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Review Paper

Role of mushroom in anxiety disorder

Prachi Kolambe^{*1}, Reema Rani², Disha Koli³

¹³Department of pharmacy, Yadavrao Tasgaonkar Institute of Pharmacy, Mumbai University

²Department of pharmaceutical science, Punjab university, patiala

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ABSTRACT

Anxiety disorder is a mental health condition worldwide. It affects more than 300 million people worldwide. Conventional pharmacological interventions such as selective serotonin reuptake inhibitors and benzodiazepines often provide only partial relief, but long-term use can lead to adverse effects and dependency risks. This has increased the novel therapeutic agents derived from natural sources, including edible and medicinal mushrooms. Recent research suggests that mushrooms are rich in bioactive compounds such as, polysaccharides, terpenoids, phenol acids, and insole alkaloids, which exhibits neuroprotective, anti inflammatory and anti oxidant properties.. Remarkably psilocybin containing mushroom have shown results in reducing anxiety in both clinical and sedative care settings by regulating serotonergic signaling and enhancing emotional flexibility. Likely, edible species such as *Hericium erinaceus* (lion's mane) and *Ganoderma lucidum* (reishi) have been studied for their anxiolytic potential, largely attributed to their capacity to promote neurogenesis and regulate gut brain axis. This will provide comprehensive synthesis of current evidence on role of mushrooms in anxiety management. This also signifies the biological mechanisms, preclinical findings, clinical trials, and coming ideas. By combining pharmacological and nutraceutical approaches, mushrooms may help for anxiety disorders, validating further inventions.

INTRODUCTION

Anxiety disorder is the prominent public health challenge, ranking among prevalent psychiatric conditions. According to WHO about 4% of world's population experiences an anxiety disorder also known as panic disorder, social

anxiety, and phobia related disorders, which is characterized by excessive fear about something, and physical symptoms like palpitation and restlessness, which lead to impair in daily functioning.^[1] Current pharmacotherapies primarily selective serotonin reuptake inhibitors (SSRIs), serotonin nor epinephrine reuptake

***Corresponding Author:** Prachi Kolambe

Address: Dr.N.Y.Tasgaonkar Educational Complex, Bhivpuri Road, Karjat, Raigad, 410201

Email ✉: prachikolambe688@gmail.com

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inhibitors (SNRIs), and benzodiazepines have proven efficacy but are limited by delayed therapeutic arrivals, variable response rate, and adverse events like sedation, sexual dysfunctions, weight gain, dependency risk^[2]. Psychotherapeutic intermediates like cognitive behavioral therapy remains valuable but not overall effective or accessible because of cost and shortage in providers^[3]. These limitations have promoted other treatments that may enhance results and reduce adverse effects. Natural products are largely recognized as logical sources of neuropsychiatric therapeutics, as they mainly contain complex mixtures of bio active molecules with combining effects on brain function^[4]. Among these, mushrooms occupy a unique position because of different chemical constituents and long lasting use in traditional medicine across Asia, Africa, and Latin America. Edible and medicinal mushrooms are used and valued for neuroprotective, immunomodulatory, and stress reducing effects.^[5] At times, psilocybin containing mushrooms are termed as magic mushrooms, as it regulates consciousness and emotional regulation through serotonergic pathways.^[6] Emerging preclinical and clinical studies tells that mushrooms may reduce anxiety through mechanism involving serotonergic modulation, reduction of oxidative stress, suppression of neuroinflammation and regulating gut brain axis.^[7] Its shows mushroom is functional as well as potential therapeutic agents. These will give idea of role of mushroom in anxiety, by bridging traditional and modern neuroscience, and gives idea of psychiatric treatment innovations.

BIOLOGICAL BASIS:

An anxiety disorder arises from interchange of neurochemical, genetic, environmental, and psychological factors. At the neurobiological level, three primary systems have been concluded

they are, the serotonergic system, hypothalamic pituitary adrenal (HPA) axis, and the inflammatory or oxidative stress pathways.^[1]

1. Serotonergic Deregulation

One of the searches in anxiety research tells about the dysfunction of serotonergic neurotransmission. Reduced serotonin availability in synaptic clefts is associated with increased fear responses, increased amygdale activation, and impaired regulation of prefrontal cortical circuits.^[8] This is carried by the clinical efficacy of SSRIs and SNRIs, which increase extracellular serotonin and thereby decreased anxiety symptoms.^[2]

2. HPA Axis Hyperactivity

The HPA axis is primary to response to stress, and its chronic hyper activation is strongly correlated with anxiety pathology. Excessive secretion of corticotrophin releasing hormone (CRH) and cortisol leads to increased attention, disturbed cardiac rhythms, and impaired hippocampus neurogenesis.^[9] Prolonged cortisol exposure is also neurotoxin, further aggravates mood and leads to anxiety.

3. GABA and Glutamate Imbalance

The neurotransmitters like serotonin, glutamate and gamma amino butyric acid (GABA) plays a critical role in brain function and hence anxiety. If GABA inhibition is reduced it will lead to increase in neuronal excitation, while hyperactivity of glutamatergic transmission leads to excessive fear and increased alertness.^[10] Therefore, benzodiazepines enhances GABA A receptor function remains effective for short time period.

4. Inflammation and Oxidative Stress

Neuro inflammation and oxidative stress are found factors for anxiety disorders. Increased levels of



pro inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF alpha) are mainly reported in anxiety patients.^[11] As well as, marks oxidative stress like, malondialdehyde (MDA) are increased, whereas antioxidant like superoxide dismutase (SOD) are reduced^[12] Together, this process impairs synaptic plasticity and increases neuronal damage and anxiety.

5. Gut–Brain Axis Dysregulation

The interlocation between gut microbiota and the central nervous system is another factor of anxiety pathology. Dysbiosis is characterized by reduced microbial diversity and imbalance of beneficial bacteria which can alter tryptophan metabolism and serotonin synthesis which will lead to increase in anxiety behaviors.^[13] The preclinical studies suggest that restoring gut microbial balance may reduce anxiety as a promising therapeutic target. All together, these neurobiological substrates show multiple entry points for therapeutic interventions. Mushrooms, due to their diverse array of bioactive compounds have the potential to act on serotonergic, anti-inflammatory, antioxidant, and gut–brain pathways provides a multi-targeted strategy against anxiety disorders.

MUSHROOM AS BIOACTIVE SOURCES:

Both edible and medicinal Mushrooms comes from varied Variety of fungi which are rich in nutrition, traditional healing, and recently in modern biomedical research. They consist of secondary metabolites and nutraceutical compounds which help in brain health and emotional regulation. The bioactive substances like polysaccharides, terpenoids, phenolic compounds, ergothioneine, and indole alkaloids, all has certain effects.^[4]

1. Polysaccharides

Polysaccharides like β -glucans are derived from mushroom, which are responsible for **immunomodulatory properties**. Pro-inflammatory cytokines like IL-6 and TNF- α if regulated shows reduction in neuroinflammation, which lead to decreases anxiety.^[14] These compounds also help in gut microbial health, and lead to improve gut–brain axis function.

2. Terpenoids and Triterpenes

Mushroom species like *Ganoderma lucidum* (reishi) has triterpenoids present into them; they have antioxidant, anti-inflammatory, and neuroprotective properties.^[15] This compound helps in improving HPA axis activity and may reduce cortisol production leading chronic anxiety reduction.

3. Phenolic Compounds and Antioxidants

Mushrooms are an important source of **phenolic acids** and antioxidants such as **ergothioneine** contains sulfur with amino acid which is found abundantly in *Pleurotus ostreatus* and *Agaricus bisporus*. Ergothioneine functions as a cytoprotective agent by neutralizing reactive oxygen species and preserving mitochondrial integrity, and protecting neuronal circuits involved in stress and anxiety.^[16]

4. Neurotrophic Compounds

The mushroom lion's mane contains **erinacines** and **hericenones compounds into it**, which stimulates **nerve growth factor (NGF)**, which increases hippocampal neurogenesis, synaptic plasticity, and cognitive resilience, leads to reduction in anxiety disorders.^[7]

5. Indole Alkaloids

The Studies have shown that Psilocybin mushroom contains tryptamine alkaloid which is



also found in various species of fungi, those are used in psychiatric medicines. The Psilocybin is metabolized to form psilocin, which acts as a **5-HT_{2A} receptor agonist** in the brain. This serotonergic modulation enhances emotional management which reduces abnormal behaviors, and causes states of cognitive flexibility which hence reduces anxiety.^[6] Clinical evidence suggests its efficacy in treatment-resistant anxiety, particularly in soothing care and major depressive disorder with anxious distress.^[17]

6. Gut Microbiota-Modulating Molecules

By the research studies, we can indicate that certain mushroom polysaccharides act as **prebiotics**, specifically the nourishing beneficial gut bacteria such as *Bifidobacterium* and *Lactobacillus*. This microbial shift increases short-chain fatty acid production, which is linked with reduced systemic inflammation and improved mood regulation.^[18] All together, mushrooms provide a **phytochemical toolkit** capable of addressing multiple neurobiological targets of anxiety, including neurotransmitter modulation, neurogenesis, oxidative stress reduction, and gut-brain regulation. Their unique combination of compounds positions them as promising candidates for integrative psychiatric care.

MECHANISM:

Mushrooms, particularly those containing bioactive compounds like psilocybin, ergothioneine, and other phenolics, shows anxiolytic effects through multiple pathways in the central nervous system (CNS). This mechanism is essential to understand biochemical properties with observed outcomes.

1. Neurotransmitter Modulation

Mushroom species Psilocybin has naturally occurring psychedelic which gets metabolized into psilocin, it primarily acts as a partial agonist in **serotonin 5-HT_{2A} receptors**.^[19] This receptor activates and enhances **cortical connectivity** and neural circuits regulate mood and anxiety. Preclinical studies suggest that this receptors interacts and reduces the effects on **glutamatergic signaling**, which is important for synaptic plasticity and emotional management.^[20]

2. Neurotrophic Effects

Pleurotus and lion's mane are edible mushrooms species. They contain compounds that stimulate nerve **growth factor (NGF)** expression. NGF is important for the maintenance and growth of neurons in hippocampus and prefrontal cortex region of brain. This shows effect in anxiety.^[21] Regular intake of these mushrooms in the diet will improve the **synaptic density** and **neuronal resilience**, which will supports adaptive thinking and emotion regulation.

3. Anti-inflammatory and Antioxidant Pathways

Oxidative stress and neuro inflammation give rise to anxiety disorder. Mushrooms like *Pleurotus ostreatus* and *Ganoderma lucidum* has **ergothioneine, polysaccharides, and phenolic compounds**, which are good source of antioxidants.^[22] These compounds reduces reactive oxygen species (ROS) and regulates pro-inflammatory cytokines (IL-1 β , TNF- α), and stabilizes neuronal function and hence reduces anxiety symptoms.

4. Gut-Brain Axis Modulation

New research shows that mushrooms impacts the **gut microbiota**, which regulates CNS function through the **microbiota-gut-brain axis**. Prebiotics



in mushroom polysaccharides help beneficial gut bacteria to develop in **short-chain fatty acid (SCFA)** production. SCFAs balance the **neuroinflammation** and neurotransmitter synthesis which indirectly reduces anxiety.^[9] This constitute in novel, dietary-mediated mechanism connecting mushroom consumption with mental health.

CLINICAL EVIDENCES:

In recent years, there is increased number of clinical studies seen which are questing for the role of mushroom particularly psilocybin species for reducing anxiety in humans.

1. Psilocybin-Assisted Therapy in Anxiety

Psilocybin has been studied broadly in patients who have experienced anxiety related to other fatal diseases, such as cancer. Randomized controlled trials (RCTs) have shown major reductions in anxiety after including psilocybin into the diet. Many a times the effects have lasted for months after a single or limited dosing session. As per the research conducted a double-blind RCT for patients suffering from life-threatening cancer. They found substantial and lasting decreases in both depression and anxiety after a single moderate dose of psilocybin combined with psychological support.^[17]

2. Edible Mushrooms Anxiety

Non-psychedelic edible mushrooms, such as *Herichium erinaceus* (lion's mane), have also shown ability to reduce mild anxiety symptoms. A study has shown that patients who consumed lion's mane extract resulted major reduction in Anxiety.^[7] These recommend that consumption of edible mushrooms can stabilize the mood and improves brain function, even in individuals who are not diagnosed with anxiety disorders.

3. Safety

Safety is an important for any therapy. Clinical trials has shown that psilocybin, when administered in a controlled manner provides favorable safety profile. Side effects are mild and temporary, including headache, nausea, or increases in blood pressure.^[23] Similarly, edible mushrooms are generally considered **safe for daily consumption**, which doesn't have much side effects reported in human studies, mainly gastrointestinal discomfort in sensitive individuals.

INTERVENTIONS AND IMPLICATIONS:

The mushroom is a part of balanced diet. It can be regularly taken into diet to prevent anxiety and also managed through nutrition and lifestyle means.

1. Nutritional Components Beneficial for Anxiety

Pleurotus ostreatus, *Agaricus bisporus*, and *Herichium erinaceus* are the edible mushrooms containing various bioactive compounds that help in mental health:

- Ergothioneine has antioxidants which reduces stress. It also promotes protection of nerve cell and improvement in emotion management.^[16]
 - Polysaccharide (β -glucans) improves immunity as well as reduces inflammation, which results in anxiety reduction.^[24]
 - Vitamin B and minerals like selenium and zinc are important for neurotransmitter synthesis which improves mood and anxiety.^[24]
- ### 2. Including Mushrooms in diet:

Including mushroom into the diet with regular exercise, mindfulness, good sleep as lifestyle



changes will help individual to recover from the anxiety disorder.

3. Potential for Preventive Mental Health

Studies suggest that diet enriched with mushrooms will **lower the mood disorders** with anxiety. By improving oxidative balance, reducing inflammation, and enhancing gut–brain communication, mushroom-rich diets will be **preventive measures**, in high risk anxiety disorders.

4. Limitations and Considerations

- Dose can vary depending on species, cultivation method and cooking method.
- Some bioactive compounds may require specific preparation (e.g., heat or extraction) for absorption purpose.
- Genetics, gut microbiota composition, and pre-existing health conditions can dependent factor for effectiveness of mushroom consumption.

FUTURE DIRECTIONS:

As research on mushrooms for anxiety is expanding, we are getting to know more and more clinical uses and their applications.

1. Novel Bioactive Compounds

As psilocybin and ergothioneine mushroom species are well-studied, they contain multiple underexplored bioactive molecules which may have anxiolytic or neuroprotective properties. For Examples:

- Hericenones and erinacines: This Stimulates nerve growth factor (NGF) and enhances synapse development.[21]
- Triterpenoids: they have anti inflammatory and antioxidant properties. It potentially reduces neuroinflammation associated with

anxiety. Further studies can quest about other such compounds which can regulate the CNS function and can lead to find new anxiolytic treatments.

2. Personalized Medicine Approaches

Mushrooms can react with different for different individuals, taking into consideration the factors like genetics, gut microbiota, and metabolic differences.

Future goals:

- **Genetic profiling:** this may predict response to psilocybin therapy.
- **Microbiome modulation:** for enhance the anxiolytic efficacy of edible mushrooms through the gut–brain axis.
- **Tailored dietary interventions:** as with nutraceutical one can combine mushroom intake and check for mental health outcomes.

Personal history of patient and adaptability will help in safety, efficacy, and beliefs in clinical populations.

3. Incorporating Conventional Therapies:

Mushrooms can be best as traditional treatment:

- Psilocybin-assisted therapy with cognitive-behavioral therapy (CBT) has shown combine benefits for treatment-resistant anxiety and depression.^[23]
- Dietary mushrooms or standardized extracts may permit dose reduction of anxiolytic medications lead to minimize the side effects.
- Regular administration of edible mushrooms in the diet can act as a preventive measure in patients that will help in reducing the anxiety disorders.



Collectively, these aims to show mushrooms as a scientifically validated, accessible, and complete option for anxiety management.

CONCLUSION:

Worldwide, million of people are suffering from anxiety disorder. There are treatments available like medications and therapies but they usually fail or have side effects. So, it has motivated researchers now to find safer and more comprehensive approach towards the same. Here, mushroom is seen beneficial in olden or traditional medicine which is gaining attention in today's time for its capability to aid mental health and anxiety disorder. Psilocybin mushroom, which is well known species for activating serotonin pathway and emotional flexibility to edible species like lions mane and reishi helps in brain growth and reduce inflammation. They have multiple natural compounds which help reduce anxiety. They work on brain as well as gut brain connection; balances stress hormones and protect neurons from damage which can cause by stress and oxidative process. Mushroom has nutrition, neurobiology, and mental well being all together. Still more research and dept knowledge required to know how it can be used, its dose, and for which group of people it is helpful. By the research papers referred, it is encouraging that mushroom could become worthy in managing stress, anxiety by taking it as medicine or into the diet. It seems, it will form bridge between natural remedies and modern psychiatry as its safer and effective anxiety care.

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