# MUSHROOMS:

# A WEALTH OF NUTRACEUTICALS AND AN AGENT OF BIOREMEDIATION

**Editors:**

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# Mushrooms: A Wealth of Nutraceuticals and an Agent of Bioremediation


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**Mushrooms: A Wealth of Nutraceuticals and an Agent of Bioremediation**

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# FOREWORD

Limited data is available worldwide in the area of mushroom research. There is a strong need to explore the various nutraceuticals in mushrooms. Lifestyle diseases like obesity, diabetes, and atherosclerosis are very common nowadays. Researchers worldwide are working on the edible components of daily diets that can improve the chances to overcome the rate of lifestyle diseases in common people. Polysaccharide like b-glucans, is the very important nutraceuticals in this respect that have been explored recently for their therapeutic potential. Various nutraceuticals having potent medicinal properties have been discussed in this book. In this book, the editor included the chapters in a sequence-wise manner. Initially, the medicinal properties of different edible and non-edible mushrooms have been mentioned. Diabetes is the next area that is explored in this book. The treatment of both type I and type II diabetes by mushrooms and their nutraceuticals has been included in this book. The authors of this book show their hard efforts to accumulate all the information related to the therapeutic potential of mushrooms. Cancer is the next centre of attraction and one of the major portions of this book written by several authors. Anticancer properties are very well fully discussed in a couple of chapters. Figures and tables are well positioned in this book. Antimicrobial properties also have been well written in a single chapter of this book. The last portion of this book emphasizes the bioremediation aspects of various mushrooms. Overall, this book offers a complete package that includes the therapeutic and bioremediation properties of various mushrooms. All these chapters are very vital for the readers and are written in a very comprehensive manner to maintain the interest of the readers. References are recent and well-arranged in a comprehensive manner. The editor has done a fantastic job of editing this book by pinpointing and revising the major areas of this book.

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# PREFACE

Mushrooms have been an important source of nutraceuticals from the beginning, containing various nutraceuticals, like β-glucans, lectins, unsaturated fatty acids, phenolic compounds, tocopherols, ascorbic acid, and carotenoids. These nutraceuticals offer significant therapeutic potential for the treatment of a number of lifestyle diseases like obesity, diabetes, heart disease, stroke, etc. In addition, the mushroom also can be utilized as an important agent of bioremediation. Mushroom exhibits strong high metal absorption capacity and can be utilized to improve the fertility of aquatic and land ecosystem.

This book comprises a new efficient treatment strategy for the treatment of various lifestyles and other most common diseases with the help of mushrooms and their nutraceuticals. This book also shows the efficient bioremediation strategy exhibited by most common mushrooms. The starting chapters of this book exhibit the nutritional and medicinal values of various edible and non-edible mushrooms. In addition, the therapeutic activity of various bioactive components of mushrooms also has been explored in these starting chapters. Antidiabetic properties of different mushrooms are also explored in the starting chapters of this book. For both type I and type II, the therapeutic potential of mushrooms have been included in this chapter. In the middle of the chapters, the anticancer properties of various edible and non-edible mushrooms have been thoroughly discussed in this book. Various nutraceuticals present in different edible and non-edible mushrooms offer considerable anticancer properties, which are discussed in these middle chapters. A good number of figures and tables has been included regarding the anticancer properties of different mushroom and their nutraceuticals. In the last section of this book, some in silico approaches by utilizing mushrooms to treat various diseases have been included. Some of the last chapters also exhibited the application of fungal xylanase enzymes. One chapter in the last section also shows the antimicrobial properties of various mushrooms. A major portion of the last chapters explores the bioremediation properties of various mushrooms.

Overall, we can say that this book offers a combo pack of the treatment of lifestyle diseases along with an agent for bioremediation that shows a strong capacity to improve the fertility of aquatic and land ecosystems. This book attracts researchers worldwide working on the therapeutic potential of mushrooms and their nutraceuticals. In addition, students are also interested in this book to see the therapeutic activity of mushrooms. Thus, this book will be a complete package for researchers, scientists, and students working in the field of mushroom research.

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CHAPTER 1

# Nutritional and Medicinal Values of Mushroom

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**Abstract:** Humans have ingested both wild and farmed mushrooms for their nutritional and therapeutic properties. Mushrooms are a good source of protein, carbohydrates, and dietary fiber compared to energy and fat. They are rich in vitamins like riboflavin, niacin, and folates, as well as minerals and trace elements like potassium and copper. Due to their distinct flavor, they have been eaten as food for ages. Aside from being a nutrient-dense diet, certain mushrooms are also considered a rich source of physiologically active chemicals with potential therapeutic value in Chinese medicine. Phenolic chemicals, sterols, and triterpenes are examples of bioactive secondary metabolites that occur in mushrooms. Mushrooms are essential in traditional medicine for their healing powers and characteristics, as well as their long history as a food source. It has been shown to have positive benefits on health and the treatment of certain ailments. Mushrooms have a variety of nutraceutical qualities, including the prevention or treatment of Parkinson's disease, Alzheimer's disease, hypertension, and stroke risk. Due to their antitumoral properties, they are also used to lower the likelihood of cancer invasion and metastasis. Mushrooms are antimicrobial, antioxidant, immune system boosters, and cholesterol-lowering agents, and essential bioactive compounds. Mushrooms and mushroom derivatives may have health benefits if included in our daily diet.

**Keywords:** Bioactive compounds, Food supplements, Medicine, Mushroom .

## INTRODUCTION

As the world's population grows, so does interest in the production and subsequent use of mushrooms as a food source. Since 1990, the mushroom industry has gotten a lot of attention, which has resulted in a significant increase in production. In recent years, mushrooms have emerged as one of the most important sources of functional foods and medications [1]. The popularity of edible mushrooms has grown as a result of their taste, flavor, and nutritional value [2, 3]. Mushrooms are superior to animal proteins and other animal products, as evidenced by several previous research [4]. However, distinguishing edible and medicinal mushrooms is difficult since many popular edible species have thera-

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peutic characteristics, and numerous medicinal mushrooms are also edible [1]. *Agaricus bisporus* is the most widely farmed fungus, followed by *Lentinus edodes*, *Pleurotus* spp., and *Flammulina velutipes*. Mushroom output is steadily increasing, with China being the world's largest producer [5, 6]. Wild mushrooms, on the other hand, are gaining popularity due to their nutritional, sensory, and, most importantly, pharmacological properties [7].

Mushrooms are the fruiting structures of specialized fungi that can break down organic matter and recycle nutrients again in the soil. These fungi can turn lignocellulosic waste into lucrative protein-rich biomass that contains all of the needed elements. The use of mushroom fungi to convert leftovers reduces pollutants in the atmosphere while also acting as fertilizer, animal fodder, soil conditioner, and bioremediation [8]. Photosynthesis and agro-industries produce almost 200 billion tonnes of organic matter every year [9]. Firstly, mushroom cultivation began in the caves of France. In 600 AD, the Chinese attempted it again. In 1978, it produced only 60,000 tonnes. Following that, artificial mushroom cultivation began in China and Japan. Over the last 55 years, innovative and simple cultivation technologies have been created, resulting in a large increase in mushroom production from 0.30 million tonnes in 1961 to 18.58 million tonnes in 2016 [10].

China's oyster mushroom (*Pleurotus ostreatus*) is the world's third most extensively grown fungus [11]. In India, it is widely used by women's self-help groups on a small to medium level. It is presently quite popular in practically all of India's states, which have diverse climatic circumstances. The Chinese mushroom (*Volvariella volvacea*) is another tropical mushroom that has taken over Odisha and may be found in every corner of the state. It is the world's sixth most popular mushroom [12]. In India, the button mushroom has a significant market share maximum and makes up roughly 80% of the overall mushroom population manufacture. Tropical mushrooms, such as *Pleurotus* spp., *Volvariella volvacea*, and *Calocybe indica*, showed 20% of total production and are grown virtually all year in different parts of the country. The Indian subcontinent is recognized for its diverse agro-climatic regions and ecosystems that support various mushroom species [13].

Mushrooms may be a new source of antimicrobial chemicals, primarily secondary metabolites as well as primary metabolites. The best-researched species, Lentinus edodes, appears to exhibit antibacterial activity against bacterial strains [14]. They have a high nutritional value because they are high in protein, contain a high quantity of vital amino acids and fiber and are low in fat but high in critical fatty acids (Fig. **1**).


**Fig. (1).** Nutritional and medicinal properties of mushrooms (Adapted from- www.mushroom-appreciation.com).

## NUTRITIONAL COMPOSITION OF MUSHROOM

Carbohydrates make up the majority of mushroom fruiting bodies, for 50% to 65% of their dry weight (Table **1**). Free sugars account for around 11% of total sugars. *Coprinus atramentarius* contains 24 percent carbohydrate by dry weight [15]. Mannitol, commonly known as mushroom sugar, accounts for approximately 80% of free sugars, making it the most prominent. A fresh mushroom contains 0.9 percent mannitol, 0.28 percent reducing sugar, 0.59 percent glycogen, and 0.91 percent hemicellulose [16].

Protein is a significant component of mushroom dry matter. Mushroom protein concentration is affected by substratum composition, pileus size, harvest period, and mushroom species [17]. Mushroom protein level has also been noted to fluctuate from flush to flush. On a dry weight basis, the protein content in the mycelium of *A. bisporus* is 32%-42%. Mushrooms have a higher protein content than most other vegetables and wild plants. Literature survey illustrated the 14.71 to 17.37 percent protein found in the fruiting bodies of *Lactarius deliciosus* and *Lactarius sanguiffus* where as 5.20 to 18.87 percent protein in the fruiting bodies of *L. deliciosus* and *L. sanguiffus*, correspondingly [18] (Table **2**).

## CHAPTER 2

# Mushrooms Against Malignancies: from Chemo-sensitization to Immunopotentiation

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**Abstract:** Malignancies have been among the diseases which claim most of the lives around the globe. They also impact the socioeconomic level as well as emotional detriments among the near and dear ones. Various strategies and interventions have been devised to combat these life-threatening conditions. The ill effects associated with synthetic drugs comprising most of the anticancer drugs enforce looking for an alternative source for molecules with therapeutic potential. Mushrooms are one of the most prominent sources of bioactive molecules with diverse medicinal properties. Various mushrooms have shown their ability to inhibit the proliferation of neoplastic cells both in *in vitro* and *in vivo* investigations. Mushrooms and their active constituents can affect the various Hallmarks of Cancer. Mushrooms are not only able to inhibit the proliferation of cancer cells, but they also prevent the onset of carcinogenesis. The anti-angiogenic property of various mushrooms is indicated in several research investigations. The immunomodulatory potential and ability to avert metastasis also aid in the anticancer potential of this wonderful food item. Due to the high nutritive values of edible mushrooms, they have been suggested as nutraceuticals and contribute to nutritional management in diseases including cancer. The active constituents are also proven to have chemosensitizing ability. Preventive management of cancer and reverting chemoresistance have been sought as promising achievements in the clinical management of malignant conditions. Moreover, the nutritional values of mushrooms, along with their therapeutic potential at various fronts against cancer, make them a strong candidate for clinical application. This also warrants the careful

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exploration of mushrooms, their nutritive potential, and bioactive constituents against malignant disorders in laboratory and clinical settings.

**Keywords:** Angiogenesis, Cancer, Chemoresistance, Immunity, Metastasis, Mushrooms.

## INTRODUCTION

The majority of therapeutic interventions against malignant disorders attempt to impact the rapid cell division of transformed cells. The chemotherapeutic agents used in the treatment of cancer are mostly compounds synthesized or derivatized from natural compounds. Shortcomings of most of the agents used in cancer treatment include the dampening of the immunity of the host. The chemicals striking the high rate of cell division also affect the rapidly dividing cells of the immune system. Moreover, there are many other undesired consequences associated with the use of chemical anticancer drugs of synthetic nature. These undesired effects include proneness to infection, anatomical damage, physiological disorders, and discomfort to the patients [1, 2]. Therefore, natural products having medicinal properties have been explored by mankind for ages to prevent and cure human health disorders. These natural compounds mostly impose no or minimal unwanted consequences or harm to human health. Nevertheless, traditional lifestyle practices promote a connection with nature for food, medicine, and other supplements, including materials for shelter and safety. These traditional medicinal practices integrate food and medicine, and prescribe and restrict the food items or ingredients based on their nature [3, 4]. The nature of these food items is a product of their biochemical composition. Among many food items having the dual benefits of nutrient richness and medicinal properties, the mushroom is the prime [4 - 6]. Mushrooms are the nutritious fruiting body of fungi of a specific group and have been reported in human consumption for ages during human development in various parts of the world [4, 7, 8].

The mushroom itself is preventive for many human disorders by fulfilling the essential nutrient requirement, maintaining physiological and immunological homeostasis, and supplementing vitamins and minerals [4, 8 - 11]. Moreover, the medicinal benefits associated with mushrooms not only include healing potential in many human anomalies but can also boost immunity tidy and tough to counter the contract or onset of disease conditions [9, 11, 12]. Many forms of mushrooms belong to a variety of genera and species and may have distinctive bioactive compounds. This diversity in their bioactive compounds allows them to provide several advantages to humankind [5, 6, 13, 14]. The mushrooms with medicinal and rich nutritional values include *Agaricus bisporus, Grifola frondosa, Coriolus* *versicolor*, *Osmoporus odoratus*, *Pleurotu spp., Hypsizygus marmoreus, Amauroderma, Lentinula spp, Trametes versicolor*, *Cordyceps, Phellinus, Polyozellus*, and *Antrodiac innamomea* which are relatively common for their utilization as compared to many other mushroom forms [4]. The advantages of mushrooms for humans are not limited to their nutritional values and medicinal benefits; they also aid in environmental management and the production of value-added substances [4 - 6, 13 - 16].

The benefits of mushrooms for human health also encompass activity against malignant disorders [4, 17 - 23]. The anticancer properties of mushrooms are well known and depicted in many traditional medicinal practices. *Ganoderma, Pleurotus, Hericium cirrhatum, Inonotus obliquus*, *Fomitopsis pinicola*, *Agaricus*, *Phellinus, Sparassis crispa*, *Grifola frondosa*, *Cordyceps, Coriolus*, and *Hericium erinaceus*, *etc*. are few among common mushrooms being exploited for their antineoplastic abilities [4, 17 - 23]. The consumption of mushrooms has been reported to prevent the occurrence of malignant disorders of a variety of origins [18, 24, 25]. The direct action of mushrooms and their bioactive against critical molecules involved in the initiation and progression of neoplasm pave the path for therapeutic benefits [4, 17 - 23]. The 'Hallmarks of cancer', including neovascularization and metastasis, is also resisted by mushroom and their bioactive components [4, 23, 26 - 34]. Mushrooms, such as *Ganoderma, Pleurotus*, *etc*., and many secondary metabolites of peptide and polysaccharide nature derived from mushrooms can prevent the molecular players from triggering angiogenic events [31, 35, 36]. Reports also indicate that mushrooms can diminish the potential of endothelial cells to form vessels [23, 27, 37]. Nevertheless, the anti-metastatic potential of mushroom consumption and their bioactive compounds have been recorded [33, 38, 39]. Various mushrooms, including *Agaricus blazei, Cordyceps sinensis, Pleurotus*, *Ganoderma lucidum, Grifola frondosa*, *Poria cocos*, and *Lentinula edodes,* have shown their anti-metastatic potential against a variety of cancer cells, including those of breast, prostate, pancreatic, skin, colon, and lung origin. The antimetastatic potentials of mushrooms are not only confirmed in *in vitro* settings, but they have been proven in experimental models and cohort studies [4, 9, 40].

One of the major reasons for exploring natural products to identify the effective therapeutic agent is the onset of chemoresistance against chemicals classically used in clinical settings [1, 2, 4, 41 - 43]. Malignant cells often reprogram their cell physiology to prevent the anticancer effect of drugs [2, 41 - 43]. However, it is very uncommon for cancer cells to show resistance against natural metabolites derived from various living forms. Mushrooms, through their bioactive metabolites, not only directly cause cytotoxicity against cancer cells but also elicit the sensitivity of cancer cells against standard anticancer drugs [44 - 47].

## CHAPTER 3

# Anti-proliferative, Anti-angiogenic, Anti-apoptotic, and Anti-metastatic Effects of Mushroom

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**Abstract:** Cancer is the second leading cause of mortality globally after cardiovascular diseases. It is attributed to various genetic and epigenetic changes in the genome, while lifestyle and environmental factors have a say in its rate of progression. Conventional agents like chemotherapy, radiotherapy, and surgical interventions though successful to some extent, are always associated with toxic side effects. A promising alternative could be herbs that form a part of our daily consumption. Mushrooms consumed worldwide have been found to be a treasure of macromolecules like β-glucan, α-glucan, resveratrol, concanavalin A, cibacron blue affinity protein, p-hydroxybenzoic acid, ergosterol, linoleic acid, *etc*. that are responsible for mediating anti-tumor, immunomodulatory, antioxidant and anti-diabetic roles. Various experiments have demonstrated the potential of mushrooms as an anti-cancer agent. This chapter summarizes the effect of mushroom extracts and bioactive constituents against various hallmarks of cancer like sustained proliferation, evading apoptosis, angiogenesis, immune evasion and metastasis, along with underlying mechanisms. At the end of the chapter, we also talked about what still can be done and where we need to focus so that future studies can add to the already existing knowledge about this natural reservoir of anti-cancer compounds.

**Keywords:** Anti-angiogenic, Anti-apoptotic, Antimetastatic, Antiproliferative, Mushroom.

## INTRODUCTION

Since the dawn of the 20th century, finding an answer to the dilemma posed by cancer has been most challenging for man. The disease, which took a toll on millions of lives, has remained an unanswered mystery. Researches throughout the world have been going on, but a real breakthrough still evades us. The disease took in its ambit not less than 1.3 million people in 2020 [1], and is second to only cardiovascular diseases when accounting for mortality. What is really worrisome

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is the sync between the incidence of cancer, the changing lifestyle of man, and the nature of his surroundings. Who among us is not being subjected to an environment full of automobile fumes, polluted water, edibles treated with a variety of chemicals and land overwhelmed with herbicides and pesticides. Alcohol abuse, tobacco consumption, and cannabinoids are finding their presence very common among youth nowadays. And to this, what is more, intriguing is people are being alienated from meditation, exercise, a nutrient-rich diet, and many more things which can help the body to find a way from stresses developing inside it. It is worth acknowledging that an increased incidence of cancer is attributed to all the above-mentioned reasons. The picture will be more gruesome if we don't find an alternative that is more sustainanble for us in the long term. But what we have discussed so far are controllable factors and should be worked upon on an individual and collective basis but Cancer isn't this simple; it is manifested even with aging, exposure to biological entities like bacteria and viruses and *via* mutations in genetic material either by exposure to carcinogens and radiations [2]. Biologically, genetic, epigenetic and metabolic alterations taking place inside the cells when they accumulate over a considerable period of time for successive cell divisions result in Cancer. These changes trigger a plethora of genes to express themselves constitutively; thus, normal cells lose their capability to regulate homeostatic mechanisms [3]. This is manifested in uncontrolled cell cycle events leading to hyperproliferation, evasion of apoptosis and immune response, angiogenesis, epithelial to Mesenchymal transition and metastasis [4]. Additionally, malignant cells also exhibit the Warburg effect, whereby tumors display high levels of glucose uptake and lactate production even in the presence of adequate oxygen, and this increased aerobic glycolysis could contribute to the immortalization of cells [5]. These genetic and metabolic reprogramming in cancer cells support their growth, survival, proliferation and maintenance in the hostile environment [3].

Notwithstanding challenges, it has been inherent to the human mind to ponder over the problem nature poses to us. Cancer is no exception, and we found some tangible results in our basket in the form of chemotherapy, radiotherapy, hormonal therapy, immunotherapy, nanomedicines and surgical interventions [6]. These therapies, when used individually or in combination, have checked the growth of cancer cells and caused the shrinkage of tumor size to a significant level though none of them have proved to be an exclusive remedy for cancer treatment so far. What is of concern with this repertoire is the side effect they have on our bodies [7]. Chemotherapy is the main approach for the treatment of metastatic tumors. However, it is associated with serious side effects, such as bone marrow suppression, neurotoxicity, gastrointestinal reaction and liver and kidney damage. In addition, currently used chemotherapeutic agents, such as alkylating agents, mustards, anti-metabolites, spindle poisons, and DNA binders and cutters, target a specific pathway, which ultimately shrinks tumor size but often fails to eradicate tumors or prevent their recurrence. Repeated treatment with these agents eventually results in tumors that become resistant to the chemotherapies [8]. During radiotherapy, patients receive a high total dose of ionizing radiation fractionated over a period of weeks. These radiations are themselves known to possess cancerous effects that can lead to secondary tumors, thus adding to already existing criticality [9]. While surgical interventions can remove primary tumors, they may stimulate the hematogenic distribution of tumor cells, leading to increased metastases growth [10].

In the quest to resolve the shortcoming of conventional therapeutics, an option of choice was natural herbs which have been known to have several biological properties of advantages. Among many such herbs, we will discuss mushrooms' effect in treating cancer. Mushrooms have been used since the dawn of human civilization as an important constituent of our diet [11]. Not only are mushrooms rich in nutrients required by our body for normal maintenance, but in addition to that, they are also reported to have numerous biologically active compounds, *e.g.*, α- glucans, β- glucans, lentanin, lipopolysaccharides, resveratrol, cibacron blue affinity purified protein, concanavalin A which together induce pharmacological actions such as antimicrobial, anti-inflammatory, immunomodulatory, antidiabetic, cytotoxic, antioxidant, hepatoprotective, anticancer, antioxidant, antiallergic, antihyperlipidemic, and prebiotic properties [12]. All these attributes have attracted scientists to study in detail the effect of mushroom on cancer. Here we will discuss this one by one in relation to how mushroom may target hallmarks of cancer and thereby inhibit it.

## ANTI-PROLIFERATIVE EFFECT

Normal cells require mitogenic growth signals in order to move from a quiescent state to an active proliferative state. However, these factors are limited in supply, and thus, cell proliferation is restricted. Additionally, the progression of the cell cycle in somatic cells is controlled by a balance between proliferative and antiproliferative signals as well as *via* cyclin-cdk complexes [13]. Cancer cells defy the above limitation of trophic factors by a mechanism of autocrine signalling whereby they actively produce growth-inducing mitogens, and the balance is tilted in favour of proliferative signals *via* loss of function mutation in tumor suppressor gene and gain of function mutation in proto-oncogenes as listed in Table **1** [16]. Constitutive expression of Ras-ERK, PI3K-Akt and mTOR signalling pathways, nuclear factor-kappa B [NF-κB], mitogen activated protein kinase pathway [MAPK], Akt, Wnt, Notch pathways, as well as universal disruption of Rb mediated control of G1/S transition enables cancer cells to undergo sustained proliferation [14, 15]. This is further supported *via* the

## CHAPTER 4

# Antidiabetic Attributes of Mushrooms

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**Abstract:** Mushrooms are macrofungi, with distinct mycelia structure, and fruiting bodies, divided into stalk and cap that contains spores in most of the species. These mushrooms are edible with diverse therapeutic applications. Old civilizations from India, China, and Korea used these mushrooms to cure diseases, especially diabetes. Diabetes is now a newly emerging pandemic, affecting people worldwide, with special reference to developing countries. There are several medications available for the management of diabetes, but their permanent treatment is still to be explored. Due to synthetic medicines and their adverse effect, people are searching for natural therapeutic agents. Many mushroom species have shown their potential to control diabetes and its related complications, such as weight loss, lipidemia, hypertension, *etc.* In this chapter, we have discussed five different mushroom species, *i.e.*, *Auricularia auricula-judae, Agaricus bisporus, Ophiocordycep sinensis, Ganoderma lucidum,* and *Pleurotus* species with their potential therapeutic application against diabetes and its related complications.

**Keywords:** Anti-diabetic properties of mushroom, Diabetes, Diabetes type 1, Diabetes type 2, Edible mushroom, Medicinal mushrooms.

## INTRODUCTION

Mushrooms are macrofungi, having mycelia and fruiting bodies with spores, showing a variety of therapeutic activities which is beneficial to human health. Mushrooms are a good nutraceutical agent due to their medicinal and nutritional value. Recent research studies have promoted mushrooms as a biotherapeutic for new generations [1]. Besides, mushrooms are adding value to economic growth because they can be grown worldwide with fewer investments and requirements [2, 3]. Malnutrition is one of the serious concerns in the 21$^{st}$ century. It can be caused due to over intake of food or lack of nutritional aspects in food (vitamins,

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carbohydrates, minerals, saturated fats, fibers, salts) may also be called hidden hunger that may further develop many clinical symptoms, *i.e.*, obesity, loss of weight, and non-communicable diseases (diabetes, cardiovascular diseases, *etc.*). Mushrooms are a rich source of minerals (Ca, P, K, Fe, and Cu), carbohydrates, and vitamins (A, B-complex, C, D, K) [4] which can be found only in meat and animal-based food. Many secondary metabolites (*i.e.*, phenolic compounds, lectines, terpenoids, lactones, sterols, and alkaloids) have shown their potential against cancer, drug-resistant bacteria, diabetes, hypertension, and high blood pressure [5 - 10].

Due to all their nutritional values and culinary effects of secondary metabolites, mushrooms are a potential therapeutic agent against diabetes. It contains a few insulin-like enzymes that can facilitate the break-down of complex carbohydrate molecules into simple sugars and improve the resistance of insulin [11 - 13]. It smoothens the liver, pancreatic endocrine gland, and metabolic functions by stimulating the secretions of insulin and hormones. Many studies have revealed that mushrooms, if supplemented in the diet, may lower the low-density lipoprotein, triglycerides, and total cholesterol and help to increase the level of high-density lipoprotein [14 - 18]. The bioactive compounds, *i.e.*, α, and β-glucans, with other dietary fibers, aid in regenerating the pancreatic β-cells that further increase the flow of insulin in the bloodstream to regulate the glucose level in the blood. Due to their low fat and carbohydrate content, mushrooms are the best food for diabetic patients [19 - 22]. There are many hypoglycemic agents, such as gliclazide, exenatide, insulin, metformin, phenformin, rosiglitazone, tolbutamide, and troglitazone, that are mainly used in treating diabetic patients and are found to be much effective in controlling it. But the major problem is that synthetic drugs may have adverse side effects that might alter the course of diabetes into chronic diabetes complications that may associate with a high rate of morbidity and mortality. Thus, as an alternative, mushrooms can be used as an effective hypoglycemic and anti-diabetic agent in preventing and controlling diabetes because of their nutritional and medicinal values [23] control diabetes to which mushrooms can be a good candidate in terms of medicament agent.

Diabetes mellitus (DM) is one of the most rapidly growing pandemics that needs to be controlled. Developing countries are the most affected by diabetes, and these numbers are increasing day by day. DM can are considered a metabolic disorder that is caused due to the self-destruction of pancreatic β-cells by the antibodies, also called an autoimmune disorder. It is under the heterogeneous and genetic disorder groups [24]. With the destruction of β-cells, less/no insulin secretion occurs, leading to the rise of glucose levels [25]. If the high glucose level persists for a long time, then it may cause several health-related complications, such as cardiovascular disorder, cancer, hypertension, glaucoma, nephropathy, neuropathy, *etc* [26 - 38]. The most common DM is diabetes type 1, and diabetes type 2.

Diabetes type 1 is developed due to the autoimmune destruction of pancreatic β-cells, and it is a rare disorder, also called insulin-dependent diabetes mellitus (IDDM), with 5-10% of cases reported, according to Diabetes Care, 2008 report. Type 2 diabetes is caused because of insulin deficiency and resistance of the peripheral tissues, also called non-insulin-dependent diabetes mellitus (NIDM). This type of diabetes is the most common disorder, with a 90-95% occurrence rate [39].

In this chapter, we describe the anti-diabetic attributes of various mushroom species.

## DIABETES MELLITUS (DM)

DM is one of the oldest lifestyle-related metabolic disorders, developed due to less insulin secretion or absence of insulin because of β-cells self-destruction by antibodies. Insulin is a hormone that regulates the blood glucose level, secreted by the β-cells of the pancreas, and utilizes the sugars and carbohydrates to form the energy that participates in metabolic actions. The glucose metamorphosis into glycogen is hampered in the liver if the insulin level is not in the normal range which is 4.0-6.0 mmol/L in pre-prandial conditions and up to 7.8 mmol/L in post-prandial conditions [40]. If sugar levels cross the mark of more than 15 mmol/L, then it can cause some serious health-related issues, especially in terms of nerves, kidneys, and cardiovascular [41]. Generally, diabetes can be categorized into two common groups, *i.e.*, type 1 and type 2 diabetes mellitus.

### Diabetes Mellitus Type 1 (DMT-1) or Insulin-dependent Diabetes Mellitus (IDDM)

DMT-1 can be diagnosed in the early stages of age with symptoms of ketonuria, and loss of weight due to less insulin secretion/no secretion of insulin by the body of the patients, whose required daily doses of insulin. DMT-1 is an autoimmune disorder caused by the cellular-mediated obliteration of pancreatic β-cells found in Islets of Langerhans [42]. As this disease is diagnosed early, children are the victims, but adults are also affected. As it is a catabolic disorder, glucagon and insulin are not secreted in the bloodstream. In diabetes conditions, the β-cells cannot react to the stimuli received by the cellular signaling pathways [43]. Environmental toxins and other external factors such as viruses (coxsackievirus B4, and mumps virus), and chemotoxins are also contributed to developing the DMT-1. Genetic factors are also a serious concern that increases the risk of developing DMT-1. Human leukocyte antigen (HLA), a complex of genes

# CHAPTER 5

# Antimicrobial Potential of Mushrooms: Emergence of Mycotherapy

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**Abstract:** The 21st century enters a "post-antibiotic world," with just a few alternatives for combating antibiotic-resistant microbial strains. The search for new antimicrobials which could overcome the situation of antimicrobial resistance is of prime importance and the need of hour. Herbal antimicrobials pose a plethora of new antimicrobial drug discoveries. Mushrooms give rise to a number of bioactive chemicals that are known to have anti-pathogenic qualities as well as safer and more effective therapeutic effects in the treatment of human diseases. As a result, this chapter emphasises that mycoconstituents might be an alternate treatment regimen and could play a role in novel drug discovery against various infections. This chapter contains information about the potential use of mycoconstituents in the management and treatment of infectious diseases. The approaches illustrate the importance of primary screening of bioactive molecules from mushrooms as a potential step by offering new possibilities for clinical and pharmacological research and development. Traditional antibiotics can now be substituted with newer and more effective natural antimicrobials derived from mushroom extracts to treat a variety of fatal and multi-drug resistant infectious diseases. As a result, this functional food extract might play a significant role in naturally combating infections and offering a comprehensive approach to treatments. Finally, we will go through the mechanics of mushroom antimicrobial potentials and presents an insight into "Mycotherapy".

**Keywords:** Antibiotics, Mushrooms, Mycoconstituents, Pathogenic, Resistance.

## INTRODUCTION

Infectious diseases caused by drug-resistant germs can lead to high mortality and hospitalization, placing a huge financial burden on patients and healthcare sys-

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tems while hindering long-term growth goals [1, 2]. The WHO has reported that AMR is one of the top ten public health challenges facing humanity. The cost of AMR in the economy is high. In addition to death and injury, chronic illness leads to long-term hospital visits, the need for more expensive medications, and financial hardship for those affected [3]. Antimicrobial Resistance (AMR) poses a major global challenge to human, animal and environmental health. This is due to the emergence, distribution and spread of multidrug-resistant pathogens (MDR) or 'superbugs'. MDR bacteria live around a triangle or niche between animals, humans and the environment, and these viruses are linked to this triangle. Potential causes of "global resistance" or AMR include overuse of antibiotics in animals (food, livestock and water) and humans, inadequate sanitation/hygiene and removal of weakened antibiotics or residues from the environment through manure/surface. These factors contribute to the suppression of genetic selection in the emergence of MDR bacterial infections in society [4, 5]. Currently, antibiotic resistance is a growing health threat worldwide and is the cause of nosocomial and often fatal infections [6]. The 21st century enters a "post-antibiotic world," with just a few alternatives for combating antibiotic-resistant microbial strains. The European Union (EU) expects that by 2050, this outcome will be responsible for 10 million fatalities per year. One of the primary drivers of the development of novel medicines derived from natural antimicrobial sources is the global increase of AMR versus current treatments [7]. As a result, it is vital that a new class of medication should be developed to fight this resistance. The demand for alternative therapies for epidemics is growing. This, in fact, prompted the emergence of new mycopharmaceuticals with no side effects focused on mushroom bioprospecting. Globally, mushrooms are one of the most important weapons in dietary medicine and can be seen as an effective tool in combating malnutrition as well as numerous ailments and conditions [8, 9]. Many countries use these traditional foods as a nutraceutical or their derivatives have been developed as drug molecules. Several antimicrobial agents are found within mushrooms, making them an excellent source of "green" antimicrobials. Fruit and mycelium bodies contain substances that have different antibodies. In the treatment of human diseases, certain mushrooms have been shown to possess antibacterial properties. In the decades to come, mushrooms can be considered a magic plant that can create a positive reaction because of their soothing properties [2].

## CLASSIFICATION OF ANTIMICROBIAL AGENTS

The term antibiotics refer to any substance, natural or synthetic, that inhibits or kills microorganisms, when used therapeutically, antibiotics are referred to as antimicrobial drugs. Antibiotics are broadly classified into five categories on the basis of their source of origin, mode of action, spectrum or range of susceptible/resistant microbes, function and chemical structure [10].

### Classification According to the Type of Action

The activity shown by antibacterials can be either bactericidal or bacteriostatic. The bactericidal effect is demonstrated by attacking bacteria's cell wall or cell membrane and ultimately destroying it completely, while bacteriostatic acts to inhibit or suppress the growth of bacteria by acting on their metabolic pathways or pathways for protein synthesis [11].

### Classification based on the Source of Antibacterial Agents

On the basis of their origin, antimicrobial drugs can be divided into three categories: natural and synthetic. Natural antimicrobials are those found in natural organisms which possess life, such as plants, animals, or microorganisms. They comparatively have high toxicity than synthetic antibacterials. Cephalosporins, benzylpenicillin, cefamycins, and gentamicin are natural antibiotics or antibacterials that are well-known examples. In terms of effectiveness, synthetic antimicrobials are comparatively more effective as they are not present in nature, and the microorganism is not exposed to them until they are released. Moxifloxacin and norfloxacin are promising synthetic antibiotics [12]. Aside from natural antimicrobials and synthetics, semisynthetic are those antibiotic drugs found in nature that have little change in their chemical structure and function to benefit from natural ones, *e.g.*, Ampicillin which is based on penicillin.

### Classification based on Activity Spectrum

On the basis of their effectiveness, the easy-to-resistant / resistant pesticides can be divided into two groups: narrow-spectrum antibiotics are effective only against either Gram-positive or Gram-negative bacteria, *e.g.*, vancomycin. While broad-spectrum antibiotics are those effective against a wide range of Gram-positive as well as Gram-negative bacteria, *e.g.*, tetracycline [10, 11].

### Classification based on Chemical Structure

The unique composition and chemical composition of antibiotics give them unique therapeutic properties. Therefore, basically and in the formulation of antimicrobials, it is divided into two groups: group A and group B, *i.e.*, β - lactams and aminoglycosides, respectively.

## CHAPTER 6

# *In silico* Interactions of the Biomolecules of Edible Mushrooms Against Lifestyle Diseases

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**Abstract:** Mushrooms are fungi that are consumed all over the world and contain bioactive nutritive components with nutritional and therapeutic qualities. Protein, minerals, vitamins and antioxidants are all found in edible mushrooms. Selenium, vitamin C, and choline are antioxidants that help the human body remove free radicals. Antimicrobial, antiviral, anticancer, anti-allergic, immunomodulation, anti-inflammatory, anti-atherogenic, hypoglycemic, hepatoprotective, and antioxidant properties of mushrooms. Primary and secondary metabolites can be found in mushrooms. The primary metabolites are energy-producing, but the secondary metabolites have therapeutic qualities. As the bioactive molecule has a pharmacological effect, researchers have recently focused on extracting it. As a result, the mushroom has the potential to be a recipe for human health and play a key role in the battle against COVID-19 pandemics and other infectious illnesses. Mushrooms and their biomolecules have therapeutic properties in a variety of diseases, including cardiovascular, diabetes, reproductive problems, cancer, and neurological disorders. A computer method, or *in silico* technology, is promising early evidence for drug development. Molecular docking studies have discovered bioactive chemicals from natural items like mushrooms as possible inhibitors against various diseases.

**Keywords:** Biomolecules, Diseases, *In silico*, Mushroom.

## INTRODUCTION

Mushrooms have been used as food and nutritional value from ancient times to modern days. Mushrooms are a potential source of biomolecules that include large macromolecules (protein, carbohydrate, lipid, and nucleic acid) as well as small molecules (primary metabolites, secondary metabolites, and natural products) [1]. Mushrooms contain secondary metabolites, including polysaccha-

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rides and phenolic compounds. Secondary metabolites contain polyphenols, acids, terpenoids, alkaloid sesquiterpenes, lactones and sterols. In edible mushrooms, many vitamins B1, B2, B12, C, D, and E are present. A mushroom is a macro fungus with a distinctive fruiting body, either epigeous or hypogeous, and large enough to be seen with the naked eye and picked by hand [2]. In several countries, mushrooms are used as food and medicine. Mushrooms are a good source of protein, carbohydrates, minerals and vitamins (including thiamin, riboflavin, cobalamin, ascorbate, tocopherols, and b-carotene) [3]. Mushrooms are a rich source of phenolic compounds. Several studies reported that mushrooms are a nutritionally functional food and a rich source of biologically active agents responsible for medicinal properties, including antimicrobial, antioxidant, antiviral, anti-diabetic and anticancer substances [4 - 6]. Regular consumption of mushrooms in diet may enhance the immune system and cure several diseases [7]. Edible mushrooms possess polyphenolic compounds, and dietary fiber composition may help in the modulation of gut microbiota. The medicinal properties of mushrooms may help prevent several lifestyle diseases cancer, neurodegenerative disease, cardiovascular disease, and diabetes. Medicinal mushrooms such as *Hericium erinaceus* are used to cure tumor disease such as gastric cancer, and duodenal cancer [8, 9]. Several research reports show that some edible mushrooms, including *Pleurotus ostreatus*, *Lentinula edodes*, *Agaricus bisporus*, *Flammulina velutipes*, and *Auricularia auricular-judae* are used as a treatment for ND [10, 11]. Oudemansin, strobilurins A, D, illudin S and pterulone B are antibiotic metabolites extracted from *Collybia nivalis, Omphalotus olearius, Flavolaschia* sp. and *Pterula* sp [12]. Heart disease and diabetes are age-related diseases that have been treated by ingesting mushrooms. *Cordyceps sinensis* regulates insulin sensitivity and reduces cholesterol levels. Sun mushrooms, such as *Agaricus blazei* used to cure hepatitis, congested arteries, diabetes, and cancer, are found in Japan and China.

Mushrooms are a source of polysaccharides used as anticancer and immune-stimulating properties. Turkey tail mushroom extract uses polysaccharopeptide (PSP) and polysaccharide-K to stop cancer cells [13]. Chemotherapy drug paclitaxel is produced from fungus are used to cure lung, bladder, pancreatic, and breast cancer. Mushrooms that contain polysaccharides compound does not directly attack cancer cells but stimulate antitumor properties to enhance immune cells. There can be four categories of mushrooms such as edible, poisonous, medicinal and miscellaneous category- mushrooms are used as folk medicine in several countries. Most of the mushrooms' secondary metabolites possess drug-like structures (*i.e.*, Lipinski's Rule of Five compliant) and could be considered a significant natural inspiration for drug discovery purposes. Multi-target drugs have advantages over single-target drug co-administration, mainly higher efficacy, an improved safety profile, and better compliance.

Furthermore, virtual screening methods help identify sources of off-target drug effects and investigate their potential to cause adverse or desirable side effects. In this work, a database of compounds has been created from the extracts of mushroom species (both edible and toxic). Furthermore, docking studies were carried out to theoretically comprehend their polypharmacological activity and guide the design of promising new multi-target agents (MTAs). The genomic analysis of the gut microbiota and the changes that happened at the genetic level of the microbiota upon the mushroom feeding (metagenomics or ecogenomics) [14]. In this chapter, we also describe the interaction between the bioactive compound of mushrooms and lifestyle diseases. Various computational techniques, including molecular docking, virtual screening, and molecular dynamics simulation, are used against various life-threatening diseases.

## Biomolecules of Mushrooms

Medicinal mushrooms play a beneficial role in United Nations Sustainable Development Goal in Good health and well-being. Healthy human health problems are publically considered, including life-threatening diseases, cancer, diabetes, cardiovascular disease, and neurodegenerative disorders influenced by food consumption and lifestyle [13]. There are various drugs and therapeutics for human diseases, but they have some side effects. The Sustainable Development Goals (SDGs) of the United Nations challenge authorities globally to cease hunger, achieve food safety, and update nutrition through 2030, especially for the poor and vulnerable members, including children. Due to their therapeutic potential, mushrooms have recently generated a lot of attention as a source of physiologically functional food and medication. In the main world, researchers focus on a mushroom in their therapeutic properties. Mushrooms are not only utilized as food but also used as potential therapeutics against numerous ailments. Mushroom is the "elixir of life" for the remedy of human disease due to the proximity of different secondary metabolites. Secondary metabolites, such as phytochemical compounds and low molecular weight molecules, are generated in reaction to stress. Edible mushrooms are *Ganoderma lucidum, Lentinula edodus, Schizophyllum commune, Hericium erinaceous* and *Cordyceps sinensis* function as medicinal mushrooms [15]. *Ganoderma lucidum* is the unique power of medicinal mushrooms. Edible mushrooms include a vast amount of biochemical compounds, including polysaccharides, terpenes, bioactive proteins, phenolic compounds, Lentinan, Adenosine, Ling Zhi 8, Polysaccharide Krestin (PSK), Polysaccharide Peptide (PSP), Entadenine butyric acid and antioxidants that make therapeutic threatening many diseases [13, 16]. Medicinal mushrooms possess diverse pharmacological and remedial traits including immune improvement, maintenance of homeostasis and coordination of biorhythm, antioxidant, anti-atherosclerotic, anti-inflammatory, analgesic, anti-tumor, anti-bacterial, anti-viral,

**CHAPTER 7**

# An Eco-friendly Practice of Decontamination of Toxicants using Fungi

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**Abstract:** The advent of industrialization and urbanization has caused rapid production of various types of domestic, agricultural, medical and technological goods, such as different types of pesticides, herbicides, cyanotoxin, heavy metals, antibiotics, dyes, phthalates, *etc.* Production of these substances has led to the production of enormous amount of waste materials. Inappropriate discharge and uncontrolled drainage of these waste materials into the environment have caused their accumulation in the surrounding environment, causing serious health problems and destroying our ecosystem. Different methods such as physical, chemical and biological have been adopted to eliminate these waste materials. However, these methods are cost-effective and have some side effects. Hence, in this chapter, efforts have been made to understand the fungal enzymes involved in remediation processes, and their role and the mechanism of action of fungi have been depicted. Besides that, we have also discussed different categories of waste and their remediation using fungi, which is an eco-friendly biological approach to remediate toxic materials.

**Keywords:** Contaminants, Detoxification , Fungal enzymes, Mycoremediation.

## INTRODUCTION

Production of anthropogenic waste has been increased in recent years. In the past centuries, it was limited both in terms of quantity and variety owing to smaller production and less industrialization. In the ancient period, only small amount of waste was contributed by industries, while majority was primarily due to domestic practices. In contrast, increased population augmented the human need and all sorts of requisites which led to the advent of urbanization and industrialization.

To alleviate the needs of the growing world population, the rapid progress in industrialization has led to the generation of more and more medicines, pesticides,

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and herbicides for human health as well as the betterment of agricultural fields. Apart from these, there are many medium and small industries that, along with their useful products, produce a massive amount of hazardous products, such as several types of useless inorganic and organic compounds. The hazardous products are considered waste materials which are mostly toxic and harmful. Improper disposal and continuous mixing of these wastes into the environment led to their accumulation many times higher than their tolerable limit, causing various kinds of health hazards that could be detrimental to living world.

In the report of the world health organization, it is mentioned that 144 million people are using contaminated water while 2200 million people are unable to get clean water for drinking as well as other purposes [1]. It is expected that 50% of the world's population will face water stress by 2025 [1].

Pollution caused by industrialization and urbanization has become havoc for developing countries leading to a loss of their GDP (5%), 16% global death, as well as 25% polluted regions. Besides its effect on the economy and the health of people, it can be responsible for threatening the availability of drinking water, food security, and biodiversity. Therefore, it is necessary to develop and generate some methods and strategies to overcome water pollution caused by toxicants.

In order to deal with the problem of water contamination, there is an urgent need to treat wastewater or effluents before their release into the aquatic environment. To decontaminate the contaminated water number, techniques like ion exchange methods, chemical precipitation, electrochemical method, and membrane technologies are used in different industries at large scales [2]. However, these techniques are not environmentally friendly, very costly, and also less effective [3]. Hence, it is important to develop an eco-friendly method that will be fast and cost-effective in eliminating polluted water. In recent years, the use of fungi has increased many folds to remediate toxic elements owing to their high metal binding capacity as well as a high percentage of the cell wall [4]. Although there are numbers of *in vitro* studies to remediate various toxicants from the synthetic media in which fungi are used, information regarding the in vivo studies to decontaminate natural waste using fungi is scanty. Mycoremediation, *i.e.,* the use of fungi for remediation purposes, is considered an economical and environmentally friendly method to mitigate the problem of contamination of water. The unique characteristics of fungi, like sturdy growth, resistance to toxicants, production of ligninolytic enzymes, vast hyphal network, resistance to changing temperature and pH, and presence of chelating proteins to combine metals make them crucial agents for the elimination of various toxicants [5, 6]. The present chapter discusses the role and importance of fungal species to degrade different toxicants such as heavy metals, pesticides, herbicides, pharmaceuticals, antibiotics, dyes and phthalates. The role of various enzymes involved in mycoremediation processes has also been described. Moreover, the mechanism or cellular response in the mycoremediation process has been explained (Fig. **1**).

## ROLE OF FUNGI IN MYCOREMEDIATION

Bioremediation is considered a very effective, economical and eco-friendly method to decontaminate toxins and harmful compounds into nontoxic substances. This is the natural and biological way of decontamination [7, 8]. The use of plants, *i.e.,* phytoremediation has been recognized as an economical and environmentally friendly method to decontaminate waste materials. But researchers found some limitations, such as tolerance to toxicants, selectivity of plants and climatic inhibitors, which cannot solve all the strategies to decontaminate waste materials [9].

Fungi can be an effective alternative to plants to remediate contaminated waste materials [5, 6-9]. Some characteristics of fungi, such as robust morphology, diverse metabolic capacity, and resistance to extreme temperature and pH, play significant roles in removing the different toxicants. Fungi have metal-chelating proteins that bind with metals and make them hyperaccumulators [4]. Apart from these qualities, reactive oxygen species, which are produced directly or indirectly by toxicants, can be counteracted by an antioxidant system that exists in fungi.

Various fungi have been recognized to play an important role in the mycoremediation of varieties of toxicants [10]. Some filamentous fungi such as *Acrimonium, Aspergillus*, *Pithium*, and *Curvularia* species are known for their tolerance ability to various toxicants [11]. Some other fungi, like *Trametes versicolor*, *Pleurotus ostreatus*, *Hypholoma dispersum* and *Trametes pavonia* are also known to have the degradation ability of various toxicants [12, 13]. Similarly, *Aspergillus and Penicillium* are also involved in remediating different toxicants [14, 15].

## ROLE OF FUNGAL ENZYMES INVOLVED IN MYCOREMEDIATION TECHNIQUES

### Extracellular Oxidoreductases

Some specific enzymes, *i.e.,* extracellular enzymes of fungi, make them able to catalyze toxic substances into nontoxic forms. These enzymes are likely produced to enhance fungal growth on toxic substrates of various structures which are not accessible to most of the bacteria [16, 17]. Therefore, these enzymes contribute to

# CHAPTER 8

# Application of Mushroom in Bioremediation of Toxic Heavy Metal Ions

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**Abstract:** Heavy metals have economic importance in industrial applications and are presently becoming a significant environmental concern. Components of heavy metals like As, Cd, Cr, Pb, Se, and Hg are considered systemic toxicants and induce various organ damage even at lower levels of exposure. Natural sources include metallurgy of metal-bearing rocks and volcanic eruptions, whereas mining and different industrial and agricultural operations are human sources to release them into the environment. In recent times, remediation of toxic metal pollution has been a major environmental and technological challenge all over the world. Several physiochemical strategies have been used in the past to remove heavy metals from the environment. But, it has adverse repercussions, including power dissipation, incompetence for inherently dangerous ions, pernicious by-products, and high cost; hence, alternative strategies are necessary. Biosorption and its operational processes have been very effective in the removal of hazardous heavy metals and display features like eco-friendly, high efficiency, and economic viability, and can be used repeatedly, showing selective metal binding, effective desorption, and recycling of adsorbents. Different biological agents like algae, bacteria, fungi, and yeast can be employed to carry out bioremediation, especially mycoremediation. The potential of fungal biomass (Mushrooms) as a biosorbent is well accepted for the removal of toxic heavy metals and radionuclides from the environment because of its excellent metal-binding characteristics and tolerance towards metals and unfavourable environmental conditions like diverse pH and temperature conditions. Mushrooms, macro-fungi, have fruiting bodies that grow out of a mass of mycelium and can build up heavy metals in high concentrations in their bodies above maximum permissible concentrations and may also act as an effective biosorption tool. High

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accumulation potential and shorter life span are some of the advantages of using mushrooms as biosorbents and exhibiting excellent mycoremediation potential.

**Keywords:** Bioremediation, Macro-fungi, Miosorbents, Mycoremediation.

## INTRODUCTION

Heavy metals are naturally occurring elements having high atomic mass and at least five times the density of water, prevalent mainly in the earth's crust [1]. The heavy metals also include metalloids like arsenic (As), antimony (Sb) and silicon (Si), and can induce toxicities even at low levels of exposure to the living organism, including humans [2]. These metals have numerous agricultural, domestic, industrial, medical, and technological applications to meet the demands of the ever-growing modern human population [1, 2]. Several inorganic metals like calcium (Ca), chromium ($Cr^{3+}$), copper (Cu), magnesium (Mg), manganese (Mn), nickel (Ni), sodium (Na), and zinc (Zn) are vital components for living organisms and required in a small amount for various biochemical, metabolic and physiological functions [3, 4]. However, metal ions like arsenic (As), cadmium (Cd), chromium (Cr), lead (Pb), mercury (Hg), and silver (Ag) do not have significant biological roles but adversely affect the environment and living organisms. These metals enter the environment by various natural and anthropogenic means, such as mining, natural weathering of the earth's crust, industrial effluents, fossil fuel burning, soil erosion, sewage discharge, urban runoff, insect or disease control agents to crops, and many others [5 - 7]. An increasing ecological and global public health concern has been associated with environmental contamination by these metals. Heavy metals are non-biodegradable and persistent in the environment, contaminate the food chains, and cause different health abnormalities due to their toxic nature. At present, there is a significant rise in bio-accumulation and bio-intensification of heavy metals (above threshold levels) in biological species, which causes various anomalies in humans and the environment [8 - 10]. Bioaccumulation of these metals above the permissible limits exhibits its lethal toxic effects and negatively affects the microbiota and ecological equilibrium of soils, animal species, and humans. Therefore, remediation of heavy metals requires special attention to protect air quality, water quality, soil quality, human and animal health, and all spheres as a collection. In this scenario, it is critical to choose economically viable and effective treatment methods free of shortcomings and translate the need for heavy metal alleviation from the environment in terms of an eco-friendly approach [11, 12]. Bioremediation is the most potent and ideal for removing heavy metals and degrading various pollutants, recognized as heavy metal hyper-accumulators by numerous studies as efficient and sustainable. Additionally, it poses multiple advantages over conventional methods, including economic viability and repeated use of biomass, selective metal binding, effective desorption, and recycling of bio-adsorbents [13, 14]. Mycoremediation, for example, is a biological approach for removing trash from the environment that relies on the usage of fungi or mushrooms. Fungi have chitin in their cell walls, which can tolerate high concentrations of metals, grow in diverse pH and temperature conditions, and exhibit excellent mycoremediation potential [15]. Macro-fungi, a member of Phylum Basidiomycota and Ascomycota of the Fungi kingdom, have diverse epigeous or hypogeous fruiting bodies that grow out of a mass of mycelium and are collectively called a mushroom. The ability of mushroom species to digest heavy metals by secretion of a range of hydrolysing and oxidizing enzymes has attracted researcher's attention toward its application in waste remediation/ mycoremediation [16, 17]. Mushroom is a multicellular, heterotrophic and achlorophyhous species that belongs to Basidiomycetes family and mycota kingdom. The present review paper discusses about bioremediation of heavy metals and biodegradation with mushroom diversity. The edible mushroom *Lactarus deliciosus, Russula delica and Hizopogon roseolus* are known to dissociate Cd, Cr, Cu, Pb and Zn. Agaricus bisporus assimilates heavy metals like Cr, Cu, Cd and Zn whereas, *Pulveroboletus amarellus* absorbs Zn metal. *Agaricus macrospores* accumulate Cd metal. *Pleurotus ostreatus* absorbs more heavy metals like Cd, Hg, Zn and Cu [18 - 20].

## SOURCE OF HEAVY METAL TOXICITIES

Sources of heavy metals in the environment are both natural and anthropogenic. The natural or geological sources of heavy metals in the environment include weathering of metal-bearing rocks and volcanic eruptions. The primary rocks, such as magmatic or igneous rocks, crystallize upon the cooling down of magma. Magma contains a large amount of heavy metal in small quantities [21 - 23]. These heavy metals are incorporated into the crystal lattice of magma during the cooling of magma. Magma crystallization is a function of temperature and pressure conditions, which change constantly during cooling. Different metal ions concentrate according to their stability field at limited ranges of temperature, pressure and chemical composition conditions. One such example is Cr deposited as chromite, and another is Zircon contains uranium and other rare earth materials. These infiltrate into the enclosing rocks; a chemical reaction takes place between enclosing rock and hydrothermal fluids and mineral precipitate as ores such as arsenic as arseno-pyrites (FeAsS), lead as galena (PbS), Zinc as sphalerite. Repeatedly, the ore is an assemblage of several minerals, so smelting and processing of one metal often result in releasing other metals in the environment. Physical and chemical weathering dissolves these heavy metal ions and is

## CHAPTER 9

# Mushrooms - A Promising Candidate for the Biosorption of Heavy Metals from the Environment

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**Abstract:** Heavy metal pollution has become an emerging issue worldwide owing to its high toxicity, non-biodegradability and persisting nature. Thus, it shows high bioaccumulative ability in the living system that may lead to carcinogenicities and several health complications in humans, even at trace concentrations. Their genesis occurs *via* both natural as well as anthropogenic activities that have contributed to an unusual increase in the concentration of toxic heavy metals across the globe. Several conventional methods, namely chemical precipitation, ion exchange, and membrane filtration, are being implied for the elimination of recalcitrant metals persisting in the ecosystem. But these methods have their own shortcomings and offer many limitations when applied to large volumes and fewer metal concentrations. In this regard, an alternative treatment method is needed that will overcome major demerits while remediating pollutants at a large scale without generating any secondary pollutants. Hence, a variant of the sorption technique, *i.e*., biosorption, appeared as economical and eco-friendly alternative treatment technology which is characterized by utilizing a material of biological origin. Further, in this process, the binding of passive cations might occur through living or nonliving biomass and aid in the elimination of contaminants from the aquatic system. The origin of biosorbents may vary in terms of the different microorganisms used. However, the biomass of macrofungi or mushrooms has been apprehended as a reassuring class of low-cost adsorbents in effacing toxic ions. This is because the cell walls of macrofungi are enriched with several functional groups that provide key aspects in the biosorption process. In this chapter, the biosorptive propensity of different mushrooms toward metal ions has been accented, and also insights into mechanisms of biosorption are discussed.

**Keywords:** Biosorption, Environment, Heavy metal, Mushroom.

## INTRODUCTION

During the last centennial, industrialization and urbanization have increased progressively to meet human necessities. This leads to increased demand for the

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exploitation of natural resources at a high level and thus aggravates pollution across the globe [1]. The environment is gradually contaminated through the entrance of many pollutants; inorganic ions are of great concern. Since the 1940s, heavy metal pollution has been alarmingly increased owing to their high rates of mobilization and transport in the living systems [1]. These are considered leading contaminants because of their toxicity, perseverance and bioaccumulative nature. Their genesis occurs through both natural as well as anthropogenic sources in which natural activities include weathering of metal-bearing rocks, soil erosion, and volcanic eruptions and anthropogenic activities comprise mining and several other manufacturing and farming activities [2]. Therefore, the term 'heavy metal' is used to represent the metallic chemical elements and metalloids that show a negative impact on the environment and living organisms. However, certain metalloids and lighter metals (like selenium, arsenic, and aluminum) also have toxic effects. Some elements (such as gold) are non-toxic even though they are known to be heavy metals [3, 4]. Although, some heavy metals appear to show biological importance when trace amounts occur. The elements with biological significance especially belong to the 4th period in the modern periodic table. These elements involve the functioning and production of many enzymes, hormones, and the cellular and metabolic growth of the living organism. But their importance is limited to only low concentrations and above the required concentration, which instigates many adverse impacts on human health [5]. Several industries of chemical fertilizers, pesticide, metallurgy, tannery, mining, electroplating, iron, and steel discard their heavy metal-containing wastes into the aquatic ecosystem and contribute negative consequences to aquatic biota also. The most widely distributed heavy metals which have engrossed the researcher's attention due to their ubiquitous nature are chromium (Cr), lead (Pb), zinc (Zn), arsenic (As), copper (Cu), nickel (Ni), cobalt (Co), cadmium (Cd), mercury (Hg) and others [3]. Hence, it becomes vital to remove such non-biodegradable and recalcitrant pollutants from the environment.

Various efforts have been made to eliminate such pollutants using conventional methods like chemical precipitation, cation or anion exchanger, membrane filtration, ultrafiltration, microfiltration, nanofiltration, reverse osmosis, electrolysis, photocatalysis, and activated carbon adsorption [6]. These treatment methods have their shortcomings and offer many limitations when applied to large volumes and fewer metal concentrations. Furthermore, other drawbacks are they precipitate metals slowly, remove metals partially, require expensive reagents, are less effective for mixed metal concentrations, and release secondary pollutants in high quantities that further need proper disposal. In this criterion, it becomes essential to elite such processes that are fast, worthwhile, eco-friendly, and efficient approaches for the treatment. Moreover, it should be devoid of the limitations and enhance the ability to translate the need for eliminating toxic heavy metals released from industries or originating from other sources [7 - 9]. Recent research has approached green technologies for cleaning and remediating recalcitrant pollutants. Hence, the process of adsorption is found to be efficient, reasonable, and worthwhile for the eradication of these pollutants and shows a high degree of efficaciousness while using feasible biosorbents. In addition to other advantages, biological methods have the propensity to remediate huge quantities of effluents using low biomass concentration in a short period. In the biosorption process, microbial biomass is a biosorbent for detoxification and removal of several recalcitrant pollutants, particularly toxic inorganic ions, from the ecosystem [10]. Moreover, it can perform dual mechanisms as active and passive transport. The first phase is generally signified as passive uptake that exhibits fast and reversible accumulation at the earliest, whereas the second phase represents active uptake owing to slow bioaccumulation inside the cell's organelles, often irreversible and associated with metabolic activities [11]. Initially, dead microorganisms were used mostly for decontamination, but a later approach initiated the utilization of living microorganisms to express better endures in the contaminated environment and high metal accumulation [12].

However, the biomass of various microbes is being employed as biosorbents. While numerous biosorbents have also been designed using different live or dead constituents of mushrooms, such as mycelium, fruiting bodies, and spent mushroom substrates (SMS). These are found to be effective in heavy metal sorption, and their mechanism of action, including extracellular and intracellular accumulation in the biosorption process, displayed the tolerance potential of heavy metals to macrofungi [13]. Further, they have huge dimensions to accumulate heavy metals above their threshold concentration inside the fruiting body and other parts, so the mushrooms emerged as an operative agent for biosorption [14]. Various species related to the genera, such as *Agaricus, Boletus, Armillaria, Polyporus, Russula, Pleurotus,* and *Termitomyces,* have been explored for the sorption of toxic heavy metals [15]. Hence, the macrofungi or mushrooms are considered a scavenger of pollutants and the foremost part of the ecosystem. This chapter aims to highlight the mechanisms of biosorption, the potentials of macrofungi (mushrooms) in heavy metal sequestration, the efficiency of different biosorbents, and comparative analysis of dead and live fungal biomass as biosorbent for heavy metal removal from the contaminated sites.

## BIOSORPTION

In the early 1970s, nuclear power stations discarded their wastewater containing heavy metals and radioactive elements in large amounts into the aquatic system; meanwhile, many microorganisms have appeared to show a remarkable process called biosorption which aid in the concentration of these toxic elements.

**CHAPTER 10**

# Application of Fungal Xylanase Enzymes

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**Abstract:** The enzyme xylanase breaks down the linear polysaccharide β-1,4-xylan into xylose, therefore breaking down hemicellulose, one of the primary components of plant cell walls. It is essential for the breakdown of plant materials into usable nutrients by microorganisms that thrive on plant sources. Fungi, bacteria, yeast, marine algae, protozoans, snails, crustaceans, insects, seeds, and other organisms generate xylanases. However, the amount of xylanase produced by fungal cultures is generally significantly larger than that produced by yeasts or bacteria. There is a growing demand for low-cost microbial xylanolytic enzymes that have industrial uses and are commercially manufactured. The chlorine-free whitening of wood pulp preparatory to the papermaking process and the enhanced digestibility of silage are two commercial applications for xylanase. Aside from the pulp and paper industry, xylanases are used in wheat flour for ethanol production, improving dough handling and quality of baked products, as food additives in poultry, clarification of fruit juices, biofuel production, textiles, pharmaceuticals, and chemical industries. Improved knowledge of the biological characteristics and genetics of fungal xylanase will allow these enzymes to be used in a variety of novel biotechnological and commercial applications.

**Keywords:** Biofuels, Biotechnological applications, Pharmaceuticals, Textiles, Xylanase.

## INTRODUCTION

Global demand for sustainable renewable fuels has been spurred by rising energy costs and environmental concerns [1]. Governments are now funding considerable research into the development of alternative transportation fuels generated from renewable energy sources, recognising the impending global energy problem caused by the depletion of petroleum-derived fuels. The US Department of Energy has launched a programme to produce biofuels, with a goal of 60 billion gallons per year by 2030. Europe has set a similar goal of replacing 25% of petroleum-based liquid transportation fuel with biofuels by that time [2].

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However, because biofuel production utilising substrates such as sugar cane and corn has limited ability to produce such large volumes, it is a difficult goal to achieve. Researchers discovered that lignocellulose biomass, which contains 75 percent polysaccharide sugars, may be used as a significant feedstock for biofuel production as a solution [3]. If that isn't enough, lignocellulose biomasses are a sustainable energy source that can be procured mostly from agricultural wastes and are plentiful in nature [4].

Agricultural and industrial activity, notably related to agro-allied industries like breweries, paper pulp, and textiles, creates lignocellulosic wastes worldwide. Wood residues (such as sawdust and paper mill waste), waste paper and agricultural leftovers (such as straw and bagasse), household garbage (lignocellulose waste), food industry residues, and municipal solid wastes are just a few examples of waste [5].

These wastes tend to build up in the environment, resulting in pollution [6]. These wastes, on the other hand, are biodegradable and may be turned into useful goods like biofuels, chemicals, and low-cost energy sources for fermentation-improved animal feeds, food processing, sugar, paper pulp, ethanol, pharmaceutical, and agro-industries [7 - 9]. There has been much concern regarding the use of lignocellulosic wastes in the production and recovery of various value-added products because of their availability and renewability [10, 11]. Its increasing need for more efficient usage looks to be transforming into one of the most crucial areas of enormous industrial interest.

Plant biomass wastes that are mostly made up of lignin, cellulose, and hemicelluloses are referred to as lignocellulosic wastes. Hemicullose has a significant structural component called xylan, which accounts for 20–40% of total plant biomass. The degradation of lignocellulosic biomass necessitates the use of a variety of hydrolyzing enzymes. The availability of enzymes for lignocellulosic biomass hydrolysis remains a key problem in the efficient degradation of plant biomass. Under ideal industrial conditions, biomass may be degraded successfully by combining multiple enzymes that hydrolyze complex polysaccharides into fermentable sugars. These enzymes must function in a range of environments, including those with high temperatures and pH [12].

Xylanases are a kind of depolymerizing enzyme that hydrolyzes xylan, which is a major component of hemicellulose. The development of thermophilic xylanases that are more efficient at higher temperatures than those currently accessible commercially is essential. The relevance of xylanase-producing thermophilic bacteria is critical, and they are well-suited for industrial applications. As a result, researchers are increasingly interested in studying thermophilic bacteria from harsh environments for biotechnological applications in biomass breakdown. Xylanases are most often generated from microorganisms for industrial purposes due to their biotechnological features. Xylanases have recently piqued the curiosity of the industry for biofuel production, chemical and pharmaceutical production, bioleaching of wood pulp, papermaking, food and beverage production and animal nutrition.

## XYLAN

Plant biomass that remains in agricultural trash contains an essential structural component called xylan [13, 14]. It is the second most common biopolymer after cellulose and the most abundant hemicellulosic polysaccharide in plant cell walls [15]. The angiosperms, grasses, and grains constitute a family of structurally varied plant polysaccharides [16]. It is a heterogeneous polymer composed largely of a linear-(1,4)-D-xylose backbone that is partially acetylated and partially replaced by a variety of side chains, principally-D-glucuronosyl and L-arabinosyl units, to varying degrees.

Multiple hydrolases are necessary for full xylan breakdown due to their structural complexity. Endo-xylanase (EC3.2.1.8) is the main enzyme in this process, which cleaves the xylan backbone into xylooligosaccharides [17, 18]. Its primary role appears to be structural, preserving the cell wall's integrity in conjunction with other components, such as hemicellulose, cellulose, pectin, and lignin. It also works in tandem with lignin to protect cellulose microfibrils from biodegradation [19 - 22].

Xylans have characteristics that influence our well-being. One of the essential functional ingredients in baked goods is xanthan gum. They may be turned into xylitol, a natural food sweetener. They affect the brewing characteristics of grains. They can also aid in the diagnosis of various human illnesses. Due to the variety and complexity of plant xylan's chemical composition, it takes a combination of hydrolytic enzymes with distinct specificities and modes of action to completely break it down. As xylan has a complicated structure, it necessitates the use of many enzymes for full hydrolysis. However, endo β-1, 4-xylanase plays a significant role in xylan depolymerization [23].

## XYLANASES

Biological catalysts, such as enzymes, mediate the vast majority of metabolic processes that make life possible. Enzymes are the catalytic cornerstones of metabolism, and as such, they are the area of extensive research worldwide, not just among biologists but also among process designers/engineers, chemical engineers and other scientists. Enzymes perform a number of functions inside

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