Do Mushrooms also Cause Cancer in Human?

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Abstract

Mushrooms are not usually known to cause cancer. But this is a poignant truth that some of these poisonous mushrooms containing mycotoxins develop various ailments, diseases and even cancer in human. Peoples are unknowingly consuming the poisonous mushrooms as they are unable to identify them. It appears that no such integrated study has done so far in the past to make the people aware that how some of these mushrooms are toxic in developing cancer in human. The present paper deals with the study of some of these poisonous mushrooms containing mycotoxins causing several ailments, diseases and cancer in human.

Keywords: Mushrooms; Mycotoxins; Diseases and Cancer

Abbreviations

AGT: Agaritine; ALF: Acute Liver Failure; RNA: Ribonucleic Acid; DNA: Deoxyribonucleic Acid; MMH: Mono Methyl Hydrazine; CNS: Central Nervous System; mRNA: Messenger Ribonucleic Acid; LD 50: Lethal Dose, 50%; IARC: International Agency for Research on Cancer

Introduction

In the past, mushrooms have never been the part of man's original diet. But, nowadays, they are popular edibles of modern society. How good are they for us? Do they have a positive effect on our health? Some growing reports suggest that some of these mushrooms are not fit for consumption and they harm our health [1]. And, this is all due to a variety of mycotoxins especially the hydrazines found therein [2]. Most of these hydrazines tested so far are either carcinogenic or mutagenic in nature. For example, one of the most common hydrazines is agaritine found in *Agaricus bisporus*, which is metabolized into diazonium derivative, a very potent carcinogen in a very small amount [3]. *Agaricus bisporus* is widely cultivated to produce low-cost mushroom fruiting bodies casting about a multibillion-dollar world industry [4]. It causes lung, bladder and stomach cancer [5-8]. Similarly, the gyromitrin isolated from *Gyromitra* is also hydrolyzed into a more toxic compound monomethylhydrazine (MMH) causing cancer in human and animals [9-12]. Further, the "death cap", *Amanita phalloides* is an extremely poisonous mushroom killing an individual in a very small amount. It contains a variety of amanitins developing liver failure and prostate cancer [13-15]. In addition, the fruiting bodies of *Podostroma cornu-damae* have also been found to be highly toxic as it contains several trichothecenes developing diseases and cancer in human [16-18]. As we have exemplified some of these mushrooms documenting their roles in causing cancer in human, the present review is an attempt to describe them in detail. The basic aim of the paper is to make the people aware of the fact that some of these mushrooms are extremely toxic to human health.

Discussion

Mushroom mycotoxins caused a variety of adverse health effects ranging from acute poisoning to long term effects such as immune deficiency and cancer. Since most mushrooms are rarely eaten, many toxins are poorly documented for their cancer-causing efficiencies. However, some of these mycotoxins found in mushrooms capable of causing cancer are tabulated (Table 1) and discussed as under:

<table>
<thead>
<tr>
<th>S.N.</th>
<th>Name of Mushroom</th>
<th>Mycotoxins Produced</th>
<th>References</th>
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**Table 1: A List of some Mushroom Mycotoxins Causing Cancer in Human.**

**Agaritine**

Agaritine (AGT) is produced by a mushroom named as *Agaricus*. This is worldwide in occurrence and popularly known as the button white or table mushroom. *A. bisporus* is a very popular species of *Agaricus*. This is one of the most consumed mushrooms of the world being cultivated in more than seventy countries [19,20].

Agaritine is an aromatic, hydrazine derivative and IARC Group 3 carcinogen (Figure 1) [2,7,19]. It causes lung and bladder cancer [5,7]. Agaritine has also been shown to be a mutagen by Ames test [21]. It covalently binds with DNA *in vivo* [22]. This is metabolized in kidney and toxic metabolites thus produced can cause stomach cancer in mice [6,8].

![Skeletal Formula of Agaritine.](image)
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Though agaritine causes cancer in human and animals, their clinical implications have also shown to inhibit the cell proliferation of HL-60 leukaemia cells via the induction of apoptosis [23,24]. Similarly, it has some antiviral properties against HIV too [25]. Clinically, this is observed that Agaricus brasiliensis has some advantageous effects on the human to decrease the body weight, fat, blood glucose and cholesterol significantly. It activated the immune system and normalize the liver function [26].

Gyromitrin

Gyromitrin is produced by several species of Gyromitra especially reported from G. esculanta. This is one of the false morels and an edible mushroom mostly found in America and Europe. Gyromitrin is a volatile, water-soluble and unstable compound. It can easily be hydrolyzed into rather more toxic compound monomethylhydrazine (MMH) [9]. Several hydrazines have been isolated from G. esculanta. The raw mushroom of G. esculanta, gyromitrin, methylformylhydrazine and its precursor, all have been reported to cause cancer in experimental animals [10,11,27-29]. Their effects are cumulative and even in a very small amount it could be carcinogenic in future (Figure 2) [12]. Its toxicity from raw mushroom can be removed by cutting into small pieces and repeatedly boiling with adequate water under good ventilation. Prolong period of air drying also reduces the level of toxin.

A poisoned person may usually recover within 2 to 6 days having a mortality rate of about 10% [30]. Its toxicity may result in stomach cramps, nausea and vomiting, diarrhoea, CNS disturbances with convulsions, jaundice, coma and death. It also causes liver and kidney damage, methemoglobinemia, cyanosis and respiratory arrest [11]. Recently, this is observed that gyromitrin can develop amyotrophic lateral sclerosis [4].

Clinical systemic symptoms of poisoning are often delayed. The patient is kept under supportive care and the symptomatic relief is given. The stomach is emptied as soon as possible. And, the charcoal blood filtration therapy is also performed. As Gyromitrin decomposes in the stomach to form rather more toxic and irritating monomethylhydrazine which reduces pyridoxine in the central nervous system, the high dose of pyridoxine is given in cases of severe CNS toxicity. The patient is also treated with benzodiazepine-like diazepam for the control of seizures [31-35].

Amatoxins (Amanitins)

Amanita phalloides is one of the most poisonous toadstools known to science. Originally found in Meghalaya, this is popularly known as the "Death Cap" mushroom. This is an extremely poisonous mushroom to such an extent that only one death cap is enough to kill an individual and their toxicity is not even reduced by cooking, freezing or drying [13].

Amatoxins include at least eight related mycotoxins produced by the death cap, Amanita phalloides and several other members of the same genus as well as some other mushrooms like Conocybe, Galerina and Lepiota. They are: α-amanitin, β-amanitin, Y-amanitin, Σ-amanitin, amanullin, amanullinic acid, amaninamide and amanine. They were for the first time isolated in 1941 by Heinrich O. Wieland and Rudolf Hallermayer and are oligopeptides made of eight amino acids. They are very lethal and thermostable mycotoxins. The main target organs of amatoxins poisoning are liver, heart and kidney failure (Figure 3) [12,13,15].

The Clinical picture of amanitin intoxication ranges from a mild subclinical presentation to a lethal fulminant course. Gastrointestinal decontamination is a preliminary step to be followed immediately after ingestion. The gastrointestinal phase is characterized by nausea, vomiting, diarrhoea abdominal cramp and hematuria. Acute liver failure (ALF) is caused by the poisoning of amanitins followed by kidney involvement [36]. Currently, the most important antidote used to Amanita phalloides mushroom poisoning is an antioxidant silybin [37].

Amatoxins are a group of complex cyclic polypeptides which damage tissues by inhibiting the RNA synthesis within each cell [38]. Amatoxins are potent inhibitors of RNA polymerase II, a vital enzyme for the synthesis of mRNA. In the lack of mRNA, protein synthesis does not progress, cell metabolism stops and lysis takes place [11,39]. α-Amanitin is a cyclic polypeptide of eight amino acids and is the most poisonous of all amatoxins. The oral LD50 of amanitin is approximately 0.1 mg/kg for rats. This is also an inhibitor of polymerase II and III [40]. Inhibition of RNA polymerase II, amanitin binding not only leads to apoptosis of dividing cells but also of slowing the growing cells which is often observed in prostate cancer [14,15].

Trichothecenes

Trichothecenes are produced by the mushroom Podostroma cornu- damae. The mushroom was first discovered from China in 1895 and was originally described as Hypocrea cornu – damae. Later on, a Japanese mycologist described it as Podostroma cornu- damae [41]. This is native to Korea, Japan, China and Java and has been a rare deadly fungal species of Ascomycetes belonging to the family Hypocreaceae. Its fruiting bodies are highly toxic containing trichothecenes as roridin E, verrucarin J and satratoxin H. Researchers have further identified the trichothecenes as satratoxin H, H12, H12-acetate, H13-acetate and H13-diacetate (Figure 4) [42,43].

Figure 3: Chemical Structure of alpha Amanitin.
Several fatalities of *Podostroma cornu-damae* intoxication have been reported in Japan but none from Korea up to 2013. This is easily mistaken either for a healthy traditional food of *Cordyceps sobolifera* or an antler *Ganoderma lucidum* [41]. While early clinical symptoms of intoxication of this mushroom are gastrointestinal disturbances such as dehydration, nausea and vomiting, diarrhoea, anuria, polypnea, unconsciousness and multiple organs failures, the late symptoms are alopecia, desquamation of palms and soles, anaemia, leukocytopenia, thrombocytopenia, pancytopenia and sepsis leading to death. The main cytotoxic and malignant effects of *Podostroma cornu-damae* are inhibition of cell division, protein biosynthesis and apoptosis [16-18].

**Conclusion**

Among thousands of species of mushrooms worldwide, only a few of them are known to be fatally poisonous. And, due to some of these poisonous mushrooms, the entire population is blamed causing it as an atypical dish worldwide. One of the most toxic mushrooms is *Amanita phalloides*, the death cap containing amatoxin [17,43]. The paper is an attempt to describe some of these cancer-causing mushrooms found in nature. Mushrooms contain potent mycotoxins mainly developing multiple organs failure causing death in those unlucky enough to consume them. And, if survived, in the long run, they usually found to suffer from cancer. Further, this is advisable to consume them with caution as peoples are quite unable to differentiate them perfectly and only an expert can do the job safely. The pieces of information given in the paper might be useful for better treatment in future for patients showing the symptoms of mushroom poisoning as mycetism, pancytopenia with desquamation of scalp, palms and soles. The physicians should also consider the possibility of ingesting any poisonous mushroom when such symptoms appear.

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**Conflict of Interest**

The authors have declared no conflict of interest. They have approved the final version of the manuscript contributing equally.

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