The Pharma Innovation Journal 2023; 12(5): 4654-4659

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2023; 12(5): 4654-4659

www.thepharmajournal.com
Received: 07-02-2023
Accepted: 18-03-2023

Omprakash Mishra
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Ashish Kumar
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Jinat Rehena
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Krishanu Ghosh
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Sudipta Nandi
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Debosmita Roy
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Kashish Gupta
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Archana TS
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Devendra Kumar
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Corresponding Author:
Omprakash Mishra
Department of Plant Pathology, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Amanita - the wild impersonator: A narrative review

Omprakash Mishra, Ashish Kumar, Jinat Rehena, Krishanu Ghosh, Sudipta Nandi, Debosmita Roy, Kashish Gupta, Archana TS and Devendra Kumar

Abstract
A portion of the human diet consists of mushrooms because of their delicious flavour, high protein content, and the positive health impacts that scientific study has revealed. When collectors and consumers are misled by the physical similarities between hazardous and non-toxic mushrooms, mycotoxicity results. Several types of mushrooms are classified as "poisonous" because they create toxic byproducts. For instance, the genus Amanita has species that can have severe and even fatal negative effects. These species include A. phalloides, A. virosa, and A. Verna. The fact that mushroom poisoning causes a significant number of deaths each year makes it a critical healthcare concern on a global scale. Nevertheless, there is currently no known antidote for this poisoning. The characteristics of A. virosa in terms of epidemiology, toxicity mechanisms, and poisoning traits are discussed in this article.

Keywords: Bioluminescence, luciferin, bioluminescence imaging, biosensors

Introduction
Since ancient times, eating mushrooms has been a tradition, especially in areas with a suitable climate. They have a longstanding reputation for excellent cuisine. Although delicious, mushrooms have a reputation for "killing tables." The variety of foods that people put on their tables has progressively increased in recent years, but the psychological tendency of seeking for novelty, delectable food, and mushroom poisoning remains pervasive (Trabulus and Altiparmak 2011; Yang *et al*. 2020) [24, 25]. According to a case study published in June 2022, Amanita led the patient to experience typical neuropsychiatric symptoms as tiredness, salivation, and vertigo. The primary methods of therapy were symptomatic and supportive measures such infusion, gastric lavage, and liver protection. High-performance liquid chromatography-tandem determined the mushroom toxin content using mass spectrometry (Chen *et al*. 2022) [26]. Additionally, severe kidney damage and rhabdomyolysis have been linked to mushroom poisoning and should be actively treated (Evans *et al*. 2012; French *et al*. 2011) [27, 28]. Additionally, it has been noted that some patients who suffer from mushroom poisoning may exhibit severe arrhythmia, overt precardiac discomfort, cardiac dysfunction, markedly elevated troponin, and decreased ejection fraction. These symptoms usually improve with active symptomatic treatment (Li *et al*., 2021b) [29]. The most deadly of the Amanita poisons is -amanitin, which is a substantial cause of mortality in the event of mushroom poisoning (Rosenthal 2002) [30]. Clinical care for amanitin poisoning is continually improving and now includes measures to stop the absorption of the toxin and employing the antidote that is most likely to be successful (Nieminen and Mustonen 2020) [31].

Active detoxification of ingested toxins by increased excretion, such as diuresis, gallbladder, and diarrhoea. Currently, a number of pharmaceutical therapies are also accessible to treat -amanitin. For instance, silibinin blocks the organic anion transport polypeptide (OATP), which prevents-amanitin from entering cells. Inhibitors of -amanitin entry into cells include Rifampicin, Penicillin, and Cyclosporine A (Ganzert *et al*. 2008; Letschert *et al*. 2006) [32, 33]. Additionally, supportive care such as plasma exchange is used in the treatment of -amanitin before the final strategy, such as liver transplantation, is chosen (Andera and Wasylyk). However, the outcomes are still unsatisfactory when using the current treatment plan. Although specialised detoxification medications are being developed, amanitin poisoning frequently results in serious consequences like multiple organ failure. Exploring and illuminating the pathogenic mechanism of -amanitin will have a significant impact on research into the therapy and study of this substance.

Classification and toxicity of *Amanita* mushrooms

There are many poisonous mushrooms, including those that contain cyclopeptides, which are typically regarded as the most poisonous species, all over the world. The majority of hazardous mushrooms for humans are found in the genus Amanita, which is a member of the Amanitaceae family. Nine of the approximately 900–1000 the species of Amanita are known to produce dangerous amatoxins. Although the genus Lepiota has the biggest figure of amatoxin-producing species, species from the genus Amanita are primarily responsible for mushroom poisoning-related mortality. It's interesting that A. muscaria and A. pantherina contain ibotenic acid and muscimol, which can cause acute renal failure and hallucinogenic effects. Its flavour and aroma are sweet, just like those of other Amanita mushrooms. The A. virosa cap is white, and as it ages, the centre turns yellow or brown in colour. White spores of A. virosa measure 8 to 10 mm in diameter and have a length-to-width ratio of 1.25. (Lee E 1997) [1]

The majority of mushroom intoxications begin with only gastrointestinal symptoms and eventually go away, resembling viral gastroenteritis, however Amanita may cause potentially fatal liver damage. The most frequent symptoms in those who have been poisoned by A. virosa are nausea and vomiting. Additionally possible symptoms include hepatitis, diarrhoea, agitation, vertigo, and nausea. Three clinical stages of A. virosa poisoning occur 8–12, 12-–48, and 72 hours after intake, respectively. During this intoxication, the blood, testicles, and pancreas are also impacted. The phalloidin toxin and its active metabolites are often blamed for the first stage's stimulation of the gastrointestinal tract. Abdominal symptoms in the second stage of amanita poisoning are significantly reduced, but hepatic and renal failure are still possible side effects. In the third phase, death occurs due to encephalopathy (muscular twitching, delirium, coma, seizures), coagulopathy (epistaxis, hematuria, melena, and hematemesis), and seldom cardiomyopathy. The most popular technique for analysing Amanita mushroom toxins in biological specimens, both quantitatively and qualitatively, has been high performance liquid chromatography (HPLC).

When either fungus is consumed alone, the clinical symptoms of poisoning by Amanita muscaria are remarkably similar to those in Amanita phalloides intoxication and should allow doctors to distinguish between the two diseases readily. Because different kinds are combined so frequently, the symptoms experienced by patients typically indicate the combined action of several hazardous principles. The time between intake and the onset of symptoms in A. muscaria poisoning is typically quite short-between a half-hour and an hour, or at most three hours. Small meals may cause even five or six hours to pass. This characteristic is crucial for determining the type of intoxication that the instances involve. Severe cases include extreme sweating and salivation, tears streaming down the face, a sense of laryngeal constriction, nausea, retching, vomiting, and diarrhoea that is watery. The final two almost usually happen. Typically, the pulse is sluggish and erratic. The pupils are tiny and there is no fever. Accelerated respirations and clypnoea are present in the patient, and the bronchi are mucus-filled. Additionally, there are mental symptoms, most notably giddiness, thought confusion, and very infrequently hallucinations. The severity of each of these symptoms may vary, with the mental symptoms occasionally outweighing the gastrointestinal ones. Only salivation or sweating may be seen in mild cases, along with stomach and intestinal discomfort for a few hours. In extreme circumstances, the gastrointestinal tract may be quickly cleared of the problematic material by vomiting and diarrhoea, at which point the mental symptoms-delirium, violent convulsions, and loss of consciousness-become more prominent and the patient may fall into a profound coma-take over. Rarely does someone die from paralysis of the breathing muscles while still conscious. After the nausea and diarrhoea, the patients frequently fall asleep and wake up later thoroughly prostrated but on the road to recovery. Two to three days is how quickly normal health returns. The intoxication caused by Muscaria has no lasting repercussions like that caused by Amanita phalloides, which causes internal organ degeneration. If the patient overcomes the initial symptoms, the prognosis is always favourable. Excitation and hallucinations can occasionally mimic alcohol intoxication when anxious symptoms predominate the digestive system.

Traditional methods for spotting poisonous wild mushrooms

Brightly coloured poisonous mushrooms are poisonous. Although no documented human fatalities, fly agar is a narcotic and psychedelic that is typically bright red to orange or yellow. The deadly destroying angel, however, is a bland white. Dig up the mushroom below the surface with your knife. There will be an obvious ball-shaped swelling where the mushroom hits the soil. Cut the stem open. Any mushroom with a hollow stem ought to be regarded as extremely poisonous. It most likely carries harmful poisons if the stem has an interior that resembles a hollow straw. Popular edible morel mushrooms have towering, conical tops that are severely wrinkled. You should not consume a morel that you find after the first day of summer since it is a false morel. Boiling rice with a poisonous mushroom will turn it crimson and give it a pointed cap. The caps of edible ones are flat and rounded. This is not a reliable way to distinguish between edible and toxic species since the shape of the mushroom cap does not correlate with the presence or absence of mushroom toxins.

Clinical Features and Diagnosis

Amanita phalloides poisoning can appear clinically as anything from a minor preclinical symptom to a fatal fulminant outcome. As a result, not all Amanita phalloides poisoning patients g*et al*F and die. The quantity of toxin consumed and the duration of time between consumption and the start of treatment determine how severe the intoxication is overall.

Four sequential phases are traditionally used to describe the clinical picture of amanita phalloides poisoning:

Lag Phase, first. Since the poisons do not cause irritation on their own, there are no symptoms or indicators during the initial period. The typical incubation period is 10 hours, ranging from 6 to 40 hours. Since other toxic mushrooms that do not cause liver involvement typically induce gastrointestinal symptoms much earlier, 1-2 h after ingestion, it is crucial for an early diagnosis to suspect amatoxin intoxication in any case of a relatively prolonged latency period between mushroom consumption and onset of symptoms.

Phase II, the digestive system. This stage is marked by severe secretory diarrhoea, crampy stomach pain, nausea, and vomiting. Bloody emesis and diarrhoea are both possible. This gastroenteritic phase could be so bad that it causes

electrolyte imbalances, hypoglycemia, dehydration, and hypotension, among other things. For 12 to 24 hours, this second phase lasts. If the dehydration has been corrected, the patient appears to be clinically improving within a few hours. Tests of kidney and liver function are often normal at this stage of the illness. If the connection between toxic mushrooms is not discovered, these individuals may be mistakenly given the diagnosis of gastroenteritis and, if hospitalised, discharged home.

(3) Pretended recovery. There may be liver involvement symptoms 36–48 hours after consumption. The impacts of toxins are harming the liver and kidneys in this third stage, despite the apparent healing of gastrointestinal symptoms, which causes a steady decline in liver enzyme tests and an increase in blood transaminases and lactic dehydrogenase. When jaundice first appears, clinical indicators of liver damage eventually appear.

(4) Severe Liver Failure. Transaminases sharply increase and liver and renal function worsen in the last stage, causing hyperbilirubinemia, coagulopathy, hypoglycemia, acidosis, hepatic encephalopathy, and hepatorenal syndrome. Within 1-3 weeks following intake, multiorgan failure, diffuse intravascular coagulation, mesenteric thrombosis, seizures, and death may occur.

Treatment Strategies

There isn't a known amatoxin antidote. Since no reported randomised, controlled clinical trials have been conducted, it is impossible to demonstrate the clinical efficacy of any method of diagnosis for amatoxin poisoning. Amatoxin poisoning is treated with initial medical attention, supportive measures, targeted medicines, and liver transplantation. The specific therapy include chemotherapies and detoxication techniques.

Initial Medical Attention. Gastrointestinal decontamination methods make up first medical care. Early execution is closely related to these treatments' success. The therapeutic value of these measures appears to be fairly constrained because to the prolonged asymptomatic delay.

Data are insufficient to support or disprove the use of entire bowel irrigation as well as the emesis brought on by the administration of ipecac syrup. Only when it is possible to execute it shortly after eating should gastric lavage be taken into consideration.

Extraction Techniques. The two different tactics used in detoxification processes are to decrease intestine absorption and increase elimination.

1. Oral cleansing. There is no proof that using activated charcoal improves clinical outcomes, although repeated administration should prevent reabsorption of the poisons due to their enterohepatic circulation. To remove bile fluids and stop enterohepatic circulation, gastroduodenal aspiration with a nasogastric tube has been advocated as a solitary approach or in combination with activated charcoal, although the benefits of these treatments have not been proven. Cathartics should be used if diarrhoea has stopped.
2. Detoxification of the urine. The renal clearance of amatoxins can be increased by urine output of 100–200 mL/h for 4–5 days instead of intense forced neutral diuresis, which is no longer advised.
3. Techniques for extracorporeal purification. Recently described treatments use the Molecular Adsorbent Recirculating System (MARS). Even though the true effectiveness of this technique, as well as that of the other liver support systems, needs be evaluated in suitable trials, their use may represent a viable additional treatment option for individuals with severe amanitina poisoning. By moving protein-bound and water-soluble hazardous metabolites from the blood stream into a dialysate compartment via a specific membrane, MARS is a modified dialysis technique that mimics the biological characteristics of the hepatocyte membrane. By consistently eliminating chemicals that are bound to proteins, the approach has been demonstrated to be effective in enhancing liver function. To be effective, extracorporeal decontamination therapy must be initiated as soon as possible following the onset of gastrointestinal symptoms, according to universal consensus.

Chemotherapies. Most publications suggest that silibinin and N-acetylcysteine (NAC) may be useful in the treatment of patients with Amanita phalloides poisoning based on retrospective evidence.

Antibiotics, antioxidants, thioctic acids, hormones, and steroids were among the many additional medications once used to treat amatoxin poisoning. All of these medications have since been discontinued. A water-soluble silymarin derivative called silibinin competes with amatoxins for transmembrane transport and blocks amanitin's entry into hepatocytes, providing a direct hepatoprotective effect.

In addition, silibinin appears to have an impact on the liver's secondary uptake via enterohepatic recirculation. If the patient is observed within 48 hours of ingesting, it is advised to administer silibinin. The dosage is 20–50 mg/kg/day administered intravenously, and the course of treatment should last 48–96 hours. Silymarin capsules can be taken orally in doses ranging from 1.4 to 4.2g/d.

Similar to penicillin G, amanitin is displace from the binding to plasma protein by penicillin G, increasing excretion and blocking hepatic absorption. High dosages of Na/K penicillin G (1,000,000 IU/kg on the day 1, then 500,000 IU/kg for the following two days) are administered continuously intravenously. Although silibinin and penicillin combined therapy has been proposed, there is no clinical evidence to suggest that this strategy is superior to silibinin monotherapy.

Indicators and liver transplantation prognosis

If a liver transplant (LT) is not carried out, amatoxin poisoning could develop into ALF and possibly result in death. Based on the information that is currently available, the death rate following Amanita phalloides poisoning varies from 10 to 20%. Patients with serious liver damage should be hospitalised to an ICU with a liver transplant centre nearby. There are now two surgical procedures available: auxiliary partial liver transplantation (APOLT) and orthotopic liver transplantation (OLT). Long-term immunosuppression is necessary for OLT, a well-established surgery, to prevent graft rejection. APOLT can be an alternate method since some patients who have temporary assistance and partial hepatectomy may fully recover their own liver in terms of morphology and functionality.

Pathogen types and mushroom varieties

The edible species of the genus Agaricus (button, portabella, and criminis mushrooms), the genus Pleurotus (oyster

mushrooms), and the genus Volvariella (straw mushrooms) are all examples of mushrooms. Mushrooms are the fleshy fruiting bodies of fungus. The look of mushrooms varies greatly depending on the type and stage of growth. The cap of an agaricus mushroom is rounder while it is juvenile, flattens out as it matures, and can measure 5–10 cm (2-4 in) in diameter. The stem has a pale grey or brown colour. Pleurotus mushrooms can form lateral attachments to a growing substrate, like the bark of a tree, rather than a stem. Smooth and elongated, pleurotus mushrooms have a diameter of 4-5cm (1.5-6.0in). The little volvariella mushroom has pink gills and a distinctive volva-like coating at the base of the stem. The cap has a diameter range of 5–15 cm (2–6 in). Mushroom illnesses can be either biotic or infectious and are brought on by fungus, bacteria, viruses, etc.

Global sickness caused by pleurotus green mould

The first considerable crop losses of farmed Pleurotus ostreatus due to this disease were reported in South Korea by Yu (2002) [18]. Sharma and Vijay (1996) observed green mould of oyster mushroom caused by *T. viride* in North America. More than 100 Trichoderma strains isolated from oyster mushroom substrate were examined for their cultural and morphological traits. Based on the findings, the following species were identified: *T. viride* (13.6%), T. harzianum (8.2%), and *T. koningii* (5.5%), with an unidentified species of Trichoderma making up the majority (65.5%) of the isolates. These isolates were supposed to belong to T. harzianum based on DNA banding pattern, internal transcribed spacer 1 and 2 (ITS1 and 2) sequences, random amplified polymorphic DNA (RAPD), and restriction fragment length polymorphism (RFLP) analysis. However, because they formed different phylogenetic clades, they were regarded as a new variety. On mushroom beds, Hypocrea species 1 and 2 were also discovered, with the former producing brown stroma and the latter producing white stroma. While Hypocrea sp. 2 did not develop the asexual stage on mushroom beds, Hypocrea sp. 1 formed an anamorph with gliocladium-like shape. Trichoderma isolates predominated Pleurotus on both potato dextrose agar and in situ and *in vitro* interactions between P. ostreatus and the green mould strains.

Table 1: Anti-Viral Properties of Selected Mushrooms

Serial No.	Mushroom	Antiviral activity shown against	Molecule identified	Mechanism of Action
1	*Lentinus edodes*	Infectious Hematopoietic Necrosis Virus (IHNV)	Lentinan (LNT-1)	Direct viral inactivation and viral replication inhibition. Proinflammatory cytokines such TNF-, IL-2, and IL-11 have significantly reduced expression. FN-1 and IFN- produce actions that areantiviral, antiproliferative, and immunomodulatory. IFN-1 and IFN- expression are both increased.
2.	*Grifola frondosa*	Herpes Simplex Virus type-1 (HSV-1)	Antiviral protein (GFAHP)	Directly rendered HSV-1 inactive and prevented its invasion of Vero cells.
3.	*Grifola frondosa*	Hepatitis B Virus (HBV)	NA (Fraction D-GF-D)	Human IFN -2b has a synergistic impact on the inhibition of the virus.
4	*Inonotus obliquus*	Herpes Simplex Virus type-1 (HSV-1)	NA (Aqueous extract)	Viral glycoproteins were directly inactivated, and membrane fusion and entrance into the host cell were stopped.

Cyclosporine as a therapeutic remedy for amatoxin-containing mushroom poisoning

A calcineurin inhibitor called cyclosporine is used to treat autoimmune diseases and the rejection of organ transplants. Most hospitals carry cyclosporine in a parenteral formulation, which is a well-known and extremely strong inhibitor of the OATP1B3 transporter. since OATP substrates' pharmacokinetics are changed by OATP inhibition.

Table 2: Clinical cases related with mushrooms intoxication

Cortinarius	After consuming mushrooms from the Cortinarius species, a 26-year-old lady developed anuria after experiencing nausea and vomiting for many days. She also had increased BUN and creatinine levels at the time. She was diagnosed with interstitial nephritis during a kidney biopsy, and she eventually needed continuous dialysis for more than a year.	Wessely *et al*., 2007
Amanita	The Toxicological Unit at Careggi General Hospital (University of Florence, Italy) treated amatoxin poisoning patients from 1988 to 2002. A retrospective analysis of each patient's medical history and treatment results was done. A review of 111 patients' clinical data was conducted, and biological parameters were checked every 12 to 24 hours till discharge. Two individuals passed away; both were hospitalised more than 60 hours after consuming mushrooms, and 105 made a full recovery.	Giannini *et al*., 2007
Amanita	Abdominal pain, vomiting, and diarrhoea were reported by two patients, ages 54 and 51, respectively; these symptoms started 9 and 15 hours after eating soup. The findings of the urinalysis later verified the poisoning with the species Amanita phaloides. Eight days later, the patients were released in good condition.	Enecker-Jans *et al*., 2007

Table 3: Molecular properties, mechanism of toxicity and sources of mushrooms's toxins

Toxin name	Molecular properties, mechanism of toxicity and sources	References
Ostreolysin	Aegerolysin is a family of proteins that includes a 16 kDa acidic protein that is expressed in the primordia and fruiting bodies of Pleurotus ostreatus. It has 137 amino acid residues, 13 positively charged and 16 negatively charged residues, and a disproportionately high percentage of aromatic residues. The nativelike conformation of ostreolysin is defined by rigid tertiary structure and mostly b-sheet secondary structure when the pH is between 6 and 9, which is at 25 °C.	Berne S *et al*; 2005
Phallotoxin	Peptides with a trans-anular thioeter bridge on the bicyclic structure. According to current thinking, the toxin of F-specific actin's attachment to liver cells, which prevents F-actin from polymerizing into G-actin, is the cause of intoxication.	Kobayashi N *et al*;

Amatoxin	Amanita genus species include a thermostable bicyclic octapeptide. A-amanitine is the most active of the nine amatoxins that have already been found. Amatoxin's toxicity is caused by the inhibition of RNA polymerase-II, which in turn prevents DNA transcription and stops protein synthesis, leading to cell necrosis. Bédry R and Saviuc P. Intoxications Bédry R and Saviuc P. Intoxications	Bédry R and Saviuc P. Intoxications

Conclusion

Every year, a number of intoxications are documented in nations where mushrooms are widely ingested, mostly as a result of species misidentification. These species contain dangerous poisons that, depending on the dosage consumed, can result in a variety of symptoms that can be lethal. It is challenging to prevent accidental mushroom consumption, especially in nations where consuming wild species is widespread. The effectiveness of therapy depends on early detection of symptoms and indicators of intoxication. Proper identification is crucial to prevent accidents. Intoxications brought on by commonly consumed mushrooms have already been reported; as a result, it is important to carefully study edible mushrooms and those with pharmacological potential in order to identify the possibility of intoxications. Additional research must be carefully conducted, including clinical and experimental assays with medicinal species to look into any potential side effects.

The fatal amanita toxin is the subject of ongoing research. Its mechanism likewise continues the in-depth elaboration from several perspectives. The capacity of -amanitin to suppress RNA polymeraseII activity in the nucleus, which results in reduced protein synthesis and cell death, is one of the processes described in this article. Additionally, it has become increasingly important to consider how the -amanitin transport system contributes to the disease's pathophysiology. Through mostly enterohepatic circulation, amanitin continually destroys cells in the body. Two receptor molecules implicated in the transport mechanism are NTCP and OATP1B3. In conclusion, research on the mechanism of -amanitin-induced cell death has been ongoing. Apoptosis and autophagy have received the greatest attention. We make an effort to use the aforementioned process to create a specialised antidote for amanitin. There are still a lot of obstacles to overcome, and it has to be determined whether -amanitin uses other transport routes to harm the body because its fatal mechanism is not entirely evident. Further investigation and research are still required to determine whether -amanitin also induces pyroptosis and necroptosis in addition to apoptosis and autophagy.

References

1. Lee E. Extraordinary mushrooming. The San Diego Tribune, 1997 Apr 9.
2. Kleven R. Farming mushrooms. San Diego Tribune. 1989 Aug 17.
3. Ellenhorn MJ, Barceloux DG. Medical toxicology diagnosis and treatment of human poisoning. New York: Elsevier. 1988, 1324.
4. Von Clarmann M. Pilzvergiftungen. Fortschr Med. 1964;82:508–9.
5. McClain JL, Hause DW, Clark MA. *Amanita phalloides* mushroom poisoning: a cluster of four fatalities. J Forensic Sci. 1989;34:83-7.
6. Mitchel DH. Amanita mushroom poisoning. Annu Rev Med, 1980.
7. Beutler JA, Vergeer PP. Amatoxins in American mushrooms: evaluation of the meixner test. Mycologia, 1980.
8. Pinson CW, Daya MR, Benner KG, *et al*. Liver transplantation for severe Amanita phalloides mushroom poisoning. Am J Surg, 1990.
9. Lampe K, McCann MA. AMA handbook of poisonous and injurious plants. Chicago: American Medical Association, 1985
10. McCormick DJ, Avbel AJ, Gibbons RB. Nonlethal mushroom poisoning. Ann Intern Med, 1979.
11. Pacioni G, Lincoff G. Simon and Schuster's guide to mushrooms. New York: Simon and Schuster. 1981:9:14.
12. Lincoff G. Field guide to North American mushrooms. New York: Alfred A. Knopf. 1988, 11_30,871_4.
13. Agarwal KC, Russo FX, Parks RE Jr. Inhibition of human and rat platelet aggregation by extracts of Mo-er (Auricularia auricula). Thromb Haemost. 1982;48:162-5.
14. Kabir Y, Yamaguchi M, Kimura S. Effect of Shiitake (Lentinus edodes) and Maitake (Grifola frondosa) mushrooms on blood pressure and plasma lipids of spontaneously hypertensive rats. J Nutr Sci Vitaminol. 1987;33:341–6.
15. Nanba H, Kuroda H. Potentiation of host-mediated antitumor activity by orally administered mushroom (Agaricus bispora) fruit bodies. Chem Pharm Bull (Tokyo). 1988;36:4, 1437_44.
16. Ford & Clark-A Consideration of the properties of poisonous fungi: Mycologia, 1914 July, 4(4).
17. Bagnall-Mushroom poisoning, with atypical cases: Boston Med. & Surg. Jour., July 16, 1914
18. Yu SH. Integrated control of oyster mushroom green mould, 2002.
19. Yu SH, Seo GS. Integrated control of oyster mushroom green mould, 2002.
20. Ren G, Xu L, Lu T, Yin J. Structural characterization and antiviral activity of lentinan from Lentinus edodes mycelia against infectious hematopoietic necrosis virus. Int. J Biol. Macromol. 2018 Aug;115:1202-1210. Doi: 10.1016/j.ijbiomac.2018.04.132. PMID:29704603
21. Gu CQ, Li JW, Chao F, Jin M, Wang XW, Shen ZQ. Isolation, identification and function of a novel anti-HSV-1 protein from Grifola frondosa. Antivir. Res. 2007 Sep;75(3):250-257. Doi: 10.1016/j.antiviral.2007.03.011
22. Gu CQ, Li JW, Chao FH. Inhibition of hepatitis B virus by D-fraction from *Grifola frondosa*: Synergistic effect of combination with interferon-α in HepG2 2.2. 15. Antivir. Res. 2006 Nov;72(2):162-165. Doi:10.1016/j.antiviral.2006.05.011
23. Pan HH, Yu XT, Li T, Wu HL, Jiao CW, Cai MH, *et al*. Aqueous extract from a Chaga medicinal mushroom, *Inonotus obliquus* (higher Basidiomycetes), prevents herpes simplex virus entry through inhibition of viral-induced membrane fusion. Int J Med Mushrooms. Page | 87. 2013;15(1):29-38. Doi: 10.1615/intjmedmushr.v15.i1.40. PMID: 23510282
24. Trabulus S, Altiparmak MR. Clinical features and outcome of patients with amatoxin-containing mushroom poisoning. Clin Toxicol (Phila). 2011;49(4):303–310
25. Yang Y, Shao RF, Chen GB. Research progress on the

mechanism of mushroom poisoning. J Clin Emerg 2020;21(8):675–678
26. Chen JZ, Fu WS, Xu F, *et al*. Acute mushroom poisoning of *Amanita pseudosychnopyramis*: A case report from Fujian, China with exact species identification and descriptive study. Toxicon. 2022;212:55–61
27. Evans N, Hamilton A, Bello-Villalba MJ, Bingham C. Irreversible renal damage from accidental mushroom poisoning. BMJ. 2012;345:e5262.
28. French LK, Hendrickson RG, Horowitz BZ. Amanita phalloides poisoning. Clin Toxicol (Phila). 2011;49(2):128–129.
29. Li Y, Qiu Z, Huang L, Cao C. Extracorporeal membrane oxygenation combined with sequential blood purification in the treatment of myocardial damage and cardiac arrest caused by mushroom poisoning. Toxicon. 2021b;197:65–69.
30. Rosenthal P. Mushroom poisoning and auxiliary partial orthotopic liver transplantation. Am J Gastroenterol. 2002;97(5):1272–1273.
31. Nieminen P, Mustonen AM. Toxic potential of traditionally consumed mushroom species-a controversial continuum with many unanswered questions. Toxins (Bas el), 2020.
32. Ganzert M, Felgenhauer N, Schuster T, Eyer F, Gourdin C, Zilker T. Amanita poisoning–comparison of silibinin with a combination of silibinin and penicillin. Dtsch Med Wochenschr. 2008;133(44):2261–2267.
33. Letschert K, Faulstich H, Keller D, Keppler D. Molecular characterization and inhibition of amanitin uptake into human hepatocytes. Toxicol Sci. 2006;91(1):140-149.