely used in Brazil, there is no traditional use of mushrooms in Brazilian practical medicine, although there has recently been greater interest in mushroom

consumption with the growing awareness of the isolation of substances with medicinal properties from various mushroom species. Besides their medicinal properties, edible mushrooms have been considered a health food because they are low in fat, rich in vitamins and amino acids and, compared to most vegetables, high in protein (Crisan & Sands, 1978). With the greater popularization of these properties and of their culinary qualities there has been a slow but noticeable change in the habits of Brazilians regarding the consumption of mushrooms, and as a result, there is currently a considerable number of Brazilian mushroom growers interested not only in *A. bisporus* but also in other mushrooms, such as *Pleurotus ostreatus* (hiratake and shimeji), *Pleurotus sajor-caju* (houbitake) and, especially, *Lentinula edodes* (shiitake), all valued not only for their medicinal properties but also for the preparation of gourmet food.

Since the 1990s, there has been a growing interest in Brazil in the cultivation not only of the mushrooms above mentioned but also in the 'new' mushroom species, discovered in the Brazilian town of Piedade in the Brazilian state of São Paulo in 1960 by a grower and researcher named Furumoto, who sent it to Japan in 1965 for investigation (Mizuno, 1995b). This mushroom was identified as *Agaricus blazei* Murrill by the Belgian scientist Dr. Heinemann in 1967 (Heinemann, 1993; Mizuno, 1995b) and was given the common name of Himematsutake in Japan, while in Brazil it was named the Piedade mushroom after the town where it was discovered, and later known as either medicinal mushroom or Sun Mushroom® (Cogumelo do Sol® in Portuguese) in Brazil and the Royal Sun Agaricus® in other countries. After the death of Mr. Furumoto, cultivation of *A. blazei* was abandoned and it was only in 1990 that its cultivation was revived as a result of the interest of some Japanese businessman who brought *A. blazei* strains back from Japan where they had been used in antitumor activity studies (Fujimiya et al., 1998; 1999; Kawagishi et al., 1988; 1989; Osaki et al., 1994; Itoh et al., 1994; Ito et al., 1997). According to Ernesto N. Uryu, an agronomist at an organization for technical assistance (Coordenadoria de Assistência Técnica Integral - CATI, Sorocaba, São Paulo, Brazil) and a contemporary of Mr. Furumoto, the mushrooms originally grown by Mr. Furumoto had a very strong aroma and flavor which made them difficult to eat, but the strains brought from Japan had lost many of their original characteristics and had acquired a more pleasant smell, a lighter coloration, and were bigger (personal communication, 1998).

Because of the interest of the Japanese market a new phase in the cultivation of mushrooms was initiated in Brazil in which *A. blazei* had the status of an export product, with higher prices in comparison to other mushrooms, and *A. blazei* began to represent an optimal alternative cash crop for small rural growers. The lack of sci-

entific studies on *A. blazei* meant that it was cultivated empirically based on the cultivation of *A. bisporus*, which has a very similar life cycle, although differing in the terms of environmental factors, *A. bisporus* being a temperate species with optimal fruit body initiation at 17°C, while *A. blazei* is a tropical species, with optimal fruit body initiation at 25°C.

Several Brazilian publicly funded institutions are currently engaged in research on *A. blazei*, studying biochemical, physiological and genetic aspects of this fungus and carrying out applied research on the selection of compost, soil casing techniques and optimization of the environmental conditions needed for the growth of *A. blazei*. Such research means that the cultivation of this mushroom can be carried out on a scientific basis taking into account the particularities of the species.

Studies describing the antimutagenic properties of *A. blazei* have already been published in Brazil. Delmanto et al. (2001) used mice to show the antimutagenic activity of an aqueous extract of *A. blazei*, antimutagenic activity only being observed when the extract was obtained by mixing extracts from three different *A. blazei* strains. These results indicated that differences between strains or growth conditions might influence the medicinal properties of *A. blazei*. Menoli et al. (2001) observed that a mixture of extracts from the same strains described by Delmanto et al. (2001) showed antimutagenic activity against Chinese hamster V79 lung cells treated with methyl methanesulfonate. Research has also been published on clinical studies employing the mushroom described as *Agaricus sylvaticus* (Gennari, 2000a) (which may in fact be *A. blazei*), including studies of the effects of this mushroom on cancer and AIDS (Gennari, 2000b) and on increased numbers of natural killer cells in cancer patients (Gennari et al., 2001).

### Medicinal mushrooms: science versus profit

With the discovery of the antitumor properties of *A. blazei*, many companies began to commercialize the dehydrated mushroom for export and, on a smaller scale, for the Brazilian market. In Brazil, a prominent feature of the mushroom industry has been the broad popularization of the medicinal properties-bearing mushrooms, but because of the unethical way that these medicinal properties were marketed, the health claims have been viewed with suspicion. Some accusations have been made, especially on television, that companies were selling mushroom products and promising results that had not yet been proved scientifically because of the lack of research showing the same antitumor activity in humans as had been demonstrated in animals. Decree 396/1999 of the Brazilian Ministry of Health prohibits the sale of foods with medicinal properties or the suggestion that they can be used for the treatment or prevention of diseases.

Another negative aspect created by purely economic interests is the attempt to exclusively exploit this mushroom. Despite the fact that the term Cogumelo do Sol<sup>®</sup> became popular among growers as a common name for the species *Agaricus blazei*, the name Cogumelo do Sol<sup>®</sup> was registered as a trademark by a company in São Paulo. In addition to appropriating a name already in common use, the same company reported that, based on a study by Dr. Pegler of the Royal Botanic Gardens London (see below), their Cogumelo do Sol<sup>®</sup> was very similar to *Agaricus sylvaticus* Shaeffer and that it was the result of the fusion of several fungi and a hybrid not found in nature. There is a series of contradictions in the information regarding *A. blazei* presented by this company. First, there is no report whatsoever in the scientific literature of a fungus with the name *Agaricus sylvaticus* Shaeffer although there is an *Agaricus silvaticus* Schaeffer. Because of the similarity between these names it is almost certain that the so-called *A. sylvaticus* Shaeffer was identified as a species (*Agaricus silvaticus* Schaeffer) already known for decades. Someone, probably by mistake, took it upon themselves to change or omit some letters, substituting the letter 'i' in the scientific name by 'y' and omitting the letter 'c' in the author's name. The mushroom *A. silvaticus* is described in the literature as being native to temperate regions, contrary to what is known for the mushroom found in the Piedade region of São Paulo and which was sent to Japan for identification, this mushroom growing well at about 25°C. Some samples of the Piedade mushroom were sent from Japan to Dr. Heinemann in Belgium, who identified them as *Agaricus blazei* Murrill, while the Biological Institute of São Paulo sent other samples to Dr. Pegler who Fellippe Jr. (1999) erroneously reported as having identified them as *Agaricus sylvaticus* Shaeffer. It looks like the samples were identified as different species and that Dr. Pegler probably did not consider it a new species but that it was similar to *Agaricus silvaticus* Schaeffer.

The few scientific reports on the Cogumelo do Sol<sup>®</sup>, citing it as the Royal Sun *Agaricus*<sup>®</sup>, refer to it as a natural variant of *A. blazei*, but if this is true, then *royal agaricus* could never have been considered as a new species but only as one of the numerous strains of *A. blazei*. As far as we know no paper has been published in scientific journals on the antitumor properties, or any other therapeutic action, of *A. silvaticus*, although some internet sites mention it as a poisonous species capable of causing flue-like symptoms.

The claim that the Cogumelo do Sol<sup>®</sup> was a result of the fusion of various fungi does not have any scientific support, because the fusion of fungi to produce a new species does not readily occur. If this did indeed happen there should have been a detailed description of the methodology, preferably published in a peer-reviewed journal, and the fact that there is no scientific support for strain fusion casts doubts on the consistency of much of



the information published on the sun mushroom, which may not necessarily be true.

Considering all the above, it is evident that there is a need to clarify the identity of the Cogumelo do Sol<sup>®</sup>. Dr. Mizuno, one of the icons of Japanese medicinal mushroom research, referred to what is now known as Sun Mushroom (Cogumelo do Sol<sup>®</sup>) as the Royal Agaricus or *Agaricus blazei* Murrill (Mizuno, 2000), while in a technical study, Stamets (2000) referred to it as the Royal Sun Agaricus<sup>®</sup> or *A. blazei* Murrill. Scientific recognition of the medicinal properties attributed to the Sun Mushroom (Cogumelo do Sol<sup>®</sup>) always refer to it as *A. blazei* Murrill, this being the nomenclature adopted by the scientific community in both Brazil and Japan.

Colauto et al. (2002) genetically characterized several *A. blazei* Murrill isolates using random amplified polymorphic DNA (RAPD) and found little genetic variability between the isolates, with isolates ABL 97/11, ABL 99/25 and ABL 99/29 being identical and isolates ABL 99/28 and ABL 99/26 (isolate Jun 17, which has been used in studies in Japan and at the University of the State of São Paulo, Brazil) being more divergent, isolate ABL 99/26 showing the greatest genetic distance. Although there is a close genetic relationship between the strains commercialized in Brazil, it is possible to detect some genetic variability among them. From our point of view, it would be very interesting if the mushroom commercialized as *Agaricus sylvaticus* could be genetically compared with all known strains of *A. blazei* to establish its genetic distance.

Since *Agaricus blazei* Murrill is of North America origin, Wasser et al. (2002) has proposed that the Piedade mushroom constitutes a new subspecies, *Agaricus blazei* Heinemann native to South America. In fact Wasser et al. go further and suggest that *A. blazei* Murrill and *A. blazei* Heinemann represent two different species and that *A. blazei* Heinemann should be renamed as *Agaricus brasiliensis* S. Wasser, M. Didukh, de Amazonas et Stamets sp. Nov., syn: *A. blazei* Murrill ss. Heinemann., Bull. Jard. Bot. Belg. 62: 365-368, 1993. The synonym *A. blazei* Murrill ss. Heinemann may be more useful commercially for the producers because the Piedade mushroom is well-known by the name *A. blazei* not only in Brazil but also in Japan, which is the main market for this mushroom, changing its name to one more obviously Brazilian could affect consumer perception of this product.

## FINAL CONSIDERATIONS

Whether or not the mushroom commercialized exclusively as the 'Sun Mushroom' or the 'Royal Agaricus' possesses medicinal properties is not disputed here. Instead, what we are questioning is the lack of consistency in the taxonomy of the species and its origin.

While it is important to have clinical studies of the medicinal properties of mushrooms it is also important to have a solid scientific basis in terms of microbiology and genetics and health professionals who carry out such studies need the support of professionals with taxonomic experience to avoid the use of inappropriate terms and expressions. Another important point is that these professionals should be objective and not compromised by the need to produce the results desired by commercial interests.

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