RESEARCH ARTICLE

Mushroom Poisoning in Thailand: Incidence and Intoxication to Human Health

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ABSTRACT

Mushroom poisoning is one of the public health issues related to food-borne diseases in Thailand and worldwide. This paper revealed the incidence of mushroom poisoning in Thailand between 2008 and 2017 and discussed relevant information involved. About 1,200 to 2,000 reported cases were reported each year with morbidity rates from 1.86 to 3.34 per 100,000 population and mortality rates from 0.12 to 1.12%. Overall, 15,680 patients of mushroom poisoning were reported in Thailand during the 10-year period from 2008 to 2017 with an average of 1,568 patients annually. The cases were reported mainly from northeast and north Thailand. Actually, the incidence of mushroom poisoning increased during rainy season between May and September. The highest risk was found among patients aged between 55 and 64 years and over 65 years followed by the group of 45-54 years. The poison risk to women was always greater than to men with ratios varying between 1.13:1 and 1.70:1 and the incidence was found mainly among farmers and general workers. Four groups of toxins have been found in Thailand including protoplasmic poisons, neurotoxins, gastrointestinal irritants and disulfiram-like toxins. The protoplasmic poisons are a major cause of death in most cases and are found among some mushrooms, such as *Amanita exitialis*, *A. fuliginea*, *A. fuligineoides* and *A. gleocystidiosa*. Gastrointestinal irritants are the most common toxins found in all regions of Thailand and found among some mushrooms, such as *Chlorophyllum molybdites*, *Russula* sp., *Cantharocybe virosa*, *Entoloma* sp., *Lactarius* sp.and *Tricholoma* sp. Commonly, consumption of poisonous mushrooms is usually a result from misidentification of some poisonous ones, closely similar to those of the commonly edible mushrooms. Therefore, educating the public to recognize poisonous mushrooms to avoid to harvesting them for consumption or sale is urgently needed.

Keywords: Mushroom, Poisoning, Toxin, Consumption, Health, Thailand

INTRODUCTION

Mushrooms are commonly found throughout the world and are an important source of food for humans. About 140,000 species of mushrooms have already been identified.[1] Among these, approximately 2,000 species are recognized as edible mushrooms while about 700 species are considered as medicinal ones.[1] Thailand is located in a tropical area in Southeast Asia with a high degree of biodiversity; and as a result, many species of mushroom can be found in forest areas. Almost 2,000 species of edible and inedible mushrooms are distributed around the country.[2] Mushrooms have been commonly consumed by Thais. However, mushroom poisoning is also one of the major public health issues related to food-borne diseases in Thailand. Mushroom poisoning resulting in death is reported by the Ministry of Public Health yearly and remains a significant cause of poisoning-related mortality in the country.[3] This study intended to investigate the epidemiology of mushroom poisoning in Thailand during the past decade. Information about poisonous mushrooms and their toxins found in Thailand were revealed and discussed.Some attempts to minimize the incidence were also investigated and solutions suggested.

MATERIALS AND METHODS

The data on the incidence of mushroom poisoning in Thailand between 2008 and 2017 was obtained using online published annual reports of the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand.[4-13] The information about mushroom species identification using molecular techniques and laboratory detection of toxins in mushroom samples was obtained from the Toxicology Center, National Institute of Health (Thai NIH) and the published annual reports of the National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Thailand.[14] The molecular techniques for species identification of mushrooms included DNA extraction, PCR amplification, DNA sequencing, fungal identification using BLAST and BOLD-IDS, sequence alignments and phylogenetic analyses while the liquid chromatography mass spectrometry (LC-MS) method was used to detect toxins in the mushrooms.[15] All data were statistically calculated and presented as proper figures.

RESULTS AND DISCUSSION

The annual incidence of mushroom poisoning in Thailand from 2008 to 2017 is shown in Figure 1. As can be seen, about 1,200 to 2,000 cases were reported each year with a morbidity rate between 1.86 and 3.34 per 100,000 population during that period. The lowest incidence of mushroom poisoning was found in 2016 with 1,220 reported cases while the highest in 2012 reported 2,148 cases. Overall, 15,680 mushroom poisoning patients were reported in Thailand during the 10-year period between 2008 and 2017 with an average of 1,568 patients/year. This incidence is dramatically high as compared with other countries, such as Japan (192 patients/year),[16] Switzerland (79 patients/year),[17] Hong Kong (67 patients/year)[18] and Korea (21 patients/year).[19] Therefore, minimizing the incidence of mushroom poisoning in Thailand is urgent needed as much as possible using various strategies. However, the number of people reporting mushroom poisoning in Thailand yearly should be higher than those reported in the Figure 1 because people presenting only mild symptoms after ingesting the mushrooms do not want to visit hospitals, especially those living in remote areas with poor access to health services. Normally, the number of reported mushroom poisoning cases increases during the rainy season between May and September. In fact, this is the best period for mushroom growing in Thailand, especially for those residing in forests. Thais collect many mushrooms from the forests nearby their homes for consumption in their families as well as for local sale.

Some commonly edible mushrooms, such as *Termitomyces fuliginosus*, *Termitomyces globulus* and *Astraeus hygrometricus* have relatively high prices in the market, approximately 600-1,000 THB/kg (USD 20-35/kg). Therefore, many Thais are active in harvesting edible mushrooms in the forests during rainy season yearly to supplement their income.

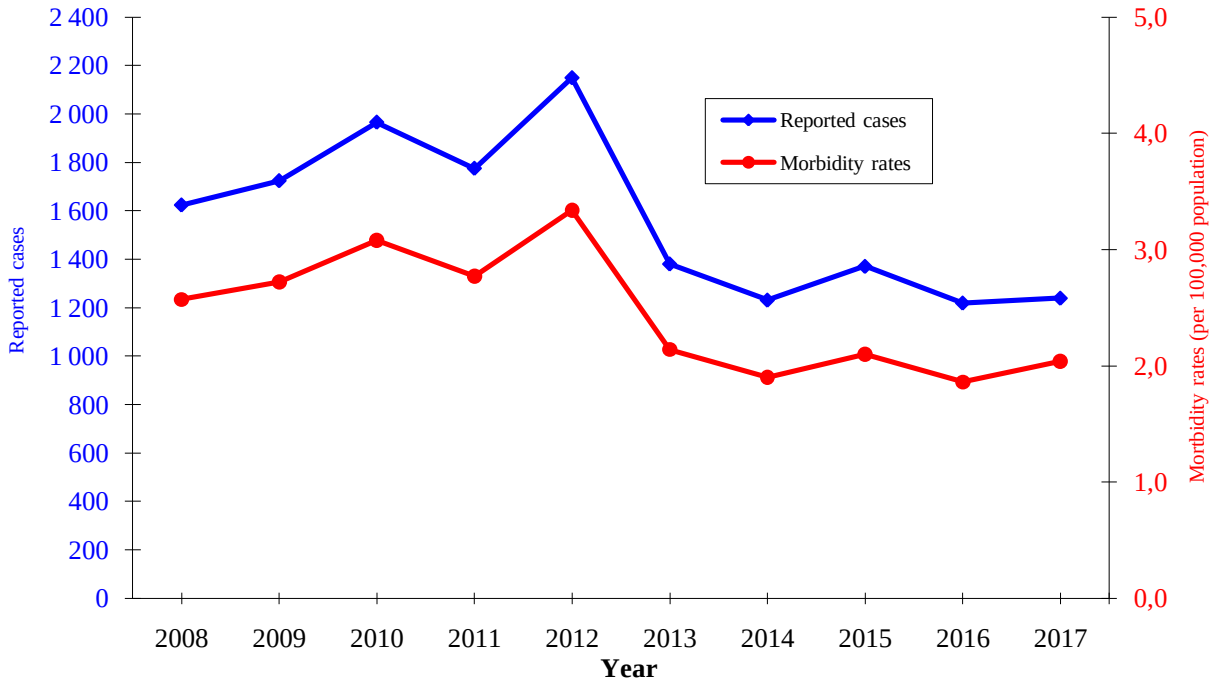

Figure 1. Reported cases and morbidity rates of mushroom poisoning in Thailand, from 2008 - 2017.

The number of reported deaths because of poisonous mushrooms and mortality rates (%) between 2008 and 2017 are presented in Figure 2. The lowest incidence (2 deaths) was found in 2009 with 0.12% mortality whereas the highest (24 deaths) was found in 2012 with a 1.12% mortality rate. Overall, 79 patients died by mushroom poisoning in Thailand from 2008 to 2017 with an average of about 8 deaths annually. Most cases were caused by consuming poisonous mushrooms from the genus *Amanita*. Actually, the severity of mushroom poisoning depends mainly on the species poisonous mushrooms ingested, the amount of toxins received, the cooking process and individual response to the toxins. Many toxins produced by poisonous mushrooms can affect the organs, varying from mild to severe symptoms. Cooking methods, such as boiling, grilling or stir-frying cannot affect the toxicity of some mushrooms because the toxins are heat stable. As for the individual response, the elderly and children are at higher risk for the serious effects from mushroom poisoning than healthy young adults.[20] In this study, the highest risk was usually found among the patients aged between 55 and 64 years and over 65 years, followed by the group 45-54 years. As can be seen, most cases of mushroom poisoning in Thailand commonly occurred among adults with ages at least 45 years old. Additionally, the poison risk to women was always greater than men from 2008 to 2017, with ratios varying between 1.13:1 (in 2011) and 1.70:1 (in 2017) and was found mainly among farmers and general workers.

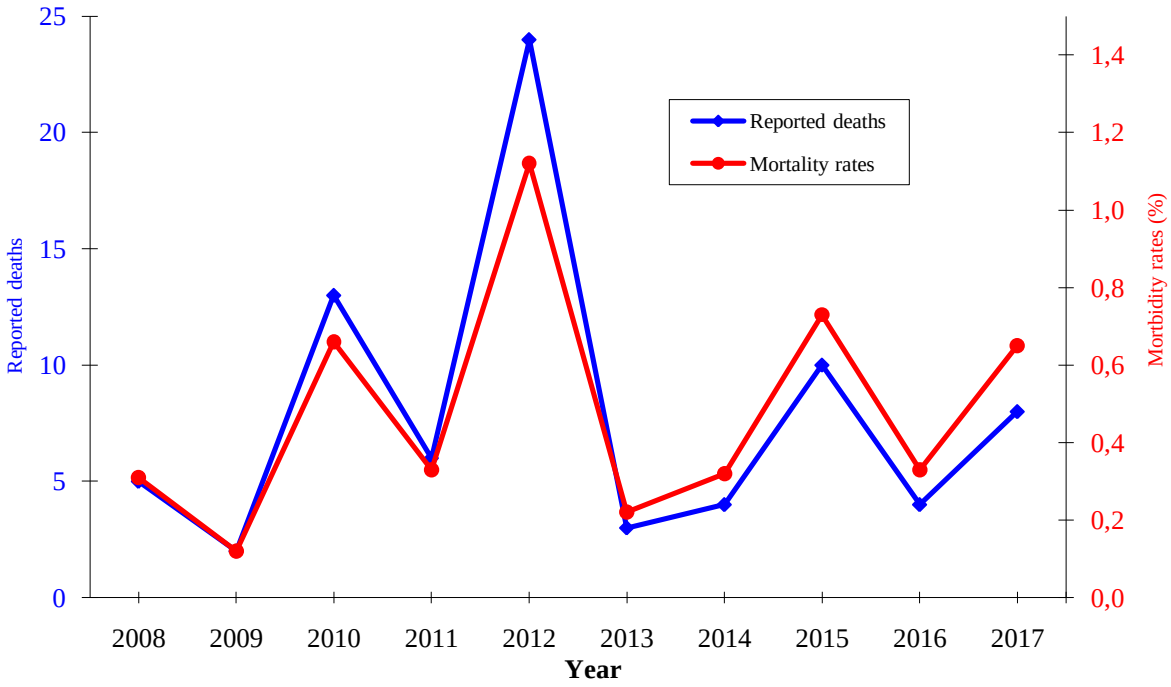

Figure 2. Reported deaths and mortality rates of mushroom poisoning in Thailand, from 2008 - 2017.

Mushroom poisoning can be classified in four groups by the physiological effects: protoplasmic poisons, neurotoxins, gastrointestinal irritants and disulfiram-like toxins.[21] These poisoning categories have been found in various regions of Thailand (Figure 3). Firstly, the protoplasmic poisons are toxins that destroy cells of some organs, such as the liver and kidney; as a result the organs fail and possible death. The toxins found in this group include amatoxins, gyromitrins and orellanine that produce hepatotoxicity.[22-23] Among these, amatoxins are the most toxic and cause over 95% of mushroom-related fatalities in the US.[22] The ten known amatoxins, include alpha-, beta- and gamma-amanitins, etc., and alpha-amanitin is the primary toxin damaging liver and kidney cells.[24] A single mushroom may contain about 5-7 mg of amatoxin and could cause death when ingested; even the small amount of 0.1 mg amatoxin/kg body weight could cause human death.[25] The four stages of clinical symptoms comprise latency phase, gastrointestinal phase, clinical remission and multiple organ failure.[24] The latency phase, without presenting any symptoms could last about 6-24 hours after mushroom ingestion. Later, the gastrointestinal phase occurs among patient with symptoms such as nausea, vomiting, profuse watery diarrhea and abdominal pain, typically lasting 1-2 days then followed by brief clinical remission.[24] Multiple organ failure is the final stage when at the start damaged liver and kidney cells, leading to systemic failure in both organs within 2-7 days after mushroom consumption and death could occur in severe case within 4-16 days.[24,26] However, rapid diagnosis and appropriate treatment could substantially alter mortality by amatoxin poisoning as fatalities may be reduced from 50-60% to less than 5% with good supportive care.[20] Mengs et al[27] pointed out the reasonable use of silibinin as Legalon® SIL in almost 1,500 amanita poisoning cases. Among these, the mortality rate among patients treated with intravenous silibinin (Legalon® SIL) is less than 10% as compared with more than 20% when using penicillin alone or a combination of silibinin and penicillin.[27] On the other hand, treatment with oral high dose silymarin could

be one of the principal treatments in amatoxin poisoning when silibinin is unavailable as it could provide about a 87% survival rate in severe cases.[28] In addition, liver transplantation could be lifesaving for those severe cases with acute liver failure.[29] Some poisonous mushrooms in Thailand containing protoplasmic poisons include *Amanita exitialis*, *A. fuliginea*, *A. fuligineoides*, *A. gleocystidiosa* (Figure 4, no.1-4) and *A. virosa* and are found in the north, northeast and central regions of Thailand (Figure 3).

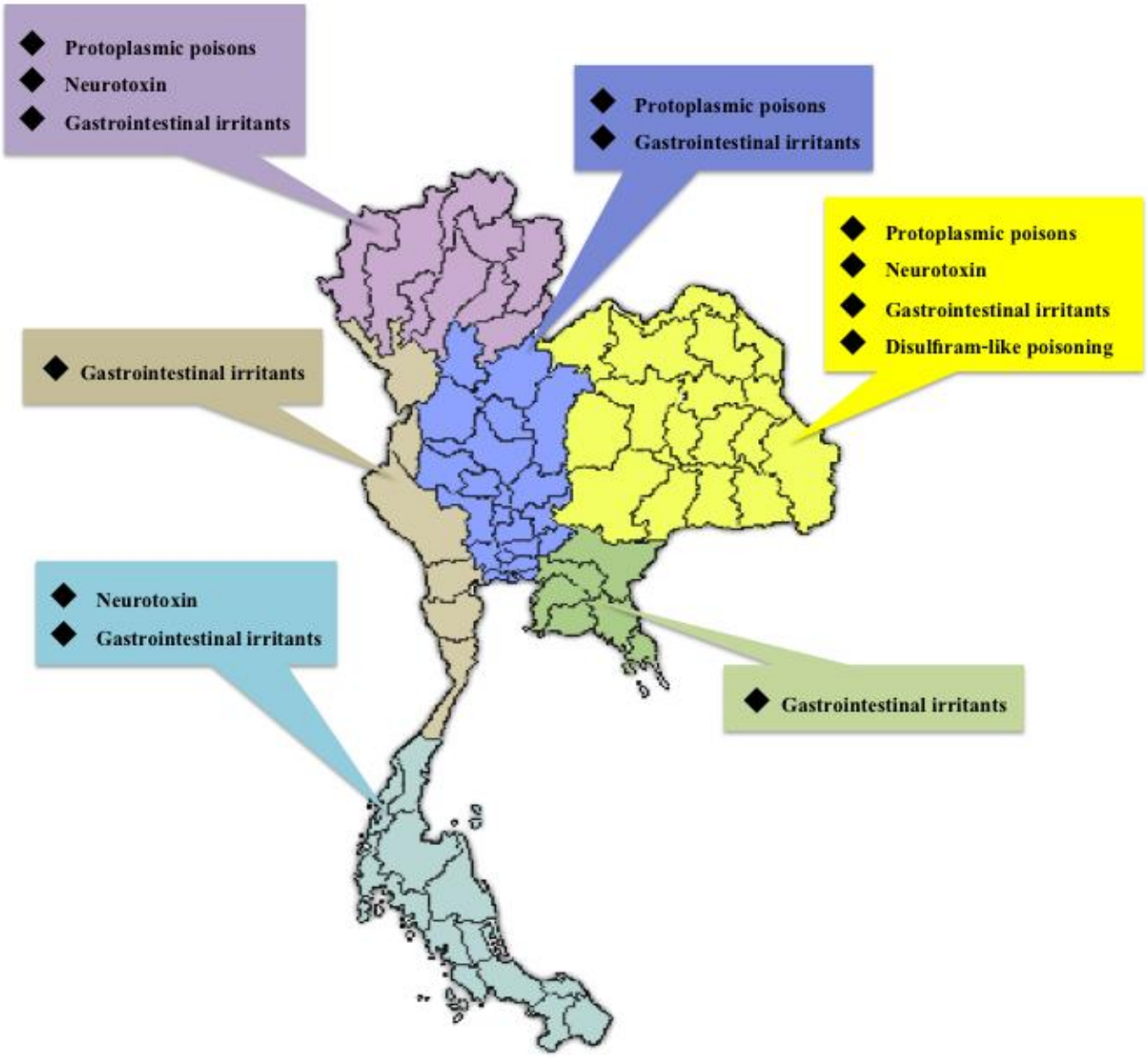

Figure 3. Distribution of mushroom toxins found in various regions of Thailand

Secondly, the neurotoxins cause neurological symptoms including three: muscarine, ibotenic acid/muscimol and psilocybin poisoning.[22] The muscarine toxin causes various symptoms, such as hypersalivation, perspiration, lacrimation, blurred vision, bronchospasm, vomiting, diarrhea, abdominal pain, tremor and bladder contraction. These symptoms usually occur 15 minutes to 5 hours after ingestion of the poisonous mushroom.[24] Symptoms caused by ibotenic acid/muscimol poisoning include drowsiness, delirium, dysphoria and vertigo that may last for a few hours, whereas those of psilocybin poisoning

involve hallucinations that may decrease within 2 hours.[22] Fatalities by mushrooms containing neurotoxins are rarely found among adults but may among children when large amounts of the mushrooms are ingested.[22] Supportive treatment with fluid and electrolytes may be necessary for those neurotoxins.[24] *Amanita muscaria, A. pantherina*, *Clitocybe* sp., *Inocybe* sp. (Figure 4, no. 6-7), *Entoloma* sp. (Figure 4, no. 10) are poisonous mushrooms containing neurotoxins and are found in north, northeast and south regions of Thailand (Figure 3).

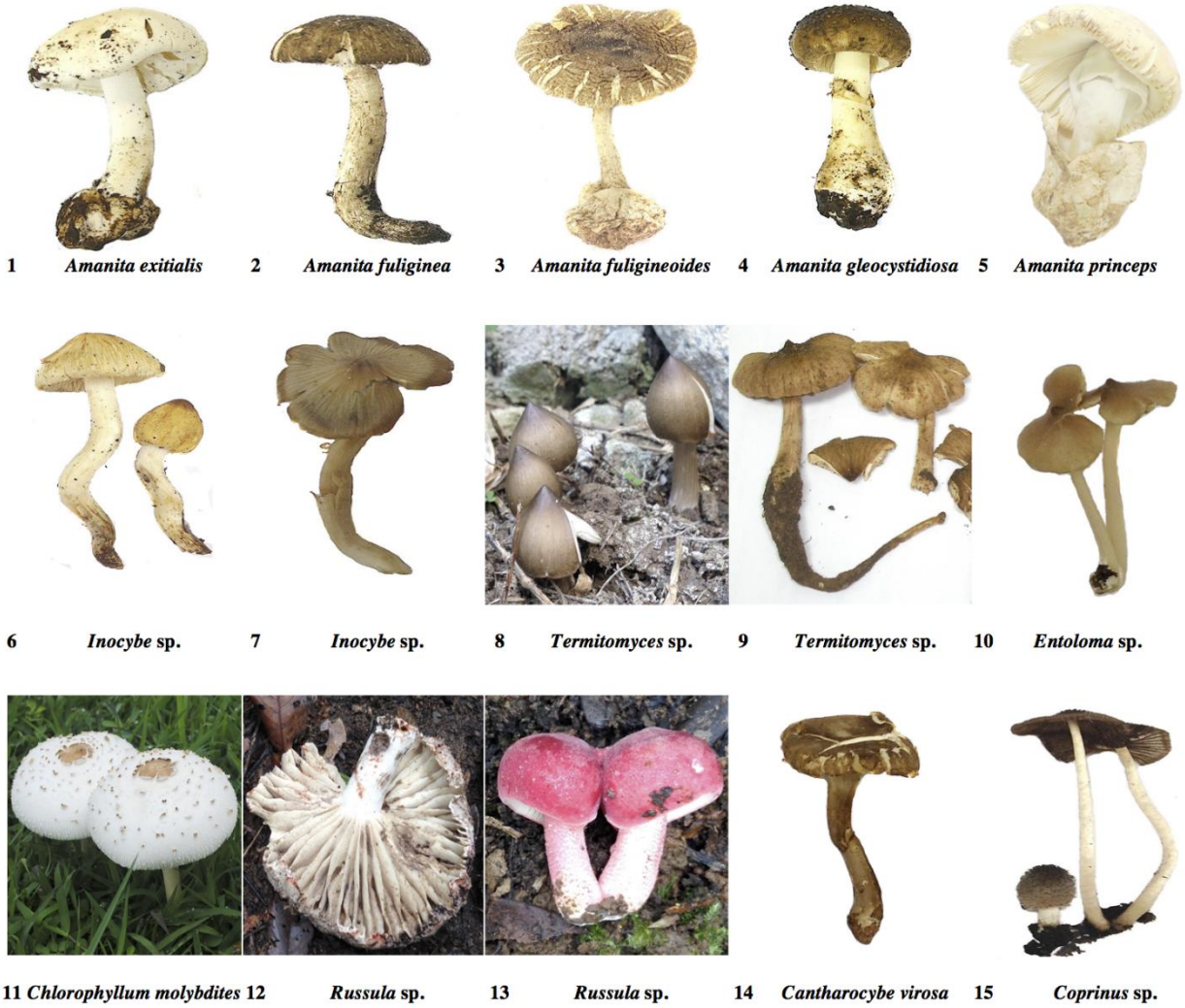

Figure 4. Species of poisonous mushrooms containing various toxins: Protoplasmic poisons (1. *Amanita exitialis*, 2. *Amanita fuliginea*, 3. *Amanita fuligineoides*, 4. *Amanita gleocystidiosa*), Neurotoxins (6-7. *Inocybe* sp., 10. *Entoloma* sp.), Gastrointestinal irritants (11. *Chlorophyllum molybdites*, 12-13. *Russula* sp., 14. *Cantharocybe virosa*), Disulfiram-like toxins (15. *Coprinus* sp.) and nonpoisonous mushrooms (5. *Amanita princeps*, 8-9. *Termitomyces* sp.) found in Thailand

Thirdly, gastrointestinal irritants are toxins that cause abdominal pain, nausea, vomiting and profuse diarrhea.[24] Symptoms usually occurred between 30 minutes and 4 hours after ingesting the suspected mushroom. Fatalities caused by these toxins are rare; however, the severity could occur among very old or young patients due to extensive dehy-

dration and electrolyte imbalances.[22] Therefore, fluid and electrolyte replacement are the actual treatment.[24] Some poisonous mushrooms in Thailand containing gastrointestinal irritants include *Chlorophyllum molybdites*, *Russula* sp., *Cantharocybe virosa* (Figure 4, no. 11-14), *Entoloma* sp., *Lactarius* sp. and *Tricholoma* sp. Notably, mushrooms having gastrointestinal irritants are found in all regions of Thailand (Figure 3). Similarly, *C. molybdites* is commonly found on lawns in the US and it is also recognized as the representative GI toxic mushroom of the country.[24]

Lastly, disulfiram-like toxins are normally nontoxic among humans but will cause illness when consumed with alcohol within 72 hours after ingesting the poisonous mushroom. *Corprinopsis atramentaria*, *Corprinopsis* sp. and *Coprinus* sp. (Figure 4, no.15) are poisonous mushrooms containing disulfiram-like toxins found in Thailand. Actually, the mushrooms produce coprine, a toxin inhibiting the breakdown of alcohol beverages consumed within 72 hours after ingesting the mushroom.[22] The illness includes headache, flushing, diaphoresis, nausea, vomiting, tachycardia, hypotension, palpitations, dizziness and dyspnea and symptoms may last for a few hours.[22,30] Actual treatment is supportive using fluid and electrolyte replacement[24]; however, patients with severe symptoms may benefit by receiving fomepizole.[22] Surprisingly, poisonous mushrooms having disulfiram-like toxins are found only in the northeast region of Thailand at present (Figure 3).

In a study conducted in Thailand in 2012, a total of 113 samples received from mushroom poisoning cases were collected between 2008 and 2012 and examined for species and their toxins.[31] Among these, only 58 samples could be identified whereas the 55 samples remained unclassified. Of the 58 known mushrooms, 35 samples were revealed to be poisonous, belonging to various genera, such as *Amanita*, *Entoloma*, *Clitocybe*, *Agaricus*, *Lepiota*, *Russula*, *Boletus*, *Hygrocybe*, *Alboleptonia*, *Geastrum*, *Lactarius*, *Pisolithus*, *Psilocybe*, *Scleroderma*, and *Mycena*. However, only 15 species could be identified and these included *Amanita* cf. *bisporigera*, *Boletus* cf. *rubiicolor*, *Chlorophyllum molybdites*, *Clitocybe* cf. *odora*, *Clitocybe* cf. *atrobrunnea*, *Entoloma* cf. *rhombispora* var. *rhombispora*, *Entoloma* cf. *occultipigmentatum*, *Entoloma* cf. *pallidaavum*, *Entoloma* cf. *strictius*, *Entoloma talisporum*, *Gaestrum saccatum*, *Inocybe* cf. *agardhii*, *Pisolithus tinctorius*, *Psilocybe cubensis* and *Scleroderma verrucosum*.[31]

From 1 October 2014 to 30 September 2015, a total of 225 samples of mushrooms were sent to the Toxicology Center, National Institute of Health, Thailand (Thai NIH) for laboratory identification of mushroom species and toxin.[14] These samples were collected from patients admitted in hospitals with a diagnosis of food poisoning after mushroom ingestion. Three groups of toxins were identified as gastrointestinal irritants (75%), protoplasmic poisons (α-amanitin 9.9%, β-amanitin 3.4%) and alkaloid muscarine (11.7%). The toxins of gastrointestinal irritants were identified from the poisonous mushrooms in the genus *Chlorophyllum*, *Entoloma*, *Lactarius*, *Russula* and *Tricholoma*. The cyclopeptides were from *Amanita* while the alkaloid muscarines were from *Clitocybe* and *Inocybe*.

The correct diagnosis of mushroom poisoning should be based on clinical features, laboratory investigations and mushroom identification. The clinical features of patients are always observed by physicians and laboratory investigations are also conducted in hospital whereas the suspected mushrooms must be sent to the Toxicology Center, the reference laboratory in Thailand to identify the mushroom species. Identifying mushrooms when the sample is inappropriate is difficult. The right identification requires an appropriate sample of the suspected mushroom. The whole mushroom should be preserved as much as possible for the original characteris-

tics of the stem, bulb and cap. In addition, the mushrooms should be individually kept in a dry paper bag, not cloth or plastic. Transporting the mushrooms with these practices could minimize destruction of their natural characteristics.[22] However, mushroom samples usually sent to the Toxicology Center for the laboratory to identify the mushroom species and toxins were frequently inappropriate because they were sent from a remote areas taking many days to transport. The mushroom samples were then usually decayed and unable to be identified by morphological characteristics. Also, some mushrooms were already cooked. Therefore, attempts have been made by staff of the Toxicology Center, Thai NIH to develop methods for detecting poisonous mushroom species using DNA barcoding, a technique that can be used to identify species of organisms quickly and precisely using standard DNA fragments compared with reference databases.[15] The internal transcribed spacer (ITS) region of nuclear ribosomal DNA was then selected to be used for this purpose. Widely used to study genetic variability and the divergence of closely related species of various mushrooms,[32] it is also recognized as the universal barcode region for fungal identification.[33] As a result, Parnmen et al[15] in 2016 succeeded in molecular identification of poisonous mushrooms using nuclear ITS sequence data in 26 mushroom samples eaten in nine fatal cases from 2008 to 2014. Three species of mushrooms: *Amanita exitialis*, *Amanita fuliginea* and *Amanita* sp. 1 were identified and newly recorded as the causes of death in those fatal cases. Interestingly, this was also the first time to reveal the presence of *A. exitialis* in Thailand.[15] Presently, we can use the molecular technique to precisely identify many species of the poisonous mushrooms, especially those in the genus *Amanita* which is the most important one that always cause fatal cases in Thailand. Additionally, the technique was also applied to identify some wild mushrooms in the genus *Tylopilus* and *Parvixerocomus* that caused two fatal cases.[34] However, we are going to expand this technique to identify other genera of poisonous mushrooms found in Thailand as well.

To explore as many poisonous mushrooms in Thailand as possible, attempts have been made by staff of the Toxicology Center and the Regional Medical Science Centers, Department of Medical Sciences (DMSc) to survey fresh mushrooms found in forests throughout Thailand, especially those in the areas with reported cases of mushroom poisoning. The collected mushrooms have been identified properly by their morphological characteristics and molecular techniques to identify species. According to the genus and species identified and the relevant literature review, the collected mushrooms were also investigated for the potential toxins that they may contain. The information obtained from these investigations will be established as a database of poisonous mushrooms in Thailand. This will be valuable for local people to know more about the poisonous mushrooms in particular areas that they must avoid harvesting for consumption or sale, especially those species that closely semble edible mushrooms. In Figure 4, for instance, poisonous mushrooms containing protoplasmic poisons: *A. exitialis* (no. 1), *A. fuliginea* (no. 2), *A. fuligineoides* (no. 3) and *A. gleocystidiosa* (no. 4) are closely similar to the edible mushroom *A. princeps* (no. 5), while those containing neurotoxins: *Inocybe* sp. (no. 6-7) also closely resemble the edible mushroom, *Termitomyces* sp. (no. 8-9). In addition, a detailed comparison of similar mushrooms of the genus *Amanita* was also conducted by staff of the Toxicology Center to discriminate the differences between (a) *Amanita princeps*, an edible mushroom commonly consumed by Thais and (b) *Amanita exitialis*, a poisonous mushroom containing fatal toxins (α-amanitin, β-amanitin and phallacidin) (Figure 5). Obviously, it provides three significant points of differences that can help people to easily distinguish poisonous mushrooms when they harvesting them.

(a) (b)

Figure 5. Comparison of similar mushrooms of the genus *Amanita*, (a) *Amanita princeps*, an edible mushroom commonly consumed by Thais (b) *Amanita exitialis*, the poisonous mushroom containing fatal toxins (α-amanitin, β-amanitin and phallacidin)

In Thailand, misconceptions abound from folk knowledge about mushroom consumptions, such as boiling or stir-frying mushrooms make them safe for human consumption, a silver spoon will turn blackish in contact with poisonous mushrooms, mushrooms that have been partially bitten by insects are safe for humans, vinegar or salt can detoxify toxins in poisonous mushrooms, poisonous mushrooms tarnish garlic or rice grains, the soup will turn blackish when boiling poisonous mushrooms with onions and poisonous mushrooms are always colorful while the edible ones are usually white or pale. This local knowledge false needs to be corrected by government agencies for the right understanding by the public. Recently in 2018, the DMSc published a handbook of poisonous mushrooms (in Thai) for people to easily learn about poisonous mushrooms found in Thailand (Figure 6). This book provides important information relevant to poisonous mushrooms, such as the toxins found in particular mushrooms, discriminating between poisonous mushrooms from edible ones, misconceptions on testing poisonous mushrooms, suggestions for safe consumption of mushrooms, first aid treatment after ingesting poisonous mushroom and proper treatment and appropriate collection and transportation methods of suspected poisonous mushrooms for laboratory identification. Additionally, the DMSc has also attempted to develop a mobile application to distinguish between poisonous and edible mushrooms. This alternative advanced device could help people to easily differentiate poisonous mushrooms in the field for safer harvesting mushrooms.

Figure 6. A handbook of poisonous mushrooms (in Thai) for public awareness published by the Department of Medical Sciences (DMSc) for Thais to easily learn about poisonous mushrooms found in Thailand

In conclusion, mushroom poisoning remains an important health issue in Thailand. Annual incidence has been relative high with some reported of deaths during the past decade. Therefore, educating the public to recognize poisonous mushrooms and avoid harvesting them for consumption or sale is urgently needed. Public awareness plays an important role to prevent and minimize the incidence of mushroom poisoning.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

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