

Adverse effects and intoxications related to medicinal/harmful plants

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ABSTRACT

Many wild plants around us have beneficial effects on our body and can be used as food. People are more and more interested in the medicinal plants. Many of them began gathering and preparing plants for the relief of symptoms of diseases or as a food dietary. Due to the lack of knowledge of plants, mistaking plants that contain toxins for medical plants may happen and cause adverse effects or even poisoning. The Poison Control Centre in Ljubljana keeps records of patients who have been admitted to the department because of adverse effects from the ingestion of certain plants. We analysed 64 cases, which were registered by the Poison Control Centre between January 2000 and December 2013. The aim of the present study was to determine which plants cause the most intoxications in Slovenia.

Key words: medicinal plants, intoxication, misidentification, abuse, suicidal attempt

IZVLEČEK

ŠKODLJIVI UČINKI IN ZASTRUPITVE Z ZDRAVILNIMI/STRUPENIMI RASTLINAMI

Mnogo rastlin, ki nas obdaja, ima blagodejen vpliv na naše zdravje in so lahko dodatek k prehrani. Ljudje se vse bolj zanimajo za zdravilne rastline. Ljudje so začeli sami nabirati divje rastoče rastline in jih pripravljati za lajšanje bolezenskih simptomov ali kot dodatke k hrani. Zaradi nepoznavanja rastlin pa se lahko dogajajo zamenjave zdravilnih rastlin z rastlinami, ki vsebujejo strupene snovi in lahko povzročajo neželene učinke ali celo zastrupitve. Center za zastrupitve v Ljubljani beleži paciente, ki so bili sprejeti na njihov oddelek zaradi neželenih učinkov, ki so jih utrpeli po zaužitju nekaterih rastlin. Preverili smo 64 primerov, ki so bili zapisani na Centru za zastrupitve v časovnem obdobju od januarja 2000 do decembra 2013. Cilj raziskave je bil prikazati, katere rastline predstavljajo največji problem v Sloveniji.

Ključne besede: zdravilne rastline, zastrupitev, napačna identifikacija, zloraba, samomorilnost

1 INTRODUCTION

Several wild plants have beneficial effects on human health. In developing countries herbal drugs play an important role in health care (Matthews et al., 1999; Philomena, 2011). In the past two decades there has been an increase in the use of medicinal herbs. People are increasingly seeking for herbal remedies in self medication which includes complement to conventional therapies, and maintaining their overall health condition and well-being (Spiteri Staines, 2011). There are

additional advantages of medicinal herbs, some of which are that they are cheap, easily produced, in proper combination they can meet nutritional needs and they are found in all climates and terrains. There is a general belief amongst consumers around the world that medical herbs are inherently safe, because they are "natural". However, just because the product is natural, that does not assure their safety (Colombo et al., 2010; Spiteri Staines, 2011; Philomena, 2011; Matthews et al., 1999).

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All medical agents have potentially unexpected effects including toxicity and interactions, and herbs are not different. However, they are less likely adverse effects than in using conventional drugs and if such effects occur, they are mild and only affecting a small number of people (Philomena, 2011; Spiteri Staines, 2011). Contact with plants was rarely responsible for serious poisoning (Fuchs et al., 2011). Flowering plants produce thousands of secondary metabolites (alkaloids, flavonoids, saponins, tanins, essential oils, etc.), which can be either useful or very noxious for human health. It is believed they are involved in the production of poison that they use for protection from browsing animals and plant-eating insects (Colombo et al., 2010). When overdosed, incorrectly used or used regularly over a long period of time, some plants that possess "harmful effects", have the potential to induce adverse effects (Matthews et al., 1999). Consumers are largely uninformed about the possibility of adverse effects. Although most botanical products are probably safe under most conditions, some are known to be toxic at high doses and others may have potentially adverse effects under some conditions. Just as with many foods and pharmaceuticals, there is a possibility of allergic reactions (Philomena, 2011). Any pharmaceutically active agent has the potential to result in synergistic or antagonistic interaction when consumed with other pharmaceutically active compounds. Increased self-medication also increases the chance of adverse reactions to these products as well as adverse drug/herb or herb/herb interactions (Matthews et al., 1999). Patients may also substitute more conventional therapies for herbal remedies without informing the doctor. Negative effects can result from bad communication between the patient and a healthcare professional, which include adverse effects or drug-herb interactions (Kosalec et al., 2009; Spiteri Staines, 2011; Ghosh and Ghosh, 2009). The solution for that problem would be proper education and effective communication. Occasionally, plants can grow in contaminated environments. There are biological and chemical contaminants in the air and in the soil, which accumulate into the herbs (Kosalec et al., 2009). Plants can therefore contain unwanted constituents, such as heavy metals, or can be even deliberately adulterated with pharmaceutical ingredients (Philomena, 2011).

Accidental poisoning with plants should also be mentioned. Using plants as food can lead to accidental poisoning. In order to eat fresh or cooked herbs and plants, mainly during spring and summer, some people prefer to spend their free time outdoors picking up young shoots, young leaves and buds of wild plants without having sure knowledge of plant identification (Colombo et al., 2010). They use them to make fresh salads or cook them in soups. In Europe, severe plant poisoning is a rare event for which a small number of specific plants appear to be mainly responsible. In Slovenia serious poisoning in adults is most commonly caused by autumn crocus (*Colchicum autumnale* L.). Wrong identification between autumn crocus and wild garlic (*Allium ursinum* L.) leads to poisoning. The use of wild garlic has increased dramatically in the last few years. This plant, often used as a spice, grows wild in groundlayer vegetation of several broadleaved forests in Central Europe. Leaves of wild plants collected during spring for food purpose may be responsible for intoxications. Its raw leaves are mainly used to flavour spreads based on cottage cheese, soups and sauces (Gilotta and Brvar, 2010; Fuchs et al., 2011). Dried leaves usually have a very faint odour (Colombo et al., 2010). Because of their great similarity the patients mistakenly ingested autumn crocus instead of wild garlic. Accidental colchicine poisoning is not uncommon. All parts of autumn crocus are toxic and contain an alkaloid called colchicine, which blocks the cell division by inhibition of mitosis (Gilotta and Brvar, 2010; Sundov et al., 2005). Concentration of colchicine reaches a maximum content in the seeds (Gaillard and Pepin, 1999). Crude seeds were used for medical purposes (Sundov et al., 2005). Two to five hours after ingestion the patient develops nausea and diarrhoea, along with gastrointestinal symptoms (Gilotta and Brvar, 2010; Brvar et al., 2004; Nagesh et al., 2011; Brnčić et al., 2001; Sundov et al., 2005). In cases when patients consumed higher doses, they died of multi-organ dysfunction (Klitschar et al., 1999). However, there are other poisonous plants with similar elliptical leaves as wild garlic which grow in similar environments and their vegetation period falls into the same time as wild garlic: white hellebore (*Veratrum album* L.) and other species from the genus *Veratrum* and Lily-of-the-Valley (*Convallaria majalis* L.). Both of them contain a mixture of different alkaloids.

Accidental poisoning with white hellebore or Lily-of-the-Valley mistaken for wild garlic is possible. Both plants do not show even traces of garlic odour, but their leaves are particularly similar (Gilotta and Brvar, 2010; Columbo et al., 2010; Klintschar et al., 1999; Meyer et al., 2009). Poisoning with Lily-of-the-Valley rarely occurs, but it is possible because both of them have elongated-elliptic leaves (Meyer et al., 2009). It contains digitalis toxins and is considered a mildly poisonous plant (Klintschar et al., 1999; Gaillard and Pepin, 1999). Interestingly, in accidentally poisoned patients white hellebore was nearly always mistaken for yellow gentian (*Gentiana lutea* L.) (Gilotta and Brvar, 2010; Rauber-Lüthy et al., 2010). Roots of yellow gentian are used to aromatize home-made distilled products. These roots have to be harvested in the autumn, when the yellow flowers disappear and its leaves go brown. Unfortunately, the stem and the leaves of gentians are very similar to those of *Veratrum* species, plants containing a mixture of toxic alkaloids called veratrin. The alcohol in brandy is able to extract the toxic alkaloids from the roots and the “grapa” becomes toxic (Columbo et al., 2010; Grobosch et al., 2008). White hellebore that can be mistaken for yellow gentian contains alkaloids that are soluble in alcohol, so the use of it in an alcoholic drink leads to faster absorption of toxic alkaloids and more rapid onset of symptoms (Gilotta and Brvar, 2010). Symptoms that occur after ingestion are mainly nausea, vomiting, vertigo and in some cases headache (Rauber-Lüthy et al., 2010).

There are plants containing psychoactive chemicals and other abusable substances around us. When taken for nonmedical reasons, usually for their mind-altering effects, they are called drugs and their use abuse. The most affected are adolescents and young adults (Ghosh and Ghosh, 2009). Jimson weed (*Datura stramonium* L.), especially seeds, is used because of its psychoactive hallucinatory effects. Concentrations of hallucinogen alkaloids vary from plant to plant, the anatomical part of the plant, the preparation method, and various environmental factors. Positive or negative effects depend on the dose (Krenzelok and Mrvos, 2011). There are many signs of poisoning with jimson weed, some of

which are abnormal behavior (delirium), agitation, blurred vision, dry mouth and mucous membranes, thirst, tachycardia, nausea and vomiting, difficulty in swallowing and speech, disturbed bowel function, hyperthermia, hypertension, loss of consciousness and coma (Gaire and Subedi, 2013). The number of patients poisoned by deadly nightshade (*Atropa belladonna* L.), a perennial bushy herb with black, shiny and sweet berries in autumn, is also not negligible. Some patients consumed the deadly nightshade by mistake instead of blueberries (*Vaccinium corymbosum* L.). Deadly nightshade is frequently taken by adults for the purpose of suicide or to experience its hallucinogenic effect. Accidental consumption in adults is rare (Cikla et al., 2011). Unfortunately the berries of the deadly nightshade contain some tropane alkaloids (hyoscyamine, atropine and scopolamin) (Columbo et al., 2010). The part of the deadly nightshade that contains the most alkaloids is the stem (Gaillard and Pepin, 1999). Children are most vulnerable because they do not realize the danger, and are attracted by the smell or color of plants. The number of death cases is slightly higher in adults, because most of the deaths are the result of deliberate poisoning by certain toxic plants (Krenzelok and Mrvos, 2011). At greater risk to adverse health effects associated with medicinal herbs may be young children, pregnant women and the elderly, who are more sensitive and thus more vulnerable to adverse effects. Intensity of adverse effects also depends on users age, gender, genetics, nutrition status, concurrent disease states and treatments (Matthews et al., 1999; Staines, 2011). Another important limitation is the difficulty determining the quality of the toxin the patient had been exposed to, because leaves or seeds of the same plant species may contain variable amounts of toxins, depending on the vegetation period, soil, exposure to light, and age of the plant (Fuchs et al., 2011).

The aim of this study was to define the clinical relevance of plant toxicity for humans in Slovenia and to identify which plants may actually lead to severe poisoning. The study obtains an overview of the more common and more relevant plant exposures reported to the University Medical Centre in Ljubljana, Poison Control Centre.

2 MATERIALS AND METHODS

We checked the records of the patients admitted to the Poison Control Centre. In the Poison Control Centre only adults are treated. Among these we further investigated only patients who suffered from the side effects of plant ingestion. In the study we investigated cases that occurred during the

13-year period between January 2000 and December 2013. We analysed 64 cases of human plant exposure, which were reported to the Slovenian Poison Control Centre. Data were edited and graphically staged using Microsoft Excel.

3 RESULTS

During the 13-year period, the Poison Control Centre in Ljubljana recorded a total of 64 cases of human exposure to toxic plants. Annual the number of poisonings with ingested plants varied. Peak intoxications with plants occurred in 2011 (12 cases) and in 2003 (7 cases) (Fig 1). The year with the fewest human intoxications with plants was 2008, with just 2 cases. In 2000 there were no reports of human poisoning with plants.

In 46 cases, the exposure was accidental. From these 46 accidental cases, 39 were because of mistakenly ingested plants (Table 1) and 8 because

of incorrectly usage (Table 2). In 15 cases it was the result of the abuse and in 3 cases the result of a suicidal attempt. In the case of accidental exposure the most frequent plant was autumn crocus. In the case of abuse, jimson weed was the most common plant. *Aconitum*, *Atropa belladonna* and *Lonicera* species were the plants used in suicide attempts. 13 different plants were responsible for the poisonings and side effects in this study. Autumn crocus was at the top of the list with 20 cases, followed by jimson weed with 15 cases, and white hellebore with 13 cases.

Table 1: Number of poisoned patients that mistakenly ingested wild plants reported in the register book between 2000 and 2013

Wild plant used as food	Ingested part of plant	Use	Misidentified plant	Adverse effects	Cases
<i>Allium ursinum</i> L. Wild garlic	Leaves	Cardiovascular benefits	<i>Colchicum autumnale</i> L. Autumn crocus	Abdominal pain, diarrhoea, vomiting, nausea and dizziness, at high doses multi-organ dysfunction	20 (2 fatal)
<i>Allium ursinum</i> L. Wild garlic	Leaves	Cardiovascular benefits	<i>Veratrum album</i> L. White hellebore	Vomiting, nausea, increased sweating	6
<i>Gentiana lutea</i> L. Yellow gentian	Roots soaked in brandy	For stomach problems	<i>Veratrum album</i> L. White hellebore	Vomiting, nausea, increased sweating,	7
<i>Asarum europaeum</i> L. European wild ginger	Roots	Expectorant	<i>Ranunculus ficaria</i> L. Lesser celandine	Nausea, vomiting and diarrhoea	1
<i>Pinus pinea</i> L. Stone pine	Seeds	Food additive	<i>Ricinus communis</i> L. Castor bean	Nausea, headache, heavy breathing, vomiting and diarrhoea	1
<i>Robinia pseudoacacia</i> L. Black locust	Flowers	For inflammation	<i>Laburnum anagyroides</i> Medic. Golden chain or <i>Laburnum alpinum</i> J. Presl Alpine golden chain	Nausea, dizziness, visual disturbances and diarrhoea	3
<i>Ruta graveolens</i> L. Rue or herb-of-grace	Leaves soaked in brandy	For stomach problems	<i>Arnica montana</i> L. Arnica	Nausea, dizziness and vomiting	1

Of the 64 cases included in this study 39 were due to accidental exposure, because of mistakenly ingested plants, and all of them were adults (Table 1). The most frequently accidentally ingested plant was autumn crocus (20 case reports of accidental poisoning with (*Colchicum autumnale*), and white hellebore (*Veratrum album* L.) (13 cases). Of the 64 cases included in this study, mistletoe (*Viscum album* L.) caused adverse effect because of overdose. One patient suffered adverse effects from regularly consuming club moss (*Lycopodium clavatum* L.) over a long period of time. The plant used as a drug was jimson weed. Shoots of Norway spruce (*Picea abies* (L.) H. Karst.) triggered allergic reactions in one case. Of the 64 poisonings included in this study, 2 adult patients attempted suicide by poisoning using *Aconitum napellus* L.Em. Skalicky, deadly nightshade and *Lonicera*

species. In this study 6 different plants were responsible for poisoning, because they were mistakenly ingested. 20 patients ingested autumn crocus, and 13 white hellebore. 26 of the patients ingested the said poisonous plants instead of wild garlic. 7 patients ingested white hellebore instead of yellow gentian. The Poison Control Centre also lists a case, when one patient ingested lesser celandine (*Ranunculus ficaria* L.) instead of European ginger (*Asarum europaeum* L.), and when one patient ingested castor bean (*Ricinus communis* L.) instead of stone pine (*Pinus pine*). 3 patients ingested golden chain species (*Laburnum* spp.) instead of black locust (*Robinia pseudoacacia* L.). One case reported that woman drunk flowers of arnica (*Arnica montana* L.) soaked in brandy instead of rue (*Ruta graveolens* L.).

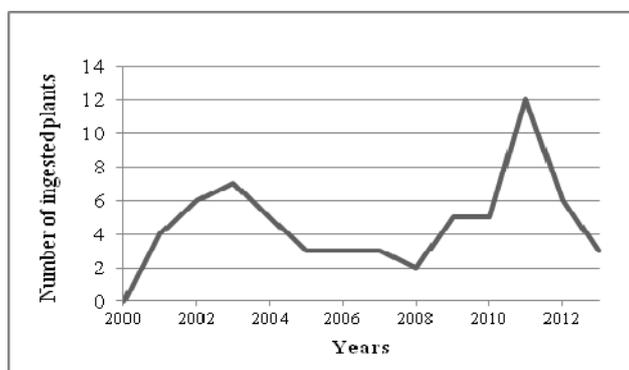


Figure 1: Plant ingestions by year: 2000-2013

Table 2: Number of poisoned patients that incorrectly used wild plants reported in the register book between 2000 and 2013

Plant	Use	Harmless effects	Cases
<i>Viscum album</i> L. Mistletoe	Antispasmodic performance, for regulation of neurosis and high blood pressure	Chest tightness, abdominal pain and diarrhoea	1
<i>Lycopodium clavatum</i> L. Club Moss	For liver and biliary disorders	Fatigue and vomiting	2
<i>Picea abies</i> (L.) Karsten Norway spruce	For respiratory diseases	Allergic reaction	1
<i>Atropa belladonna</i> L. Deadly nightshade	Abuse in some cases	Disorientation, hallucinations	4
<i>Datura stramonium</i> L. Jimson Weed	Abuse	Hallucinations	15
<i>Aconitum</i> spp. Aconite	For suicide attempt	Nausea, vomiting	1
<i>Lonicera</i> spp. Honeysuckles	For suicide attempt	Nausea, vomiting	1

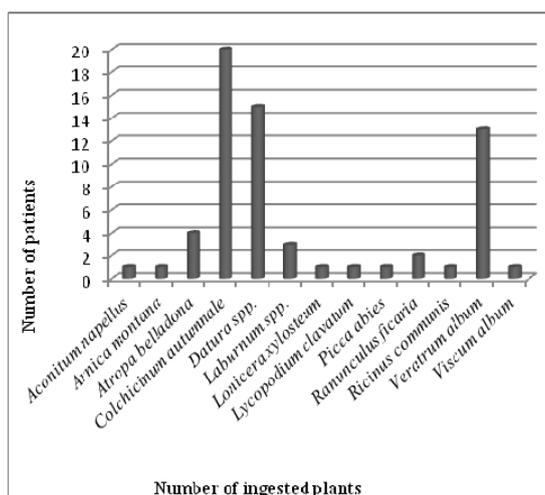


Figure 2: Plants which were ingested by patients in the period between 2000 and 2013

Over 13-year period patients aged 15 to 85 came in contact with poisonous plants (Fig. 3). There were no significant differences between the frequency in

males and females. Most adverse effects occurred to those younger than 18 (10 patients) and those adults aged 45 to 60 years (23 patients).

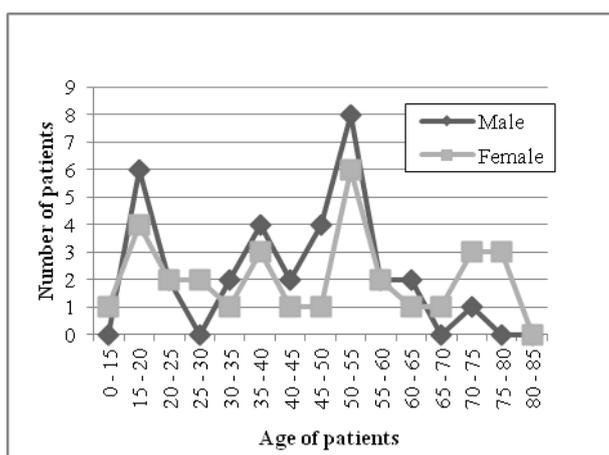


Figure 3: Number of intoxications with plants by sex and age of the patients

4 DISCUSSION

Side effects that occur after the ingestion of plants products are rare. However, the number of such cases is not negligible, and they occur every year. The problem is that people believe just in the benefits of plant products, but there were many more adverse effects about which we do not know about. People would need to be aware that plants contain a number of bioactive compounds which cause adverse effects and toxicity to humans.

Small doses of highly toxic plants are sufficient to induce severe symptoms. Severe and fatal poisoning could also be observed in the accidental settings. At the Poison Control Centre in Ljubljana the most frequent cause of poisoning with toxic plants is accidental poisoning. It was followed by deliberate abuse and suicidal intent. Plant intoxications vary according to the season. Thus the most cases of poisoning were reported in spring

and at the end of summer. Many people prepared salads and soups from wild plants. Ingestion of plants for suicidal intent was performed exclusively by adult patients. Since wild garlic became widely known, many people have tried to pick the plant in the nature. Since there are other toxic plants with similar leaves, several cases of poisoning have been reported in recent years. Particularly similar are autumn crocus (20 cases, 2 of which were fatal), and white hellebore (6 cases). Especially in spring, the leaves of these two plant species look very much alike and are often confused. In these reports, the most common plant species to have caused poisoning was autumn crocus in 20 cases. Two patients, an elderly couple, died after ingestion. The elderly are more sensitive and they died of multiorgan-failure. Intoxications with autumn crocus are followed by jimson weed, which caused serious poisoning in adolescents. The third most commonly ingested toxic plant, which caused seven intoxications, was white hellebore. People mistakenly soaked roots of white hellebore instead of yellow gentian roots in brandy. Four patients accidentally ingested white hellebore instead of wild garlic because of their great similarity, particularly their elliptic leaves and the fact they grow in the same places during spring even though they have different in smell and taste. Two adults ingested species of golden chain flowers (*Laburnum* spp.). Both of them mistakenly used flowers of said plant instead of black locust. Both of the plants have hanging flowers. One

reported case of poisoning was with the castor-oil plant. A man that mistakenly ingested the seeds of that plant thought the seeds belonged to stone pine (*Pinus pinea* L.). There were four cases of poisoning with the deadly nightshade. An elderly woman mistakenly ingested the berries of the deadly nightshade and suffered minor poisoning. That was probably because of her years. In two cases, the mode of poisoning remained unknown. In one case the man ingested the berries of mentioned plant to make a suicide attempt. Mistletoe (*Viscum album* L.) caused adverse effects because of overdose. One patient suffered adverse effects because he had been taking the plant club moss (*Lycopodium clavatum* L.) over a long period of time. The plant taken as a drug was jimson weed: 15 cases were reported, and all of them were adolescents. Shoots of Norway spruce (*Picea abies* (L.) H. Kerst.) triggered allergic reactions in one case. Of the 64 poisonings included in this study, 3 adult patients poisoned themselves with *Aconitum napellus* L. Em. Skalicky and with *Lonicera* in an attempted suicide respectively. Plant-associated poisoning affected all age groups, most frequently adults. In 15 cases, the affected were adolescents and an elderly person, who were poisoned by autumn crocus and the deadly nightshade. There is no significant difference between males and females. The most commonly exposed age groups were those younger than 18 years and those between the ages of 45 and 60 years.

5 CONCLUSION

There are many poisonous plants containing alkaloids that cause adverse effects when ingested. Active molecules in certain plants can cause adverse effects in our body. Serious poisoning with plants seems to be a very rare event in Slovenia. Nevertheless, even accidental ingestions can be responsible for fatal poisonings. When people picking edible wild plants, it is crucial that they are correctly identified, because many are similar to poisonous plants in appearance. Every year in spring such misidentification mistakes regularly

result in poisoning accidents. Autumn crocus and white hellebore are easily mistaken for wild garlic. In addition, many edible plants have poisonous parts. It is important to learn how to identify poisonous plants that grow in the house, yard and neighbourhood. We should only eat plants that we can positively identify and know that they are safe to eat. It is suggested to use caution when picking outdoor wild plants. Warnings in the media about such potentially very dangerous mistakes are far too rare.

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