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Review

Poisoning associated with the use of mushrooms: A review of the global pattern and main characteristics

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ABSTRACT

Worldwide, special attention has been paid to wild mushrooms-induced poisoning. This review article provides a report on the global pattern and characteristics of mushroom poisoning and identifies the magnitude of mortality induced by mushroom poisoning. In this work, reasons underlying mushrooms-induced poisoning, and contamination of edible mushrooms by heavy metals and radionuclides, are provided. Moreover, a perspective of factors affecting the clinical signs of such toxicities (e.g. consumed species, the amount of eaten mushroom, season, geographical location, method of preparation, and individual response to toxins) as well as mushroom toxins and approaches suggested to protect humans against mushroom poisoning, are presented.

1. Introduction

For millennia, mushrooms have been used as a part of the human diet (Wang et al., 2014). Mushrooms are regarded as a low-calorie food that is rich in various vegetable proteins, minerals, and vitamins. In some countries, mushrooms are even called "*meat for the poor*". In addition, mushrooms have been widely used for medical purposes (De Silva et al., 2013; Filippova, 2018; Hsieh and Ju, 2018; Jo et al., 2014; Money, 2016; Van derMolen et al., 2017; Wani et al., 2010; Wasser, 2011; Wu et al., 2016; Zhang et al., 2016). Medicinal use of mushrooms dates back to over 5 thousand years ago (Halpern, 2010). Besides, Taofiq et al. (2016) described the use of mushrooms extracts and compounds in cosmetics.

1.1. Poisonous, toxic and pathogenic fungi

Within the phyla of kingdom of fungi, those that are of clinical interest, Basidomycota and Ascomycota, present themselves at the end stage of their development as spore-bearing full-bodied fruits referred to as mushrooms (Fig. 1). For consumers of mushrooms, there are very few edible and delectable genera and species that are suitable for consumption determined by limitations including flavor, texture and toxicity. The mechanisms of toxicity of these phyla are well understood. In this context, we recently discussed toxins and mechanisms of toxicity of *Amanita virosa* belonging to Basidomycota (Tavassoli et al., 2019).

Although mushroom poisoning occurs following ingestion of these large bodied fungi, it is interesting that these phyla are not invasive and they do not produce infection and related diseases that are known to be associated with many in the phyla of the Deuteromycota. Within this phyla, exist two subclasses, the hyphae and spore bearing mold and distinctly separate are pleomorphic yeast fungi.

In clinical settings, from the subclass of the molds, the genera of highest interest of invasive fungi in the practice of medical mycology, are in the species of *Aspergillus*. Although many mold infections are diagnosed as fungal infections, there are many deep invasive and enzymatic necrotic invaders of sinus, brain and lungs that are diagnosed as malignancies or cancers. Histopathology by medical mycologists (Gray et al., 2015) have, in cases, diagnosed these conditions as a mycosis which can be resolved by antifungal therapy.

The systemic presence of the subclass of the pleomorphic yeast fungi including species of *Candida albicans* and *C. uris* (Quindós et al., 2018) that are well understood in otolaryngology, urology and dermatology in

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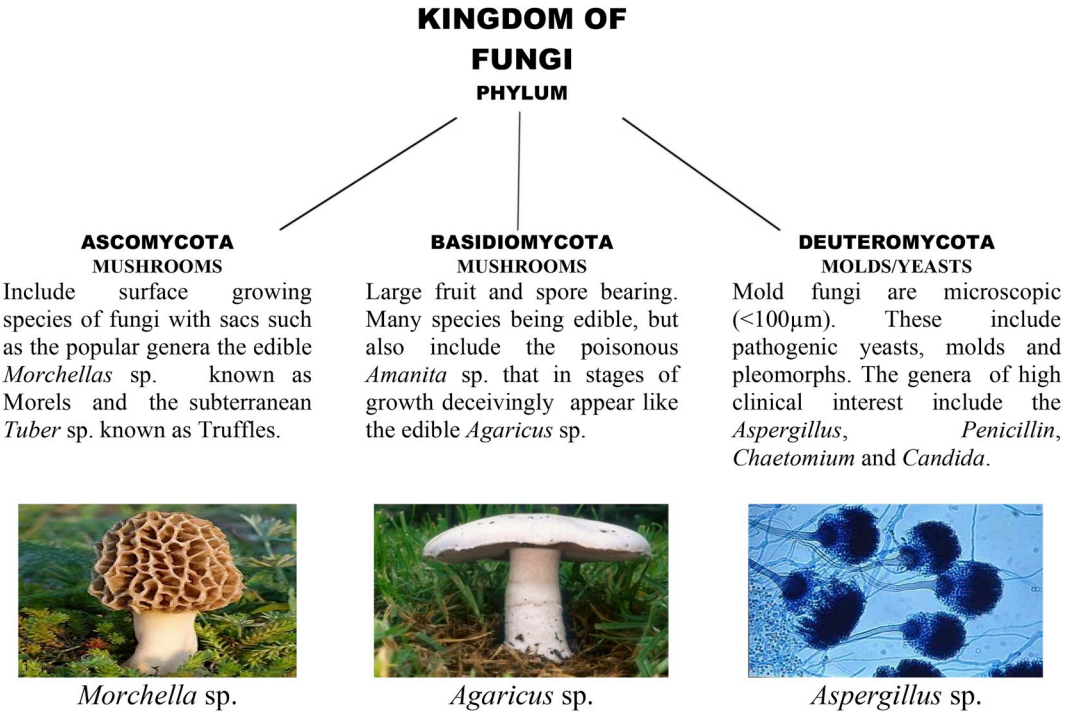

Fig. 1. Kingdom of fungi.

cases of thrush, vaginosis, and systemic and cutaneous candidiasis.

Hallucinogenic fungi were used in religious rituals/behaviorsin ancient times. In this regard, around 2000 B.C., juice of hallucinogenic mushroom, fly agaric (*Amanita muscaria*) (Wax, 2011) was usedin India. Psilocybe mushrooms were used in religious ceremonies of Aztecs (Babu, 2011; Pérez-Moreno and Ferrera-Cerrato, 1995; Musha et al., 1986; Pérez-Moreno et al., 1994). Prehistoric rock art near Villar del Humo, Spain, reflects utilization of *Psilocybe hispanica* in religious rituals 6000 years ago (Akers et al., 2011).

The oldest rock carvings of rituals in which psychoactive mushrooms (presumably *Psilocybe mairei*) were used, were found in Africa, estimated to be done 6500–9000 years ago. Such drawings were also discovered in Algeria (Tassili caves), Libya (mount Tadrart Acacus), Chad (Ennedi Plateau), and Egypt (Mount Jebel Uweinat) (Guzmán, 2008). The current use of hallucinogenic fungi was recently described (Guzmán, 2015). However, the main issue that threatens human health is the use of mushrooms for culinary purposes.

2. Use of wild mushrooms as food

There are 500 (Yildirim et al., 2016) to 140,000 species of fungi (Soltaninejad, 2018), of which 200–300 (Trakulsrichai et al., 2017) to > 2000 are edible species (Varma et al., 2011). Communities of some countries and regions (e.g. China, Southeast Asia, the Venezuelan Amazon, Slavic countries and Italy) have a long history of collecting and eating wild mushrooms. Since the inhabitants of these countries are truly fond of mushrooms, such countries are called “mycophilic”. On the other hand, in some countries (for instance in the United Kingdom) mushrooms are rarely picked and consumed; thus, these countries are named “mycophobic” (Peintner et al., 2013).

In some parts, wild mushrooms are largely harvested for export to other countries. For example, according to the Ministry of Commerce of the People's Republic of China, in the year 2012, 8963 metric tonnes of wild edible fungi harvested in Yunnan Province were exported to other countries, 50% of which were European states (Liu et al., 2015).

Many countries have legislations on collection and trade of mushrooms. Depending on the development of traditions related to use of wild mushrooms as food, such policies/legislations significantly differ. Countries with a mycophile population have specific guidelines or legislations concerning wild mushrooms marketing and consider a comparatively large number of mushroom species; however, countries with a mycophobic population, allow the use and trade of very few mushroom species. Regulatory and licensing systems established in European countries were reported by Peintner et al. (2013), and Radomir et al. (2018).

3. Classification of mushrooms according to their nutritional properties

Traditionally, fungi are divided into edible, conditionally edible, almost inedible, and poisonous categories. These concepts are fairly conventional. Importantly, the same fungus cultivated in different regions can belong to different categories. For example, all the mushrooms with acrid, milky juice (including milk mushrooms, coral milky caps, etc.) are considered inedible in some countries of Western Europe and America (Karaseva and Butvilovsky, 2014).

Conditionally, edible fungi are those that are poisonous in raw form or have a bitter taste; Poisonous or bitter substances dissolve in water after cooking, and mushrooms become suitable for human consumption. Moreover, some mushrooms may become edible after drying, soaking and other pre-treatments. It should be noted that some conditionally-edible mushrooms (for example, morels, wood blewitt, and coral milky caps) have very high taste qualities (Tietel and Masaphy, 2018).

Almost all inedible mushrooms are those that cannot be used in food because of their fatal bitter taste, tough flesh, and unpleasant odor. Pepper mushroom (*Lactarius piperatus*), poison pie (*Hebeloma crustuliniforme*), and common earth ball (*Scleroderma citrinum*) represent this category (Kompanets, 2015).

The chemical composition and nutritional value of different fungi species were previously discussed by Jedidi et al. (2017); Manikandan (2011); Tietel and Masaphy (2018); and Wani et al. (2010).

Table 1
Number of toxic mushroom species reported for different countries and the world.

Region	Toxic species	Potentially fatal species	Source
China	421		Chen et al. (2014)
China	435		Sun et al. (2017)
Iran	50		Soltaninejad (2018)
Japan	30	–	Gonmori and Yoshioka (2005)
Norway	60–100		Holsen and Aarebrot (1997)
Russia	40		Suliga and Yarovova (2017)
Russia	> 150		Vishnevsky (2017)
Turkey	20		Sönmez et al. (2015)
North America	< 100	–	Broussard et al. (2001)
Europe	32	11	Karaseva and Butvilovsky (2014)
Europe	100	–	Schmutz et al. (2018)
Globe	170	–	Boa (2004)
Globe	100	< 10	Kintziger et al. (2011)
Globe	150	–	Eren et al. (2010); Erenler et al. (2016)
Globe	< 100	–	Cervellin et al. (2018); Pinson and Bradley (1996)
Globe	50–100	–	Gawlikowski et al. (2015); Pajoumand et al. (2005)
Globe	100	15–20	Horowitz (2015)
Globe	400	–	Benjamin (1995)
Globe	100	50	Barman et al. (2018); Graeme (2014)
Globe	100	–	Diaz (2016); Smith and Davis (2016)
Globe	50–100	10	Sönmez et al. (2015)
Globe	30–50	10	Rajarathnam and Shashirekha (2003)

4. Mushroom poisoning

Consumption of toxic mushrooms that are mistakenly collected instead of edible mushrooms, leads to poisoning. The incidence of mushroom poisoning markedly varies among different corners of the world depending on local traditions, lifestyle, nutritional factors, climate and the occurrence of wild mushrooms. Information on the number of poisonous mushrooms in separate countries, regions and the world as a whole, is given in Table 1. As seen in Table 1, there is a huge discrepancy among different reports on this topic.

5. Epidemiology of mushroom poisoning

Countries where mushroom poisoning is a serious problem include Bulgaria (Marinov et al., 2018); Czechia (Kieslichova et al., 2018; Krenova et al., 2007); China (Zhou et al., 2012; Sun et al., 2018); Iran (Dadpour et al., 2017; Pajoumand et al., 2005; Rahmani et al., 2015; Soltaninejad, 2018); Mexico (Pérez-Moreno et al., 1994; Pérez-Moreno and Ferrera-Cerrato, 1995; Méndez-Navarro et al., 2011; Ruiz-Gonzalez et al., 2017); Italy (Cervellin et al., 2018; Costantino, 1978; Fineschi et al., 1996); Hungary (Vetter and Vetter, 2014); Japan (Yamaura et al., 1997; Matsuura et al., 2009); Nepal (Chaudhary et al., 2013; Das et al., 2007); Poland (Ferenc et al., 2009; Krakowiak et al., 2017; Zuber et al., 2011); Romania (Precup et al., 2012); Russia (Shen et al., 2013; Shilov et al., 2010; Ivleva et al., 2017; Vishnevsky, 2017); South Korea (Kim et al., 2017; Sohn, 2015); Thailand (Chaiear et al., 1999; Parnmen et al., 2016; Trakulsrichai et al., 2017); Turkey (Ahishali et al., 2012; Colak et al., 2015; Erenler et al., 2016; Gurbuz et al., 2015; Kavalci et al., 2010; Unluoglu and Tayfur, 2003); and Ukraine (Kurdil et al., 2016).

Single cases and series of cases have also been reported from Argentina (Romano et al., 2013); Australia (Nicholson and Korman, 1997); Brazil (Meijer et al., 2007); Canada (Berch et al., 2017; Fleury et al., 2008); Chile (Sierralta et al., 1994; Valenzuela et al., 1992); Colombia (Vargas et al., 2011); Guatemala (Logemann et al., 1987); France (Varvenne et al., 2015); India (Barman et al., 2018; Latha et al., 2018); Ireland (Cassidy et al., 2011); Israel (Bentur et al., 2014); Kenya (Tagwireyi et al., 2016); Malaysia (Chin, 1988); Portugal (Garcia et al., 2015a); Slovenia (Vendramin and Brvar, 2014); South Africa (Flegg, 1981); Spain (de la Higuera-Vila et al., 2010; Sanz et al., 1989); Sri-Lanka (Fernando and Fernando, 1990); Sweden (Hedman et al., 2017); Switzerland (Floersheim, 1985; Schenk-Jaeger et al., 2016; Schmutz et al., 2018); Taiwan (Yang et al. 1995, 2006); the United States (Diaz, 2018; Vo et al., 2017; Ward et al., 2013); Zambia (Tagwireyi et al., 2016); and Zimbabwe (Tagwireyi et al., 2016).

Several reports indicated mushroom poisoning in animals. It is believed that toxic effects of mushrooms in mammals are comparable to those observed in humans; however, other animal groups show lower susceptibility (Beug et al., 2006; Vetter and Vetter, 2014).

6. Groups of poisonous mushrooms

Poisonous mushrooms are divided into three groups with respect to their poisoning. The first group includes fungi that contain locally acting poison(s) (yellow-staining mushroom (*Agaricus xanthodermus*), dark scaled mushroom (*Agaricus moelleri*), Satan's bolete (*Rubroboletus satanas*) and some others). They disturb the gastrointestinal tract, and their toxicity develops in 1–2 h after consumption (Mahdizadeh et al., 2016; Morel et al., 2018).

The second group includes the mushrooms with toxins that affect the nervous centers (panther cap (*Amanita pantherina*), fly agaric (*Amanita muscaria*) and destroying angel (*Amanita virosa*), as well as fungi of the genus *Inocybe*). Nausea, vomiting, diarrhea, and sweating occur within 2 h after digestion. They produce a state of intoxication with uncontrolled laughter/crying, and hallucinations. Also, there is the possibility of loss of consciousness (Kosentka et al., 2013; Yildirim et al., 2016).

The third group of fungi (death cap (*Amanita phalloides*), sulphur tuft (*Hypholoma fasciculare*), etc.) contains toxic substances affecting the liver, kidneys and other vital organs. The toxic effects appear very late, after 8–48 h, resulting in irreversible damage to the human body vital organs, cells and the central nervous system. Lethality is observed following consumption of such mushrooms. Consumption of a half or even a third of these fungi usually cases intoxication (Barman et al., 2018; Cai et al., 2016; Garcia et al., 2015b).

Diaz (2006) reviewed medical publications from 1951 to 2004, and reported descriptions of 28,018 mushroom poisoning. In this report, 14 major syndromes were introduced to be caused by different taxonomic groups of poisonous mushrooms.

7. Other causes of poisoning

In addition to poisoning due to consumption of mistakenly collected mushrooms, poisoning can also occur for the following reasons (Comelli et al., 2013; Gawlikowski et al., 2015; Guillen and Baeza, 2014; Musha et al., 1986; Musselius and Ryk, 2002): 1) long-term storage of collected mushrooms without culinary treatment, 2) improper cooking; 3) long-term storage of already prepared mushrooms; 4) contamination of fungi by pests, in particular, flat-footed flies (Platypezidae); 5) concurrent use of certain types of mushrooms (for example, shaggy ink cap (*Coprinus comatus*), midden ink cap (*C. sterquilinus*) and common ink cap (*Coprinopsis atramentaria*)) with alcohol; 6) contamination with toxic agents (heavy metals, radioactive substances, etc.); 7) frequent consumption of mushrooms of family *Morchellaceae*; and 8) use of hallucinogenic fungi.

In general, poisoning by edible fungi occurs much more often than intoxications by poisonous mushrooms. For example, Department of Clinical Toxicology in Krakow reported a total of 457 cases of mushroom poisoning in 2002–2009. Of these, edible mushrooms accounted for 400 cases, and the rest were of the poisonings were caused by consumption of poisonous mushrooms (Gawlikowski et al., 2015). However, the consequences of consumption of edible mushrooms were

Table 2
Morbidity and mortality reported from different regions and countries.

Country	Average number of poisoned/year	Average number of fatalities/year	Period	Source
Belarus	125 (2013–2015)	3.8	2006–2015	Mikhasiova and Pleshkunova (2016)
Bulgaria (Varna region)	74.9	1.0	1991–2015	Marinov et al. (2018)
China	336.5	71.5	2004–2014	Sun et al. (2018)
China (Guizhou)	69.8	8,5	2004–2013	Xiang et al. (2018)
China (Yunnan)	145.6	20,4	1985–2000	Li et al. (2003)
China (Yunnan)	662	24,7	2001–2006	Chen et al. (2014)
Czechia (Prague Toxicological centre)	146	7	1991	Pelclová and Rakovcová (1993)
France	8000–10,000[a]	–	1998	Jo et al. (2014)
Iran	1247	19	2018	Soltaninejad (2018)
Iran (Razi Hospital of Rasht)	14.6		2006–2012	Badsar et al. (2013)
Italy (Province of Parma)	21.1		1996–2016	Cervellin et al. (2018)
Japan	192	1,0	2001–2010	Yamaura (2013)
Japan	184.2	2,0	1988–1997	Gonmori and Yoshioka (2005)
Japan	364.1	2,4	1959–1988	Ishihara and Yamaura (1992)
Japan	500–600	15		Pérez-Moreno and Ferrera-Cerrato (1995)
Japan (Nagano Prefecture)	20.0	0.1	1970–1994	Yamaura et al. (1997)
Mexico	–	9.5	2005–2006	Beug (2007)
Nepal	–	15–20	–	Adhikari (2004)
Poland	–	31	1931	Boa (2004)
Russia	1128.3	66.5	1995–2007	Govorushko (2012)
Russia	806.5	26,0	2005, 2010, 2013–2016	Public Health Service in Russia (2017)
Spain (Barcelona)	15.3	1.3	1986–1988	Sanz et al. (1989)
Switzerland	247.5[a]	–	1966–2014	Schenk-Jaeger et al. (2016)
Switzerland	375.9[a]	–	1995–2009	Schenk-Jaeger et al., 2012
Switzerland	7.9[b]	0	1995–2009	Schmutz et al. (2018)
Taiwan	4.4	0	1986–1993	Yang et al. (1995)
Thailand	–	8.1	2008–2014	Parnmen et al. (2016)
Turkey (Middle Black Sea region)	52.8		2002–2007	Yardan et al. (2010)
Ukraine	361.4	31.0	2005–2014	Kurdil et al. (2016)
Ukraine		112	2000	Boa (2004)
Ukraine (Lugansk oblast)	39.2	4.9	2001–2010	Romaniuk et al. (2012)
United States	7976 (1993)	20	1900–1994	Broussard et al. (2001)
United States	–	100–200	–	Mengs et al. (2012)
United States	8314	–	2001–2011	Horowitz (2015)
United States	9208	3	1989	Trestrail (1991)
United States	7000–9000	–	–	Kintziger et al. (2011)
United States (27 from 37 regional poison centers)	3419.5	–	1987–1988	Trestrail and Lampe (1990)
United States (Florida)	85.6	0	2003–2007	Kintziger et al. (2011)
United States and Europe	–	100–200	–	Pinson and Bradley (1996); Smith and Davis (2016)
WesternEurope	–	50–100	–	Dadpour et al. (2017); Kavalci et al. (2010)
Zambia	50	6	1980–1981	Tagwireyi et al. (2016)

[a] – Number of calls to Poisons Information Centers.
[b] - Hospitalization of patients with mushroom poisoning.

much less serious, usually limited to gastrointestinal disorders.

It is clear that poisoning mainly occurs due to collection and use of wild edible mushrooms, and the risk of poisoning following ingestion of cultivated mushrooms is lower. Nevertheless, in the Osmangazi University Hospital in Turkey, 8 out of 12 patients who died during 1996–2000 due to mushroom poisoning, had consumed cultivated mushrooms (Unluoglu and Tayfur, 2003).

8. Contamination of edible mushrooms

Mushrooms significantly absorb heavy metals from the environment leading to the accumulation of such toxic agents in them. Therefore, mushrooms are generally used for evaluation of the level of environmental pollution (Melgar et al., 2016; Türkmen and Budur, 2018). Heavy metals that are considered most dangerous for human health are arsenic (As), cadmium(Cd), mercury (Hg) and lead (Pb) (Chen et al., 2009; Liu et al., 2015; Mleczek et al., 2018; Muszynska et al., 2018; Türkmen and Budur, 2018; Wang et al., 2017). Other elements including iron (Fe), cobalt (Co), copper (Cu), manganese (Mn), chromium (Cr) and zinc (Zn) are less harmful.

Heavy metal concentrations in mushrooms are considerably higher than those found in agricultural crop plants, vegetables, and fruits (Liu et al., 2015). This concentration can be extremely high in heavily polluted areas such as roads with heavy traffic, landfills of sewage sludge, and emission areas such as mines and cities (Melgar et al., 2016). Health risks posed by consumption of contaminated edible fungi were previously discussed by Khani et al. (2017); Liu et al. (2015); Melgar et al. (2016); and Nharingo et al. (2015). In general, such effects are much less serious than those caused by poisonous mushrooms, and they occur following prolonged (i.e. chronic) use.

Also, radionuclides accumulate in mushrooms. The most dangerous element is Cs-137 (radiocesium), and its highest accumulation rate was found in fungi (Tereshkina et al., 2011). Consumption of such radionuclides-contaminated mushrooms only occur in the areas where nuclear accidents happened (Chernobyl, Fukushima, nuclear plant Mayak, etc.). However, long-term consumption of mushrooms collected from the emission sites of nuclear power plants, can lead to health damage. For example, it was shown that mushrooms collected from lands near

the Leningrad nuclear power plant (NPP) in Russia had Cs-137 at levels much higher than the permissible norms (Blinova and Nedbaesvkaya, 1995).

According to the degree of accumulation of Cs-137, edible mushrooms are divided into four groups (Shishkin, 2003): 1) weakly accumulating (more secure): oyster mushroom (*Pleurotus ostreatus*), winter fungus (*Flammulina velutipes*), common puffball (*Lycoperdon perlatum*), parasol mushroom (*Macrolepiota procera*), and honey fungus (*Armillaria mellea*); 2) moderately accumulating: brown birch bolete (*Leccinum scabrum*), orange-cap boletus (*Boletus edulis*), dingy agaric (*Agaricus portentosus*), chanterelle (*Cantharellus cibarius*), red-capped scaber stalk (*Leccinum aurantiacum*), orange birch bolete (*Leccinum versipelle*), and white birch bolete (*Leccinum holopus*); 3) strongly accumulating: mushroom (*Lactarius resimus*), ugly milk-cap (*Lactarius turpis*), downy milk cap (*Lactarius pubescens*), woolly milkcap (*Lactarius torminósus*), and mushrooms of the genus *Russula*; 4) the concentrators of radioactive cesium (the most dangerous): bay bolete (*Imleria badia*), velvet bolete (*Suillus variegatus*), suede bolete (*Xerocomus subtomentosus*), rufous milkcap (*Lactarius rufus*), brown roll-rim (*Paxillus involutus*), weeping bolete (*Suillus granulatus*), slippery jack (*Suillus luteus*), and larch bolete (*Suillus grevillei*).

Radiation actively goes into the mushrooms with a well-developed mycelium. The concentration of radionuclides in the mushroom caps is 1.5–2 times higher than in the stipe, in particular, it is typical for fungi with a well-developed stipe (white mushroom, brown birch bolete, orange-cap boletus, and bay bolete) (Guillen and Baeza, 2014).

9. Mortality due to toxic mushroom poisoning

The incidence of mushroom poisoning varies a lot over the world depending on local traditions, lifestyle, nutritional factors, climate and the occurrence of wild mushrooms. Information about morbidity and mortality in different regions is given in Table 2.

Countries where food traditions assign a rather important role to wild mushrooms, exert higher rates of mushroom poisoning. This includes, first of all, Russia and Eastern European countries, followed by China. For example, in Eastern Europe, about 150 species of mushrooms are harvested (Musselius and Ryk, 2002). The peak of poisoning was observed during the Second World War and immediately after it when the mushrooms were one of the main sources of nutrition (Grossman and Malbin, 1954).

There are numerous cases of mass poisoning. In this context, in 1952 in the region of Poznan (Poland), simultaneous poisoning of 102 people, of which 11 people died, was recorded. It is assumed that the cause of poisoning was the fool's webcap (*Cortinarius orellanus*), which is mistaken for edible species gypsy mushroom (*Cortinarius caperatus*) and Goliath webcap (*Cortinarius praestans*) (Shao et al., 2016). From 1952 to 1964, 144 poisoning cases were reported following consumption of this fungus, killing 25 people (Dinis-Oliveira et al., 2016).

During July-November 1981, 160 cases (out of which, 4 subjects died) were registered with mushroom intoxications, due to ingestion of *Amanita phalloides* in the north of Italy (Fantozzi et al., 1986). In March 2000 in Guangdong Province, 6 mushroom-poisoning incidents, with 33 poisoned people and 20 deaths were registered; the lethal mushroom caused the poisoning was Guangzhou destroying angel *Amanita exitialis* (Sun et al., 2018).

From April 28 to May 28, 2018, an outbreak was registered in 13 west and northwestern provinces of Iran. It was reported that 1247 persons were poisoned due to ingestion of wild poisonous mushrooms including deadly dapperling (*Lepiota brunneioncarnata*), sulphur tuft (*Hypholoma fasciculare*), and common ink cap (*Coprinopsis atramentaria*), 19 persons died (Soltaninejad, 2018); however, authorities held *Amanita virosa* responsible for the poisoning (Tavassoli et al., 2019).

The problem of mushroom poisoning is quite serious in some Asian countries. The highest mortality rates are reported from China, with the highest number of deaths occurring in Yunnan and Guizhou provinces (Sun et al., 2018). In Nepal, the annual mortality due to ingestion of poisonous mushrooms is 15–20 people (Adhikari et al., 2005). Also, significantrates of mortality were reported from Turkey (Yardan et al., 2010), Thailand (Parnmen et al., 2016), and Iran (Soltaninejad, 2018).

In Japan, during 1959–1988, 2096 incidents were recorded, in which 10,924 patients were poisoned, and 72 of them died. Thus, on average, there were70 cases of poisoning with 364 victims (5.2 patients per case), the death rate was 2.4 people/year, with a gradual decrease in the number of victims from year to year. Most often, poisoning occurs in the North-Eastern part of Japan (Nagano, Hokkaido, Niigata, Iwata and Fukushima prefectures), their peak falls in September and October. The species responsible for the highest number of poisonings are wood pinkgel (*Rhodophyllus rhodopolius*) and burnt knight (*Tricholoma ustale*) (Ishihara and Yamaura, 1992).

In North America, Mexico has the highest rates of mushroom-caused mortality (Méndez-Navarro et al., 2011). Deaths in the US and Canada are rare (Berch et al., 2017; Fleury et al., 2008; Leathem and Dorran, 2007) which is, to some extent, due to better medical care. For example, in Chiapas, a remote state in southern Mexico, death rates due to eating “death caps” and “destroying angels” are much higher than 50%. However, in the United States and Canada, mushroom-poisoned cases who seek prompt medical treatment have over 90% chance of life preservation (Beug, 2008).

In Australia, mushroom-induced mortality is also rare. For example, between 1999 and 2012, public hospitals in Canberra and Sydney recorded 4 deaths (Roberts et al., 2013). Mushroom poisoning also occurs in other continents and mortality was documented in Africa (Tagwireyi et al., 2016) and South America (Meijer et al., 2007); however, not sufficient quantitative data were reported from these continents.

It is difficult to determine a reliable average rate of annual morbidity and mortality on a global scale. Often, inconsistent information for the same country is reported by different sources. For example, estimates of annual mortality due to mushroom poisoning for the United States vary from 20 persons (Broussard et al., 2001) to100-200 (Mengs et al., 2012). More reliable information was reported by Brandenburg and Ward (2018) who noted 133,700 cases (7428/year) of mushroom exposure during 1999–2016. Approximately 704 exposures (39/year) resulted in major harm. Fifty-two fatalities (2.9/year) were reported, mostly from cyclopeptide (68–89%)-producing mushrooms unintentionally ingested by older adults.

On the other hand, sometimes there is a lack of registration of deaths. For example, according to the official information of the Russia Ministry of health, an average of 26 deaths occur annually due to mushroom poisoning (Public Health Service in Russia, 2017). It is obvious that these data are substantially understated. First, according to an analysis of news Internet sites during 1995–2007, mortality was 66 people/year in Russia (Govorushko , 2012). Second, the mortality rate of mushroom poisonings in Russia is always two times higher than in Ukraine where 31 deaths occurred during 2005–2014 (Kurdil et al., 2016).

Apparently, China, Russia, and Ukraine have the highest rate of deaths caused by mushroom-poisoning. Belarus, Poland, Turkey, Iran, Nepal, and Mexico also have high rates of mushroom-poisoning deaths. In general, the world average annual mortality due to consumption of poisonous mushrooms is estimated to be 200–250 people.

10. Importance of different toxic mushroom species

Reliable identification of cause of poisoning is hampered by the fact that the mushroom species responsible for poisoning, are rarely identified. The highest rate of correct identification of mushrooms was 17% (Mowry et al., 2013) indicated by the American Association of Toxicological centers for 6600 cases of mushroom poisoning in 2012. In other cases, this value is much lower. For example, the China Centre for Disease Control and Prevention recorded 576 patients with mushroom

poisoning from 2004 to 2014, but less than 10% of the responsible species were identified (Sun et al., 2018). In 1989, the North American Mycological Association recorded 9208 cases of exposure to fungi from the United States and Canada; in this report, only in 313 cases (3.4%), mushroom species were identified (Trestrail, 1991).

There is an opinion that the most toxic mushroom known to man is *Galerina sulciceps* which is distributed in Indonesia and Sri Lanka. Series of poisonings in Indonesia were registered in the 1930s which resulted in 14 deaths following consumption of this species (Ammirati et al., 1986). However, if global mortality is taken into account, it is believed that the undisputed championship here belongs to the death cap. There is a large amount of data about mortality rate (10–40%) due to *Amanita phalloides* (death cap) poisoning (Pelclová and Rakovcová, 1993; Iliev et al., 1999; Shilov et al. (2010); Lawton 2013; Roberts et al., 2013; Trakulsrichai et al., 2017; Kieslichova et al., 2018; Marinov et al., 2018). However, more recent studies report mortality rates of around 10% (Kim et al., 2017).

It is believed that *Amanita phalloides* accounts for more than 90% of all deaths (Ye and Liu, 2018). However, an analysis of the available information shows that this is true only for temperate latitudes.

For example, in Mexico, 10 individuals died in 2005 because of eating death cap (Beug, 2007). In Bulgaria (near Plovdiv) during 1991–1998, among 270 cases of poisoning with toxic mushrooms, 25 (9.26%) had ingested death cap; however, all deaths (10) occurred due to consumption of death cap (Iliev et al., 1999). In 1991, the Prague toxicology centre reported 146 cases of mushroom poisoning, of which 27 subjects had consumed death cap and 7 individuals died (Pelclová and Rakovcová, 1993). In Australia also almost always (except for one case) death due to mushroom poisoning was caused by death cap (Pauli and Foot, 2005).

However, in the tropics, mushrooms-induced deaths are often caused by related death cap species. For example, in South China, the main causes of death were *Amanita* species, such as East Asian brown death cap (*Amanita fuliginea*), Guangzhou destroying angel, *A. exitialis*, *A. pallidorosea* and *A. subpallidorosea*. East Asian brown death cap is the main lethal species that accounts for 41.3% of all poisoning cases, 43.2% of all deaths and a mortality rate of 22.4% (Zhou et al., 2017). In China, about 78% of poisoning and 70% of fatal cases were provoked by species of the genus *Amanita* (Fu et al., 2017). Now, about 50 lethal *Amanita* spp. are described worldwide (Cai et al., 2016).

The list of famous characters that died due to mushroom poisoning supposedly includes Siddhartha Gautama (known as Buddha), the Roman Emperor Claudius, Pope Clement VII, the Holy Roman Emperor Charles VI and the mother of Peter the Great Natalia Naryshkina, composer Johann Schobert (together with his wife, one of his children, his maid, and four acquaintances), and parents of physicist Daniel Gabriel Fahrenheit. It is believed that death cap was the cause of death of all these persons. However, the case of Emperor Claudius is not so obvious. It is believed that some other poisons were added to the dish of Caesar's mushroom (*Amanita caesarea*), at least, the symptoms did not correspond to the typical poisoning induced by death cap (Marmion and Wiedemann, 2002).

11. Clinical types of mushroom poisoning

There are 6 clinical types of mushroom poisoning (Wong and Ng, 2006; Gonmori et al., 2011; Puschner, 2012; Marinov et al., 2018): 1. Cytotoxic mushroom poisoning; 2. Neurotoxic mushroom poisoning; 3. Myotoxic mushroom poisoning; 4. Metabolic-toxicity mushroom poisoning; 5. Gastrointestinal mushroom poisoning; 6. Miscellaneous adverse reactions due to mushrooms. Most of them, are further divided into subgroups.

11.1. Cytotoxic mushroom poisoning

This large group involves just those types of intoxication where a specific organ is affected and either initial hepatotoxicity, or initial nephrotoxicity is provoked. It is divided into3 subgroups of mushrooms that leads to: (1A) Primary hepatotoxicity; (1B) Primary nephrotoxicity; or (1C) Delayed primary nephrotoxicity.

Subgroup 1A is represented by mushrooms that contain amatoxins. They cause potentially lethal hepatotoxicity, with a specific set of clinical signs. A variety of fungal species possess enough amatoxins to generate considerable toxicity. Among them are some *Amanita* spp. (e.g. *Amanita phalloides*, as well as *Lepiota* spp. and *Galerina* spp.). Several studies discussed this type of mushroom poisoning (Wong and Ng (2006); Vargas et al. (2011); Mengs et al. (2012); Ward et al. (2013); Varvenne et al. (2015); Yilmaz et al. (2015); Zhou et al. (2017)).

Subgroup 1B includes mushrooms that produce direct kidney damage as an acute effect; such mushrooms have aminohexadienoic acid (AHDA), such as *Amanita smithiana* and *Amanita pseudoporphyria*. The poisoning caused by this group of mushrooms was explained by Karlson-Stiber and Persson (2003) and Apperley et al. (2013).

Subgroup 1C includes fungi that cause deferred kidney failure, and contain orellanine, especially several *Cortinarius* spp. Poisoning caused by subgroup 1C mushrooms was described by Dinis-Oliveira et al. (2016); Anantharam et al. (2016); and Hedman et al. (2017).

11.2. Neurotoxic mushroom poisoning

This wide group incorporates classic types of fungal poisoning that trigger initial neurotoxicity. It is represented by 4 subgroups: (2A) Hallucinogenic mushrooms; (2B) Autonomic toxicity mushrooms; (2C) Central nervous system toxicity mushrooms; and (2D) Morel neurologic syndrome.

Subgroup 2A includes fungi that cause hallucinations or related effects as a major symptom. This group of mushrooms contains psilocybin, psilocine, gymnopilus and related toxins. A variety of mushrooms are involved, including *Psilocyb*e spp., *Conocybe* spp., *Gymnopilus* spp., *Panaeolus* spp., *Copelandia* spp., *Pluteus* spp., and possibly *Stropharia* spp. This type of poisoning was shown by Kosentka et al. (2013); Dydak et al. (2015); and Murray et al. (2015).

Subgroup 2B includes fungi that cause a direct vegetative effect (i.e. they affect the internal organs, glands of internal and external secretion, blood and lymph vessels). This is due to the presence of muscarine and related toxins; this subgroup includes selected *Inocybe* spp., *Clitocybe* spp., *Mycena* spp. and *Rubinoboletus* spp. (Kosentka et al. (2013); Mikaszewska-Sokolewicz et al. (2016); Yilmaz et al. (2018)).

Subgroup 2C includes fungi that cause neuroexcitatory effects, and occasionally hallucinations. Ibotenic acid and muscimol are their toxins. This subgroup includes *Amanita muscaria*, *A. patherina*, *A. ibotengutak* (Zinkand et al. (1992); Michelot and Melendez-Howell (2003); Ginterova et al. (2014)).

Subgroup 2D includes an ill-defined syndrome of neurologic and gastrointestinal effects after eating various morel mushrooms. No specific toxin was introduced for this subgroup, and the status of this type of “intoxication” is uncertain. Almost all cases were found to be related with consumption of *Morchella* spp. Only one article discussed this type of poisoning (Saviuc et al., 2010).

11.3. Myotoxic mushroom poisoning

This group encompasses intoxication characterized by rhabdomyolysis (acute skeletal muscle necrosis) as the main characteristic. It is divided into 2 subgroups of mushrooms that leads to: (3A) Rapid onset myotoxicity; and (3B) Delayed onset myotoxicity.

Subgroup 3A includes fungi that cause rapid onset myotoxicity (partial or complete damage to red bone marrow myeloid tissue cells). The causal toxin that mediates the poisoning caused by mushrooms of this subgroup, is cycloprop-2-ene carboxylic acid. Such cases are related with consumption of some *Russula* spp. (Nisekurohatsu (*Russula subnigricans*)) (Lin et al. (2015); Cho and Han (2016); Matsuura et al.

(2016)).

Subgroup 3B includes fungi that cause deferred onset myotoxicity. Toxins responsible for the poisoning induced by such mushrooms, have not been yet fully understood; however, recent studies showed that saponaceolide B and M are potentially the major toxins (Yoshikawa et al. (2002); Clericuzio et al. (2018); Gozzini et al. (2018); Klimaszyk and Rzymski (2018)).

11.4. Metabolic-toxicity mushroom poisoning

This large group produce a wide range of toxic syndromes and clinical manifestations, so it can be recognized as a group with various clinical manifestations, rather than similar clinical outcomes.

Subgroup 4A includes fungi that cause metabolic pathology secondary to blocking gama-aminobutyric acid (GABA) synthesis, which affects multiple organs. This includes mushrooms containing gyromitrins, in particular some *Gyromitra* spp. (Saviuc and Flesch (2003); Wong and Ng (2006); Sohn (2015)).

Subgroup 4B includes the fungi that provokes disulfiram-like responses similar to those observed in case of alcohol intoxication. Such a reaction is caused by mushrooms containing coprines, for example some *Coprinus* spp. (Saviuc and Flesch (2003); Wong and Ng (2006); Sohn (2015)).

Subgroup 4C includes fungi that cause neurological effects and may damage other organs. It is represented by mushrooms containing polyporic acid, in particular tender nesting polypore (*Hapalopilus rutilans*) (Kraft et al. (1998); Diaz (2005); Villa et al. (2013)).

Subgroup 4D includes fungi that cause specific multi-organ failure syndrome, such as bone marrow failure and lamellar desquamation of the palms, soles of the feet and face. It is represented by mushrooms containing trichothecenes, for instance *Podostroma cornu-damae*. Information about this type of mushroom poisoning was reported by Saikawa et al. (2001); Gonmori et al. (2011); Kim et al. (2016); and Park et al. (2016).

Subgroup 4E involves mushrooms that cause rapid hypoglycemia, such as mushrooms reported from Yunnan, China, in particular *Trogia venenata*. As previously reported, causal agent is unusual amino acids (2R-amino-4S-hydroxy-5-hexynoic acid and 2R-amino-5-hexynoic acid) (Shi et al. (2012a); Shi et al. (2012b)).

Subgroup 4F poisoning was reported from France, where seven patients developed hyperproinsulinemia following intake of Satan's bolete (*Rubroboletus satanas*) (Kretz et al. (1991); Schenk-Jaeger et al. (2012); Patocka (2018)).

Subgroup 4G includes an uncommon poisoning that was presented by only two cases in Japan, after long-term consumption (for a few days) of a herbal medicinal mixture containing *Ganoderma neojaponicum* (Yoon et al., 2011).

11.5. Gastrointestinal mushroom poisoning

This group contains those fungal species which produce a “poisoning” that does not fit in the previous 5 groups. Such mushrooms produce gastrointestinal disturbances rather than specific toxicities and from a practical clinical point of view, they are included in this classification scheme.

Usually mushroom intoxications that cause gastroenteritis are characterized by a mild and short gastrointestinal syndrome (McPartland et al. (1997); Sohn (2015); Leudang et al. (2017); Brandenburg and Ward (2018); Marinov et al. (2018)).

11.6. Miscellaneous adverse reactions due to mushrooms

Subgroup 6A includes mushrooms causing acute dermatitis post-consumption. It is related to Shiitake mushroom (*Lentinola edodes*). The pathophysiology is unclear, but it appears to be non-allergic and most likely associated with the presence of a thermolabile polysaccharide, lentinan, found in these mushrooms (Boels et al. (2014); Mossong et al. (2015); Saupe et al. (2016)).

Subgroup 6B encompasses mushrooms causing an erythromelalgia-like syndrome. It was observed following ingestion of *Clitocybe acromelalga* (also known as *Paralepistopsis acromelalga*), and paralysis funnel (*Clitocybe amoenolens*). Acromelic acid is considered to be the causal toxin (Taguchi et al. (2009); Miyazaki et al. (2013); Yoshioka et al. (2017)).

Subgroup 6C includes mushrooms causing an autoimmune haemolytic anaemia after repeated exposure. It is related to brown roll-rim mushrooms, specifically *Paxillus* spp. (Poison Pax (*Paxillus involutus*) (Brzostowski et al. (2009, 2011); Chen et al. (2014)).

Subgroup 6D poisoning which presents encephalopathy syndrome, reported from Japan, is speculatively considered to be the result of hydrogen cyanide (HCN) poisoning following ingestion of mushrooms containing high HCN levels. Mushrooms implicated in this type of poisoning are *Pleurocybella porrigens*, *Grifola frondosa*, and *Pleurotus eringii* (Gonmori et al. (2011); Yamada et al. (2012); Nomura et al. (2017)).

12. Mushroom toxins

Each poisonous fungi species contains one or more toxins with marked differences in the toxicity they produce. Poisons may be classified on the basis of the mushroom's physiologic and clinical effects in humans, the target organ toxicity, and the time of symptom onset. The clinical spectrum and toxicity differs based on the following factors (Horowitz, 2015): 1) eaten species; 2) amount consumed; 3) season: 4) geographic location; 5) preparation method; and 6) individual response to the toxins.

The characteristics of fungal poisons were given in a variety of publications (Goldfrank (2011); Gonmori and Yoshioka (2005); Horowitz (2015); Jo et al. (2014); Karimi and Razavi (2015); Karlson-Stiber and Persson (2003); Kim et al. (2017); Li and Oberlies (2005); Michelot and Melendez-Howell (2003); Puschner (2012); Sun et al. (2018); Vargas et al. (2011); Yilmaz et al. (2014)).

Main toxin groups that could be found in toxic mushrooms are (Goldfrank, 2011; Kim et al., 2017): 1) Cyclopeptides – amatoxins and phallotoxins; 2) Gyromitrin; 3) Orellanine; 4) Muscarine; 5) Psilocybin; 6) Muscimol and ibotenic acid; 7) Coprine; 8) Nephrotoxins (norleucine); 9) Myotoxins; 10) Immunoactive toxins; 11) Hemolytic toxins; and 12) Gastrointestinal irritants. Considering the seriousness of their toxicity, they can be subdivided in the following categories: a) deadly (for instance, amatoxins and orellanine); b) potentially deadly (muscarine, and ibotenic acid); and c) non-lethal (phallotoxins, coprine, muscinol, psilocybin, and gastrointestinal irritants).

Amatoxins are found in some species of *Amanita*, *Galerina*, and *Lepiota*. For the genus *Amanita*, especially *A. phalloides*, *A. virosa* and *A. verna*, the main causes of poisoning are associated with their high content of amatoxins. Some species of *Galerina* (the most common being *Galerina marginata*) and *Lepiota* (*Lepiota brunneoincarnata*, *Lepiota brunneolilacina*, *Lepiota helveola*, and *Lepiota josserandii*) are also extremely toxic but less frequently cause human poisoning compared to the *Amanita* species (Garcia et al., 2015b; Kose et al., 2015). Toxin content of *Amanita* species (mg/kg dry weight) was given by Sun et al. (2018). Amatoxins cannot be denatured by cooking or digestive enzymes (Broussard et al., 2001).

Worldwide, amatoxin-containing mushrooms are a leading cause of mortality. Various reports showed that they account for more than 90% (Cai et al., 2016; Eren et al., 2010; Karvellas et al., 2016; Rahmani et al., 2015) and even > 95% of mushroom poisoning-related deaths (Barman et al., 2018; Latha et al., 2018; Yilmaz et al., 2015).

Orellanine is a principal toxin in genus *Cortinarius*. Most often lethal poisonings are caused by fool's webcap (*Cortinarius orellanus*) and deadly webcap (*Cortinarius rubellus*) (Shao et al., 2016). These mushrooms are typically found in Europe and North America (Goldfrank,

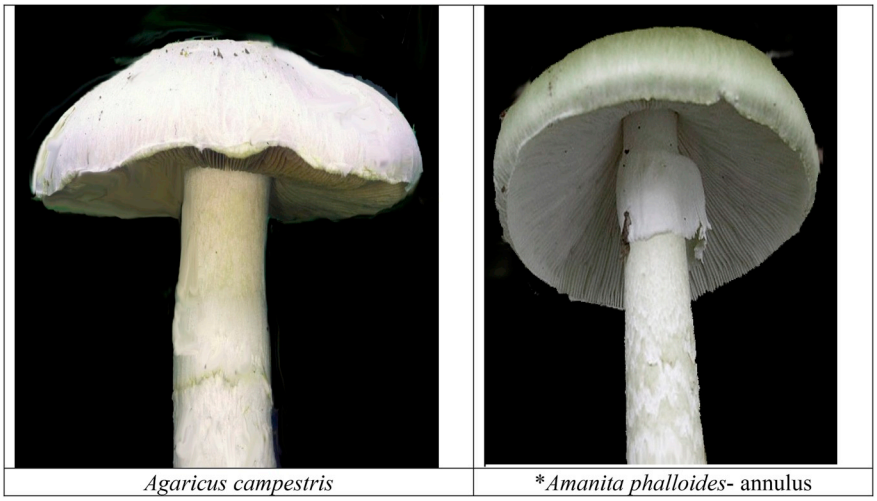

Fig. 2. A misidentification may occur when poisonous mushrooms appear edible as in the case of *Amanita phalloides* as it can look identical to *Agaricus campestris* as they may be viewed in similar shape, form and color. For these mushrooms, it is critical to note the difference, mushroom pickers must recognize between the two of the presence of distinguishing annulus (a ring) on the stipe (stem) of the * *Amanita phalloides* under the pileus (cap) that only appears at the later stages of growth. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Methods of treatment of mushroom poisoning[a].

Toxins	Mushrooms	Clinical presentations	Treatments
1. Amatoxins	*Amanita verna*, *Amanita virosa*, *Amanita phalloides*, *Lepiota helveola*, *Galerina marginata*	Initial phase: latency 2nd phase: GI disturbances 3rd phase: recovery 4th phase: liver and renal failure	Gastrointestinal decontamination procedures, rehydration, metabolic acidosis and electrolyte correction, specific therapies (silibinin, N-acetylcysteine, penicillin G, MARS) and liver transplantation
2. Gyromitrin	*Gyromitra esculenta Gyromitra californica*	GI irritations, neurotoxicity, liver/renal failures, and hemolysis	Methylene blue, pyridoxine, folinic acid, NAC, and vitamin K
3. Orellanine	*Cortinarius orellanus*	Renal impairment due to severe interstitial nephritis, acute focal tubular damage, and interstitial fibrosis	Prevention of secondary complications of kidney failure, adequate dialysis and, in the case of incomplete recovery, management of chronic renal insufficiency
4. Muscarine	*Clitocybe* (*Citocybe gibba*) and *Inocybe* (*Inocybe rimosa*)	Bradycardia, miosis, salivation, lacrimation, diarrhea and bronchospasm	Supportive, anticholinergic agents such as atropine in the presence of severe toxicity
5. Psilocybin and psilocin	*Gymnopilus spectabilis*, *Panaeolus foenisecii*, *Conocybe cyanopus*, *Psilocybe caerulescens*, *Psilocybe cubensis* *Psilocybe argentipes*	Euphoria, hallucinations, tachycardia and blood pressure, mydriasis, tremors, and fever	Supportive, and diazepam
6. Muscimol and ibotenic acid	*Amanita gemmata*, *Amanita pantherina*, *Amanita muscaria*	Lethargy, stupor, alterating mania, delirium Continues periods of excitation and inhibition in the nervous system	Supportive, sedative, and hypnotic agents
7. Coprine	*Coprinus atramentarius*	Flushing, headache, dyspnea, sweating, arrhythmia, hypotension, and confusion	Propranolol, and fomepizole
8. Nephrotoxins (norleucine)	*Cortinarius* spp., *Amanita smithiana*, *Amanita proxima*	GI disturbances, chills, headache, myalgia, paresthesia, and renal dysfunction	Hemodialysis, hemoperfusion, plasmapheresis, and kidney transplantation
9. Myotoxins cycloprop-2-ene carboxylic acid, and saponaceolide B and M	Some *Russula* spp. (*Russula subnigricans*)	Rhabdomyolysis (acute skeletal muscle necrosis) as well as (for severe cases) severe electrolyte disturbance (hyperkalemia, hypocalcemia), respiratory failure, acute renal failure, pulmonary edema, ventricular tachycardia, and circulatory shock	Aggressive repletion of fluids and continuous venovenous hemofiltration or hemodiafiltration
10. Immunoactive toxins	*Agaricus* sp.	Data not found.	Data not found.
11. Hemolytic toxins	*Paxillus involutus*	GI disturbancesfollowed by haemolysis, anaemia, potential secondary renal failure, and shock	Plasma exchange and hemodialysis for treatment of acute renal failure
12. Russuphelins	*Tricholoma equestre*, *Russula subnigricans*	GI disturbances, weakness, myalgia, rhabdomyolysis and renal failure	Supportive
13. Gastrointestinal irritants	species of *Agaricus*, *Amanita*, *Boletus*, *Entoloma*, *Gomphus*, *Lactarius*, *Omphalotus* (*O. olearius*), *Tricholoma*, *Tylopilus* and *Verpa molybdites*	Gastroenteritis	Supportive

[a] Therapeutic approaches were extracted from reports published by Gonmori et al., (2011); Ward et al., (2013); Karimi and Razavi (2015); Smith and Davis, 2016; Zuliani et al., (2016); Dinis-Oliveira et al., (2016).

2011). The nephrotoxicity induced by *C.orellanus* was first recognized in the 1950s, when this mushroom was identified as the cause of a mass poisoning in Poland (Dinis-Oliveira et al., 2016). The characteristic feature of orellanine late detection of symptoms, as a rule, patient will seek medical advice 3–7 days post-consumption (Hedman et al., 2017).

Muscarine was first isolated from *A. muscaria* in 1869. It was also found in *Inocybe* and *Clitocybe* species, such as the deadly ivory funnel (*Clitocybe dealbata*). The symptoms of early onset (within 15 min to 2 h) include headache, vomiting, nausea, etc. Later begins diarrhea, asthma attacks, severe shortness of breath and bradycardia in combination with

hypotension and severe vasodilation. This leads to a blood circulation shock. Death occurs after 8–9 h in 5% of cases (Kosentka et al., 2013).

Ibotenic acid occurs in fly agaric (*Aminita muscaria*), panther cap (*Amanita pantherina*), and related species of mushrooms, which are distributed in the boreal and temperate regions of the northern hemisphere. Ibotenic acid is a powerful neurotoxin, and typically affects the central nervous system and influences consciousness, perception and emotions (Zinkand et al., 1992).

Phalltoxinis any of several closely-related poisonous peptides present in the death cap (*A. phalloides*), destroying angel (*A. virosa*), fool's mushroom (*A. verna*). Phallotoxin is 20 times less toxic than amatoxins but it has a shorter onset of action (Sun et al., 2018).

Coprine was first isolated from the common inkcap (*Coprinopsis atramentaria*). It is also found in other fungi of the genus *Coprinopsis* and in the brawny bolete (*Imperator tarsus*). In combination with alcohol use, it provoked "Coprinus syndrome" with redness of the face, malaise, vomiting, excitement, and heart palpitations within 5–10 min after drinking. If not taken with alcohol, the symptoms usually subside after 2–3 h. The severity of symptoms is proportional to the quantity of alcohol consumed (Wong and Ng, 2006). Muscinolis found in fly agaric (*A. muscaria*), panther cap (*A. pantherina*), and some others. Similar to ibotenicacid, this toxin is thermostable and not destroyed by cooking.

Psilocybin mostly occurs in the fungal genus *Psilocybe*. Psilocybin is also produced by members of genera *Gymnopilus* (14 species), *Panaeolus* (13), *Copelandia* (12), *Pluteus* (6); *Hypholoma* (6), *Inocybe* (6), *Panaeolina* (4), *Conocybe* (4), *Gerronema* (2), *Mycena* (1), *Galerina* (1) and *Agrocybe* (1). More than 200 species of fungi produce psilocybin (Guzmán, 2008). Psilocybin-containing mushroom species are distributed throughout the world but mostly they are typical for tropical and sub-tropical environments (Dydak et al., 2015).

Some members of *Agaricus*, *Amanita*, *Boletus*, *Entoloma*, *Gomphus*, *Lactarius*, *Omphalotus*, *Tricholoma*, *Tylopilus* and *Verpa* provoke gastrointestinal irritation (Goldfrank, 2011). Symptoms can take place from a few minutes to several hours after eating. Poisoning signs and symptoms involve abdominal pain followed by nausea, profuse sweating, vomiting, and diarrhea (Marinov et al., 2018).

13. Methods of protection against poisoning

Protection against poisoning caused by toxic mushrooms is possible in two directions: 1) precautions; and 2) assistance measures. The first group of measures is the knowledge of the distinctive features of edible mushrooms, because most often, poisoning is caused by mushrooms that are mistakenly assumed to be edible ones (Fig. 2). It is also necessary to avoid long-term storage of collected mushrooms without cooking and long-term storage of already prepared mushrooms.

Measures to help with the poisoned patients include, first of all, removing the toxins from the stomach and intestines, for which the stomach is washed, vomiting is induced, a laxative is administered and an enema is made. Since treatment of poisonings induced by different fungi is different, to clarify the diagnosis, all not eaten mushrooms are preserved. It is forbidden to use any alcoholic beverages, as alcohol facilitates the absorption of fungal poisons. In case of severe poisoning, a doctor is needed. Methods of treatment of mushroom poisoning are described in Table 3.

14. Conclusion

Countries are very heterogeneous with respect to their nutritional traditions of using wild mushrooms as there are mycophile and mycophobe states, but in the vast majority of countries of the world, mushrooms are used in food. As expected, countries where consumption of wild mushrooms is widespread, are leaders in mushrooms-induced mortality.

In addition to poisoning due to errors made during mushrooms collection, mushrooms poisoning can occur for the following reasons: 1) long-term storage of collected mushrooms without their culinary treatment; 2) improper cooking; 3) long-term storage of already prepared mushrooms; 4) damage of fungi by pests, in particular, flat-footed flies (Platypezidae); 5) concomitant use of certain types of mushrooms (for example, shaggy ink cap (*Coprinus comatus*), midden ink cap (*C. sterquilinus*) and common ink cap (*Coprinopsis atramentaria*) with alcohol; 6) accumulation of harmful agents (heavy metals, radioactive substances, etc.) in the mushrooms during their growth; 7) frequent consumption of mushrooms of the family *Morchellaceae*; and 8) use of hallucinogenic fungi.

China, Russia, and Ukraine have the highest rate of mortality due to mushroom poisoning. Countries such as Belarus, Poland, Turkey, Iran, Nepal, and Mexico also have high numbers of death due to mushroom ingestion. World average annual mortality because of consumption of poisonous mushrooms is estimated to be200-250 people. Death cap (*Amanita phalloides*) in temperate latitudes, and Guangzhou destroying angel (*A. exitialis*), and East Asian brown death cap (*A. fuliginea*) in the tropics are deadly species for humans.

List of abbreviations

There are no abbreviations.

Conflict of interest

The authors declare that they have no conflict of interest.

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