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Review Article

Evaluation of the effects and side effects of pyrrolizidine alkaloids in medicinal plants

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Medicinal plants are rich in secondary metabolites, the most important of which are alkaloids. Alkaloids are organic compounds that have diverse structural and physiological activity. Pyrrolizidine alkaloids are non-polar compounds that have side effects and harmful effects especially hepatotoxicity in addition to its medicinal properties. Therefore, due to the presence of these materials in some medicinal plants and the importance of these materials and consumption of plants, and monitoring and more precision in these cases, this study was carried out. In this paper, the information has been collected from electronic library resources and from reputable sites such as Google Scholar and Scopus, PubMed, ISI (Web of Science), and the related keywords, which was the benchmark for the period between 1991 and 2019, and about 90 articles and non-electronic resources for pyrrolizidine alkaloids, Medicinal plants, their effects, and their experiences and experiences were evaluated. Pyrrolizidine alkoxides in some dark Vegetable plants such as Leguminosae, Asteraceae, Orchidaceae, Boraginaceae family have been reported. Consumption of herbal products has been commonplace from centuries ago and is vital importance in various parts of the world, today. Many alkaloids are mutagenic and carcinogenic to humans. PAS-containing plants are present in most parts of the world and cause poisoning and damage to humans, livestock and wildlife. Pyrrolizidine alkaloids, which are found in some plants, can be harmed to body tissues, important properties and medicinal effects, of course, have also been reported, which requires it to be used for studying, knowing and recognizing the structure, organs and plants.

Keywords: Pyrrolizidine Alkaloids, Toxic Medicinal Plants, Hepatotoxicity

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Introduction

Medicinal plants and natural products are of great importance since ancient times. They have different biological properties and effects due to their active medicinal ingredients [1]. Because of its climate, soil, agriculture and medicinal plants, Iran is a very important country. Different researches have been carried out to achieve plants' substances and their specifications; also to understand their medicinal and biological properties in order to use them as drugs or medicine [2]. Medicinal plants are enriched with secondary metabolites, of which is Alkaloids. Alkaloids are organic compounds with at least one nitrogen atom in their heterocyclic ring (apart from alkalamines). They have structural varieties and different biological activities [3]. Some of them are important medicinal agents and are used in medicine and pharmacy. Morphine, quinine, atropine, and vincristine are some alkaloids that were used to treat malaria, cancer and other diseases [4]. Some others, like Senecio alkaloids (pyrrolizidine alkaloids or PAs) are toxic. In 6000 angiosperm species, which are only 3 percent of them, there are more than 200 types of PAs [5].

Materials and Methods

In this review article, information was collected from electronic libraries and scientific websites including Scopus, PubMed, Web of science and

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google scholar. Keywords were pyrrolizidine alkaloids, medicinal plants and their specifications, properties and side effects, which had inclusion criteria, between the years 1991 and 2019. 90 articles were found and most of them were used.

Results

Pyrrolizidine alkaloids

Pyrrolizidine alkaloids are non-polar substances. Despite so many varieties, all are divided into two groups: containing toxic N-oxide and non-toxic. (Figure 1)

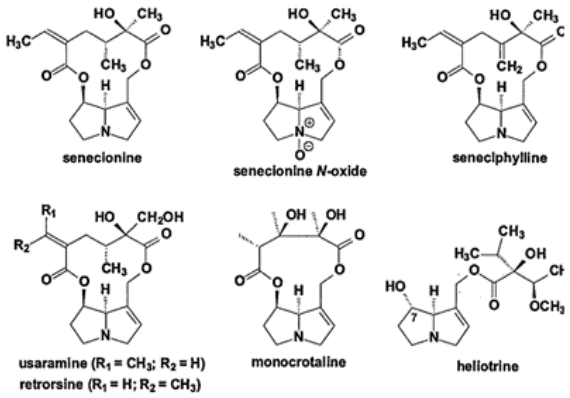

Figure 1 chemical structure of some extracted pyrrolizidine alkaloids

These substances are secondary metabolites of plants, of which are highly toxic [6-8]. Different effects have been observed in these substances including chronic liver toxicity, teratogenicity and carcinogenicity. Others, have therapeutic, anti-cancer and anti-tumor effects [9]. These substances are mostly found in Boraginaceae species [10, 11]. Pyrrolizidine alkaloids are generally hydroxylated 1-methyle pyrrolizidine; unsaturated forms mostly have liver toxicity (Figure 2) [12, 13].

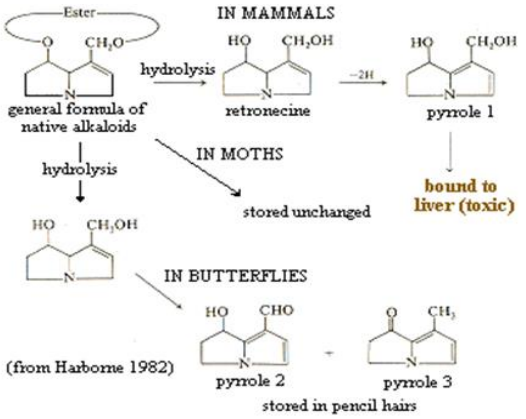

Figure 2. Mechanism of transformation of Pyrrolizidine alkaloids into toxic substances

Many researches have been done on the toxicity of the plants containing Pyrrolizidine alkaloids; because they change to alkylating pyrroles (alkylating agent) in the liver and with connection to DNA, RNA and liver cell proteins, cause Ascites, cirrhosis, and liver cancer [14].

Discussion and Conclusion

For centuries, plants have been used as the source of drugs and food. They have different effects due to their active ingredients. One of these ingredients which has the most abundance between natural substances are alkaloids. [16-19]. Medicinal plants have acceptable efficacy and availability. These specifications have been mentioned in ancient books, holy books and various religions [20, 21]. Some of alkaloids are toxic; for example, ergo alkaloids are the cause of epidemic poisoning and were widely used for this reason; Arecoline and caffeine are included as well. Alkaloids exists in animals, fungous, bacteria and plants, which are the richest one [22]. One of these substances are Pyrrolizidine alkaloids which exists in common plants affecting human and wildlife. These alkaloids have mutagen and destructive effect on DNA. They are able to transform to alkylating pyrroles and with connection to DNA, RNA and liver cell proteins, cause ascites, cirrhosis and even liver cancer [10, 23-26]. Plants containing Pyrrolizidine alkaloids exists all over the world and cause poisoning and damage to human, domesticated animals and wildlife. Although some of these plants are used as food and drug [27]. Besides extracting from plants, Pyrrolizidine alkaloids can be produced in synthesizing procedure of senecionin from tissue culture of Senecio sp's root. An increase in biosynthesis of this plant have been done with suspension cell culture of plants [28]. Pyrrolizidine alkaloids are exist in animal and plants generating foods. Research suggests that honey and tea can be carcinogen as well. In a research by Mulder et al, (2017), in Europe, Pyrrolizidine alkaloids were identified in dairy products, egg, meat and meat by-products, tea and plant supplements, grains collected from supermarkets, shops and online shops. Largest mean concentration was in robios tea with 559 microgram per kilogram in dried tea and 7.99 microgram in one-liter tea. Lowest mean concentration was in oily tea with 274 microgram per kilogram in dried tea and 3.65 microgram per liter. On the other hand, only 2 percent of animal

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by-products were contained PAs, especially 6 percent of milk samples and 1 percent of egg samples. No kind of PAs was found in other

animal by-products [29]. Neuman et al (2015) claimed that treatments including Pyrrolizidine alkaloids can induce liver damage disease, liver sennosoide obstruction or venal obstruction. Avoiding long term treatment with these substances prevent glutathione reservoir from depleting, so mitochondrial and liver cell damages are prevented [30]. Allgaier et al (2015) evaluated the risk of consuming medicinal plants containing PAs. It was concluded that encountering PAs can be because of either plant products or related foods [31]. Researches have shown that PAs existing in Compositae, legominosae. Orchidoceae or Borginaceae families, can be carcinogen and toxic. [32, 33]. In a research by Azadbakht et al (2002), amount of Pyrrolizidine alkaloids in Senecio vulgare in wheat and flour samples of Mazandaran province, Iran, were evaluated. All of these substances and their N-oxides in 0.512 gram of samples were 0.02-0.05 milligram and in 0.512 gram of Senecio vulgare were 0.4 [27] Comparing senecionin LD50) 24.2±12.64mg/kg(, lethal dose of these substances (6-167 mg/kg) and their non-lethal dose (2-27 mg/kg) wheat and floor samples of Mazandaran province practically did not have the acute side effects of these substances, though being exposed to even low amounts of PAs, can cause increasing damage to body organs especially to liver. Given current daily diet, the possibility of chronic toxicity is high [34]. In a research done by Letsyo et al (2017), toxic PAs were evaluated in common medicinal plants of Ghana and Africa [35]. In recent years, articles have shown that PAs detected in honey, herbal foods, tea. Regarding possible contamination, concerns about herbal treatments are increasing [36]. Azadbakht et al (2012) evaluated the quality and quantity of PA in Persian Borage. All these substances and their N-oxides in 0.500 gram of petal samples were 0.026, leaf samples 0.369 milligram, root 0.031-0.053 milligram. PAs in seeds did not detected. Comparing senecionin LD50) 24.2±12.64mg/kg(, lethal dose of these substances (6-167 mg/kg) and their non-lethal dose (2-27 mg/kg), leaf sample did not have the ability of generating acute side effects and seed, petals and root samples could not cause these toxic effects. Long term exposition to PAs, even short amounts of them, has the possibility of organ damage and liver toxicity [29]. Chen et al (2017) evaluated toxicity of PAs in medicinal plants including Gynura bicolor and Gynura divaricata from Asteraceae family collected from different districts of china. In south eastern Asia these two species are known and used as nutritional and medicinal plants. Late phytochemical investigations on Gynura species have shown these substances which indicates the risk following their consumption. Genotoxicity was not observed in these species but subtle cytotoxic activity was detected at the concentration of 100 mg/ml. this point suggests that Gynura species should be observed [36]. Special attention has also been paid to pyrolizidine alkaloids in food and food security in developed countries [37]. Pyrrolizidine alkaloids (PAs) protect the plants from biotic stresses by stimulating defense mechanisms as well as adaptability.So many pyrrolizidine alkaloids and their N-oxides possess anticancer activity. Some PAs have demonstrated cytotoxic effects also. In the study of Singh et al. (2019), these effects are also mentioned for Pas [38]. Pyrrolizidine alkaloids are important and medicinal plants are widely used by common people and researchers [39]. They can cause damage to human and domesticated animals; therefore, it is necessary for researchers and consumers to have a complex investigation about it to know structure, organs and properties of medicinal plants. Important properties and medicinal effects, of course, have also been reported. People should be informed about them and cultural, laboratorial measures should be taken in order to genetically correct these plants to have less toxicity and side effects.

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Conflicts of interest

There is no conflict of interests

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