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Mushroom poisonings

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- **Conflicts of Interest Disclosure:**
  No Conflicts of Interest to declare
- This lecture for health education only

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- Mushroom species vary widely regard to xenobiotics they contain
- Identifying them with certainty difficult
- Clinical system of classification more useful

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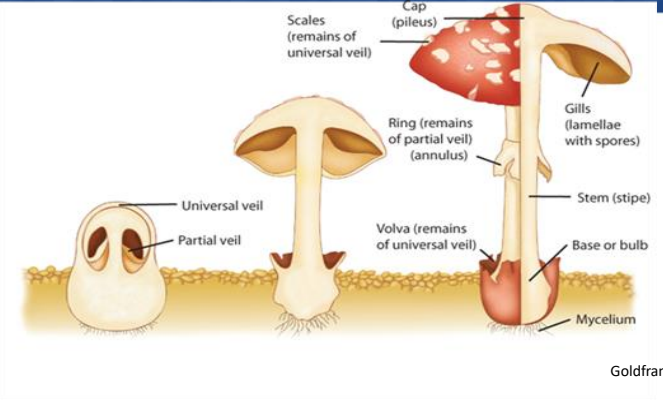

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Mushrooms Identification

- Visualizing and analyzing the gross, microscopic, chemical characteristics of the ingested mushroom: infrequently used
- The diagnosis: based on the clinical presentation
- Best to **rely on symptomatology**, not mushroom appearances, to confirm a diagnosis
- No rapidly available studies in EDs or clinical chemistry laboratories available to assist with management

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- The toxicology of any species: vary depending on geographic location
- Staining of silver, presence of insects or slugs, peeling off the mushroom cap, the area of mushroom growth: unreliable or false
- If toxicity is suspected, attempt to obtain samples of the mushrooms eaten, and identify
- Rule out infections or other diseases

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- Cooking may inactivate some xenobiotics but not others
- Only some people who ate mushroom manifested characteristic toxicity should not exclude the diagnosis of mushroom poisoning
- One person may show significant effects, whereas others may be asymptomatic are ingesting the same mushroom
- Mushroom allergy can manifest as an anaphylactic reaction
- Most poisonous mushrooms resemble edible mushrooms at some phase of their growth

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The Mycological Society of Japan

Full paper

Mushroom poisoning in Thailand between 2003 and 2017

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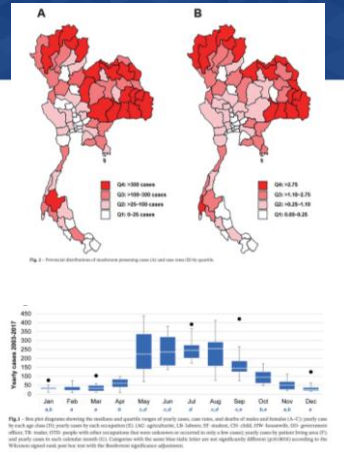
ABSTRACT

The frequent occurrence of mushroom poisoning cases in the wet season in Thailand has long been recognized but has never been quantitatively analyzed. This study aims to analyze mushroom poisoning cases in Thailand between 2003 and 2017 and focused on their association with the rainfall. The results revealed 22,571 cases and 106 deaths in this period. Cases were higher for females than males, adults than children, and agriculturists than people in other occupations. Cases were higher in the northeastern and northern regions than in the central, south, and east regions. There are strong effects of seasonality on mushroom poisoning cases. Over the 15-y period, 17,337 cases occurred in the wet season (May–Sep) compared with 5,234 cases in the dry season (Oct–Apr). The number of monthly poisoning cases were high in men, mature adults, agriculturists, people living in the rural areas and people living in the Northeastern and Northern provinces. Moreover, a strong positive correlation was shown between the number of monthly poisoning cases and the amount of monthly rainfall.



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Grouping by Onset

- Muscarine Containing Mushrooms
- Ibotenic Acid and Muscimol Containing Mushrooms
- Coprine Containing Mushrooms
- Psilocybin Containing Mushrooms
- GI Toxin Containing Mushrooms

→ **Acute**
Onset < 5 hours

- Rhabdomyolysis Associated Mushrooms

→ **Onset ??**

- Cyclopeptide Containing Mushrooms
- Gyromitrin Containing Mushrooms

→ **Delayed**
Onset ≥ 5 hours

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TABLE 117–1 Mushroom Toxicity Overview

Representative Genus/ Species	Xenobiotic	Time of Onset of Symptoms	Primary Site of Toxicity	Clinical Findings	Mortality	Specific Therapy*
I *Amanita phalloides, A. bisporigera, A. ocreata, Galerina autumnalis, G. marginata, G. venenata, Lepiota josserandi, L. helveola*	Cyclopeptides Amatoxins Phallotoxins	5–24 h	Liver	Phase I: GI toxicity—N/V/D Phase II: Quiescent Phase III: N/V/D, jaundice, ↑ AST, ↑ ALT ↑ Bilirubin	30%	Potential benefit early Activated charcoal Hemoperfusion/hemodialysis Silibinin Polymyxin B Potential benefit late *N*-acetylcysteine
II *Gyromitra ambigua, G. esculenta, G. infula*	Gyromitrin (metabolite: monomethylhydrazine)	5–10 h	CNS	Seizures, abdominal pain, N/V, weakness, hepatorenal failure	Rare	Benzodiazepines, pyridoxine 70 mg/kg IV (max 5 g)
III *Clitocybe dealbata, Omphalotus olearius, most Inocybe spp, Boletus eastwoodiae*	Muscarine	0.5–2 h	Autonomic nervous system	Peripheral muscarinic effects—salivation, bradycardia, lacrimation, urination, defecation, diaphoresis	Rare	Atropine—Adults: 1–2 mg Children: 0.02 mg/kg with a minimum of 0.1 mg
IV *Coprinopsis atramentaria, C. insignis*	Coprine (metabolite: 1-aminocyclopropanol)	0.5–2 h	Aldehyde dehydrogenase	Disulfiramlike effect with ethanol, tachycardia, N/V, flushing	Rare	Antiemetics Fluid resuscitation Fomepizole for refractory toxicity
V *Amanita gemmata, A. muscaria, A. pantherina, Tricholoma muscarium*	Ibotenic acid, muscimol	0.5–2 h	CNS	GABAergic effects, rare delirium, hallucinations, dizziness, ataxia	Rare	Benzodiazepines during excitatory phase
VI *Psilocybe cyanescens, P. cubensis, Gymnopilus spectabilis, Psathyrella foenisecii*	Psilocybin, psilocin	0.5–1 h	CNS	Ataxia, N/V, hyperkinesis, hallucinations, illusions	Rare	Benzodiazepines for agitation

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VII *Clitocybe nebularis, Chlorophyllum molybdites, C. esculentum, Lactarius spp, Paxillus involutus*	Various GI irritants	0.3–3 h	GI	Malaise, N/V/D	Rare	Symptomatic care
VIII *Cortinarius orellanus, C. rubellus, C. gentilis*	Orellanine, orellinine	>1 d– weeks	Kidney	Phase I: N/V Phase II: Oliguria, Acute kidney injury	Rare	Hemodialysis for acute kidney injury
IX *Amanita smithiana, A. proxima, A. pseudoporphyria*	Allenic norleucine	0.5–12 h	Kidney	Phase I: N/V Phase II: Oliguria, Acute kidney injury	None	Hemodialysis for acute kidney injury
X *Tricholoma equestre (Europe)* *Russula subnigricans (Japan, China)*	Cycloprop-2-enecarboxylic acid	24–72 h 0.5–2 h	Muscle (skeletal and cardiac)	Fatigue, nausea, vomiting, muscle weakness, myalgias, ↑ CK, facial erythema, diaphoresis, myocarditis	10%	Sodium bicarbonate, hemodialysis for acute kidney injury
XI *Tragia venenata* *Amanita franchetti* *Ramaria rufescens*	2*R*-amino-4,5-hydroxy-5-hexynoic acid	1–5 d 2–15 h 2–15 h	Cardiac and skeletal muscle	Tachycardia, GI symptoms, myalgias, tremor, seizures, dizziness, weakness, syncope, palpitations, ventricular fibrillation	High?	Intensive care monitoring

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TABLE 117–1 Mushroom Toxicity Overview (Continued)

Representative Genus/ Species	Xenobiotic	Time of Onset of Symptoms	Primary Site of Toxicity	Clinical Findings	Mortality	Specific Therapy*
XII *Clitocybe acromelalga, C. amoenolens*	Acromelic acids	24 h	Peripheral nervous system	Erythromelalgia paresthesias—hands and feet, dysesthesias, erythema, edema	None	Symptomatic care
XIII *Pleurocybella porrigens*	Unknown	1–31 d	CNS	Encephalopathy, convulsions, myoclonus in patients with chronic kidney failure	High (30%)	Hemodialysis
Hapalopilus rutilans	Polyporic acid	>12 h	CNS	N/V, abdominal pain, vertigo, ataxia, drowsiness, encephalopathy	None	Symptomatic care
XIV *Paxillus involutus, Clitocybe clavicepsᵗ, Boletus luridusᵗ*	Involutin	Following repeated exposure 0.5–3 h	Red blood cell, kidney	Hemolytic anemia, acute kidney injury	Rare	Hemodialysis
XV *Lycoperdon perlatum, L. pyriforme, L. gemmatum*	Spores	Hours	Pulmonary, GI	Cough, shortness of breath, fever, nausea, vomiting	None	Corticosteroids

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TABLE 220-1 Mushrooms: Symptoms, Toxicity, and Treatment

Symptoms	Mushrooms	Toxicity	Treatment
GI symptoms			
Onset <2 h	*Chlorophyllum molybdites* *Omphalotus illudens* *Cantharellus cibarius* *Amanita caesarea*	Nausea, vomiting, diarrhea (occasionally bloody)	IV hydration Antiemetics
Onset 6–24 h	*Gyromitra esculenta* *Amanita phalloides* *Amanita bisporigera*	Initial: nausea, vomiting, diarrhea Day 2: rise in AST, ALT levels Day 3: hepatic failure	IV hydration, glucose; monitor AST, ALT, bilirubin, BUN, and creatinine levels, prothrombin time, partial thromboplastin time For *Amanita*: multiple-dose activated charcoal Consider *N*-acetylcysteine 150 milligrams/kg loading dose (see text) Consider penicillin G, 300,000–1,000,000 units/kg/d Silymarin, 20–40 milligrams/kg/d, where available Consider cimetidine, 4–10 grams/d Consider transfer to a center with active liver transplant program (see text)
Muscarinic syndrome Onset <30 min	*Inocybe* *Clitocybe*	SLUDGE syndrome (**s**alivation, **l**acrimation, **u**rination, **d**efecation, **G**I hypermotility, and **e**mesis)	Supportive; atropine, 0.02 milligram/kg (minimum dose 0.1 milligram, maximum dose 1 milligram), repeated as needed for severe secretions
CNS excitement Onset <30 min	*Amanita muscaria* *Amanita pantherina*	Intoxication, dizziness, ataxia, visual disturbances, seizures, tachycardia, hypertension, warm dry skin, dry mouth, mydriasis (anticholinergic effects)	Supportive; sedation with benzodiazepines (e.g., lorazepam 0.05 milligram/kg, maximum dose 4 milligrams)
Hallucinations Onset <30 min	*Psilocybe* *Gymnopilus*	Visual hallucinations, ataxia	Supportive; sedation with benzodiazepines, external cooling
Disulfiram reaction 2–72 h after mushroom, and <30 min after alcohol	*Coprinus*	Headache, flushing, tachycardia, hyperventilation, shortness of breath, palpitations	Supportive; IV hydration, β-blockers for supraventricular tachycardia Norepinephrine for refractory hypotension
Renal compromise	*Cortinarius* spp *Amanitia smithiana*	GI symptoms initially, followed by flank pain, polyuria, anuria,	Supportive; monitor urine output, renal status, delayed renal transplant; IV hydration β-Blockers for supraventricular tachycardia Norepinephrine for refractory hypotension
Dermatitis 1–2 d after ingestion	Shiitake	Whip-like, linear, erythematous wheals, blanching erythematous patches, scattered petechiae, pruritus	Oral antihistamines, 0.1% triamcinolone ointment twice daily; spontaneously resolves within 1–3 wk

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase.

Tintinalli 9th ed

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- Coprine Containing Mushrooms
- Psilocybin Containing Mushrooms
- GI Toxin Containing Mushrooms

→ **Acute**
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- Rhabdomyolysis Associated Mushrooms

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- Cyclopeptide Containing Mushrooms
- Gyromitrin Containing Mushrooms

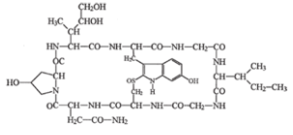
→ **Delayed**
Onset ≥ 5 hours

Mahidol University Wisdom of the Land | Cyclopeptide Containing Mushrooms

- Amanita species: A. verna, A. virosa, and A. phalloides; Galerina spp: G. autumnalis, G. marginata, and G. venenata; Lepiota species: L. helvelola, L. josserandi, L. brunneoincarnata
- Delayed onset: typical and critical consideration in assessing

Amanita phalloides

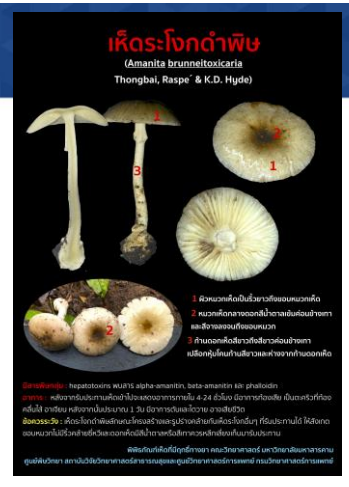
Amanita virosa.



α-Amanitin

เห็ดไข่ตายซากหรือเห็ดระโงกหิน **(Amanita verna และ Amanita virosa)**

https://gnews.apps.go.th/news?news=42188



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- A. phalloides: 15-20 cyclopeptides
- Amatoxins, phallotoxins, virotoxins
- Phallotoxin: causing early GI symptoms
- Amatoxins: the most toxic, 9 amatoxins identified, but α-amanitin (amanitin) appears the most physiologically active
- Amanitins: highly bioavailability, rapidly absorbed from the GI tract
- Heat stable
- A 20-g mushroom contains > of 0.1 mg/kg amanitin considered lethal for humans

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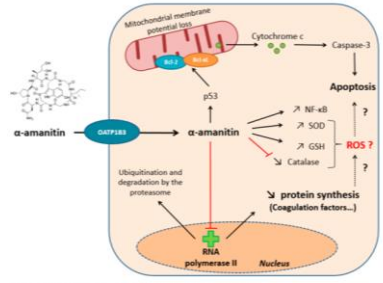

Figure 2. Main toxic mechanisms of amanitins within hepatocytes.


toxins

Review

Toxic Effects of Amanitins: Repurposing Toxicities toward New Therapeutics

- Amatoxins are excreted in large quantities in the urine (80 to 90% of the dose is found unchanged) during the first 72 h of intoxication

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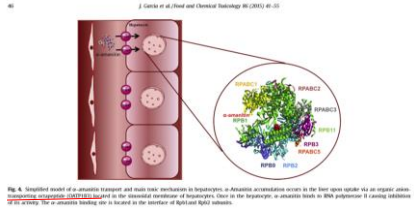
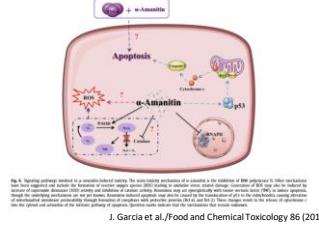
- Amatoxins: limited protein binding, in the plasma for 24-48 hours
- α-Amanitin hepatocellular entry: facilitated by a sodium-dependent bile acid transporter
- Sodium taurocholate cotransporter polypeptide, a member of organic anion–transporter polypeptide **OAT polypeptide family**, in the sinusoidal membranes of human hepatocytes, facilitates hepatocellular α-amanitin uptake
- Inside the cells, **interference with RNA polymerase II**, preventing the transcription of DNA, suppressing protein synthesis, resulting in cell death

Mahidol University — Cyclopeptide Containing Mushrooms

- α-Amanitin: **enterohepatically** recirculated
- Target organs: the highest rate of cell turnover; **GI tract** epithelium, **hepatocytes, kidneys**
- Amatoxins: not appear to cross the placenta, absence of fetal toxicity in severely poisoned pregnant women





J. Garcia et al./Food and Chemical Toxicology 86 (2015) 41–55

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Cyclopeptide Containing Mushrooms

Clinical

Phase I: severe gastroenteritis, with profuse watery diarrhea not occurring until 5-24 hours after ingestion

- Typically considered: **onset of symptoms < 5 hours** strong support for another **non-Amanita species** cause

Phase II: Supportive fluid and electrolyte replacement leads to transient improvement during phase II, occurs 12-36 hours

- Initial hepatotoxicity begins within the 2nd phase

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Cyclopeptide Containing Mushrooms

Phase III: hepatic and renal toxicity and death, 2-6 days after ingestion

- Clinical hepatotoxicity with elevated bilirubin, AST, ALT, hypoglycemia, jaundice, hepatic coma
- Until 2-3 days after ingestion
- Pathologic: steatosis, central zonal necrosis, centrilobular hemorrhage, viable hepatocytes remaining at the rims of the larger triads
- Endocrine abnormalities: hormones that regulate glucose, calcium, thyroid homeostasis

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Cyclopeptide Containing Mushrooms

Table 2 Clinical Phases of Amatoxin Poisoning.

Phases	Onset from ingestion	Symptoms and signs
Stage 1.	Lag phase 0–24 h	Asymptomatic
Stage 2.	Gastrointestinal phase 6–24 h	Nausea, vomiting, crampy abdominal pain, and severe secretory diarrhea
Stage 3.	Apparent convalescence 24–72 h	Asymptomatic, worsening of hepatic and renal function indices
Stage 4.	Acute liver failure 4–9 days	Hepatic and renal failure → multi-organ failure → death

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- Acute liver injury: a moderately severe coagulopathy (INR ≥ 2),
  presumed onset of acute illness < 26 weeks,
  absence of cirrhosis
- Acute liver failure: the presence of hepatic encephalopathy of any degree
  evidence of moderately severe coagulopathy (INR ≥ 1.5)
  presumed onset of illness of < 26 weeks
  absence of cirrhosis

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Cyclopeptide Containing Mushrooms

Treatment

- **Fluid and electrolyte repletion**: IV 0.9% sodium chloride, electrolytes, dextrose repletion
- **Multiple Dose Activated charcoal** 1 g/kg orally every 2 to 4 hours or by continuous nasogastric infusion
- Continuous nasogastric duodenal aspiration: inadequate clinical data to support gastroduodenal or biliary drainage
- **Penicillin G** 1 g/kg (l g = 1,600,000 Units):
  - displacing α-amanitin from albumin, blocking its uptake from hepatocytes, binding circulating amatoxins, preventing α-amanitin binding to RNA polymerase.

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Cyclopeptide Containing Mushrooms

- **The active complex of milk thistle** (Silybum marianum): silymarin, 3 isomeric flavonolignans: silibinin, silychristin, silydianin
- Silibinin, a mixture of Silibinin A and B
- competitively inhibits the organic anion transporter (OATP1B3)
- responsible for the uptake and enterohepatic recycling of α-amanitin
- diminishes α-amanitin enterohepatic circulation

- Currently, an amatoxin poisoning clinical trial utilizing Legalon SIL (Silibinin) at 20 mg/kg/day IV

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Cyclopeptide Containing Mushrooms

- **N-acetylcysteine**: hepatoprotective effects
- Cimetidine (a potent CYP2C9/2D6 inhibitor): hepatoprotective effect against α-amanitin
- Forced diuresis, hemodialysis, plasmapheresis, hemofiltration, hemoperfusion: may be effective shortly after ingestion, but most neither clinical evidence of benefit nor supportive pharmacokinetic data for these therapies
- Extracorporal albumin dialysis, **molecular adsorbent recirculating system (MARS),** fractionated plasma separation and adsorption system (FPSA; Prometheus system)

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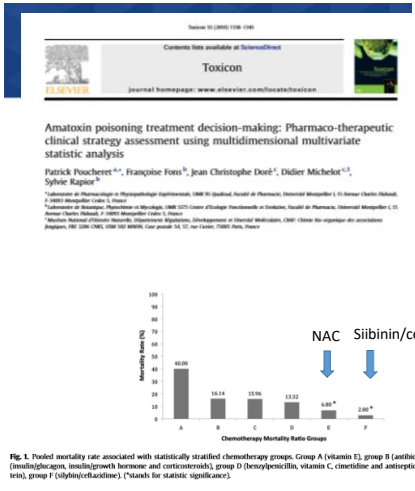
Statistical Analysis of Amatoxin-Poisoning Therapies

#		No. LTi	No. LTe	MRLTi (%)	MRLTe (%)
	Applied therapies				
1	BpThioca	207	207	16.9	16.9
2	BpwSilybTriPoly	299	297	15.4	14.8
3	BpSter	95	95	14.7	14.7
4	Bp	164	163	11.6	11.0
5	Detox alone	385	379	10.4	9.0
6	BpantiOx	111	110	9.1	8.2
7	NAC	89	89	6.7	6.7
8	BpSilyb	391	382	8.2	6.0
9	BpSilybTriPoly	151	148	7.3	5.4
10	Silyb	74	71	5.4	1.4
11	Supportive measures alone	91	85	47.3	43.5
	Pooled therapies				
12	Bp/Silybin combinations (8, 9)	542	530	7.9	5.8
13	Combined nine chemotherapies (1–4, 6–10 above)	1586	1,567	11.2	10.1
14	Combined 10 specific therapies (1–10 above)	2062	2,031	12.6	11.3
15	Bp bi-chemotherapies without Silybin (1, 3, 6)	413	412	14.3	14.1
16	Combined three worst chemotherapies (1–3)	601	599	15.8	15.5

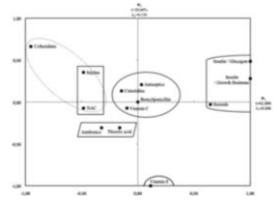
No. LTi = number of patients including liver transplants; No. LTe = number of patients excluding liver transplants; MRLTi = mortality rate including liver transplants; MRLTe = mortality rate excluding liver transplants.

F Enjalbert *et al*, 2002



Toxicon

Amatoxin poisoning treatment decision-making: Pharmaco-therapeutic clinical strategy assessment using multidimensional multivariate statistic analysis



Potential benefit early
Activated charcoal
Hemoperfusion/hemodialysis
Silibinin
Polymyxin B

Potential benefit late
N-acetylcysteine

toxins

Toxic Effects of Amanitins: Repurposing Toxicities toward New Therapeutics

Table 1. Clinical efficacy data of the main antidotes used in the management of *Amanita phalloides* poisoning in humans. Patient survival rates are associated with various drug classes after multidimensional statistical analysis.

Empiric Therapeutic Strategy	Molecules	Putative Mechanism of Action	Associated Mortality Rate (11.6% Average Mortality)	References
First-line	Silibinin (alone or in combination) (n = 624)	Inhibitor of the OATP1B3 transporter Antioxidant effectsAnti-inflammatory effects Tissue repair	5.6%	[39,41]
	N-acetyl-cysteine (n = 192)	Antioxidant effects	6.8%	
	Ceftazidime (combined with silibinin) Positive impact on a small number of patients (n = 12); interest to be demonstrated on larger samples	OATP1B3 transporter inhibitor	0%	
Second-line If first-line treatments are not available	Benzylpenicillin alone or in combination (n = 1411)		10.7%	
Interest still to be demonstrated No positive impact on care or deleterious impact on patient survival observed in a small number of patients	Vitamin E (n = 25)	Antioxidant effects	40%	
	Vitamin C (n = 60), cimetidine (n = 21), thioctic acid (n = 450)		12–20.3%	
	Gentamycin, neomycin, streptomycin, vancomycin, clindamycin (n = 63 in the entire group)	Unknown		
	Insulin + growth hormone (n = 69), insulin + glucagon (n = 128)	Stimulation of the hepatic metabolism	16%	
	Steroids (n = 459)	Anti-inflammatory		

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- **Introduction:** Amatoxin leads to the majority of deaths by mushroom poisoning around the world. Amatoxin causes gastrointestinal disturbances and multiple organ dysfunction, including liver and renal failure. As a potential treatment for amatoxin poisoning, *N*-acetylcysteine (NAC) has been used for decades but its benefit is still unproven.
- **Objectives:** We undertook a systematic review to evaluate the performance and safety of *N*-acetylcysteine on patients suffering amatoxin intoxication.
- **Methods:** We searched Pubmed, EMBASE, CENTRAL and SinoMed databases, from inception to August 31, 2019. Articles were eligible if there were five or more patients with amatoxin poisoning and *N*-acetylcysteine was included in the therapeutic regimen. Mortality rate including liver transplant cases (MRLTi) was the primary outcome. Mortality rate not including liver transplant cases, liver and renal function, clinical complications, as well as any adverse reactions to intravenous NAC were secondary outcomes.
- **Results:** **Thirteen studies with a total of 506 patients** were included. **The MRLTi of amatoxin-poisoning patients with NAC treatment was 11% (57/506), and a MRLTe of 7.9% (40/506) and a liver transplantation rate of 4.3% (22/506). Transaminase concentrations generally peaked around 3 days after ingestion,** prothrombin time/International Normalized Ratio (PT/INR) generally worsened during the first 3–4 days after ingestion before returning to normal four to 7 days after ingestion, and Factor V levels normalized in about 4–5 days after ingestion in patients treated with NAC. Renal failure was reported in 3% (3/101) and acute kidney injury was reported in 19% (5/27). Gastrointestinal bleeding occurred in 21% (15/71). Anaphylactoid reactions were the principle adverse reaction to NAC treatment in amatoxin-poisoning patients with an incidence of 5% (4/73).
- **Conclusions:** **NAC treatment combined with other therapies appears to be beneficial and safe** in patients with amatoxin poisoning. Until further data emerge, it is reasonable to use NAC in addition to other treatments for amatoxin poisoning.

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Polymyxin B:

- In silico study, significant **chemical similarities and molecular dynamics** that successfully competed at the same interface and displaced a-amanitin from binding sites with RNA polymerase II
- Potential to protect RNA polymerase II from inactivation, preventing hepatic injury leading to survival

- All patients who have ingested amatoxin- or gyromitrin-containing mushrooms (or suspected) should be closely monitored for 48 hours for the development of hepatic and renal failure (Tintin 9th ed)

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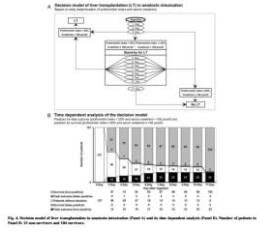
Cyclopeptide Containing Mushrooms

Liver transplantation: the criteria and timing

- Criteria for selection: essential to avoid unnecessary risk while offering the potential for survival to appropriate candidates
- Consider for encephalopathic patients with prolonged INRs (INRs > 6), persistent hypoglycemia, metabolic acidosis, increased serum ammonia and AST, hypofibrinogenemia
- Rapidly transferred to liver transplantation center



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Indications for liver transplant

- Clichy
- King's College criteria
- Ganzert
- Escudié

- Escudié's criteria show the best accuracy for emergency liver transplant in ALF induced by A. phalloides

Ferreira R, Romãozinho JM, Amaro P, Ferreira M, Sofia C. Assessment of emergency liver transplantation criteria in acute liver failure due to Amanita phalloides. Eur J Gastroenterol Hepatol. 2011 Nov;23(12):1226-32.

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Clinical Toxicology

Current fatality rate of suspected cyclopeptide mushroom poisoning in the United States

Objective: This study was designed to determine the fatality rate of suspected cyclopeptide-containing mushroom ingestions reported to the National Poison Data System (NPDS).
Background: Although silibinin reportedly improves survival in suspected cyclopeptide-containing mushroom ingestions, the greater than 20% untreated fatality rate that is often cited is based on decades-old data. An ongoing open-label silibinin trial will likely use historical cases as comparators. A recent single poison control center (PCC) study showed a fatality rate of 8.3%. This study was designed to validate those findings in the NPDS.
Methods: This study was an 11-year (1/1/2008-12/31/2018) retrospective review of suspected cyclopeptide-containing mushroom ingestions reported to NPDS. Inclusion and exclusion criteria were the same as the ongoing silibinin trial: Age >2-years-old; history of eating foraged mushrooms; gastrointestinal symptoms within 48 h of mushroom ingestion; and aminotransferases above the upper limit of normal within 48 h after ingestion. Each original participating PCC confirmed eligibility, diagnosis, treatment, and outcome on included cases.
Results: During the study period, 8,953 mushroom exposures were reported to NPDS, of which 296 met inclusion criteria. The PCC survey response rate was 60% (28/47 PCCs), and the individual case response rate was 59% (174/296). Twenty-six cases were subsequently excluded leaving 148 included cases. The overall mortality rate was 8.8% (13/148). **Mortality in silibinin/silymarin-treated vs untreated cases was 9.5% (4/42), vs 8.5% (9/106), respectively.** A mycologist identified mushrooms in 16.9% of cases (25/148), of which 80% (20/25) were cyclopeptide-containing. Among these confirmed cases, the mortality rate was 10% (1/10) in both silibinin/silymarin-treated and untreated cases.
Conclusions: The contemporary mortality rate of patients with presumed cyclopeptide-mushroom poisoning is only 8.8%. This likely represents improved supportive care for patients with acute liver injury and should be considered the current standard for historical controls in the United States

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International Journal of General Medicine — Dovepress

ORIGINAL RESEARCH

Clinical characteristics and outcome of toxicity from Amanita mushroom poisoning

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Sunun Wongvisavakorn[2]
Sahaphume Srisuma[2,4]
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2 November 2017
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Objective: To describe and analyze the clinical characteristics and outcome of amatoxin poisoning cases.
Methods: We performed a retrospective cohort study of amatoxin poisoning cases from Ramathibodi Poison Center Toxic Exposure Surveillance System, from May 2013 to August 2015.
Results: There were 30 consultations with a total of 55 poisoning cases. Most cases were male and from the north-east region. Hepatitis, acute kidney injury, jaundice, and coagulopathy accounted for 74%, 46.3%, 44.7%, and 52.8% of the cases, respectively. Almost all of the patients were admitted to the hospital, and the median duration of hospital stay was found to be 4 days. Mortality rate was found to be 27.3%. Most patients (75%) received the treatment including multiple-dose activated charcoal (67.5%), intravenous N-acetylcysteine (87.5%), and benzylpenicillin (45%). In 60% of the cases, the treatment was initiated within 24 h after eating mushrooms. Exchange transfusion and liver transplantation were performed in one severe case. However, this patient died eventually. Because intravenous silybinin is not available in Thailand during the study period, 8 patients received oral silymarin instead. All 8 patients had hepatitis and were treated with high dosage of oral silymarin (5 patients with 4.48 g/day, 2 patients with 1.68 g/day, and 1 patient with 1.4 g/day) for a couple of days. One of these patients died as she received treatment very late; she was treated with silymarin at 1.68 g/day dosage. Thus, the fatality in oral silymarin treatment group was 12.5%. We performed the analysis between the dead and survival groups. We found that in hepatitis, initial and maximum serum aspartate transaminase, initial and maximum serum alanine transaminase, and acute kidney injury were significantly different between the two groups.
Conclusion: Amanita mushroom poisoning caused high fatalities. Serum transaminase and creatinine were the factors associated with death. Treatment with oral high dose silymarin should be investigated further as one of the principal therapies in amatoxin poisoning.
Keywords: amatoxin, clinical characteristic, outcome, treatment, silymarin

Mortality rate: 27.3%

Table 1 Baseline characteristics of the patients

Characteristics	Number of patients
Gender	
Male	28 (50.9%)
Female	27 (49.1%)
Age (year), mean ± SD	43.85 ± 21.65
Region	
North/east	39 (71%)
North	7 (12.7%)
West	6 (10.9%)
East	2 (3.6%)
Central	1 (1.8%)
Underlying diseases	
No	46 (83.6%)
Yes	9 (16.4%)
The onset of GI symptoms after consuming mushrooms (hours), median (min–max)	9 (0.5–24)
Time between consumption of mushrooms and hospital admission (51 cases)	
Within 24 hours	19 (37.3%)
More than 24 hours	32 (62.7%)
Admitted to the hospital	
Yes	51 (92.7%)
No	4 (7.3%)

Abbreviations: SD, standard deviation; GI, gastrointestinal ; min, minimum; max, maximum.

Table 2 The clinical features of the patients during the hospitalization

Clinical features (total cases recorded)	Number of patients (%)
Hepatitis (50 cases)	37 (74%)
AKI (54 cases)	25 (46.3%)
Jaundice (47 cases)	21 (44.7%)
Coagulopathy (36 cases)	19 (52.8%)
Elevated indirect bilirubin (>50% of total) (48 cases)	13 (27%)
Bleeding (all had GI bleeding) (53 cases)	12 (22.6%)
Hepatic encephalopathy (53 cases)	11 (20.8%)

Abbreviations: AKI, acute kidney injury; GI, gastrointestinal.

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Table 3 Laboratory findings of all patients

Laboratory finding	Results
Initial AST results (IU/L), median (min-max)	159.5 (18–12,592)
Max AST results (IU/L), median (min–max)	871 (18–12,592)
Initial ALT results (IU/L), median (min–max)	122 (12–18,871)
Max ALT results (IU/L), median (min–max)	1426.5 (12–18,871)
Max total bilirubin results (mg/dL), median (min–max)	1.4 (0.19–28.3)
Max direct bilirubin results (mg/dL), median (min–max)	0.5 (0.1–18.49)
Max INR results, median (min–max)	1.43 (0.95–21.67)
Max creatinine results (mg/dL), median (min–max)	1.13 (0.33–7.8)

Abbreviations: AST, aspartate aminotransferase; ALT, alanine transaminase; INR, international normalized ratio; min, minimum; max, maximum.

Trakulsrichai et al

Table 4 The mortalities based on the mode of treatment for the patients

Mode of treatment (total cases treated)	Number of deaths (%)
Supportive therapy only (15 cases)	3 (20%)
The treatment regimen	
MDAC in the regimen (27 cases)	5 (18.5%)
NAC in the regimen (35 cases)	12 (34.3%)
Pen G in the regimen (18 cases)	4 (22.2%)
Oral silymarin in the regimen (8 cases)	1 (12.5%)
Single therapy	
NAC alone (7 cases)	4 (57.1%)
Oral silymarin alone (1 case)	0 (0%)
MDAC alone (1 case)	0 (0%)
Double therapy	
MDAC + NAC (7 cases)	3 (42.9%)
MDAC + Pen G (2 cases)	0
NAC + Pen G (3 cases)	3 (100%)
Oral silymarin + NAC (2 cases)	0
Triple and quadruple therapy	
MDAC + NAC + Pen G (12 cases)	1 (8.3%)
Oral silymarin + MDAC + NAC (4 cases)	1 (25%)
Oral silymarin + MDAC + NAC + Pen G (1 case)	0

Abbreviations: MDAC, multiple-dose activated charcoal; NAC, N-acetylcysteine intravenous; Pen G, penicillin G; Oral silymarin, oral high dose silymarin.

Table 5 The statistically significant differences of the clinical characteristics and the laboratory findings between the fatality and the survival group for every patient and for only the patients who developed hepatitis

Clinical characteristics	All patients			Patients with hepatitis		
	Patients who survived (40)	Patients who died (15)	p value	Patients who survived (23)	Patients who died (14)	p value
AKI (%)	11/39 (28.2%)	14/15 (93.3%)	<0.001	10/23 (43.5%)	13/14 (92.9%)	0.003
Jaundice (%)	9/34 (26.5%)	12/13 (92.3%)	<0.001	7/22 (31.8%)	12/13 (92.3%)	0.001
Coagulopathy (%)	6/23 (26.1%)	13/13 (100%)	<0.001	5/14 (35.7%)	13/13 (100%)	0.001
Initial AST results (IU/L), median (min–max)	42.5 (18–5,500)	2,350 (44–12,592)	<0.001	61 (21–5,500)	3,137 (289–12,592)	<0.001
Initial ALT results (IU/L), median (min–max)	44.5 (12–6,268)	1,787 (23–18,871)	<0.001	68 (13–6,268)	2,100 (200–18,871)	<0.001
Max AST results (IU/L), median (min–max)	323 (18–12,300)	5,750 (2,641–12,592)	<0.001	532 (135–12,300)	5,750 (2,641–12,592)	<0.001
Max ALT results (IU/L), median (min–max)	451 (12–9,899)	3,436.5 (1,684–18,871)	<0.001	607 (76–9,899)	3436.5 (1,684–18,871)	<0.001
Max total bilirubin results (mg/dL), median (min–max)	1.2 (0.19–17.9)	6.56 (0.5–28.3)	0.011	1.34 (0.23–17.9)	6.56 (0.5–28.3)	0.004
Max direct bilirubin results (mg/dL), median (min–max)	0.4 (0.1–12.75)	3.2 (0.2–18.49)	<0.001	0.5 (0.1–12.75)	3.2 (0.2–18.49)	0.001
Max creatinine results (mg/dL), median (min–max)	0.9 (0.33–3.9)	3.5 (0.4–7.8)	<0.001	0.9 (0.33–3.9)	3.5 (0.4–7.8)	<0.001

Abbreviations: AST, aspartate aminotransferase; ALT, alanine transaminase; AKI, acute kidney disord ; min, minimum; max, maximum.

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Oral high dose silymarin

- Extract from milk thistle, Silybum marianum
- No silibinin IV available in Thailand
- Oral high dose silymarin used in our poison center instead
- Dose silibinin IV: 5 mg/kg IV loading dose then 20mg/kg/day
- Recommended dose 1.4-4.2 g
- Oral bioavailability: 23-47%
- Use the dose: **4.48 g**, **7 US$/day**
- Combined with other treatment, interval 3 hours with AC
- No conflict of interest

POISINDEX System. Micromedex Healthcare Series.

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> Clin Toxicol (Phila). 2021 Sep;59(9):843-845. doi: 10.1080/15563650.2021.1887492.
Epub 2021 Feb 19.

Intravenous rifampicin use in the management of amanita phalloides toxicity

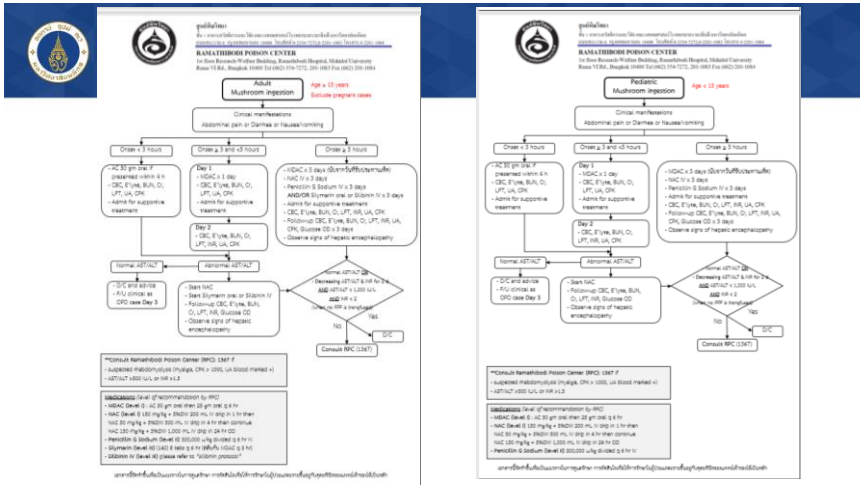
Rona Zuker-Herman [1], Roger Tong [1], Anselm Wong [2]

Affiliations + expand

PMID: 33605821 DOI: 10.1080/15563650.2021.1887492

Abstract

Context: Amanita phalloides related toxicity from amatoxins can result in acute liver and multi-organ failure and is responsible for 90% of all mushroom poisoning death. However, more evidence is needed in regards to different management strategies.**Case details:** We present two cases of amanita mushroom ingestion who were treated with intravenous rifampicin.**Discussion:** Further study is needed to establish the efficacy and role of rifampicin in amatoxin related mushroom poisoning.



Mahidol University — Cyclopeptide Containing Mushrooms

- Amatoxins
- Heat stable
- **Clinical:** Delayed onset(≥5 hours) of GI symptoms, hepatotoxicity in 12-36 hours
- **Treatment:**
  - Fluid and electrolyte repletion
  - Multiple Dose Activated charcoal
  - N-acetylcysteine
  - Penicillin G
  - The active complex of milk thistle
  - Liver transplantation

Mahidol University — Gyromitrin Containing Mushrooms

Gyromitrin containing mushrooms. A true morel (Morchella spp) on the left is compared to a false morel (Gyromitra esculenta) on the right.

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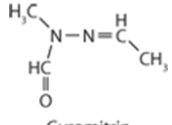
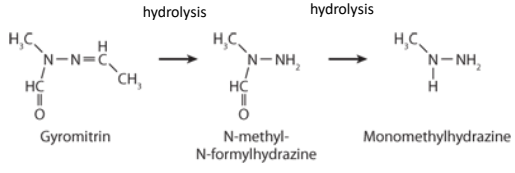


Goldfrank 11th ed

Mahidol University — Gyromitrin Containing Mushrooms

- Brainlike appearance
- Contain gyromitrin: volatile **heat-labile** toxin, hydrolysis to a family of N-methyl-formyl hydrazines, subsequent hydrolysis yield N-methyl-N-formyl hydrazine and monomethylhydrazine
- Decrease in GABA



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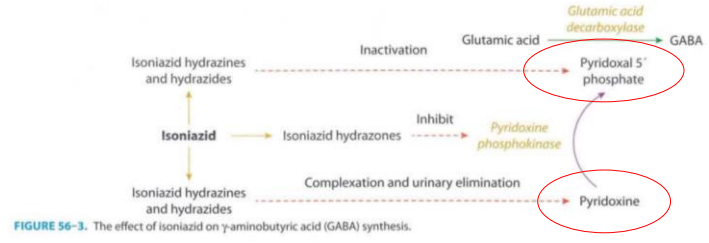

FIGURE 56–3. The effect of isoniazid on γ-aminobutyric acid (GABA) synthesis.

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Gyromitrin Containing Mushrooms

Clinical

- 5-10 hours after ingestion: nausea, vomiting, diarrhea, abdominal pain
- Headaches, weakness, diffuse muscle cramping
- 12-48 hours: delirium, stupor, convulsions, coma
- Most improve dramatically, return to normal function within several days
- Infrequently: hepatorenal syndrome

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Gyromitrin Containing Mushrooms

Treatment

- Activated charcoal: 1 g/kg BW
- Benzodiazepines: initial management of seizures
- Most circumstances: supportive care
- **Pyridoxine:** 70 mg/kg IV up to 5 g: may be useful in limiting seizures

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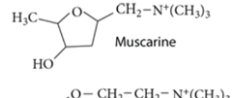
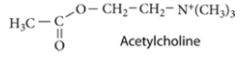
Muscarine Containing Mushrooms

- Clitocybe species: C. dealbata (the sweater), C. illudens (Omphalotus olearius)
- Inocybe species: I. iacera, I. lanuginosa, I. geophylla
- A. muscaria and A. pantherina contain limited quantities of muscarine, A. muscaria contains substantial amounts of muscimol





Muscarine and acetylcholine: similar structurally and comparable clinical effects at the muscarinic receptors

Clitocybe dealbata

Omphalotus olearius.

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Muscarine Containing Mushrooms

Clinical

- Typically mild, usually 0.25-2 hours, last several additional hours
- Complete resolution within 24 hours
- Peripheral manifestations: bradycardia, miosis, salivation, lacrimation, vomiting, diarrhea, bronchospasm, bronchorrhea, micturition
- Central muscarinic manifestations: not occur because muscarine not cross the blood–brain barrier
- **No nicotinic** manifestations e.g. diaphoresis or tremor occur
- Because muscarine lacks an ester bond, not hydrolysed by acetylcholinesterase, effects of muscarine often last longer than acetylcholine

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Muscarine Containing Mushrooms

Treatment

- Supportive care
- Rarely, atropine (1–2 mg given IV slowly for adults) titrated and repeated to reverse symptomatology

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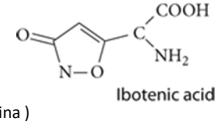
Ibotenic Acid and Muscimol Containing Mushrooms

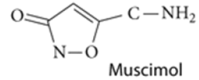
- Most primarily in the Amanita species: A. muscaria (fly agaric), A. pantherina, A. gemmata

Amanita muscaria highlights different developmental forms and colors

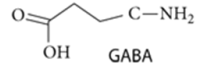
เห็ดเกล็ดดาว
(Amanita pantherina)



Ibotenic acid



Muscimol



GABA

Mahidol University — Ibotenic Acid and Muscimol Containing Mushrooms

Clinical

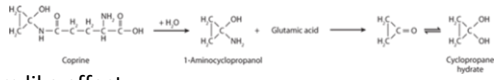
- Ibotenic acid: structurally similar to glutamic acid
- Muscimol: very similar to GABA and may act as a GABA agonist
- Within 0.5-2 hours of ingestion
- **GABAergic manifestations**: somnolence, dizziness, hallucinations, dysphoria, delirium **in adults**
- **Excitatory glutamatergic manifestations**: myoclonic movements, seizures **in children**

Treatment

- Supportive treatment
- Benzodiazepine for excitatory CNS manifestations

Mahidol University — Coprine Containing Mushrooms

- Coprinus mushrooms: C. atramentarius, (Coprinopsis atramen¬taria)
- known as “inky caps”



- Contain coprine: disulfiram like effect
- Inhibition of acetaldehyde dehydrogenase, accumulation of acetaldehyde

เห็ดหิ่งห้อย, เห็ดน้ำหมึก, เห็ดถั่ว

(A) Coprinopsis atramentaria; (B) and (C) show Coprinus comatus (shaggy mane). Image (B) shows an early form which later is self digested demonstrating the gill liquefaction in image (C).

Mahidol University — Coprine Containing Mushrooms

Clinical

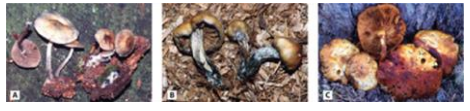
- At least 0.5-2 hours if ingests alcohol and coprine containing mushroom concomitantly
- Acute disulfiram effect: tachycardia, flushing, nausea, vomiting
- Usually mild, resolve within several hours
- if ethanol ingestion 48-72 hours following coprine-containing mushroom ingestion, toxicity may ensue

Treatment

- Symptomatic with fluid repletion
- Antiemetics e.g. metoclopramide or ondansetron

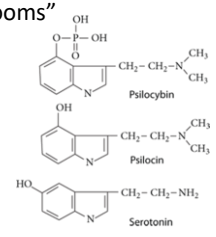
Mahidol University — Psilocybin Containing Mushrooms

- Psilocybe cyanescens, Psilocybe cubensis, Conocybe cyanopus, Panaeolus cyanescens, Gymnopilus spectabilis, and Psathyrella foenisecii
- Drug culture magazines and Internet sources advertise mail-order kits containing P. cubensis spores to grow “magic mushrooms” domestically



(A) Psilocybe cyanescens, (B) Psilocybe caerulipes, (C) Gymnopilus spectabilis.

เห็ดขี้ควาย เห็ดขี้วัว เห็ดโอสถลวงจิต (Psilocybe cubensis)



Psilocybin Containing Mushrooms

- Psilocybin: rapidly and completely hydrolyzed to psilocin in vivo
- Serotonin, psilocin, psilocybin: very similar structurally and presumably act at a similar 5-HT2 receptor site
- The effects as a serotonin agonist and antagonist
- Like lysergic acid diethylamide (LSD)

Psilocybin Containing Mushrooms

Clinical

- Rapidly (within 1 hour) CNS effects: ataxia, hyperkinesis, visual illusions, hallucinations
- Some: manifest GI distress, tachycardia, mydriasis, anxiety, lightheadedness, tremor, agitation
- Most manifestations: within 4 hours of ingestion with a return to normalcy within 6-12 hours
- Rare cases: renal failure, seizures, cardiopulmonary arrest

Treatment

- Usually supportive
- Benzodiazepine may be necessary

Gastrointestinal Toxin Containing Mushrooms

- Boletus spp, Lactarius spp, O. olearius, Rhodophyllus spp, Tricholoma spp, Chlorophyllum molybdites, and Chlorophyllum esculentum
- The toxins: not identified
- The malabsorption of proteins and sugars or ingestion of a mushroom infected or partially digested by microorganisms or allergy

- เห็ดหัวกรวดครีบเขียว (Chlorophyllum molybdites)
- เห็ดแดงน้ำหมาก (Russula emetica)

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Gastrointestinal Toxin Containing Mushrooms

Clinical

- GI toxicity 0.3-4 hours after ingestion: epigastric distress, malaise, nausea, vomiting, diarrhea
- Clinical course: brief
- Prognosis: excellent

Treatment

- Fluid resuscitation
- Control of vomiting and diarrhea
- When symptoms seem to persist, must consider a mixed ingestion of another potentially toxic mushroom group
- Not give antidiarrheal agents, because may prolong exposure to toxin

Acute Onset Mushroom poisoning

- **Muscarine Containing Mushrooms**
  - Cholinergic
- **Ibotenic Acid and Muscimol Containing Mushrooms**
  - GABAergic, glutamatergic
- **Coprine Containing Mushrooms**
  - Disulfiram
- **Psilocybin Containing Mushrooms**
  - Hallucinogen
- **GI Toxin Containing Mushrooms**
  - GI symptoms

→ Supportive treatment

Rhabdomyolysis Associated Mushrooms

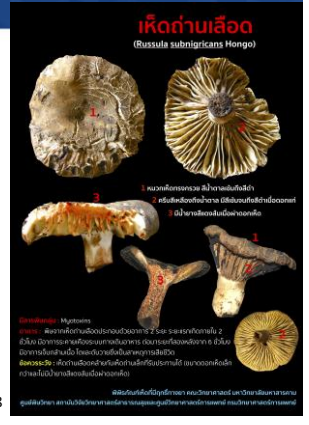
Tricholoma equestre (Tricholoma flavovirens)

- Fatigue, muscle weakness, myalgias
- 24-72 hours following the last mushroom meal
- Facial erythema, nausea without vomiting, profuse sweating
- Dyspnea, muscle weakness, acute myocarditis, dysrhythmias, congestive heart failure, death

Rhabdomyolysis Associated Mushrooms

Russula subnigricans

- Rhabdomyolysis
- Severe electrolyte disturbance (hyperkalemia, hypocalcemia)
- Acute renal failure
- Respiratory failure, pulmonary edema
- Ventricular tachycardia
- Cardiogenic shock
- Circulatory shock



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WILDERNESS & ENVIRONMENTAL MEDICINE, 26, 380–383 (2015)

CASE REPORT

Russula subnigricans Poisoning: From Gastrointestinal Symptoms to Rhabdomyolysis

Shishi Lin, MD; Maoyuan Mu, MM; Fangwan Yang, MM; Chunfu Yang, BSM

From the Department of Infectious Diseases, First Affiliated Hospital of Zunyi Medical College, Zunyi, China (Dr Lin, Ms Mu, and Mr F Yang); and the Department of Internal Medicine, People's Hospital of Dejiang County, Dejiang, China (Mr C Yang)

Wild mushroom poisoning is often reported to cause acute liver or renal failure. However, acute rhabdomyolysis caused by wild mushroom poisoning has rarely been reported. We describe 7 patients of 1 family with *Russula subnigricans* Hongo poisoning. Their clinical manifestations varied from gastrointestinal symptoms to rhabdomyolysis, with 1 fatality. Our report provides supporting evidence that rhabdomyolysis may result from ingestion of *R subnigricans* mushrooms. A key to survival for patients with rhabdomyolysis caused by *R subnigricans* poisoning may be early recognition and intensive supportive care.

Key words: rhabdomyolysis, mushroom poisoning, *Russula subnigricans*, hemodialysis

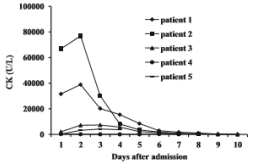

Figure 1. Serum creatine kinase (CK) levels in 5 patients who survived during hospitalization.

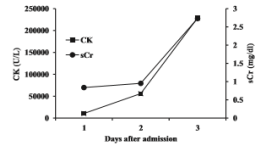

Figure 2. Serum creatine kinase (CK) and serum creatinine (sCr) levels in the patient who died during hospitalization.

Figure 3. *Russula subnigricans* mushrooms.

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International Journal of General Medicine
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ORIGINAL RESEARCH

Myotoxic Mushroom Poisoning in Thailand: Clinical Characteristics and Outcomes

This article was published in the following Dove Press journal:
International Journal of General Medicine

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Purpose: To describe the clinical characteristics and outcomes of myotoxic mushroom poisoning in Thailand.

Patients and Methods: We performed a retrospective cohort study of cases of myotoxic mushroom poisoning from the Ramathibodi Poison Center Toxic Exposure Surveillance System during a 5-year period (2012–2016).

Results: Forty-one cases were included. Most (53.7%) were male with the average age of 49 years. In three cases, the mushrooms were identified as *Russula* species by an experienced mycologist. Common presenting symptoms were gastrointestinal (GI) symptoms and myalgia. The median onset of GI symptoms and symptoms suggesting rhabdomyolysis after consuming mushrooms was 2 hours (0.17–24 hours) and 24–48 hours (2–120 hours), respectively. Eight patients who ate the mushrooms together with other patients with rhabdomyolysis had GI symptoms but did not develop rhabdomyolysis. For patients with rhabdomyolysis, acute kidney injury (AKI) and hyperkalaemia occurred in 51.5% and 33.3% of cases, respectively. Median initial and maximum creatine phosphokinase (CPK) levels in patients with rhabdomyolysis were 31,345 and 47,861 U/L, respectively. Fifteen of 17 patients who were investigated for troponin levels had elevated troponin. Three patients had a low ejection fraction. Most patients (95.1%) were admitted to hospital, with a median stay of 5 days. The mortality rate was 26.8%. Treatments included intravenous fluid, urine alkalinization, haemodialysis and peritoneal dialysis. Among patients with rhabdomyolysis, AKI, hyperkalaemia during hospitalisation, maximum CPK level, maximum creatinine level and initial and maximum potassium levels were the factors found to be significantly different between patients who died and those who survived.

Conclusion: Myotoxic mushroom poisoning had a high mortality rate. Most patients had early or delayed onset of clinical symptoms after mushroom ingestion. Some patients developed severe cardiovascular effects. Early detection, close monitoring (especially serum potassium, creatinine, CPK and cardiac effect) and good supportive care were the main treatment modalities.

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Table 1 Clinical Characteristics of the Patients (41 Patients)

Characteristics	Value
Age (year), mean ± SD	48.85 ± 16.02
Season -Rainy -Winter -Summer	 24 (58.54) 9 (21.95) 8 (19.51)
Onset of gastrointestinal symptoms after consuming mushrooms (h) (27 cases)–median (min–max)	2 (0.17–24)
Onset of myalgia after consuming mushrooms (h) (15 cases)–median (min–max)	24 (3–96)
Onset of dark urine after consuming mushrooms (h) (16 cases)–median (min–max)	48 (2–120)
Time to hospital after consuming mushrooms (h) median (min–max)	21 (2–120)

Table 3 Clinical Features of Patients with Rhabdomyolysis (33 Patients) During Hospitalisation

Clinical Features Reported (Number of Cases with Recorded Data)	Number (%) of Patients
Elevated AST and ALT	32 (97)
AKI	17 (51.5)
Elevated cardiac enzymes - Troponin (I or T) (17 cases) - CK-MB (14 cases)	 15 (88.2) 14 (100)
Hyperkalaemia (30 cases)	10 (33.3)
Abnormal chest X-ray (20 cases)	13 (65)
Abnormal electrocardiogram (20 cases)	13 (65)
Abnormal echocardiogram (4 cases)	3 (75)

Abbreviations: AST, aspartate aminotransferase; ALT, alanine transaminase; AKI, acute kidney injury; CK-MB, creatine kinase-MB.

Table 5 Differences in Clinical Characteristics and Laboratory Findings Between Patients Who Survived and Patients Who Died for Patients with Rhabdomyolysis (33 Patients)

Clinical Characteristic or Laboratory Finding	Patients with Rhabdomyolysis		
	Survived (22)	Died (11)	*P*-value
Age (years), mean ± SD	50.09 ± 14.20	58.45 ± 12.41	0.107
Sex (%) Male Female	 10 (45.5) 12 (54.5)	 6 (54.5) 5 (45.5)	0.622
AKI (35 cases) (%)	6 (27.3)	11 (100)	<0.001
Shock during hospitalisation (%)	5 (22.7)	6 (54.5)	0.117
Hyperkalaemia during hospitalisation (32 cases) (%)	2 (of 20) (10)	8 (of 10) (80)	<0.001
Initial CPK results (IU/L), median (min–max)	27,882.5 (1221–284,720)	39,157 (2746–179,506)	0.492
Maximum CPK results (IU/L), median (min–max)	36,245.5 (8616–330,000)	86,544 (34,449–179,506)	0.029
Initial AST results (IU/L), median (min–max)	709 (51–8066)	200 (33–4083)	0.456
Maximum AST results (IU/L), median (min–max)	1141 (538–8066)	2157 (69–4083)	0.593
Initial ALT results (IU/L), median (min–max)	225.5 (30–4080)	76 (30–1103)	0.302
Maximum ALT results (IU/L), median (min–max)	460 (135–4080)	464 (32–1791)	0.819
Maximum CK-MB results (IU/L), median (min–max)	1313.5 (300–2800)	3018.5 (50–7649)	0.439
Initial potassium results (mmol/L), mean ± SD	4.03 ± 0.46	4.68 ± 0.85	0.045
Maximum potassium results (mmol/L), mean ± SD	4.25 ± 0.74	5.60 ± 0.98	<0.001
Initial creatinine results (mg/dL), median (min–max)	0.84 (0.36–3.11)	1.31 (0.58–3.60)	0.054
Maximum creatinine results (mg/dL), median (min–max)	0.84 (0.36–9.96)	2.46 (1.31–7.70)	0.001

Abbreviations: AKI, acute kidney injury; AST, aspartate aminotransferase; ALT, alanine transaminase; CPK, creatine phosphokinase; CK-MB, creatine kinase-MB.

- AKI
- Hyperkalaemia during hospitalization
- Maximum CPK level
- Maximum creatinine level
- Initial and maximum potassium levels w

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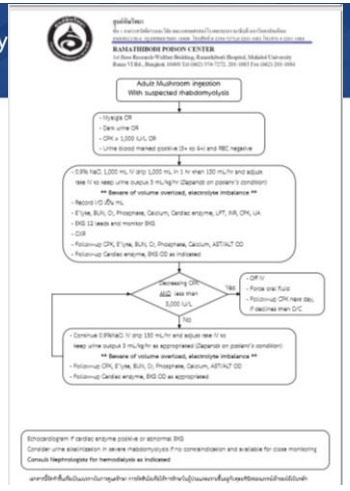

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Rhabdomyolysis Associated Mushrooms

- **Russula subnigricans**
- **Onset ?**
- **Clinical:** Fatigue, muscle weakness, myalgias, acute myocarditis, dysrhythmias, congestive heart failure, death
- Rhabdomyolysis
- Severe electrolyte disturbance
  (hyperkalemia, hypocalcemia)
- Acute renal failure
- **Treatment:** Supportive, Observe and monitoring

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Shitake dermatitis

- Well-known entity in Japan, China, Korea, reported in Europe, US
- เห็ดหอม (Shiitake Mushroom)
- Flagellate erythema appearing as whip-like, linear wheals that appear within 1 or 2 days of ingesting raw or cooked shiitake mushrooms
- The rash tends to be pruritic and can also involve branching patches of erythema and scattered petechiae
- The pathophysiology is not fully understood but is thought to be toxin induced, involving the thermolabile polysaccharide lentinan
- Skin biopsy results are nonspecific

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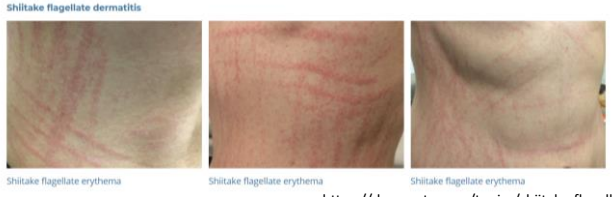
- Treatment: 0.1% triamcinolone ointment, oral antihistamines
- Regardless of treatment, the rash resolves spontaneously without hyperpigmentation in 1-4 weeks
- The rash is self-limited, and no sequelae have been reported



https://dermnetnz.org/topics/shiitake-flagellate-dermatitis/

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Special populations

Pregnancy

- In one series, a slightly lower birth weight was noted in infants born to mothers with toxic mushroom exposure than in infants of mothers with no such exposure.
- Most infants appeared to be healthy and developmentally normal, in keeping with the findings that amatoxins do not cross the placental barrier

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Toxicon

Review

Mushroom poisoning: A proposed new clinical classification

J. White et al.

Table 2
Proposed classification scheme for clinical types of mushroom poisoning.

Group	Suspected toxin	Indicative species
Group 1 - Cytotoxic mushroom poisoning.		
Subgroup 1.1 - Primary hepatotoxic mushroom poisoning		
Group 1A - Primary hepatotoxicity.	amatoxins	*Amanita phalloides*
Subgroup 1.2 - Primary nephrotoxic mushroom poisoning		
Group 1B - Primary nephrotoxicity.	AIHDA	*Amanita smithiana*
Group 1C - Delayed primary nephrotoxicity.	orellanine	*Cortinarius* spp.
Group 2 - Neurotoxic mushroom poisoning		
Group 2A - Hallucinogenic mushrooms.	psilocybins	*Psilocybe* spp.
Group 2B - Autonomic toxicity mushrooms.	muscarines	*Inocybe* spp.
Group 2C - Central nervous system toxicity mushrooms.	Ibotenic acid/muscimol	*Amanita muscaria*
Group 2D - Morel neurologic syndrome.	unknown	*Morchella* spp.
Group 3 - Myotonic mushroom poisoning.		
Group 3A - Rapid onset myotoxicity.	carboxylic acid	*Russula subnigricans*
Group 3B - Delayed onset myotoxicity.	saponacreolide B	*Tricholoma equestre*
Group 4 - Metabolic/endocrine toxicity mushroom poisoning.		
Group 4A - GABA-blocking mushroom poisoning.	gyromitrins	*Gyromitra* spp.
Group 4B - Disulfiram-like mushroom poisoning.	coprines	*Coprinus* spp.
Group 4C - Polyporic mushroom poisoning.	polyporic acid	*Hapalopilus rutilans*
Group 4D - Trichothecene mushroom poisoning.	trichothecenes	*Podostroma cornu-damae*
Group 4E - Hypoglycaemic mushroom poisoning.	unusual amino acids	*Tricaptum venenosum*
Group 4F - Hypercalcitoninemia mushroom poisoning.	unknown	*Boletus sinuspes*
Group 4G - Pancytopenia mushroom poisoning	unknown	*Ganoderma neojaponicum*
Group 5 - Gastrointestinal irritant mushroom poisoning.		
Group 6 - Miscellaneous adverse reactions to mushrooms.		
Group 6A - Shiitake mushroom dermatitis.	lentinan	*Lentinula edodes*
Group 6B - Erythromelalgia-like mushroom poisoning.	acromelic acid	*Clitocybe acromelalgia*
Group 6C - Paxillus syndrome.	unknown	*Paxillus involutus*
Group 6D - Encephalopathy syndrome.	? HydroCyanicAcid	*Pleurocybella porrigens*

Note: The suspected toxin represents only one selected toxin, but for some groups there may be several different and distinct toxins involved. Similarly the indicative species represents just one selected on the basis of available information, though for some groups, many species may be implicated.

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TABLE 117–2 Mushroom Toxicity: Correlation Between Organ System Affected, Time of Onset of Toxic Manifestations, and Mushroom Xenobiotic Responsible

	Time of Onset		
Organ System	*Early: <5 h*	*Middle: 5–24 h*	*Late: >24 h*
Cardiac muscle			2*R*-amino-4,5-hexynoic acid
Gastrointestinal	Allenic norleucine 2*R*-amino-4,5-hexynoic acid Coprine Group VII Psilocybin Muscarine	Allenic norleucine Amatoxin Gyromitrin	Orellanine and orellinine
Liver			Amatoxin
Immunologic	Involutin Spores		
Nervous	Ibotenic acid and muscimol Psilocybin	Gyromitrin	Acromelic acid Gyromitrin Polyporic acid
Kidney			Allenic norleucine Orellanine and orellinine
Skeletal muscle	Cycloprop-2-enecarboxylic acid		

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The Unknown Mushroom

- The most important determinant: deadly varieties, especially Amanita
- Onset of GI symptoms within 5 hours of ingestion: not result from amatoxin poisoning
- Collected mushrooms or detailed description of features
- Arrange for transport of the mushroom in a dry paper bag (not plastic), neither moistened nor refrigerated
- Gastric contents may contain spores that may be very difficult to find, but can be crucial for analysis
- A spore print: The spores that collect on the paper can be analyzed for color

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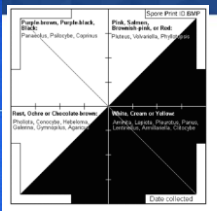
A spore print

How to: Make Spore Prints - Milkwood
Milkwood Permaculture



Spore print - Wikipedia
Wikipedia
https://en.wikipedia.org/wiki/Spore_print

How To Make A Spore Print - Wild Mushroom Spore Color Identification
Survivallandusa.com

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- Contact a mycologist and use the best resources available for identification
- Melzer reagent, solution of 20 mL water, 1.5 g potassium iodide, 0.5 g iodine, and 20 g chloral hydrate,: useful in differentiating look-alike species, defining the presence of an amatoxin
- A positive reaction: a dark blue color upon contact with Melzer reagent
- Hospitals are not typically prepared for this type of testing
- Meixner reaction: several drops of 10N to 12N hydrochloric acid applied to an amatoxin containing mushroom sample squeezed onto newspaper, resulting in a blue reaction

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Thank you for your attention

Question?