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Department of Animal Physiology, Maria Curie-Skłodowska University in Lublin
Department of Normal Human Anatomy, Skubiszewski Medical University of Lublin

KAZIMIERA GROMYSZ-KAŁKOWSKA, EWA SZUBARTOWSKA,
KAZIMIERA WÓJCIK

Cap mushroom poisonings

Cap mushroom poisonings are a key problem of toxicology, important both in the ancient and present times. Mushroom consumption causes numerous, often lethal, poisonings (Fig. 1). As shown above, the number of people suffering from poisonings decreases but is still substantial. The inability to disseminate edible mushrooms from poisonous fungi and frequently restricted access to publications on the topic make it crucial to present the most dangerous mushroom "poisoners" as well as toxins present in fungi and their activity.

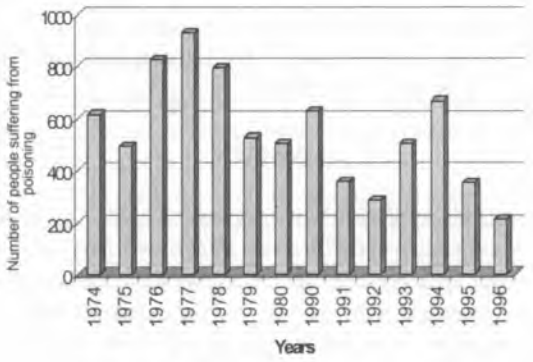

Fig. 1. The number of mushroom poisonings in 1974–1996

Three species of amanita can be mentioned as the most poisonous mushrooms. These are: the Death Cap (*Amanita phalloides*), the Spring Destroying Angel (*Amanita verna*) and the Destroying Angel (*Amanita virosa*). Sometimes *A. verna* is regarded as synonymous to *A. virosa*. These species of amanitas are very often mistaken for edible mushrooms, such as field mushrooms, parasols, knights, brittlegills, or St. George's mushroom.

The Death Cap forms medium-size fructifications. Its cap, 6–12 cm in diameter, bell-shaped in young fructifications, flattened in older ones, is green-olive and has a smooth surface with relatively large, loosely attached patches of veil tissue formed from the veil of early fructifications. As the fructification grows, the veil bursts forming a volva on a lower part of a stalk and the above-mentioned patches on the cap (7). The gills, first white and then greenish, are wide, crowded and rounded by the stalk. The characteristic feature of the Death Cap is a large rounded bulb at the base of the stalk including a well-developed sac-like volva (Fig. 2).

Fig. 2. Young and mature fructification of Death Cap

According to some systematists, the Spring Destroying Angel is a sub-species of the Death Cap as it has the same size (6–12 cm) and cap shape, young fructifications are fully covered in a veil, the gills are crowded and rounded by the stalk, and the stalk ring and vulva are well-developed. The main difference is the colour of fructifications: in case of the Spring Destroying Angel they are white or cream-white, there is no trace of green (7).

The Destroying Angel is slightly smaller than the two above-mentioned species. The cap, 7–10 cm in diameter, is conical in young fructifications and flattened in older ones with a characteristic bump at the top. The remainings of the veil are rare on the white, shiny cap surface; the ring is delicate and thin. In older fructifications only its remaining can be visible, sometimes it is absent altogether. At the bottom of the stalk there is a bulb surrounded by a vulva (6, 7).

The above-mentioned species of amanita contain three groups of toxins: amatoxins, phallotoxins, and virotoxins. Amatoxins include seven compounds: a, b, g, d, e amanitin, amanin and amanullin. These are cyclic octapeptides – Fig. 3 (10). In an amatoxin particle there is a bridge bond composed of tryptophan connected with cystein sulfur. Its cleavage leads to toxin deactivation (12). Phallotoxins include seven compounds, namely phalloidin, phalloin, phallacidin, phallisin, phallisacin, phallacin and prophalloin. Phallotoxins are cyclic heptapeptides (2). Virotoxins are cyclic hexapeptides and are characterized by smaller toxicity than ama- or phallotoxins (3).

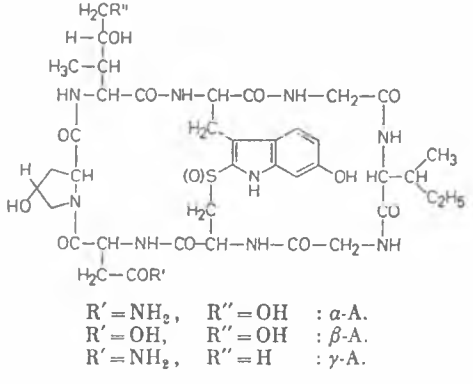

Fig. 3. Chemical structure of amanita toxins

Amatoxins constitute c. 60% of toxic substances and are more poisonous than phallotoxins (Table 1). Amatoxin toxicity for man is higher than for mice. LD_{50} values per individual vary from 0.1 to 0.2 mg/kg b.w. (3, 4).

Table 1. Amatoxin and phallotoxin toxicity in mice

Toxin	LD_{50} for mice *per os* (mg/kg b.w.)
α-Amanitin	0.1
β-Amanitin	0.4
γ-Amanitin	0.8
Phalloin	1.4
Phalloidin	1.9
Phallacidin	2.5

Poisonings with the Death Cap and its two "relatives" are particularly dangerous because of the delay of the onset of symptoms. The first stage of poisoning may not produce any symptoms at all. Only after several hours (even up to 48 hours) do we observe nausea, vomiting, abdominal pain and diarrhea. Gastrointestinal symptoms cause water-electrolyte balance disturbances and distort acid-base management. Without medical support, these symptoms may be lethal (11).

Gastrointestinal disorders are caused by phallotoxins. They are poorly absorbed in the alimentary canal. Therefore, they affect mainly intestinal epithelium destroying red blood cells and intercellural connections (3).

After 3–4 days from the onset of symptoms we can usually observe a marked improvement lasting for c. 24 hours. Then classic symptoms of liver disorders appear. They are caused mainly by amatoxin activity. These toxins easily penetrate intestine walls (especially that they have earlier been damaged by phallotoxins) and are bound by the receptors of soft organ cells (3).

It was established that the biggest amount of the Death Cap toxins go to the liver (c. 57 %), kideneys (2.7 %) and heart (0.2 %) (11). Some toxins are excreted with urine or bile. However, some toxins are transported with bile to duodenum, where they enter secondary circulation (3, 14).

Amatoxin activity mechanisms involve an irreversible blocking of nuclear RNA polymerase, which leads to disturbances in DNA/RNA transcription and then to problems with cellular protein synthesis and mRNA content decrease (2, 3, 14).

Clinical symptoms of poisoning include: hepatomegaly and liver pains, jaudice, hemorrhagic diathesis, lower body temperature, anuria, anemia and hepatic coma (3). In more severe poisonings we can observe blood clotting capability disturbances leading to nose and mucous bleeding. Disseminated intravascular clotting is another symptom of clotting capability deficits connected with liver function damage. Biochemical examinations show decreased prothrombin and increased bilirubin and transaminase levels (4, 11, 14).

Kidney failure symptoms gradually become more and more severe. Proteinuria and diuresis problems follow leading to anuria (11).

Poisonings with the above-mentioned species of amanita are almost always lethal. The possibility of saving one's life is higher when the amount of eaten mushroom was not big (below 50 g of fresh fructification). The chances are higher if a given person consumes wild mushrooms causing gastrointestinal disturbances, which makes an earlier diagnosis and treatment possible (4).

The False Morel (*Gyromitra esculenta*) is one of the most dangerous mushrooms. The fructifications of this species have a shape of an irregular round folded head: it is similar to the brain surface. The stack has little bumps. The colour of the cap can vary from light brown to maroon or dark brown. Overripe fructifications have a white coating (7, 11).

The False Morel contains a toxin called gyromytrin. It is an N-methyl-N-formylhydrazine of acetic aldehyde. It is a volatile substance of low boiling temperature: hence false morel poisoning can occur not only after eating it but also inhaling vapours of boiling or drying fructifications (4, 7, 11).

Till 1970s it was supposed that helvelic acid acting hemolytically was a toxic substance in the False Morel. The acid dissolved well in water and was sensitive to the activity of air oxygen so it was believed that it was possible to eat the mushrooms after boiling cut fungi for 10 min and pouring out the decoction or drying them at 65°C with good air access (12). It turned out, however, that toxic properties of the False Morel were not associated with helvelic acid but with gyromitrin (9, 14).

The False Morel poisonings cause hemolysis and methemoglobinemia as well as proteinuria and oliguria leading to complete kidney failure. The damage of this organ is probably caused by hemolytic activity of the False Morel toxins and water and electrolyte disturbances. We can also observe various kinds of liver functioning deficits, including hepatic coma. Central nervous system symptoms include: coordination and consciousness disturbances and convulsions. The activity of monomethylhydrazine (MMH), one of gyromitrin components, is antagonistic to pyridoxine (vitamin B_6): this toxin inhibits the pyrodoxine stage of gamma-aminobutyric acid (GABA) synthesis. Therefore, when neurological symptoms appear in the False Morel poisonings, vitamin B_6 is used as an antidote (3, 4, 11, 14).

The Fool's Webcap (*Cortinarius orellanus*) is, according to some researchers, more toxic than the Death Cap. It is a medium-size mushroom. Its cap, 5–8 cm in diameter, is bell-shaped with a characteristic bump in the middle of it. Its characteristic feature is a web-like veil connecting cap ridges with the stalk, disappearing as the mushroom grows (6). The mushroom is red, described in more detail as cinnamon-red, orange-ochre or orange with a golden shade. Only the base of the stalk can be yellow or light orange (7, 11).

A group of substances called orellanine is the toxic factor. It is a complex mixture of c. 10 compounds, probably oligopeptides. 200 g of fresh fructification contains a toxic amount. Poisoning symptoms occur very late – even after 24–36 days after consumption (4, 7, 11).

Mild poisoning cases usually do not cause many symptoms: they include a feeling of weakness and lack of strength or polyuria and they are not always associated with mushroom consumption. In case of a more severe poisoning polyuria turns into oliguria with proteinuria, and urine density is low (hyposthenuria). Kidney disturbances are the result of a particular connection between orellanine and renal tubules. This toxin causes diffuse degeneration and necrosis, and consequently leads to kidney failure (4, 11, 14). Kidney symptoms might be accompanied by nausea, abdominal pain, vomiting, diarrhea and headaches. In case of severe poisonings (after consuming a big amount of mushrooms), kidney failure can develop even after 2–3 days: proteinuria, anuria and true uremia with high urea concentration in blood are observed. The Fool's Webcap poisonings lead to death in 15% of cases. Sometimes death might follow even after 6 months since the mushroom consumption (7, 11).

Muscarine is a toxic component in numerous species of fungi. The Fibrecap (*Inocybe patouillardi*) and the Ivory and Fool's Funnel (*Clitocybe dealbata et rivulosa*) are the most poisonous muscarine mushrooms: their level of alkaloid might reach even 8% (12).

The young Fibrecap has a whitish conical cap with serrated edges. As the mushroom grows, the cap becomes flatter with a bump in the middle. The stalk is slightly bigger at the base. The Ivory Funnel is a little white mushroom. The stalk's height is 2–4 cm, and the cap's diameter is c. 4 cm. All white Funnels contain muscarine (7, 11).

Some scholars claim that the Lurid Bolete (*Bioletus luridus*), the Devil's Bolete (*Boletus satanas*), the Bitter Beech Bolete (*Boletus calopus*), as well as some species of knights (*Tricholoma pardinum*) and pinkgills (*Entoloma lividum*) are also mushrooms with muscarine activity (7, 12). Other specialists, though, classify these species as mushrooms of gastroenterotoxic activity (4, 11).

Muscarine is a quaternary base and choline derivative. It contains in its particle a tetra-hydro--furane ring. The lethal dose of muscarine is over 300 g, but 10–20 g of raw fructifiaction may cause severe poisoning, which can lead to death, particularly in case of children (4). Muscarine does not affect the central nervous system as it cannot penetrate the Blood-Brain Barrier. However, it causes a characteristic stimulation of the parasympathetic system. Typically, the first symptoms of the poisoning appear 30–120 minutes after mushroom consumption. They include sialorrhea, excessive sweating and lacrimation, excessive bile, pancreatic juice and bronchial mucus secretion. Bronchioli muscular coat contraction might lead to the attack of bronchial asthma, there are also spastic stomach and intestine cramps with diarrhea and abdominal pain. Characteristic miosis can be accompanied by accommodation disturbances and temporary blindness. Additional symptoms also include bradycardia and arterial blood pressure decrease leading to circulatory collapse. Atropin, which is a specific antidote in muscarine poisonings, is used to counteract the cholinergic effects (7, 14).

The Fly Agaric (*Amanita muscaria*), the Panthercap (*A. pantherina*), and the Jewelled Amanita (*A. gemmata*) are mushrooms whose poisoning substance is atropin. The last species is relatively rare in Poland (4).

The appearance of the Fly Agaric is so characteristic that it is impossible to mistake it with any other mushroom. The poisonings with it are occasional, usually after drinking an alcoholic tincture prepared to treat joints or eating mushrooms immersed in milk which are to be used as a fly poison. Usually children are poisoned. Sometimes suicidal poisoning take place as well (11).

The Jewelled Amanita is a middle-size fungus. Its cap, whose diameter ranges between 4 and 10 cm and which is convex in younger fructifications and flattened in older ones, is placed on a tall stalk, c. 15 cm in height. The colour of the cap is described as grayish-brown, brownish plum-like, brownish yellow, brownish ocher or dark brown. The cap is densely covered with white scales. There is a hanging unstriped ring on the stalk. The lower part of the stalk is bigger, with one or several collars which are remaining of the vulva (7, 11).

The toxic activity of the above-mentioned species is connected with the substance that used to be called mycoatropin. These are 3-hydroxyisoxazole derivatives: ibotenic acid, muscimol and muscazone. These mushrooms also include bufotenin (5-hydroxy-N,N-dimethyltryptamine) (4, 7). Isoxazole content in 100 g of the Fly Agaric is 180 mg, and in the Jewelled Amanita – 460 mg. Ibotenic acid very quickly changes into a much more active derivative, muscimol (i.e. *pantherin*) (Fig. 4). This toxin shows great affinity to GABA receptors in the central nervous system (3, 4, 14).

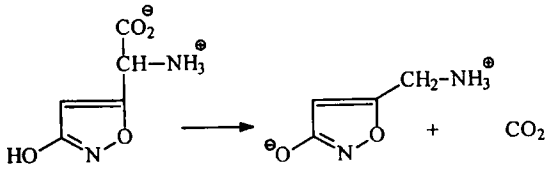

Fig. 4. Chemical structure of ibotenic acid and muscimol

Poisonings with the above-mentioned species exhibit characteristic symptoms of parasympathetic system paralysis. We can observe mydriasis, increased body temperature, consecutive periods of excitation and sedation, similar to poisonings with tropane alkaloids present in, among others, the

Deadly Nightshade (*Atropa belladonna*) or the Jimsonweed (*Datura stramonium*). Fits of madness (so-called "mushroom madness") and symptoms resembling alcoholic intoxication are typical of muscimol poisonings (3, 4).

About 20 species of conecaps, mottlegills, roundheads and brownies (*Conocybe, Panaeolus, Stropharia* and *Psilocybe*) contain hallucinogenic substances that affect central and peripheral nervous system. These are alkaloids of indole structure – psilocin (4-hydroxy-dimethyltryptamine) and psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine) (Fig. 5). These compound were isolated in 1958 and the same year they were obtained synthetically (8, 15).

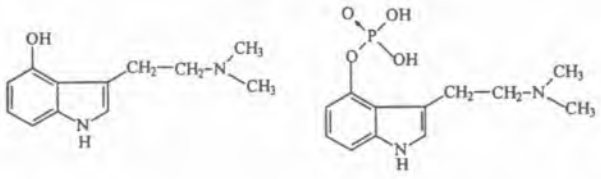

Fig. 5. Chemical structure of psilocin and psilocybin

In Poland there are two species of such fungi: the Magic Mushroom (*Psilocybe semilanceata*) and the Petticoat Mottlegill (*Panaeolus papilionaceus*). The Magic Mushroom grows in grass, on meadows and by roads or paths surrounding pine woods. The cap of this mushroom is umbrella-shaped with a characteristic "hat"; its diameter is between 0.5 and 2 cm., it is beige, its surface is smooth and gills are widely stuck to the stalk. The stalk itself is thin, hard, brown, measuring 4–12 cm in length and 2–3 mm in width – Fig. 6 (5).

Fig. 6. The Magic Mushroom

Poisonings with these mushrooms used to be accidental and very rare. Presently the described species are more and more often used to cause hallucinations (13). Psilocin and psilocybin cause aural, visual and tactile hallucinations connected with confusion of time and space as well as changes in mood, fits of aggression and sometimes symptoms resembling schizophrenia. Neurological and psychological disturbances occur after eating 10–30 g of fresh mushrooms, i.e. 5–15 mg of psilocybin (13).

There are numerous reservations as to the usefulness of species of mushrooms which can be eaten under certain conditions. The opinions on toxic properties of such species vary greatly. This may be caused by the individual response of people eating mushrooms, varying chemical composition of mushrooms which depends on their maturity, period of picking up, the kind of litter and the way of cooking.

Usefulness of the Brown Rollrim (*Paxillus involutus*) causes the biggest controversies. The cap of this species is from 4 to 20 cm in diameter. In young fructifications it is slightly convex, then it becomes flat or funnel-shaped, with rolled edges. Its colour is rusty brown or olive. The gills are dense, narrow, olive-brown. The stalk is relatively short (3–8 cm), 1–1.5 cm in diameter, slightly lighter than the cap.

This mushroom can be consumed without causing any toxic symptoms but there are reports of serious cases of haemolytic anaemia and poisonings leading to death whose cause was hemolysis. Probably hemolysis is instigated by the immunological complex adhering to the surface of red blood cells. This hypothesis is confirmed by the effectiveness of the therapy involving blood plasma exchange: hence, the above-mentioned complexes are removed (1,14).

Although the Brown Rollrim contains acetylcholine and muscarine, it seems that these substances do not play a big role in the mushroom's toxicity. Acetylcholin should principally be hydrolytically decomposed in the alimentary canal while the content of muscarine is only 0.001 % of dry mass, 96% of which is epimuscarine, an isomer of the lowest activity – Fig. 7 (1).

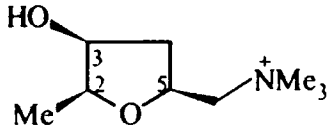

Fig 7. Chemical structure of epimuscarine

The research carried out in recent years led to the selection and identification of numerous metabolites, including involutine and involutone, two compounds whose character is that of aromatic polyphenols structurally similar to the group of cyclopentanoid pigments – Fig. 8 (1).

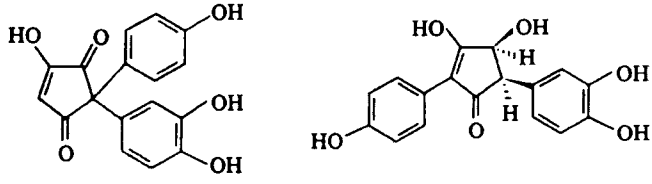

Fig 8. Chemical structure of involutine and involutone

Despite substantial research, the problem of the toxicity of the Brown Rollrim has not been solved. Therefore it seems safer to regard this species as inedible or even poisonous.

One should also mention a mushroom which can be poisonous at some conditions, namely the Common Inkcap (*Coprinus atramentarius*). Young fructifications can be eaten on condition that no alcohol is drunk either at the same time or after (even up to three days) the consumption. If ethanol is consumed even in smaller doses present in medicines, severe poisoning symptoms appear as quickly as after 15–30 minutes. They are caused by acetic aldehyde accumulating in the body. Coprine, and

more specifically its metabolite, which is an aldehyde dehydrogenase inhibitor, inhibits ethanol transformation in liver at the stage of aldehyde formation. Hence poisoning symptoms resemble an antabuse reaction, which proceeds in case of alcoholics treated with Disulfiram (Antabus, Antikol) after drinking alcohol (alcohol + Disulfiram reaction). We can observe skin reddening, chemosis, sweating, faster heartbeat, breathing difficulties, nausea, vomiting, and hypersomnia. These symptoms are accompanied by fear, headaches or dizziness. Usually these symptoms disappear after several hours but they can recur after drinking alcohol again (3,12).

Poisonings with mushrooms of the gastroenterotoxic activity constitute over a half of all poisonings and are definitely the most common. Mushrooms causing gastrointestinal disturbances include the Sickener (*Russula emetica*), the Wooly Milkcap (*Lactarius torminosus*), the Common Earthball (*Scleroderma citrinum*), the Pinkgill (*Entoloma lividum*), and species of agarics, brownies, the False Chanterelle (*Hygrophoropsis aurantiaca*) or field mushrooms (*Agaricus campestris*) (3, 4).

Eatable mushrooms can also cause alimentary tract disturbances. They might include resin substances, pectins, limited amounts of muscarine, terpenes, and other unidentified chemical substances which may irritate the mucous membrane of the alimentary canal (3).

Disturbances following eatable mushroom consumption are referred to as "non-specific poisonings". They can be caused by: consumption of raw mushrooms (e.g. the Honey Fungus) without prior thermal processing; consumption of an excessive amount of a dish made of mushrooms which are heavy to digest (e.g. boletes or chanterelles), especially by children or older people; consumption of dishes prepared from mushroom that have been stored for too long, especially in improper conditions.

Considering all these facts we might risk the statement that you need to be very careful with mushrooms. Therefore, it is crucial to get to know eatable fungi and poisonous species resembling them. It is the most effective way of avoiding poisonings, which might endanger one's health or life. In order to evade this danger one should not eat mushrooms which are controversial. Despite a popular trend, under no circumstances ought one to eat raw mushrooms. The way mushrooms are prepared is also very important – they must be cooked, stewed or fried long enough. Moreover, people suffering from alimentary tract disorders, the elderly and children should not eat mushrooms as they are heavy to digest. Following these precautions will prevent us from poisoning and enable enjoying mushroom picking and eating dishes made of mushrooms picked by ourselves.

REFERENCES

1. Antkowiak W. Z.: *Paxillus involutus* – grzyb o kontrowersyjnych właściwościach jadalnej olszówki i toksycznego krowiaka podwiniętego. Wiad. Chem., 55, 3-4, 248-261, 2001.
2. Borowiak K. et al.: Ocena mechanizmu działania hepatotoksycznego toksyn muchomora sromotnikowego (*Amanita phalloides*). Cz. I - Doniesienie wstępne. Acta Pol. Toxicol., 226, 1996.
3. Brandys J.: Toksykologia – wybrane zagadnienia. Wydawnictwo UJ, Kraków 1999.
4. Burda P. R.: Zatrucia ostre grzybami i roślinami wyższymi. PWN, Warszawa 1998.
5. Grabowska R., Sokołowska-Jabłońska Z.: Analiza substancji odurzających i psychotropowych w laboratoriach kryminalistycznych. Probl. Kryminalistyki, 207, 13-14, 1995.
6. Gumińska B., Wojewoda W.: Grzyby i ich oznaczanie. PWRiL, Warszawa 1985.
7. Henneberg M., Skrzydlewska E.: Zatrucia roślinami wyższymi i grzybami. PZWL, Warszawa 1984.
8. Kubalski J., Tobolska-Rydz H.: Środki uzależniające. PZWL, Warszawa 1984.
9. Młodecki H. et al.: Warunki oczyszczania syntetycznej gyromitryny. Bromat. Chem. Toksykol., 4, 389-391, 1971.
10. Neumüller O. A. Rompps Chemie – Lexikon. Stuttgart 1972.

11. Prokopowicz D.: Rośliny trujące, zwierzęta jadowite. Białystok 1999.
12. Rusiecki W., Kubikowski P.: Toksykologia współczesna. PZWL, Warszawa 1977.
13. Sokołowska-Jabłońska et al.: Wykrywanie i identyfikacja psylocybiny i psylocyny w grzybach halucynogennych. Probl. Kryminalistyki, 210, 7-10, 1995.
14. Szajewski J. et al.: Leksykon ostrych zatruć. PZWL, Warszawa 2000.
15. Zgirski L.: Toksykomanie w praktyce lekarskiej. PZWL, Warszawa 1988.

SUMMARY

This paper presents species of fungi of high toxicity. Their consumption might have serious consequences for health and in many cases it might lead to death. Toxic compounds present in fungi have also been characterised, mechanisms of their toxic activity have been presented and clinical symptoms of poisoning have been described. Hallucinogenic mushrooms have also been mentioned as they have recently become a serious problem: many people use them to intoxicate themselves. There are also species of mushrooms that can be consumed under certain conditions since they can occasionally trigger off serious disturbances for the functioning of organisms.

Zatrucia grzybami kapeluszowymi

W pracy przedstawiono gatunki grzybów o wysokiej toksyczności, których spożycie powoduje poważne skutki zdrowotne, a w wielu przypadkach prowadzi do śmierci. Scharakteryzowano też zawarte w tych grzybach związki toksyczne, przedstawiono mechanizmy ich toksycznego działania na organizm i opisano kliniczne objawy zatruć. Zwrócono też uwagę na grzyby halucynogenne, stające się w ostatnich latach poważnym problemem z uwagi na ich spożywanie w celu samoodurzania się, a także na tzw. gatunki warunkowo jadalne, które niejednokrotnie powodują ciężkie zaburzenia w funkcjonowaniu organizmu.