

## Revisión

# Poisonous mushrooms; a review of the most common intoxications

A. D. L. Lima<sup>1</sup>, R. Costa Fortes<sup>2</sup>, M. R.C. Garbi Novaes<sup>3</sup> and S. Percário<sup>4</sup>

<sup>1</sup>Laboratory of Experimental Surgery. University of Brasilia-DF. Brazil/Paulista University-DF. Brazil. <sup>2</sup>Science and Education School Sena Aires-GO/University of Brasilia-DF/Paulista University-DF. Brazil. <sup>3</sup>School of Medicine. Institute of Health Science (ESCS/FEPECS/SESDF)/University of Brasilia-DF. Brazil. <sup>4</sup>Institute of Biological Sciences. Federal University of Pará. Brazil.

### Abstract

Mushrooms have been used as components of human diet and many ancient documents written in oriental countries have already described the medicinal properties of fungal species. Some mushrooms are known because of their nutritional and therapeutic properties and all over the world some species are known because of their toxicity that causes fatal accidents every year mainly due to misidentification. Many different substances belonging to poisonous mushrooms were already identified and are related with different symptoms and signs. Carcinogenicity, alterations in respiratory and cardiac rates, renal failure, rhabdomyolysis and other effects were observed in toxicity studies with various species including edible and therapeutic ones. Proper identification is important to avoid accidents and toxicity studies are necessary to assure the safe use of mushrooms as food and for medicinal purposes.

(*Nutr Hosp.* 2012;27:402-408)

DOI:10.3305/nh.2012.27.2.5328

Key words: *Toxicity. Mushrooms. Toxins. Review.*

### HONGOS VENENOSOS; UNA REVISIÓN DE LAS INTOXICACIONES MÁS COMUNES

### Resumen

Las setas se han utilizado como componentes de la dieta humana y muchos documentos antiguos escritos en los países orientales se han descrito ya las propiedades medicinales de las especies de hongos. Algunos hongos son conocidos por sus propiedades nutricionales y terapéuticas y de todo el mundo, algunas especies son conocidas debido a su toxicidad que causa accidentes mortales cada año, principalmente debido a errores de identificación. Muchas sustancias diferentes que pertenecen a las setas venenosas estaban ya clasificadas y están relacionados con diferentes síntomas y signos. Carcinogenicidad, alteraciones de la frecuencia respiratoria y cardiaca, insuficiencia renal, rhabdomyolisis y otros efectos se observaron en estudios de toxicidad con varias especies incluidas las alimenticias y terapéuticas. La correcta identificación es importante para evitar accidentes y los estudios de toxicidad son necesarias para asegurar el uso seguro de las setas como alimento y con fines medicinales.

(*Nutr Hosp.* 2012;27:402-408)

DOI:10.3305/nh.2012.27.2.5328

Palabras clave: *Toxicidad. Hongos. Toxinas. Revisión.*

### Introduction

Approximately 140.000 species of mushrooms have already been catalogued all over the world, about 2.000 being considered safe for human consumption and about 700 have therapeutic properties.<sup>1</sup> A great variety of species was classified as poisonous and represents risks to health if ingested. Apart from mushrooms that contain psychoactive toxins, ingestion of toxic mushrooms is invariably accidental and caused by misidentification of species.<sup>2,3</sup>

**Correspondence:** Renata Costa Fortes.  
Science and Education School Sena Aires-GO.  
University of Brasilia-DF/Paulista University-DF. Brazil.  
QI 14. CJ J. CS 26. Guara 1/DF. Brazil. CEP: 71.015-100.  
E-mail: renatafortes@yahoo.com.br

Recibido: 1-VI-2011.  
Aceptado: 17-VI-2011.

There are some mushrooms that contain exceptionally powerful toxins that represent a real hazard to health even when ingested in small doses. Most toxins were well studied and are described in literature, such as amatoxins that are cytotoxic and cause harm to kidney and liver and orellanine that is nephrotoxic.<sup>2</sup>

Some species are well utilized for food and medicine due to the presence of pharmacologically active substances and essential nutrients. Because of these properties, mushrooms were described as popular remedies in ancient oriental documents and some of them became ingredients in traditional medicine.<sup>4,5,6</sup> Even in species with beneficial properties toxic substances were already found.<sup>7</sup>

Before using species of mushroom for human consumption it is necessary to characterize their toxicological profile because even in some edible species toxic substances have been identified. The toxicity studies consist of exposing species of mammal to a

toxic agent during a specific period of time.<sup>8</sup> The aim of the present work is to review the most common intoxications caused by toxic species and the toxic potential caused by edible and medicinal mushrooms.

### Poisonous species of mushrooms

Some species of mushrooms are known as toxic and in some countries many cases of mushroom poisoning are reported every year. In the year 1998 in France 1,675 cases of intoxications by mushrooms were reported and in this country alone it is estimated that 8-10,000 cases are expected to be registered every year. Most of these accidents are due to incorrect identification of species that is often made by empirical and traditional knowledge.<sup>3,9</sup> A wide variety of toxic mushrooms belong to different genus that will be discussed below.

#### Genus *Amanita*

The family *Amanitaceae* (genus *Amanita*) is well known as having many toxic species. Amatoxins are present in species of *Amanita* genus such as: *Amanita phalloides*, *A. virosa*, *A. verna*, *A. ocreata*, *A. bisporigera*, *A. suballiacea*, *A. tenuifolia* and *A. hygroskopica*. The family of amatoxin comprises a neutral component designated as alpha-amanitin, an acid one called beta-amanitin, gamma and delta-amanitin and the nonpoisonous component amanullin from *A. phalloides* and amaninamine from *A. virosa*.<sup>10</sup>

Other toxins also found in *Amanita* genus belong to the family of phallotoxin that includes phalloin, phalloidin, phallisin, phallacidin, phallacin and phallisacin. Virotoxin is also found in this genus and are closed related the phallotoxins.<sup>10</sup>

The specie *A. phalloides* is responsible for the majority of the fatalities caused by mushroom poisoning. The toxic effects are caused by phallotoxin and amatoxin. Phallotoxin causes alterations of enterocytes cellular membrane, while amatoxin inhibits protein synthesis at a transcriptional level within enterocytes, hepatocytes and proximal renal tubular cells. After ingestion of *A. phalloides*, amatoxin causes necrosis of liver cells with mortality rates ranging from about 10% to 20%. Only a minority of patients need emergency liver transplantation.<sup>11,12</sup>

Species with hallucinogenic effects are also found in *Amanita* genus. *A. pantherina* and *A. muscaria* are well known toxic mushrooms that have been mistaken for the edible mushroom *A. rubescens*. Two dissociative constituents such as ibotenic acid (IBO) and muscimol (MUS) are responsible for the hallucinogenic effects. IBO is a powerful agonist of N-methyl-D-aspartic-acid (NMDA) receptor and MUS is a potent GABA<sub>A</sub> agonist.<sup>13</sup> The intoxications caused by *A. muscaria* for long time were believed to be due to muscarine, but it

was demonstrated that this substance is present in small amounts.<sup>14</sup>

*A. muscaria* and *A. pantherina* grow in North America, Europe, Africa and Japan, in recent years it has been reported that young people in several countries have intentionally eaten *A. muscaria* to evoke hallucinations.<sup>15</sup> The most common symptoms of intoxication are motor depression, ataxia, changes in mood, perception and feelings, dizziness, euphoria, drowsiness, gastrointestinal disturbances and muscle twitches.<sup>13,15,16</sup>

The pantherina-muscaria syndrome is atropine-like and in the number and severity of poisoning cases fatality is rare. In most cases recovery is complete after 24 hours. The treatment is mainly symptomatic cholinesterase inhibitors may be recommended as it counteracts the effects of poisoning, benzodiazepines or phenobarbitone can be used in case of seizures.<sup>14,17</sup> The treatment of patients intoxicated with species containing amatoxins includes detoxification, careful monitoring and sometimes liver transplantation is necessary.<sup>10</sup>

#### Genus *Clitocybe* and *Inocybe*

A particular syndrome that affected five people in the region of Savoie in France was later identified as intoxication caused by the mushroom *Clitocybe amoenolens*. First symptoms appeared 24 hours after ingestion. Patients presented paresthesia of the toes and fingers followed by paroxysmal burning pain lasting 2-3 hours, notably at night. A sensation of heat, numbness, oedema and local erythema are associated with crises. Symptoms are partially relieved with cold water, acetylsalicylic acid, morphine and clomipramine. Recovery is completely after 1-4 months.<sup>18</sup>

The administration of high dose of *C. amoenolens* in rats caused weight loss, locomotor disability and erythema of the toes. Examination of the sciatic nerves showed decreased axon density and neuronal fiber degeneration.<sup>19</sup>

The poisonous specie *C. acromelalga* can be confused with the edible one *Lepista inversa*. The substances pointed out as responsible for the symptoms are the acromelic acids A-E. Acromelic acid (ACRO) is a kainate analogue that is assumed to be involved in poisoning episodes. ACRO has two isomers, ACRO-A, which is the most potent and ACRO-B. ACRO-A was demonstrated to have a powerful excitatory action on mechanosensitive unmyelinated afferents in skeletal muscle of the rat.<sup>20</sup>

Species of genus *Clitocybe* also cause muscarinic syndrome. The species *C. dealbata*, *C. rivulosa*, *C. candicans*, *C. cerussata*, and *C. phyllophila* are described in literature as poisonous mushrooms due to the presence of muscarine in their chemical composition. Approximately 15 minutes to 2 hours after ingestion patient can present gastrointestinal problems, miosis, hypersecretion and in severe cases bradycardia

**Table I**  
Clinical cases related with mushrooms intoxication

Author/year of publication	Genus	Clinical findings
Wessely et al., 2007 <sup>37</sup>	<i>Cortinarius</i>	A 26 years old woman became anuric after several days of nausea and vomiting and presented elevated BUN and creatinine after ingestion of mushrooms belonging to <i>Cortinarius</i> genus. In renal biopsy she presented interstitial nephritis and more than 1 year later she had to be submitted to chronic dialysis.
Mount et al., 2002 <sup>38</sup>	<i>Cortinarius</i>	A 17 years-old Caucasian male had picked and ingested raw and wild mushrooms hoping that they were hallucinogenic. He presented to the hospital with a one week nausea and diarrhea, for previous 3 days he was anuric and on examination he had no abnormalities. Serum biochemistry showed abnormal creatinine and urea consistent with renal failure. After 4 weeks he had no recovery of renal function and required ongoing haemodialysis.
Mount et al., 2002 <sup>38</sup>	<i>Cortinarius</i>	A 26 years-old Caucasian male ingested approximately 12 uncooked mushrooms for hallucinogenic purposes, 2 days later he went to hospital because of vomiting and epigastric pain. Following admission he became progressively oliguric and renal biopsy showed widespread cellular and oedematous interstitial fibrosis. As there was no recovery of renal function he had to be submitted to chronic haemodialysis.
Giannini et al., 2007 <sup>39</sup>	<i>Amanita</i>	A retrospective evaluation of the history and clinical outcome of each patient treated from 1988 to 2002 in the Toxicological Unit of Careggi General Hospital (University of Florence, Italy) for amatoxin poisoning was conducted. The clinical data of 111 patients were evaluated; their biological parameters were monitored every 12-24 hours until discharge. Two patients died; both were admitted to the hospital more than 60 hours after mushroom ingestion and 105 recovered completely.
Enecker-Jans et al., 2007 <sup>40</sup>	<i>Amanita</i>	Two patients, a 54-year-old man and a 51-year-old woman, presented abdominal pain, vomiting and diarrhea; these symptoms developed 9 and 15 hours, respectively, after consumption of soup. The poisoning with the specie <i>Amanita phalloides</i> was later confirmed by the results of urinalysis. The patients were discharged in good condition 8 days later.
Aygun et al., 2010 <sup>41</sup>	<i>Amanita</i>	A 24-years-old female was admitted in a hospital with abdominal pain, nausea, emesis and weakness. She had consumed a mushroom 6 hours before admission. A nasogastric tube was placed for aspiration and administration of charcoal. Simultaneously fluid and electrolyte resuscitation to treat the emesis was given in the course of intoxication. Patient developed multiple organ failure in spite of supportive treatment such as intravenous inotropic therapy and dialysis. An intra-aortic balloon counterpulsation catheter was placed because of gradual deterioration of her clinical status. After this procedure she improved gradually until complete recovery.
Bedry et al., 2001 <sup>42</sup>	<i>Tricholoma</i>	Seven women (age range, 22 to 60 years) presented severe rhabdomyolysis one week after eating wild mushrooms. All patients reported fatigue and muscle weakness accompanied by myalgia. After 3 or 4 days weakness worsened and the production of dark urine was observed. Electromyography was performed and revealed muscle injury without involvement of peripheral-nerve. Three of the patients presented increasing dyspnea at rest and signs of acute myocarditis, all three patients died.
Saviu et al., 2002 <sup>43</sup>	<i>Clitocybe</i>	A 32 years old woman ingested a specie of the genus <i>Clitocybe</i> in 3 consecutive meals. She presented paresthesia of fingers and toes, crises of paroxysmic pain lasting 2-3 hours with sensation of local heat, oedema and local erythema. Clinical examination was normal, body temperature and blood pressure was normal. Following admission to the hospital pain crises increased mainly at night. She recovered completely after several months.
Dehay et al., 2009 <sup>21</sup>	<i>Clitocybe</i>	Two patients a man and his wife, both were 67 years old, ingested the specie <i>Clitocybe rivulosa</i> wrongly identified as <i>Marasmius oreades</i> . The wife presented abdominal pain, diarrhea and intense sweating followed by and unconsciousness state. Artificial ventilation was needed because of bronchial hypersecretion. High blood pressure and alterations in cardiac rate were also noticed such as convulsions. Patient died one week after hospital admission, her husband presented moderated muscarinic syndrome 15 hours after mushrooms ingestion. He presented nausea, diarrhea, intense sweating, myosis and bronchial hypersecretion. Symptomatic treatment was instituted and administration of atropine. Recovery was completely. Patient was discharged from hospital the day after admission.
Gonmori and Yoshioka, 2003 <sup>44</sup>	<i>Psilocybe</i>	A fatal case of magic mushroom poisoning happened with a 27 years old man that was found in an irrigation canal. Two cultivation pots of mushrooms were found in his room, which was identified as <i>Psilocybe subcubensis</i> . The victim might have been influenced by these hallucinogenic substances. As a result he died of winter cold temperature.

and collapses. The treatment of this syndrome is symptomatic and atropine can be administered to counteract the effects of muscarine.<sup>21</sup>

There are approximately 40 species belonging to *Inocybe* genus in China, and they are known to be not edible. The species: *I. asterospora*, *I. fastigiata* f. *subcandida*, *I. gobeyi*, *I. lilacina*, *I. nappies*, *I. pallidicremea*, *I. patowillandii*, *I. radiate*, *I. repanda* and *I. rimosa* have toxic properties. They produce neurotoxic and psychotropic effects due to the presence of biogenic amines, muscarin, aeruginacin a thymethylammonium analogue of psilocybin which effects will be discussed later in this article.<sup>23</sup> Intoxications caused by members of this genus is similar to the ones caused by *Clitocybe* because the species contain muscarine.<sup>3</sup>

### Genus *Cortinarius*

The genus *Cortinarius* comprises between 2,000-3,000 species of mushrooms that were considered as non-toxic until 1950. One hundred-and-thirty-five cases of intoxication caused by *C. orellanus* were described from 1953-1962 in Poland. Poisoning syndrome is characterized by a delayed acute tubulopathy that can progress to chronic renal insufficiency.<sup>22</sup>

In several case reports it was demonstrated that the mushrooms *C. speciosissimus* and *C. orellanus* are nephrotoxic due to the presence of the cyclopeptide orellanine whose metabolites are supposed to be most active. In additional studies it was shown that the oxidation of orellanine in renal tissue may accumulate quinone compounds which bind covalently with biological structures leading to cell damage.<sup>2</sup>

The symptoms of orellanine intoxication may appear between 2-20 days after ingestion. Initially people can experience nausea, vomiting and abdominal pain. This is followed by intense thirst, chills, polyuria or oliguria and possibly anuria. Hemodialysis may be necessary until renal function gradually improves.<sup>23</sup>

Some species of genus *Cortinarius* can be confused with members of *Psilocybe* genus which is known as magic because of the hallucinogenic properties. This fact has led to several cases of accidental intoxication because *Psilocybe* mushrooms are used for some people for recreational purposes.<sup>24</sup>

### Genus *Gyromitra*

Species of genus *Gyromitra*, family *Helvellaceae* are really attractive to hunters and gourmets because of their taste. However, some species of *Gyromitra* contain a well known toxin named gyromitrin, whereas other species are non-toxic. This is one of the reasons why intoxications occur, toxic and non-toxic species are sometimes difficult to distinguish because they are mixed-up. The other reason is that the toxin is water

soluble and volatile, boiling for long time and drying allows ingestion without risk of poisoning, but if these procedures are not done properly intoxication may occur.<sup>2</sup>

The third reason for intoxication is the confusion with species that are consumed frequently. The species *G. esculenta* is known as false morels and is commonly confused with morels such as *Morchella esculenta* and *M. elata*. The toxin gyromitrin is the responsible for the effects of this species. Intoxications have occurred not only by eating fresh false morels but also by the inhalation of vapors from cooking.<sup>3,9</sup>

Intoxications caused by *G. esculenta* were reported by the Swedish Poisons Information Centre which handled 706 inquiries in the period of 1994-2002. Most common symptoms are gastrointestinal (vomiting and diarrhea) and neurological (vertigo, fatigue, tremor, ataxia, nystagmus). A few patients have developed mild to moderate liver damage and haemolysis. After ingestion gyromitrin is hydrolysed in stomach forming hydrazines that are cytotoxic, convulsants and irritating to mucous membranes.<sup>2,25</sup>

The other effect of gyromitrin include carcinogenesis due to the hepatic metabolism that produces free radicals with mutagenic properties in animals and are also responsible for the hepatic problems. Symptoms of intoxication start 8-12 hours after ingestion. Treatment consists of monitoring the symptoms and administering vitamin B6 intravenously considering that gyromitrin inactivates this vitamin.<sup>26</sup>

### Genus *Psilocybe*

The use of psychoactive substances of fungal origin for recreational purposes has become an increasing problem in many countries all over the world. Species of genus *Psilocybe* are known due to their psychedelic effects caused by psilocybin.<sup>27</sup> Common psilocybin containing mushrooms are: *P. semilanceata*, *P. Mexicana*, *P. bohemica*, *P. cubensis* and *P. baeocistis*.<sup>25</sup>

The symptoms of intoxication occur 30 minutes after ingestion of fresh or dried mushroom and start with anxiety, nausea, vertigo and asthenia, neurosensory symptoms consist of visual problems, disorientation, motor incoordination and sympathomimetic symptoms consist of mydriasis, tachycardia and hypertension. Recovery is completely 4 to 12 hours after ingestion. The need of hospitalization is rare and in exceptional cases myocardial infarction may occur in adult patients while children may present hyperthermia, seizures and coma.<sup>25</sup>

### Toxicity caused by commonly consumed mushrooms

Some species known as edible and medicinal also have substances that can cause harm to health, but the dose and magnitude of effects on humans must be care-

**Table II**  
*Molecular properties, mechanism of toxicity and sources of mushrooms's toxins*

Toxin name	References	Molecular properties, mechanism of toxicity and sources
<i>Ostreolysin</i>	45	16kDa acidic protein, expressed in primordia and fruiting bodies of <i>Pleurotus ostreatus</i> , is a member of the Aegerolysin protein family. It contains 137 residues of amino acids 13 positively and 16 negatively charged residues, a relatively high content of aromatic residues. At 25°C and pH between 6 and 9, ostreolysin adopt a nativelike conformation characterized by rigid tertiary structure and predominantly b-sheet secondary structure.
<i>Amatoxin</i>	46, 26	Thermostable bicyclic octapeptide found in species of <i>Amanita</i> genus. Nine amatoxins were already identified and a-amanitine is the most active. The toxicity of amatoxin is due to the inhibition of RNA polymerase-II and therefore DNA transcription resulting in arrest of protein synthesis and cell necrosis.
<i>Phallotoxin</i>	47	Peptides containing bicyclic-skeleton with a transannular thioether bridge. Intoxication mechanism is believed to be due to specific binding of the toxin of F-actin in liver cells, which consequently inhibits the depolymerization of F-actin into G-actin.
<i>Agaritin</i>	30, 48	Is an L-glutamic acid (b-N-(g-L(+)-glutamil)-4-hydroxymethyl)phenylhydrazine found in the specie <i>Agaricus bisporus</i> , it is encountered at concentrations as high as 1,7mg/g in raw mushroom. Agaritine can be enzymatically activated to a mutagenic metabolite and both substances can bind with DNA and form adducts.
<i>Orellanine</i>	49	Is a heat-stable bipyridine N-oxide (3, 3', 4, 4'-tetrahydroxy-2, 2-bipyridine-N, N'-dioxide), found in the mushroom <i>Pleurotus ostreatus</i> and <i>Cortinarius orellanus</i> . Orellanine chemically resembles the pyridine herbicides paraquat and diquat and is deoxidized in orelline that is no toxic. <i>In vitro</i> data strongly suggest that orellanine generates oxygen radicals at the target site through redox cycling and/or redox activation of iron. Further data from cellular systems indicate that a metabolite of the toxin can inhibit protein synthesis.
<i>Gyromitrin</i>	50	Gyromitrin (acetaldehyde-N-methyl-N-formylhydrazone) is a volatile liquid which is quite unstable and oxidizes at room temperature to acetaldehyde and N-methyl-N-formylhydrazine and exists free or bonded with glucosides in the specie <i>Gyromitra esculenta</i> popularly known as false morel. The typical gyromitrin content is 40-732 mg/kg (wet weight). The hydrazines are convulsants, they react with pyridoxal-phosphate forming a hydrazone which result in the decreased activity of glutamic acid decarboxylase and diminished formation of g-aminobutyric-acid (GABA).
<i>Acromelic acid</i>	20	Is a member of kainoid family a group of non-proteinogenic pyrrolidine dicarboxylic acid, found in the mushroom <i>Clitocybe acromelalga</i> . Acromelic acid -A exhibits neuroexcitatory activity, can bind glutamate receptors, mimics glutamic acid, causes characteristic behavior changes and induce selective damages to the interneurons in lower spinal cord when tested in animal model.
<i>Ibotenic acid</i>	15, 16	Is the a-amino-3-hydroxy-5-isoxazole-acetic acid, found in species <i>Amanita muscaria</i> and <i>A. pantherina</i> . Is an agonist of N-methyl-D-aspartic-acid (NMDA) receptor. Because of the acidic property of isoxazole moiety, it is similar to glutamic acid mimics its effects in animals.
<i>Muscimol</i>	15, 16	Is a 3-hydroxy-5-amino-methylisoxazole which a decarboxylated product of ibotenic acid which is found in <i>Amanita muscaria</i> and <i>A. pantherina</i> . This substance shows structural resemblance to GABA (g-amino-butyric-acid) and imitates the action of this inhibitory neurotransmitter in central nervous system.
<i>Muscarine</i>	26	Tetrahydro-4-hydroxy-N,N,N-5-tetramethyl-2-furanmethanaminium is found in small amounts in <i>Amanita muscaria</i> and in larger amounts in <i>Clitocybe serussata</i> , <i>C. dealbata</i> , <i>C. phyllophilla</i> and <i>C. rivulosa</i> . Muscarine structure is very similar to acetylcholine and bind to the same receptors. It is not hydrolyzed by cholinesterase causing a parasympathomimetic symptomatology.
<i>Psilocybin and psilocin</i>	51, 52	Component of the tyramine type, 4-phosphoryloxy-N,N-dimethyltryptamine. Cleavage of the phosphoric ester group by alkaline phosphatase and unspecific esterases indicates that psilocybin acts as a prodrug and that its hydroxyl metabolite psilocin the active agent. Activity of psilocybin is due to the activation of serotonin 2-A receptor

fully studied. Ostreolysin is a cytolytic protein that was isolated from mushrooms of the genus *Pleurotus* that was able to cause cytolytic pore formation when administered by intravenous route to rats. As a consequence it

was observed blood pressure increase, cardiac ischemia, tachycardia, hypoxia and elevated serum potassium.<sup>28</sup>

The administration of the mushroom *Phellinus linteus* to rats bearing experimentally induced prostatic

hyperplasia leads to an enlargement of prostate stroma which is involved in transforming growth factor-beta<sub>1</sub> (TGF-β<sub>1</sub>) regulation. The prostate is known to be regulated by various growth factors. Among them the TGFs have been reported to play important role in prostate cell growth regulation. The administration of *P. linteus* increased the expression of TGF-β<sub>1</sub> compared to animals treated with placebo.<sup>29</sup>

*Agaricus bisporus* is the most consumed mushroom world-wide but it has been pointed out as potentially carcinogenic due to the substantial amounts of aromatic hydrazines, an established class of direct-acting chemical carcinogens. Life-time administration of *A. bisporus* raw or baked to mice three days a week followed by balanced semi-synthetic diet for the remaining days, induced tumors in a number of tissues. The administration of the methanolic and aqueous extracts of this same mushroom is weakly mutagenic. The ethanolic extract of this mushroom is increased in the presence of fungal mammalian enzyme systems purified mushroom tyrosinase and rat hepatic cytosol.<sup>30,31</sup>

The specie *Pleurocybella porrigens* popularly known as Sugihiratake is a white mushroom widely distributed in the mountain areas of Japan and is commonly used as ingredient to various processed foods, but this was pointed out as hazardous due to the presence of substances analogous to vitamin D that are able to cause cryptogenic encephalopathy in patients with renal failure.<sup>32</sup>

The acute toxicity of *Agaricus silvaticus* was evaluated by administering the aqueous extract of this mushroom in the dose of 1.5 g/kg/day of body weight to adult male and female rats by gavage every 2 hours and 40 minutes, during a period of 24 hours, followed by a protocol of The National Health Surveillance Agency (ANVISA, Brazil). It was observed that not only the administration of *A. silvaticus* aqueous extract but also the placebo, caused the temporary appearance of apathy, respiratory alterations and piloerection, that were slightly more persistent in the group treated with the fungus. Biochemical and histopathological were not statistically significant among the groups. The administration of the *A. silvaticus* aqueous extract induced very low toxicity.<sup>33</sup>

Species of genus *Tricholoma* especially *T. equestre* (*T. flavovirens*), known as yellow tricholoma, has been implicated in 12 human poisonings causing a delayed rhabdomyolysis severe enough to be fatal in 3 cases reported in France. The symptoms were muscular weakness, fatigue and myalgias within 24-72 hours after ingestion. The substance responsible for toxic effects was not identified.<sup>2</sup>

*T. equestre* is a wild mushroom considered in Europe as a delicacy. Toxicity is observed after a consumption of considerable amounts of fresh mushroom which ranges from 100 to 400 g at 3 to 9 consecutive meals.<sup>34</sup>

A neurological syndrome appears after the ingestion of the specie *Hapalopilus rutilans* that is considered edible. Common symptoms consist of visual distur-

bances, somnolence, hypotonia and hepatic and renal insufficiency.<sup>35</sup> Hepatic cytolysis and renal insufficiency were described in children.<sup>22,36</sup>

## Conclusion

In countries where mushrooms are highly consumed, a number of intoxications are reported every year mainly due to misidentification of species. Hazardous toxins are present in these species and are able to cause different syndromes that can be fatal depending on the amount ingested. Accidental ingestion of mushrooms is difficult to avoid especially in countries where eating wild species is common. Proper identification is important to avoid accidents and the identification of symptoms and signs of intoxication as soon as possible enables the success of treatment. Intoxications caused by commonly consumed mushrooms were already described, for this reason edible mushrooms and the ones having pharmacological potential must be carefully studied in order to identify the possibility of intoxications, so more studies have to be carefully conducted, clinical and experimental assays with medicinal species must investigate the side effects that may occur.

## References

1. Lull C, Wichers HJ, Savelkoul HFJ. Antiinflammatory and immunomodulating properties of fungal metabolites. *Mediat Inflamm* 2005; 2005 (2): 63-80.
2. Karlson-Stüber and Persson. Cytotoxic fungi – an overview. *Toxicon* 2003; 42 (4): 339-49.
3. Flesch F and Saviuc P. Intoxication par les champignon: principaux syndromes et traitement. *EMC-Médecine* 2004; 1: 70-9.
4. Wasser SP. Review of medicinal mushrooms advances: good news from old allies. *HerbalGram* 2002; 56: 28-33.
5. Miyaji CK, Colus IMS. Mushroom shiitake, is it a mutagenic or antimutagenic agent? *Semina: Sci Biol Saúde* 2001; 22 jan/dez: 11-17.
6. Delu MAF, Dias ES, Schwan RF, Vilas Boas EVB. Avaliação da coloração de basidiocarpos desidratados de *Agaricus blazei* segundo a escala de Munsell. *Ciênc Agrotec* 2006; 30 (1): 162-5.
7. Nieminen P, Kirsi M and Mustonen AM. Suspected Myotoxicity of edible wild mushrooms. *Experimental Biology and Medicine* 2006; 231: 221-8.
8. Klaassen C. Casarett and Doull's Toxicology. The basic science of poisons. 1996. 5<sup>th</sup> Edition. McGraw-Hill Companies, Inc. USA
9. White J, Warrel D, Eddleston M, Currie BJ, White IM, Isbister GK. Clinical toxicology – Where are we now? 2003; 41 (3): 263-76.
10. Wong JH and Ng TB. Toxins from Basidiomycete fungi (mushroom): amatoxins, phallotoxins and virotoxins. *Handbook of Biologically Active Peptides*. 2006; Chapter 2: 131-5.
11. Escudié L, Francoz C, Vinel JP, Moucari R, Cournot M, Paradis V, Sauvanet A, Belghiti J, Valla D, Bernuau J and Durand F. *Amanita phalloides* poisoning: Reassessment of prognostic factor and indications for emergency liver transplantation. *J Hepatol* 2007; 46: 466-73.
12. Mas A. Mushrooms, amatoxins and the liver. *J Hepatol* 2005; 42: 166-9.
13. Tsujikawa K, Mohri H, Kuwayama K, Miyaguchi H, Iwata Y, Gohda A, Fukushima S, Inoue H and Kishi T. Analyses of

- hallucinogenic constituents in Amanita mushrooms circulated in Japan. *Forensic Sci Int* 2006; 264: 172-8.
14. Michelot D and Melendez-Howell LM. *Amanita muscaria*: chemistry, biology and ethnomycology. *Mycol Res* 2003; 107 (2): 131-46.
  15. Tsujikawa K, Kuwayama K, Kanamori T, Iwata Y, Inoue H, Yoshida T and Kishi T. Determination of muscimol and ibotenic acid in Amanita mushrooms by high-performance liquid chromatography and liquid-chromatography-tandem mass spectrometry. *J Chromatogr* 2007; 852: 430-5.
  16. Stormer FC, Koller GE and Janak K. Ibotenic acid in *Amanita muscaria* spores and caps. *Mycologist* 2004; 18: 114-17.
  17. Satora L, Pach D, Cizowski K and Winnik L. Panther cap *Amanita pantherina* poisoning case report and review. *Toxicon* 2006; 47: 605-7.
  18. Bessard J, Saviuc P, Chane-Yene Y, Monnet S, Bessard G. Mass spectrometric determination of acromelic acids A from a new poisonous mushroom: *Clitocybe amoenolens*. *J Chromatogr A* 2004; 1055: 99-107.
  19. Saviuc P, Dematteis M, Mezin P, Danel V, Mallaret M. Toxicity of the *Clitocybe amoenolens* mushroom in the rat. *Rev Hum Toxicol* 2003; 45 (4): 180-2.
  20. Taguchi T, Tomotoshi K and Mizumura K. Excitatory actions of mushroom poison (acromelic acid) on unmyelinated muscular afferents in the rat. *Neurosci Lett* 2009; 456: 69-73.
  21. Dehay MH, Mareville FS, Assez N, Dherbecourt V and Goldstein P. Syndrome muscarinique par ingestion de champignon: à propos de deux cas dont un mortel. *Eur J Emerg* 2009; 22: 18-23.
  22. Danel VC, Saviu PF and Garon D. Main features of *Cortinarius* spp. poisoning: a literature review. *Toxicon* 2001; 39: 1053-60.
  23. Tegzes JH and Puschner B. Toxic mushrooms. *Vet Clin Small Anim* 2002; 32: 397-407.
  24. Wormle M, Angstwurm MWA and Sitter T. Treatment of intoxication with *Cortinarius speciosissimus* using and antioxidant therapy. *Am J Kidney Dis* 2004; 43 (4): e3-e6.
  25. Berger KJ and Guss DA. Mycotoxins revisited: part II. *J Emerg Med* 2005; 28 (2): 175-183.
  26. Bédry R and Saviuc P. Intoxications graves par les champignons à l'exception du syndrome phalloïdien. *Réanimation* 2002; 11: 524-32.
  27. Keller T, Schneide A, Regenscheit P, Dirnhofer R, Rucher T, Jaspers J and Kisser W. Analysis of psilocybin and psilocin in *Psilocybe subcubensis* GUZMÁN by ion mobility spectrometry and gas chromatography – mass spectrometry. *Forensic Sci Int* 1999; 99: 93-105.
  28. Zuzek MC, Macek P, Sepsic K, Cestnik V, Franquez R et al. Toxic and lethal effects of ostreolysin, a cytolytic protein from edible oyster mushroom (*Pleurotus ostreatus*), in rodents. 2006; 48(3): 264-71.
  29. Shibata Y, Kashiwagi B, Arai S, Fukabori Y, Suzuki K. Administration of extract of mushroom *Phellinus linteus* induces prostate enlargement with increase in stromal component in experimentally developed rat model of benign prostatic hyperplasia. *Urology* 2005; 66 (2): 455-60.
  30. Walton K, Coombs MM, Walker R, Ioannides C. The metabolism and bioactivation of agaritine and of other mushroom hydrazines by whole mushroom homogenate and by mushroom tyrosinase. *Toxicology* 2001; 161(3): 165-77.
  31. Walton K, Coombs MM, Walker R, Ioannides C. Bioactivation of mushroom hydrazines to mutagenic products by mammalian and fungal enzymes. *Mutat Res* 1997; 381 (1): 131-39.
  32. Sasaki H, Akiyama H, Yoshida Y, Kondo K, Amakura Y, Kasahara Y, Maitani T. Sugihiratake Mushroom (Angel's Wing Mushroom)-Induced Cryptogenic Encephalopathy may Involve Vitamin D Analogues. *Biol Pharm Bull* 2006; 29 (12): 2514-18.
  33. Novaes MRCC, Fortes RC. Efeitos da Suplementação dietética com cogumelos Agaricales e outros fungos medicinais na terapia contra o câncer. *Rev Bras Cancerol* 2006; 52 (4): 363-71.
  34. Chodorowski Z, Waldaman W and Anand S. Acute poisoning with *Tricholoma equestre*. *Przegl Lek* 2002; 59 (4-5): 386-7.
  35. Benitez-Mácias JF, García-Gil D, Brun-Romero FM and Nogué-Xarau S. Intoxicaciones agudas por setas. *Rev Clin Esp* 2009; 209 (11): 542-9.
  36. Saviuc P, Fouilhe Sam-Lai N and Danel V. Champignons toxiques: les nouveaux syndromes. *Journal Europee des Urgences* 2003; 16 (1): 13-7.
  37. Wessely M, Schönermarck U, Raziourouh B, Jung MC, Samtleben. Orellanus syndrome: a rare cause of acute renal failure. *Dtsch Med Wochenschr* 2007; 132 (37): 1880-2.
  38. Mount P, Harris G, Sinclair R, Finlay M, Becker GJ. Acute renal failure following ingestion of wild mushrooms. *Intern Med J* 2002; 32: 182-90.
  39. Giannini L, Vannacci A, Missaneli A, Mastroianni R, Mannaioni PF, Moroni F, Masini E. Amatoxin poisoning: a 15-year retrospective analysis and follow-up evaluation of 105 patients. *Clin Toxicol (Phila)* 2007; 45 (5): 539-42.
  40. Ennecker-Jans AS, Van Daele PL, Blonk MI, Varin DS, Van Laar JA. Amatoxin poisoning due to soup from personally picked deathcap mushrooms (*Amanita phalloides*). *Ned Tijdschr Geneesk* 2007; 151 (13): 764-8.
  41. Aygul N, Duzenli MA, Ozdemir K and Altunkeser BB. A case report of unusual complication of *Amanita phalloides* poisoning: Development of cardiogenic shock and its successful treatment with intra-aortic balloon counterpulsation. *Toxicon* 2010; 55: 630-2.
  42. Bedry R, Baudrimont I, Defieux G, Creppy EE, Pomies JP, Dupon M, Gabinski C, Chapalain JC. Wild mushroom intoxication as a cause of rhabdomyolysis. *N Engl J Med* 2001; 345 (II): 798-802.
  43. Saviuc PF, Danel VC, Moreau PA, Claustre AM, Ducluzeau R, Carpentier PH. Érythralgie soudaine: cherchez les champignons! *Rev Méd Intern* 2002; 23: 394-9.
  44. Gonmori K and Yoshioka N. The examination of mushroom poisonings at Akita University. *Leg Med* 2003; 5: S83-S86.
  45. Berne S, Sepsic K, Anderlüh G, Turk T, Macek P, Ulrih NP. Effect of pH on the pore forming activity and conformational stability of ostreolysin, a lipid raft-binding protein from the edible mushroom *Pleurotus ostreatus*. *Biochem* 2005; 44: 11137-47.
  46. Wieland T, Gotzendorfer C, Zanotti G, Vaisius AC. The effect of the chemical nature of the side chains of amatoxins in the inhibition of eukaryotic RNA polymerase B. *Eur J Biochem* 1981; 117: 161-4.
  47. Kobayashi N, Endo S, Kobayashi H, Faulstich H, Wieland T, Munekata E. Comparative study on the formation of phalloidin, viroisin and related derivatives in aqueous solution. *Eur J Biochem* 1995; 232: 726-36.
  48. Kondo K, Watanabe A, Akiyama H, Maitani T. The metabolisms of agaritine, a mushroom hydrazine in mice. *Food Chem Toxicol* 2008; 46: 854-62.
  49. Nilson A, Nystrom J, Buvall L, Ebefors K, Bjornson-Granqvist A, Holmdahl J, Haraldsson B. The fungal nephrotoxin Orellanine simultaneously increases oxidative stress and down-regulates cellular defenses. *Free Radic Biol Med* 2008; 44 (8): 1562-9.
  50. Arshadi M, Nilsson C, Magnusson B. Gas chromatography-mass spectrometry determination of the pentafluorobenzoyl derivative of methylhydrazine in false morel (*Gyromitra esculenta*) as a monitor for the content of the toxin gyromitrin. *J Chromatogr* 2006; 1125: 229-33.
  51. Musshoff F, Madea B and Beike J. Hallucinogenic mushrooms on the German market – simple instructions for examination and identification. *Forensic Sci Int* 2000; 13: 389-95.
  52. Vollenweider FX, Vollenweider-Scherpenhuyzen MFI, Babler A, Vogel H and Hell D. Psilocybin induces schizophrenia-like psychosis in human via serotonin-2 agonist action. *Cog Neurosci* 1998; 9 (17): 3897-3902.