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# The Toxicity Mechanism and Treatment Methods of Poisonous Mushrooms

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**Abstract.** Poisonous mushrooms act as decomposers in the ecosystem. Because of their confusing resemblance to common mushrooms, they are often eaten inadvertently and cause serious poisoning. Different poisonous mushrooms contain different kinds of toxins, such as goitrogens and umbrella toxins. Poisoning can cause irreversible damage to organs such as the liver and kidneys. Clinical symptoms and duration of poisoning vary among different types of poisonous mushrooms in different regions. The most common clinical manifestations include gastrointestinal symptoms, liver failure and neurological disorders. Current diagnostic tools are mainly based on symptomatology and laboratory tests such as high-performance liquid chromatography. Treatment after poisoning is generally supportive therapy and antidotes, and in extreme cases liver transplantation is considered. In this research, two of the most typical poisonous mushrooms, the gooseberry and the death cap, were used as examples by analyzing open source information and cases. Their toxin composition poisoning symptoms as well as the principles of toxicogenesis were studied. Treatment strategies for poisonous mushroom poisoning are proposed, which can provide scientific basis for future prevention and treatment.

**Keywords:** Poisonous mushrooms; Toxicity mechanism; Treatment methods.

## 1. Introduction

Poisonous mushrooms play an important role as decomposers in the ecosystem by decomposing organic matter such as dead leaves of wood and converting them into nutrients to be incorporated into the soil. Its toxins are thought to maintain the biodiversity of the natural system and maintain the ecological balance by preventing overpredation by causing poisoning of a larger number of predators. Because of its similarity to common mushrooms in appearance and bright color, it is confusing and easy to be eaten, resulting in poisoning. Edible mushrooms are rich in nutrients such as vitamin B2 and folic acid, which are often regarded as nutritious ingredients, and poisonous mushrooms are also easier to be eaten by mistake because of their similar shape.

Once entered into the human body, the strong toxins in poisonous mushrooms can lead to serious poisoning reactions [1]. In different regions, the time of poisoning and the toxic reaction of different kinds of poisonous mushrooms are slightly different according to the living habits of the local residents and the measurement and manner of intake. The clinical symptoms produced after ingestion are varied, among which the gooseberry toxins (amatoxins) contained in gooseberry species are the most common targets of scientific studies [2]. This toxin disrupts cellular protein synthesis mainly by inhibiting RNA polymerase II, which ultimately leads to apoptosis [3]. The fatal Amanita muscaria and Amanita phalloides contain this toxin. In addition, toxic umbelliferin (Orellanine) impairs kidney function leading to irreversible chronic renal failure requiring long term dialysis and kidney transplantation to sustain life, and umbelliferatoxin (Monomethylhydrazine) produces a dramatic stimulating effect on the central nervous system leading to headaches, dizziness, seizures, and in severe cases, even coma or death. Gastrointestinal symptoms such as nausea, vomiting, and diarrhea caused by other species of poisonous mushrooms are usually early signs of poisoning, but they are also precursors to more serious organ damage [4]. In the case of liver damage, patients may develop acute liver failure within a few days which may be fatal if liver transplantation is not performed in time [3]. In addition to the liver and kidneys, certain toxins in poisonous mushrooms may cause direct

damage to the heart, leading to arrhythmia or myocardial damage, further aggravating the condition. Even if the patient survives the initial poisoning, long-term organ damage may lead to chronic health problems, such as persistent renal insufficiency or liver disease affecting subsequent quality of life over time. Furthermore, symptoms do not occur immediately after poisoning and patients may not realize the severity of the poisoning until hours or even days before symptoms appear, making subsequent diagnosis and treatment difficult.

Currently, the most widely used treatments are supportive therapy, application of antidotes and, in severe cases, liver transplantation. The effects of mushroom poisoning on human health are extensive, and studies analyzing the classification of poisonous mushrooms, toxin composition and types of poisoning are essential for future treatment and prevention of related poisoning events. This research will first explore the classification and identification methods of poisonous mushrooms, then analyze the biochemical mechanisms of toxins in depth, followed by a discussion of the clinical treatment of poisonous mushroom poisoning. It aims to provide a valuable scientific basis for future poisonous mushroom research and poisoning prevention by systematically analyzing the classification, toxin composition, and clinical manifestations of poisonous mushrooms.

## 2. Toxicity mechanism

Amanita phalloides alias death cap is mainly distributed in temperate and subtropical regions. Possessing the strongest mushroom toxin in the world, it is one of the deadliest poisonous mushrooms. Poisoning cases due to accidental consumption of this poisonous mushroom should not be ignored in the world, and Amanita phalloides poisoning is also a common occurrence in Asia. In Asia, mushroom poisoning also occurs frequently, where dozens of cases of poisoning are diagnosed every year [5]. Mushrooms contain toxins mainly a-Amatoxin, this toxin through the inhibition of RNA polymerase II, preventing the transcription of DNA into mRNA home production. It can lead to the inability of the cell to synthesize proteins and lead to cell necrosis and tissue damage because the liver is the most important human body metabolic organs first processed through the digestive system. Since the liver is the most important metabolic organ in the human body and is the first organ to process toxic substances entering the body through the digestive system, liver cells are the main target of a-amatoxin [6]. Once the toxin blocks protein synthesis, liver cells rapidly lose function resulting in acute liver failure and death. The CDC reports that three of the 14 cases of poisoning by this toxin in California in 2016 required liver transplants to survive.

Amanita muscaria, known for its bright red coloration and neuroactive toxin, grows mainly in temperate and sub-freezing regions of the Northern Hemisphere such as forests in North America, Europe, Asia and Siberia, usually around pine, birch and oak trees [7]. Amanita phalloides is distinguished from Amanita phalloides by its main toxins, muscimol and ibotenic acid, which is a neurological stimulant capable of activating glutamate receptors leading to hyper-excitability of the central nervous system. Muscimol, on the other hand, is a gamma-aminobutyric acid (GABA) analog that causes sedation, hallucinations, and coordination disorders by acting on GABA receptors, leading to an increase in inhibitory neuronal activity [7]. Although Amanita muscaria is not as lethal as the toxins of Amanita phalloides, and serious poisonings are relatively rare, its toxicity should not be underestimated. As both neurotoxins enter the human body, they cause severe neurological symptoms and damage to the central nervous system, and poisonings are much more common. In North America and Europe, an average of nearly 100 poisonings are reported each year, but the mortality rate is relatively low.

The chemical composition, mechanism of toxicity, and clinical manifestations of toxicity in Amanita muscaria has been investigated [7], with an in-depth study of the biochemical characterization of the toxins of Amanita muscaria and their effects on the human nervous system. There are two main toxins in Amanita muscaria: ibotenic acid and its metabolite muscimol, both of which act on the human nervous system. The severity of poisoning depends on the content of the main toxins, and the two substances have different effects on the central nervous system. Ibotenic acid is an agonist at

glutamate receptors and has excitatory neurotoxicity, while muscimol is an agonist at GABA receptors and has a sedative effect. In the early stage of gooseberry poisoning, the neuroexcitatory symptoms caused by ibotenic acid are particularly pronounced, such as ataxia, confusion and hallucinations. With the gradual metabolism of ibotenic acid to muscimol, the patients will gradually show inhibitory symptoms such as lethargy, coma and muscle relaxation. In Russia and the Nordic region, the local residents have a long history of misuse of gooseberry, and some patients already have tolerance to the toxin, the symptoms are very mild, and the treatment effect is remarkable. Of the more than 200 cases of poisoning by Pseudomonas syringae, 90% had mild symptoms and did not require specialized medical treatment. Recovery was usually achieved with fluid replacement and correction of electrolyte disturbances. The remaining 10% had more severe symptoms and required treatment such as gastric lavage or induced vomiting. In the early stages of poisoning due to the effects of ibotenic acid, patients usually experience a high degree of excitability and neurological disorders. Benzodiazepines, such as diazepam or lorazepam, are given to achieve a sedative effect, which can effectively inhibit the neurological over-excitability triggered by the ibotenic acid and reduce the symptoms such as ataxia. For patients with severe hallucinations or hyperarousal, antipsychotic medications may be needed, but the sedative effects of muscimol can cause drowsiness and coma. The patient's breathing should be monitored closely to prevent aspiration pneumonia. The treatment of thrush poisoning is very effective most patients recover completely within 24-48 hours of treatment, with a very small number of patients experiencing long term illness.

## 3. Diagnosis

There are two stages of poisoning by hydatid mushrooms, the early manifestations usually occur within 6-12 hours of use, mycological analysis and analysis of all existing cases of poisoning by poisoned mushrooms indicate that early poisoning is characterized by gastrointestinal symptoms most commonly vomiting (=82%) followed by nausea (=68%), abdominal discomfort (=58%), and diarrhea (=38%) [8]. These symptoms usually appeared 30 min-240 min after consumption and improved after 1-3 days, creating the illusion of recovery. However, by the time the symptoms worsen after 24-28 hours, the patient is at risk of liver failure, renal failure and even death [9].

Poisoning by Amanita muscaria is usually the result of accidental ingestion and early manifestations usually occur within 30 minutes-3 hours. Like the hydrilla mushroom it is also mostly gastrointestinal. Hallucinations, muscle spasms, neurological disturbances as well as ataxia and extreme psychosis occur within 4-12 hours. These symptoms result from the binding of specific toxin components in muscimol and ibotenic acid to GABA receptors in the central nervous system [10]. The vast majority of the hundreds of poisonings reported in the literature each year result in full recovery within a relatively short period of time.

The identification of the specific toxin is very important in providing timely and effective treatment, and the earliest possible information on the toxin will allow immediate treatment to prevent further deterioration of the reaction. The diagnosis of mushroom poisoning relies on symptomatology and laboratory testing for specific toxins. Commonly used assays include high-performance liquid chromatography (HPLC) and immunoassays to detect toxin levels in blood, urine or stomach contents. For example, HPLC can detect the concentration of α-epileptotoxin in blood to confirm poisoning by hydatidylcholine mushrooms [11]. In contrast, the laboratory can quickly determine the type of mushroom that caused the poisoning by analyzing the gastrointestinal tract contents for spores, but the type of material analyzed also determines the validity of the analytical comparisons. Gastrointestinal tract contents from the first few hours of poisoning contain intact spore fragments that can be used to determine the morphologic characteristics of the spores and the type of spores by comparing them to standard fungal spores under a microscope. Patients' descriptions of their symptoms, consumption and storage of poisonous mushrooms can also help to identify poisoning cases. During the period 2002-2009, about 7 million people in the south of Poland were admitted to the DCT for poisoning by wild mushrooms. Prior to their admission to the DCT they filled out a basic profile of the mushrooms they had collected, transported, stocked and consumed, and the data were

kept on file for each patient. This data also helped the doctors to determine the status of the poisoning and to build a database for future diagnosis and treatment, considering the actual symptomatology of the disease.

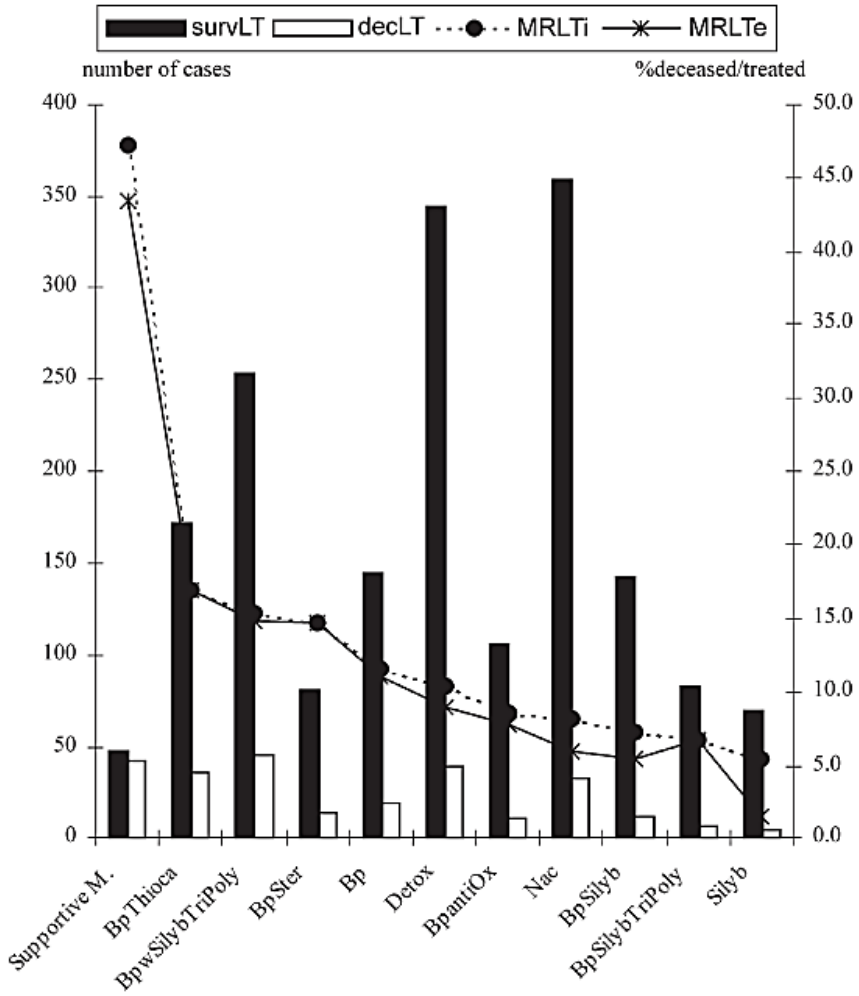


**Figure 1.** Effect of nursing mode on the distribution of treated patients [11].

## 4. Treatment strategies

The mortality rate of poisonous mushroom poisoning is extremely high, and it is estimated that the mortality rate of acute poisoning is about 5-30% in the modern medical environment [6]. The metabolism and action of poisonous mushrooms after poisoning is very fast, especially in cases like Amanita phalloides poisoning, where the toxins cause irreversible damage to vital organs such as the liver in a short period of time. Activated charcoal is usually used in the early stages of poisoning to reduce the absorption of toxins in the gastrointestinal tract (principle). In the late stages of poisoning, when liver damage has already occurred, supportive therapy is more appropriate, especially in the case of severe liver failure or accumulation of toxins in the body, to maintain the patient's blood pressure and electrolyte balance through fluids, together with hemodialysis, to remove toxins that have not been metabolized by the liver, to reduce the burden on the liver to minimize the toxin level in the blood. In extreme cases, liver transplantation may be considered to prolong the patient's life. Modern medical data show that the survival rate of liver transplantation is 70-80% [6], but the risk of postoperative complications increases, and the risk of long-term complications such as infection and cancer is also very high. In addition to the traditional basic poisoning therapies, specific antidotes for poisonous mushroom poisoning, such as silibinin and penicillin, inhibit the hepatotoxicity of α-eclampsia toxin and protect hepatocytes. This makes early intervention and accurate identification of the toxin key to reducing mortality [11], as shown in Figure 1.

The existing research has described the treatment options for patients with mushroom poisoning, analyzing more than 100 cases of mushroom poisoning and finding that acute symptoms usually appear within 6-12 hours of ingesting the mushrooms and include vomiting, dehydration and diarrhea leading to liver failure in severe cases [10]. The mainstay of treatment in the early stages of poisoning is usually the administration of activated charcoal to adsorb the toxins using the carbon structure and intravenous fluid rehydration to prevent the body from losing water through diarrhea, which can lead to severe dehydration and electrolyte disturbances. Treatment for advanced and severe poisoning is usually silibinin, which prevents the toxin from penetrating the liver cells and binding to RNA polymerase II, thereby minimizing the damage to the body's cells. This is supplemented by penicillin therapy to inhibit the circulation and distribution of amatoxin in the body and to minimize its effects on other organs. The efficacy of these treatments depends on the promptness with which they are administered. The early use of activated charcoal and silibinin is effective in slowing down the absorption of the toxin and reducing the mortality rate, whereas liver transplantation is riskier for those who need it, but the majority of patients make a good recovery. In 20% of all cases, liver transplantation was required and 70% of these patients survived successfully.

## 5. Conclusion

This research studied the chemical composition and mechanism of toxicity of the major toxins in different species of poisonous mushrooms. Mushrooms of the genus Amanita are of interest because of the amatoxins they contain, other poisonous mushrooms such as lepiota and galerina contain similar peptide toxins, whereas mushrooms of the genus. Umbellifer are mainly dominated by muscarine and other small molecule toxins. This research has analyzed the chemical composition and mechanism of toxicity of the major toxins in different species of poisonous mushrooms. These toxins inhibit the function of RNA polymerase II, preventing the normal synthesis of proteins from RNA, leading to apoptosis of liver cells and liver failure. The incidence of liver failure is high because the toxicity of this toxin causes irreversible damage to the organ. The survival rate of liver transplantation is 70-80% and that transplantation surgery is a relatively mature but risky treatment. By analyzing the clinical symptoms of poisonous mushroom poisoning, patients usually develop symptoms 6-12 hours after ingesting poisonous mushrooms. Analyzing toxin residues in blood and urine allows for early diagnosis and timely treatment to prevent further damage to the body. Toxin testing based on urine or blood samples, such as ELISA and HPLC, can provide accurate data and be a powerful tool for clinical diagnosis. This research discusses the main treatments currently available after diagnosis and their limitations. Cilibene and penicillin G are the most commonly used antidotes for early stages of gecotoxin poisoning when symptoms are mild, and both have been shown to protect the liver in in vitro experiments. Clinicians have been working to find more effective antidotes, but at present patients with severe liver damage in the later stages of poisoning are dependent on liver transplantation. The most important thing to do to prevent poisonous mushroom poisoning is to make people aware of the dangers of poisonous mushrooms and learn how to identify wild mushrooms and promote the importance of scientific harvesting to reduce the frequency of poisoning. Training in the identification of poisonous mushrooms for people in rural and suburban areas can go a long way in preventing the frequency of poisoning.

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