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REVIEW

Use of Macrofungi in Traditional and Complementary Medicine Practices: Mycotherapy

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Abstract
Modern people have increased their living standards due to the development of technology. However, health problems have increased with increasing living standards. Efforts to return to nature and natural products such as herbal drugs, medicinal mushrooms and traditional medicine practices have become popular. Medical mushrooms, which have an important place for human beings at every stage of history; in recent years, has succeeded to take its place from traditional medicine applications by separating itself from phytotherapy applications. The aim of our research is to raise awareness about this value, which is present in our country, which has a rich mycota, and to make determinations regarding its usage areas in the world and its importance in the history. Our study could be regarded as a resource for the practices and future studies in our country.
Keywords: Medicinal Mushrooms, Macrofungi, Tradional and Comlementary Medicine

INTRODUCTION

According to the World Health Organization (WHO); "Traditional medicine dates back to an ancient time. It is a collection of knowledge, skills and practices based on theory, beliefs and experiences of different cultures that are also used in the protection of health such as protection from physical and mental illnesses. It has all along been supportive and complementary methods to modern medicine"[1]. Traditional and complementary medicine practices, which have been used in folk medicine for thousands of years, have been collected under three main headings: 1. Natural products (medicinal plants, macrofungi, probiotics etc.), 2. Mind and body medicine (meditation, acupuncture etc.), 3. Physical applications (massage, osteopathy etc.)[2]. It is known that natural products in medical plants, probiotics and macrofungi have been used by every society in every period of history to protect against diseases, strengthen immunity or treat diseases. Ninova tablets dated back to B.C. 1000; founded in Mesopotamia, Assyrians, Sumerians and Akat proved that herbal treatments have an important place among traditional medicine practices. Approximately one thousand medicinal plants are mentioned in the works of Rig Veda, which is accepted as one of the important representatives of Indian medicine. Nearly 400 herbal drugs have been mentioned in the works of Eskulap, one of the important names of Greek medicine, and Hippocrates, the father of modern medicine[3]. The use of mushrooms for medicinal purposes, like plants, is as old as human history. There is evidence that mushrooms are used both in food and medicine in ancient Chinese, Egyptian, Roman and Greek civilizations. It is known that Hippocrates recommends mushrooms to treat certain complaints[4]. In Egyptian civilization, it is known that people believe that mushrooms are a gift of the god Osiris. In ancient Rome, there are sources indicating that mushrooms were accepted as "the food of the God" and that they were made of lightning thrown from Jupiter to the world during storms[5,6]. In ancient times, humankind separated edible mushrooms from poisonous mushrooms by trial and error, and as a result of these experiences

they distinguished poisonous, hallucinogenic or medicinal mushrooms[7,8]. Thus, macrofungi have played an important role in the history scene for centuries as a delicious food, a healing tea, a magic shaman cure, or a deadly poison responsible for the emperors' death[9]. With all these features, mushrooms have managed to be the passion of people since the early ages. The most important reason for this is that it is a delicious food as well as a deadly poison. Apart from being a delicious food, the magic mushroom of the shamans, the healing source of the Far East, or a deadly poison responsible for the death of emperors, mushrooms is a passion for some people. Every year, these passions bring together thousands of people from all over the world at mushroom festivals (Figure 1)[10]. Mushrooms have long been a tasty food alternative for many societies around the world in the early ages, people discovered which mushrooms are edible, poisonous or halisunogic by

Figure 1. Metropolitan Municipality Wild Mushrooms Training Festival Ida Mountains Mushroom Hunt (2017)

trial and error. Wild mushrooms in many parts of the world are regularly collected and used directly as a primary food source, or soups, stews and it is added to beverages such as tea[8].

The use of mushrooms in traditional medical practice dates back to Neolithic time[11]. Nearby the Bronze Age Ice Man discovered in the Alps in 1991; clothes, equipment and two types of mushrooms (*Fomes fomentarius* (L.) Fr. and *Fomitopsis betulina* (Bull.) BK Cui, ML Han & YC Dai (also known as *Piptoporus betulinus* (Bull.) P. Karst**.**) that he carried with him were found. While *Fomitopsis betulina* is believed to be used for medical purposes, the other species is considered to be used as a matche for making fire [12]. The use of macrofungi in traditional medicine is arguably the most popular in the Far East, especially in China. As a proof of the use of macrofungi in Chinese Traditional Medicine which dates back to a long time, the mention of Lingzhi (*Ganoderma lucidum* Curtis) P. Karst.) (Figure 2) in the 2000-year-old poem of the Chinese Han dynasty can be shown[13]. Today, commercial, ecological, pharmacological, and medical value of macrofungi are increasing. In this study, traditional and medicinal uses of medicinal mushrooms are compiled.

KINGDOM FUNGI

1. What is Fungi?

The common feature of the kingdom fungi, which contains a wide variety of groups, is the eukaryotic cell structure, the presence of chitin on the cell wall and the formation of zygote by undergoing meiosis[14]. The kingdom Fungi contains one of the most diverse groups of organisms on Earth, and they are integral ecosystem agents that govern soil

carbon cycling, plant nutrition, and pathology.

Figure 2. *Ganoderma lucidum*

Macrofungi are specific part of the kingdom fungi that include the divisions *Ascomycota* and *Basidiomycota*[15,16]. They are multicellular or single-celled eukaryotic, high-structure organisms that live as parasites or saprophytes that do not carry chlorophyll[17]. Fungus cells with a cylindrical structure are called hyphae. The intermediate wall between the hyphae is called the septum. Some hyphae are without compartments. Hyphae usually grow from their ends. The wall structures of mushrooms are usually chitin in higher forms but some fungi contain cellulose[18]. Hyphae unite to form micelium, and micelium combine to form masses of micelium called mycelia. The term "mushroom" refers to the fructification body formed by stacking mycelium stacks in appropriate ecological conditions[19,20].

2. Fungal Classification

The kingdom Fungi contains four major divisios *Chytridiomycota* (Chytrids), the *Zygomycota* (conjugated fungi), the *Ascomycota* (sac fungi) and the *Basidiomycota* (Figure 3)[14]. Among them, Basidiomycota and Ascomycota commonly grow to sufficient sizes to be recognized as larger fungi[21].

3. Commercial Value of Mushrooms

There are more than 100.000 identified fungal species[22,23] on earth, but about 2.000 of these are edible mushrooms[24,25]. Wild mushroom gathering, a popular occupation among the Khasi tribe of Northeastern India from the early ages to the present day; became an important income generating activity for gastronomic and medical uses in Japanese community, China, Turkey and more than 85 countries in Eastern Europe. Thus, it has acquired an important commercial value. Organized in various regions of the world and in our country for decades and hosting thousands of mushroom enthusiasts, Mushroom Festivals are the most important evidence of the increasing commercial value of macrofungi[10] (Figure 4-5)[26,27]**.** However, there are dozens of mushrooms, such as truffle mushrooms, morel mushrooms, Reishi mushrooms or Lingzi, which have important commercial value for their world-class taste or medicinal value.

For example; Lingzi (*G.lucidum*) extracts with a wide range of products from cosmetics to food supplements has commercial value exceeding four million dollars[28,29] in the world. Shiitake has been used as a source of medicine, especially in Asian Countries such as China and Japan. It has been cultured in the Far East since ancient times because of its medicinal properties. Today, its culture is done all over the world.

USE OF MUSHROOMS IN TRADITIONAL AND COMPLEMENTARY MEDICINE APPLICATIONS IN HISTORY

In Asian countries (Korea, Japan, China) approximately 300 mushroom species are used as drugs[30].

Olympic athletes in 7000 BC; are known to use stimulants naturally obtained from hallucinogenic mushrooms for fatigue and injury treatments[31]. About 270 mushroom species are considered therapeutic in Chinese Traditional Medicine (TCM). Some traditionally used edible mushrooms *Lentinula edodes* (Berk.) Pegler (Figure 6), *Grifola frondosa* (Dicks.) Gray (maitake), *Hericium erinaceus* (Bull.) Pers *Flammulina velutipes* (Curtis) Singer, *Pleurotus ostreatus* (Jacq.) P. Kumm., and *Tremella mesenterica* Retz. are also a source of pure bioactive compounds; non-edible rechargeable species with medical use such as, *G.lucidum*, *Schizophyllum commune* Fr. and *Trametes* versicolor (L.) Lloyd are used for medicinal properties only. The term "Medicinal Mushroom" today is accepted worldwide[7].

It is known that macrofungi have been used in folk medicine in ancient Chinese, Egyptian, Roman and Greek civilizations throughout history. Recently, as in far east medicine, the use of macrofungi in western countries has increased, especially in allopathic medicine. Europen people

therapeutically used *F.fomentarius*, *Inonotus obliquus* (Fr.) Pilát and *Fomitopsis officinalis* (Vill.) Bondartsev & Singer [32]. In Traditional Chinese Medicine, *H. erinaceus* is used to treat symptoms related to gastric ulcers[33]. In Asia, Russia, USA, Canada, Mexico, and in Venezuela; It is known that mushroom use has a long history in the treatment of various diseases[30,34–36]. According to folkloric reports from Siberia, the Baltic and Finland, a tea prepared from a premature fruiting bodies of a certain fungus were given to cancer patient until a prognosis is achieved.

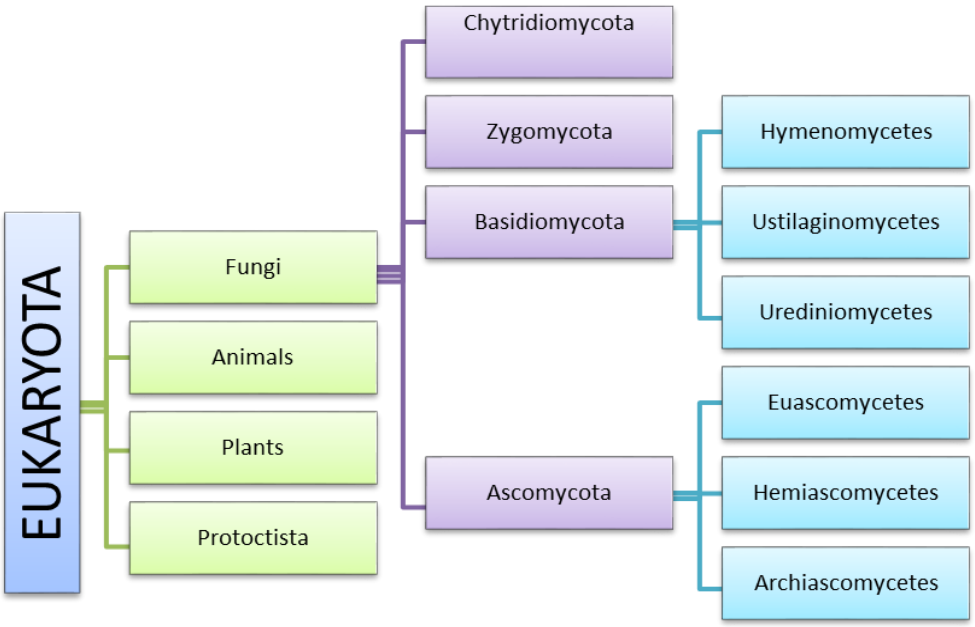

Figure 3. Major kingdoms of the Eukaryota, the four divisios of the Fungi, and the three classes of the Basidiomycota and the Ascomycota [14]

It was considered a tonic, blood purifier and pain reliever and was widely used against cancer in the 1960s in Poland[34]. According to literature, Avicenna recommended truffles, wild boar meat, phlebotomy and balanced nutrition for the treatment of Epilepsy[37].

Figure 4. Mt. Pisgah Mushroom Festival, Eugene Oregon

Figure 5. The Richmond Mushroom Festival (2019)

The blood clotting effect of *Auricularia auricula-judae* (Bull.) Quél. (Figure 7), known as the "ear fungus" among the people, in some communities, the blood stopping effect of *Lycoperdon* Pers.(Figure 8) and some *Polyporus* P. Micheli ex Adans. species in the umbilical hemorrhage of newborn babies and nasal bleedings, in some societies, the weaning effect of *Laricifomes officinalis* (Vill.) Kotl. & Pouzar in controlling the milk secretion and the healing effect of *Lactarius* (L.) Pers. milk in viral wart treatments were all along known by the people.

Figure 6. *Lentinula edodes*

Fomitopsis officinalis (Vill.) Bondartsev & Singer is known to be used in some societies to control milk secretion at the time of weaning and *Lactarius piperatus* (L.) Pers.'s milk is used against viral warts[9]. *Geastrum triplex* Jungh.; it is caustic, detoxic, strengthens the throat and lungs and regulates body temperature and lowers fever [38]. It is also said to reduce respiratory inflammation. According to the literature, laryngitis is boiled together with licorice for sore throat and cough. It is used to stop bleeding and reduce swelling[38]. The yeast used the spores of the *Geastrum* Pers. species to treat wounds[39]. There are sources in North America that Cherokee natives apply the powders of some Geastrum species to the umbilical cord after birth as hemostatic and antibiotic[40]. A mushroom used in the treatment of various cancers in the north-west of Russia and grown on birch is noted in Russian folklore. Being known as Chaga (*I. obliquus*), this fungus is well known in Russia with its anti-cancer properties[41]. *Hericium* species are edible medicinal mushrooms in the *Basidiomycota* class in *Hericiaceae* family types. In China and Japan,it is widely used as a medicine

Figure 7. *Auricularia auricula-judae*

as well as a food source[42,43]. Being known as "Red Immortal Mushroom Lingzi or Reishi"; *G. lucidum* has been used in Chinese and Japanese folk medicine for more than 2000 years.

Figure 8. *Lycoperdon perlatum* Pers.

It is preferred as a natural medicine in the treatment of diseases such as liver disorders, cancer, bronchitis, arthritis and hypertension[9]. It is known that *L.edodes*[44], whose common name is 'Shiitake' in Japan, is used in diseases that suppress the immune system such as AIDS, cancer, environmental allergies, Candida infection, recurrent flu and colds. Shiitake is also known to be good for chronic high cholesterol, where it relieves bronchial inflammations and regulates the problem of urinary incontinence. *L. edodes*, which is among the top five cultivated mushrooms in the world[45,46], is among the important medicinal mushrooms with its lentinan content.

MUSHROOMS AND COSMETICS

Today, cosmetics with commercial value contain products of herbal origin. In addition to the herbal cosmetics, cosmetic products containing fungi include anti-aging, antioxidants, skin care products (Figure 9-10)[47,48] such as skin brightening and hair products[49].

Figure 9. Cosmetic product containing mushrooms

MUSHROOMS AND MEDICINE

1. Poisonous Mushrooms

Although mushrooms are among the foods that are high in nutrients and are a cosmetic raw material with a high commercial value, they come to the fore with their hallucinogenic properties and toxins they carry. Their bad reputation due to their undeserved toxins negatively affects mushroom consumption in our country. Among the more than 22,000 species of macrofungi, the number of species with medical value is considerably higher than that of poisonous species.

2. Medicinal Mushrooms

Mushrooms are thought to possess around 130 medical functions[11]. These medical functions can be listed as antitumor, immunomodulator, antioxidant, radical scavenger, cardiovascular, antihypercholesterolemic, antiviral, antibacterial, anti-parasitic, antifungal, detoxification, hepatoprotective and antidiabetic activity. In addition to these medical effects, psychiatric science and practice also benefited from the discovery and subsequent research of hallucinogenic mushrooms[34].

Figure 10. Cosmetic product containing mushrooms

Fungi contain a wide variety of bioactive molecules, such as polysaccharides, proteoglucans, terpenoids, phenolic compounds, steroids, and lectins. These molecules have therapeutic effects and function as immunostimulating, anticarcinogenic, antiviral, antioxidant and anti-inflammatory agents[50–52]. Barros et al. (2007) *Lactarius deliciosus* (L.) Gray (Figure 11), *Sarcodon squamosus* (Schaeff.) Quél. and *Tricholoma portentosum* (Fr.) Quél. extracts have been reported to inhibit some important microorganisms for medical purposes[53]. A number of controlled clinical trials have been conducted in Japan since 1990 for supportive treatment in hospitals and clinics treatment of patients with various cancers, especially colorectal and stomach cancer, as well as breast and lung cancers[54]. Queiroz et al.(2010) methanolic extract (mainly glucan-type polysaccharides) of *Gymnopus montagnei* (Berk.) Redhead fungus have been shown to exhibit anti-inflammatory effects on the male Swiss mice and male Wistar rats. Glucans significantly reduced the inflammatory infiltrate produced by thioglycollate-mediated peritonitis by 75%. In addition, a significant reduction in nitric oxide levels was observed in exudates[51,55]. Liu et al.

(2016) reported that ethanol extracts of *H. erinaceus* fungus showed *Helicobacter pylori* inhibition[33]. *Terfezia boudieri* Chatin (Scop.) Pers. is a famous mushroom both in our country and in the world with its pleasant aroma and taste.

Figure 11. *Lactarius deliciosus*

Doğan and Aydın (2013) reported that *T. boudieri* mushroom has antimicrobial activity in gram (-) and gram (+), yeast and bacteria and also has high antioxidant capacity[56]. Zhong et al.(2011) reported that inotodiol extracts of the *Inonotus obliquus* (Fr.) Pilát fungus have an anti-proliferative effect on the human lung carcinoma cell line A549[57]. Jayakumar et al.(2006) reported that an extract of oyster mushroom *P. ostreatus* can protect Wistar rats against acute hepatotoxicity induced by CCl4 administration[58]. In 2010, a study by Nitha et al. revealed that morel mushroom (*Morchella esculenta* (L.) Pers.) mycelium is an excellent source of antioxidants that can provide different levels of protection and potential therapeutic use[59]. Based on the results of a study by Jeng-Leun et al.(2006), It can be concluded that upon the consumption of *Cyclocybe parasitica* (G. Stev.) Vizzini, the alleged antioxidant properties may be somewhat beneficial against the antioxidant protection system of the human body against oxidative damage[60]. Canli et al. (2016) reported that *Xylaria hypoxylon* (L.) Grev. (Figure 12) has in-vitro antimicrobial activity[61].

Figure 12. *Xylaria hypoxylon*

CONCLUSION

According to the literature, mushrooms have played important roles in the history scene with people, and have become an integral part of traditional and modern medicine. In the academic studies carried out since 1900s, the medicinal effects of fungi have been investigated, however, the fungal kingdom, which is assumed to be represented by 750.000–1 million species, has very few fungi whose medical properties have been defined. In addition to in vitro and in-vivo studies on mushrooms, clinical studies based on their use in traditional and complementary medicine applications are important. Clinical studies to be performed could be important steps for the solution of many diseases such as cancer.

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