

Al-Mustaqbal University
College of Pharmacy
5th stage
Clinical Toxicology
Lecture:6



Plant Toxicity

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Plant Toxicity

- ✓ A **poisonous plant** is defined as a plant that when **touched or ingested** in sufficient quantity can be **harmful or fatal** to an organism or any plant capable evoking a **toxic and/or fatal reaction**.
- Examples on poisoning plants like **mashroom, foxglove, castor bean, free tobacco ...etc.**



MUSHROOM POISONING

- ✓ **Mushrooms** are the **fruiting** bodies of a group of **higher fungi**.
- ✓ Mushroom **toxicity** occurs after the **ingestion** of mushrooms that contain toxins which are **similarly** appearing to non-toxic mushrooms.
- ✓ There are **thousands** of species of mushrooms, but only about **100 species** can cause **symptoms** when eaten by humans, and only **15-20 species** are potentially **lethal** when ingested.
- ✓ **No simple rule** exists for distinguishing **edible mushrooms** from **poisonous** one.
 - ✓ In more than **95%** of mushroom toxicity cases, poisoning occurs as a result of **misidentification** of the poisonous mushroom from edible one.



PATHOPHYSIOLOGY

- ✓ Each poisonous mushroom species contains **1 or more toxins**.
- ✓ The **severity** of mushroom poisoning may **vary**, depending on:
 1. The **geographic** location where the mushroom is grown
 2. The **amount** of toxin delivered
 3. **Genetic** characteristics of the mushroom
- ✓ Boiling, cooking, freezing, or processing **may not** alter some mushroom's toxicity.

PATHOPHYSIOLOGY

✓ Mushroom poisoning can be classified into the following **3 categories** on the basis of the **time from ingestion to** the development of symptoms :

1. **Early symptom category**
2. **Late symptom category**
3. **Delayed symptom**



PATHOPHYSIOLOGY

Early symptom category: first 6 hours

✓ of ingestion and include gastrointestinal, allergic, and neurologic syndromes.

Late symptom category: appear between 6-24 hours

✓ after ingestion and may include hepatotoxic and nephrotoxic syndromes.

Delayed symptom category: more than 24 hours

✓ after ingestion and include mostly nephrotoxic syndromes.

MUSHROOM TOXINS

Mushroom **toxins** include but not limited to the following:

1. **Amatoxin--- Cyclopeptides**



2. **Gyromitrins (monomethylhydrazine)**

- ✓ inhibits a number of hepatic systems, including cytochrome P-450 and glutathione, and causes hepatic necrosis
- ✓ inhibits pyridoxine kinase and interferes with all the pyridoxine-requiring enzymes in the body, including those involved in the **synthesis of gamma-aminobutyric acid (GABA)**.
- ✓ The **reduction** of GABA concentrations in the brain leads to CNS **hyperexcitability** and **convulsions**.

2-Orellanine

Its main effects are on the **renal tubular system**, where it causes **necrosis** with relative **sparing** of the **glomerular** apparatus.

3- **Muscimol and ibotenic acid**(is structurally similar to **GABA** and acts as a GABA-receptor **agonist**. So It is **excitatory neurotoxin** and may be **mildly hallucinogenic**)

4-Norleucine (Nephrotoxins)

5- Muscarine

Amatoxins

Amatoxins are **powerful toxins**.

- ✓ Ingested amounts as **low as 0.1 mg/kg** are sufficient to be **lethal**.
- ✓ A **single** full-grown specimen of *A. phalloides*, **weighing 20 g**, contains about **5–8 mg** of amatoxin and is, therefore, potentially lethal.

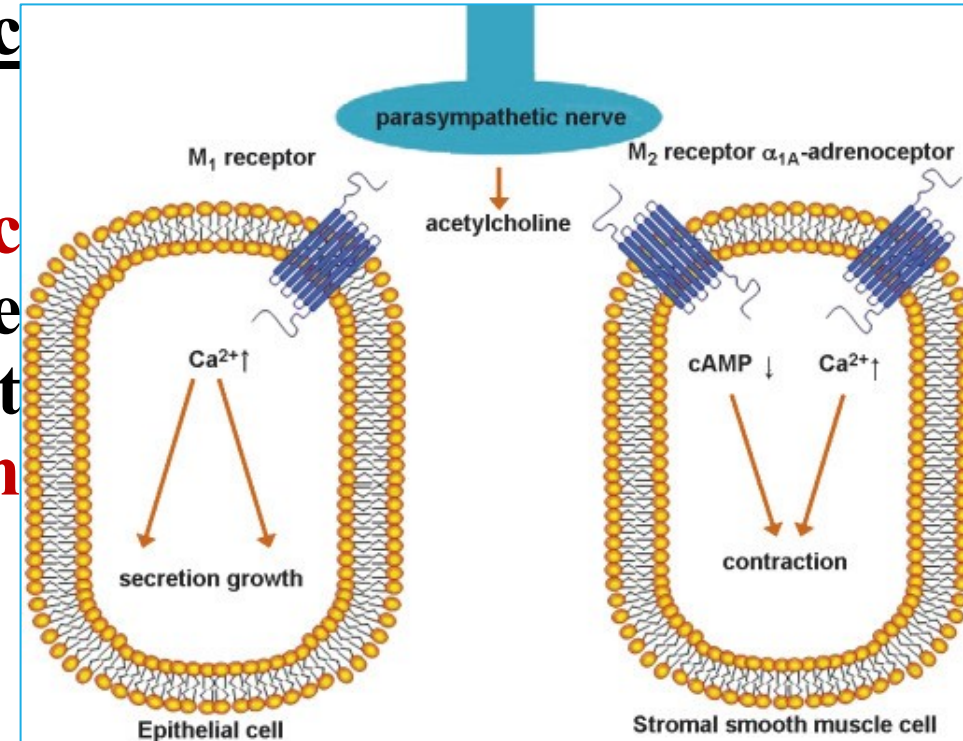


Amatoxins

- ✓ It is a **cyclic octapeptides** that are synthesized by *Amanita species*.
- ✓ Amatoxins are **absorbed** rapidly from the **GIT**.
- ✓ These toxins may be **detected in the urine** as early as 90–120 min after ingestion of the mushrooms.
- ✓ At **least 5 subtypes** of amatoxins are known, the only significant **human toxin** being **alpha-amatoxin**, which inhibits RNA polymerase II and protein synthesis.

Muscarine

- ✓ **Muscarine** stimulates **M1 and M2 types** of postganglionic cholinergic receptors (muscarinic receptors) in the autonomic nervous system.
- ✓ This action results in **parasympathetic stimulation** similar to that caused by the release of endogenous **acetylcholine** at postganglionic receptors of **smooth muscle and exocrine gland**.



Muscarine

- ✓ **Muscarine-containing mushrooms** typically produce **cholinergic symptoms** such as sweating, facial flushing, salivation, lacrimation, vomiting, abdominal cramps, diarrhea, urination, and miosis; occasionally, bradycardia, hypotension, and dizziness develop.
- ✓ Symptoms typically **occur within 1 hour** of ingestion and **last for 4-24 hours.**
- ✓ In most cases, they **resolve without drug therapy** or **with a dose of atropine.**



SIGNS OF CHOLINERGIC CRISIS



DUMBBELLS

Diarrhea (and Diaphoresis) and abdominal cramping

Urination

Miosis (pinpoint pupils)

Bradycardia (muscarinic) or Tachycardia (nicotinic)

Emesis (Nausea and Vomiting)

Lacrimation

Lethargy

Salivation



Complications Of Mushroom Toxicity

Respiratory:

- ✓ Aspiration pneumonia may occur with mushroom poisonings and involves loss of airway protective reflexes.

Neurologic:

Convulsions are common in gyromitrin poisoning, but they also may be due to hypoxia, acidosis, and metabolic abnormalities; cerebral edema may be a complication of hypoxia, acidosis, trauma, and hepatic failure.

Complications Of Mushroom Toxicity

Hepatic:

- ✓ Hepatic failure and hypoglycemia are complication of amatoxin and gyromitrin poisonings.

Renal:

Renal failure is a common complication of norleucine and orellanine poisoning but also may be due to hypoperfusion and shock.

Hematologic:

- ✓ Methemoglobinemia and hemolysis may complicate gyromitrin poisoning.

Others:

- ✓ Trauma may complicate hallucinogenic mushroom poisoning.
- ✓ Hypovolemia and electrolyte disturbances may complicate any mushroom poisoning

Treatment OF MUSHROOM TOXICITY

1. **Early volume resuscitation** (fluid rehydration) is important for liver and renal toxic syndromes.
2. **Gut decontamination**, including whole-bowel irrigation.
3. **Multiple doses of activated charcoal** (regardless of the timing of presentation) should be administered repeatedly to interrupt enterohepatic circulation of these toxins.
4. **Endotracheal intubation** is recommended in all patients at risk of aspiration, and mechanical ventilation should be initiated in all patients with hypoxia, acidemia, and shock.

TREATMENT OF MUSHROOM TOXICITY

5. **Agitation**, commonly observed with hallucinogenic mushrooms, is treated with **benzodiazepines**.
6. **Severe muscarinic symptoms** may be treated with the infusion of small doses of **atropine**.
7. Patients with severe poisoning from **disulfiram-containing mushrooms** may benefit from **fomepizole** which blocks **alcohol dehydrogenase** and, hence, the formation of the **toxic aldehyde**.

TREATMENT OF MUSHROOM TOXICITY

8. **Renal failure**, commonly observed with norleucine and orellanine poisoning, may have to be treated with **hemodialysis**.
9. Conventional **indications for dialysis** include fluid overload (with pulmonary edema), severe hyperkalemia, and acidosis.
10. **Blood transfusions** may be required in patients with hemorrhagic diarrhea, blood loss, and severe hemolytic anemia.

TREATMENT OF MUSHROOM TOXICITY

- 11. Blood pressure support** with dopamine and norepinephrine may be required when crystalloids and colloid infusions fail.
- 12. Hypoglycemia** is treated with infusions of **10% dextrose**.



**THANK YOU
FOR YOUR ATTENTION**