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# ASSESSMENT OF THE CREDIBILITY OF PUBLIC WEBSITES ABOUT MEDICINAL HERBS

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In recent decades, there has been a growing interest in the use of herbs and herbal medicinal products, both in developing and developed countries. While electronic medium has become a more and more important tool for presenting information about health-related issues, several studies demonstrated that the internet often contains inaccurate and/or misleading information. In our study we assessed 30 Hungarian websites and 2 cellphone applications intended for public use and evaluated the quality and credibility of the information presented about medicinal plants recommended. It was found that websites showed very diverse safety: most websites gave mixed information, that is, some medicinal herbs and their potential hazard were properly described, while others were not. There were, however, websites, which completely missed to give information about any potential hazard. As credibility of public websites can be in most cases questioned, it is strongly recommended for potential users to consult more than one source of information.

Key words: hazardous plants, medicinal herbs, safe use, web-based information

## INTRODUCTION

In recent decades, the popularity of herbs and herbal medicinal products has been growing both in developing and developed countries, including Hungary. In developed countries, many patients or consumers are seeking herbal therapy assuming that it will promote healthier living (Ekor 2014).

However, while there is a quite general belief that herbal medicines are safe because they are "natural" (White *et al.* 2014), traditional is not necessarily safe. There are numerous risk factors associated with the use of herbal medicinal products, including unexpected toxicity (Jordan *et al.* 2010).

Due to the continuous development of analytical technology, identification and detection of secondary metabolites have considerably improved (Masullo *et al.* 2015), revealing the presence of potentially toxic bioactive compounds such as hepatotoxic pyrrolizidine alkaloids (PAs) (Kristanc and Kreft 2016*a*). Wiesner and Knöss (2014) discuss that a complete chemical profile should be given, including not only the major ingredients but all bioactive compounds.

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Unexpected toxicity also occurs in case of misidentification (Kristanc and Kreft 2016*b*), adulteration (Techen *et al*. 2014) or contamination. Contamination can be observed in polluted habitats, where the plants accumulate heavy metals and/or polyaromatic hydrocarbons (PAHs), either from contaminated soil or from atmospheric deposition (reviewed by Tripathy *et al*. 2015). Pesticide residues have also been detected (Zhang *et al*. 2012). Herbs or herbal preparations can be contaminated with mycotoxins, which might cause adverse human health effects (Ashiq *et al*. 2014). In some cases, even parasites have been found in herbal preparations (Mazzanti *et al*. 2008). Phytochemical variability might also be an issue: chemical composition and thus mode of action of the plant can be influenced by environmental factors (reviewed by Dhami and Mishra 2015).

Clinical reports prove that interactions with other drugs, either pharmaceutical or herbal, can pose actual human health hazard (e.g. Izzo and Ernst 2001, Jordan *et al*. 2010).

For the public, diverse information sources are available on the collection, cultivation, identification, mode of action and preparation of herbs. They involve books, websites, lectures (also accessible on the internet), organised excursions and/or visits to botanical gardens. Electronic medium has become a more and more important tool for presenting information about health-related issues, including medicinal plant databases (Ningthoujam *et al*. 2012). For example, in the U.S., sixty-one percent of adults seek health information online (Kitchens *et al*. 2014).

Public websites, however, might lack quality assurance; in other words, the information provided by them might have been compiled without actual scientific review. Bearing in mind the growing interest towards herbal medicinal products and the potential hazards mentioned, the purpose of the study was to evaluate the credibility of readily available Hungarian websites about medicinal herbs. Another aspect of the evaluation was whether the database included protected species, indicating their legal status.

## METHODS

Google-based search was done, using the selective key words: medicinal plants; everyday medicinal plants; common medicinal plants (in Hungarian: gyógynövények; mindennapi gyógynövények/gyógynövényeink; gyakori gyógynövények). Websites were evaluated in order of appearance. Exclusion criteria were:

– commercial ads (for example, advertising herbal products, books, training courses, etc.);
– simple compilation of publications;
– only a narrow collection of selected herbs, e.g. for losing weight.

Websites were preferred which included a list of recommended medicinal herbs with:
– description (including taxonomy, habitat or other ecological traits);
– information on collection (methods, season, etc.);
– mode of action;
– suggested use, mode of preparation;
– additional information (e.g. photo, potential risks, etc.).

Websites were evaluated based on:
– number of potentially hazardous plants per website;
– number of potentially hazardous plants per website inadequately described;
– number of protected species per website;
– number of protected species per website inadequately described (the website did not mention the protected status of the plant and did not inform the users that collection of any part of the specimen was strictly forbidden by Hungarian national legislation).

Plants included in the list of the (Hungarian) National Institute of Pharmacy and Nutrition (OÉTI 2013) were considered potentially toxic/hazardous (Table 1). In case of any doubt, community herbal monographs or public state-

*Table 1*
List of hazardous plants, which (1) were included in at least one of the websites accessed and (2) are included in the OÉTI list

| Name of the plant | Active ingredients responsible for potential hazard |
|---|---|
| *Acorus calamus* | asarone |
| *Adonis* sp. | cardenolide glycoside, adonitoxin |
| *Alkanna tinctoria* | pyrrolizidine alkaloids, likopsamin |
| *Angelica archangelica* | furocoumarins |
| *Arctostaphylos uva-ursi* | quinone, arbutin, metlarbutin |
| *Aristolochia* sp. | aristolochid acid and derivatives |
| *Artemisia absinthium* | α-thujone |
| *Asarum europaeum* | β-asarone |
| *Berberis vulgaris* | isoquinoline alkaloids, berberine |
| *Bryonia* sp. | cytotoxic cucurbitacin |
| *Chelidonium majus* | isoquinoline alkaloids, chelidonine, protopine |
| *Cimicifuga racemosa* | actein, 27-deoxi-actein, cimicifugoside |
| *Colchicum* sp. | alkaloids, colchicine |
| *Conium maculatum* | alkaloids: coniine, coniceine |

*Table 1* (continued)

| Name of the plant | Active ingredients responsible for potential hazard |
|---|---|
| *Convallaria majalis* | cardenolide glycosides, convallatoxin, convallozid |
| *Datura* sp. | tropane alkaloids: atropine, scopolamine |
| *Digitalis* sp. | cardenolide glycosides, digitoxin, lanatoside |
| *Dryopteris filix-mas* | phloroglucin derivatives |
| *Ephedra* sp. | phenilalkilaminalkaloids, ephedrine, norephedrine |
| *Euonymus* sp. | evonine type alkaloids, evonin; cardenolide, evonoside |
| *Euphorbia* sp. | tiglinane, ingenane and daphnane type phorbol esters |
| *Fumaria officinalis* | isoquinoline alkaloids, scoulerine, protopine |
| *Genista tinctoria* | alkaloids: anagirin, cytisine, sparteine; izoflavone, genistein |
| *Gratiola officinalis* | triterpene glykoside, graciozid; cucurbitacin |
| *Hedera helix* | saponins, α(alpha)-hederin |
| *Helleborus* sp. | alkaloids, celliamine, sprintilline; cardenolide glycoside, hellebrin; toxic saponins, helleborin |
| *Hyoscyamus* sp. | tropane alkaloids, hyoscyamine, scopolamine |
| *Hypericum perforatum* | naphtodiantrones, hypericin, pseudohypericin |
| *Leonorus cardiaca* | diterpenes of labdane skeleton lactones, leocardin; alkaloids |
| *Lycopodium clavatum* | alkaloids, lycopodin |
| *Melilotus officinalis* | coumarin |
| *Oenanthe* sp. | oenantotoxin, apiol, myristicin |
| *Paeonia officinalis* | – |
| *Petasites hybridus* | (un/) insaturated pyrrolizidine alkaloids |
| *Pulsatilla* sp. | protoanemonin, ranunculin |
| *Rhamnus frangula* | hydroxyanthraquinone, frangulin, glucofrangulin |
| *Scopolia* sp. | tropane alkaloids, atropine, scopolamine |
| *Senecio* sp. | (un/) insaturated pyrrolizidine alkaloids, senecionine |
| *Solanum dulcamara* | steroidal alkaloids and saponins |
| *Symphytum* sp. | pyrrolizidine alkaloids |
| *Taxus baccata* | diterpene pseudoalkaloids, taxine A and B |
| *Teucrium chamaedrys* | neo-clerodane, teucrium lactones |
| *Tussilago farfara* | pyrrolizidine alkaloids |
| *Veratrum album* | steroidal alkaloids, protoveratrin A and B |
| *Viscum album* | Viscum lectin I–III; viscotoxin |

ments (reviewed by Chinou 2014) were consulted. In case of *Fumaria officinalis* for example, the OÉTI list states that: "not enough data are available to assess safety". The Community Monograph (HMPC 2011*a*) gives special warnings and precautions for use, such as contraindications in case of biliary diseases and hepatitis.

Description was considered safe if the website mentioned the potential toxicity of the herb, or gave another special warnings, such as potential contraindications, or safe dose (e.g. in case of *Artemisia absinthium* a daily intake of 3.0 mg/person is acceptable for a maximum duration of use of 2 weeks, due to the thujone content (HMPC 2009)).

Legal status of the species was given according to the 13/2001 (V. 9.) KöM Decree.

## RESULTS

Altogether 30 websites and 2 cellphone applications were assessed. Table 2 gives a summary about (1) number of potentially hazardous plants per website; (2) number of potentially hazardous plants per website with lacking/misleading information about the potential hazards; (3) number of protected species per website and (4) number of protected species per website with lacking/misleading information about the legal status.

Considering potential risk of herbs, credibility and safety of websites varied to a high extent. The lowest category of safety and credibility is represented by websites where no information was given about potential hazards (e.g. W1, W10 and W11). Most websites gave mixed information: some medicinal herbs and their potential risks were properly described while others

*Table 2*

Number of potentially hazardous plants per website (PH); number of potentially hazardous plants per website with missing/incorrect information on the potential hazard ($PH^-$); number of protected species per website (PS); number of protected species per website with missing/incorrect information on the legal status ($PS^-$); number of all taxa included; short description of the website. W1–W30: Websites 1–30; App1–App2: cellphone applications 1–2

| Website | PH | $PH^-$ | PS | $PS^-$ | No of all taxa | Short description |
|---|---|---|---|---|---|---|
| W1 | 7 | 7 | 2 | 0 | 31 | advices in everyday health issues |
| W2 | 10 | 0 | 5 | 3 | 102 | reliable relic of medical plants |
| W3 | 2 | 1 | 0 | 0 | 15 | gives alternative medicine option |

*Table 2* (continued)

| Web-site | PH | $PH^-$ | PS | $PS^-$ | No of all taxa | Short description |
|---|---|---|---|---|---|---|
| W4 | 3 | 1 | 0 | 0 | 53 | list of herbs recommended for different illness |
| W5 | 1 | 1 | 0 | 0 | 9 | helping in everyday health |
| W6 | 23 | 3 | 10 | 2 | 183 | herbs a–z, application, therapy, property, cultivation |
| W7 | 11 | 4 | 7 | 0 | 90 | collection of most important herbs |
| W8 | 1 | 1 | 1 | 1 | 207 | collection of herbs, herbal teas and spices |
| W9 | 14 | 3 | 7 | 5 | 49 | showing the healing power of nature |
| W10 | 9 | 9 | 4 | 2 | 10 | description of herbal products |
| W11 | 7 | 7 | 2 | 0 | 31 | suggests that 'every complaint can be cured by a herb' |
| W12 | 25 | 13 | 16 | 15 | 246 | lexicon of herbal plants |
| W13 | 3 | 2 | 0 | 0 | 32 | introduction to the world of herbs |
| W14 | 4 | 0 | 1 | 0 | 55 | herbal teas and promotion |
| W15 | 6 | 8 | 0 | 0 | 49 | general uses of herbs |
| W16 | 11 | 5 | 3 | 3 | 109 | phytotherapy guide |
| W17 | 23 | 0 | 1 | 0 | 119 | description of herbs |
| W18 | 0 | 0 | 0 | 0 | 18 | description of herbs |
| W19 | 5 | 2 | 4 | 3 | 170 | modern use of herbs |
| W20 | 13 | 3 | 6 | 3 | 239 | description of herbs |
| W21 | 1 | 1 | 0 | 0 | 53 | description of herbs |
| W22 | 1 | 0 | 0 | 0 | 16 | the most common herbs around the house |
| W23 | 17 | 10 | 7 | 0 | 73 | collection of herbs |
| W24 | 7 | 4 | 3 | 1 | 72 | schematic overview of herbs, herbs and edible (wild) plants |
| W25 | 4 | 0 | 0 | 0 | 23 | description of herbs |
| W26 | 14 | 5 | 4 | 4 | 99 | effects of herbs |
| W27 | 3 | 1 | 0 | 0 | 94 | description of herbs |
| W28 | 38 | 25 | 18 | 17 | 240 | description of herbs |
| W29 | 32 | 18 | 21 | 1 | 796 | general uses of herbs |
| W30 | 24 | 5 | 13 | 2 | 700 | description of herbs |
| App1 | 22 | 6 | 3 | 1 | 187 | description of herbs |
| App2 | 6 | 0 | 2 | 0 | 183 | description of herbs |

were not (e.g. W6 which included 23 potentially hazardous species, but only 3 were improperly described or W12, which included 25 potentially hazardous species, but gave inappropriate description for approximately half of them, 13). It is interesting to note that W28 and W29 covered the widest range of potentially hazardous plants (38 and 32, respectively) and also, number of inappropriately described plants was the highest in their case, 25 and 18, respectively. Of cellphone applications, the wider database (App1) included 22 potentially hazardous species, but description of only 6 were found as inappropriate. The other included only 6 such species, but provided correct information on the potential hazard.

Considering the protected status of medicinal herbs, websites also varied to a great extent. For example, W12 included 16 protected species and 15 were improperly described; similarly, W28 included 18 protected species and for 17 of them, no information was provided about the legal status. On the contrary, W29 included 21 protected species and the conservation status of only 1 of them was missing.

## DISCUSSION

As the number of people consulting the Internet in health-related issues is continuously rising, more and more studies attempt to assess the credibility of websites (e.g. Gao *et al.* 2015, Lederman *et al.* 2014).

Molassiotis and Xu (2004) evaluated safety issues of web-based information about herbal medicines in the treatment of cancer. In their study, a scoring system was applied to give a quantitative estimation about overall safety of the website. They concluded that based on these scores, "the safety of the web-based information on herbs in the treatment of cancer was low". While in our study commercial websites (advertising some herbal products) were excluded, the assessment of Molassiotis and Xu included such websites and found that they had the lowest safety scores.

In parallel with the growing interest in herbal medicinal products, there is an increasing concern about their safety on institutional level. The World Health Organisation (2004) recommends the safety monitoring of herbal medicines/traditional medicines. It might especially be useful in developing countries, where approximately 80% of the population relies on herbal remedies (Neergheen-Bhujun 2013). However, more and more studies prove that even such herbs, which have a long tradition can cause negative effects. For example, Haq (2004) in his review gives an extensive list of these herbs, which include ginkgo (*Ginkgo biloba*) and ginseng (*Panax ginseng*). Assessment of adverse effects is based on patients' reports and/or animal toxicological tests.

Adverse effects of alternative medicine have already been reported in Europe. Jacobsson *et al.* (2009) covered an approximately 20-year period (between 1987 and 2006) and found 967 suspected adverse reactions related to different complementary and alternative medicine (CAM) products. Surprisingly, the most reported cases (8.1%) were connected to purple coneflower (*Echinacea purpurea*), an herb, which is non-native in Hungary, but is widely used. Medicinal herbs might also be used as Plant Food Supplements (PFS). In the framework of the European Project PlantLIBRA, a survey was performed involving over 2300 adults from 6 countries (Finland, Germany, Italy, Romania, Spain and UK). Complaints regarding adverse reactions were also assessed. Causality was likely in 56 out of 87 cases (Restani *et al*. 2016).

It is not the main intention of this paper to discuss all potentially toxic/hazardous plants included in the websites assessed in details. However, some plants are taken as examples. Comfrey (*Symphytum officinale* L., family Boraginaceae) is known to contain pyrrolizidine alkaloids (PAs), which have hepatotoxic effect. Allgaier and Franz (2015) review the regulations concerning the human exposure to PAs in herbal medicine products: in most cases, daily exposure is limited and/or the maximum period for its application is given (it is interesting to note, however, that the EMA public statement (EMA 2014) does not discriminate between oral and dermal exposure). As the above mentioned list of the Hungarian National Institute of Pharmacy and Nutrition (OÉTI 2013) clearly prohibits its use, we assessed how reliable information is given by the websites presented in this study. Of the 30 websites, 18 included comfrey and 5 provided misleading information.

The use of another potentially hepatotoxic plant, greater celandine (*Chelidonium majus* L.) was causally related to liver injury according to European case reports (Teschke *et al.* 2012*a*) and hepatitis (Moro *et al*. 2009). All these authors emphasize that concern should be increased about the safety of oral use of *C. majus*. In our study, the plant was included in 12 websites, 7 of them gave proper warning. In general, reported cases of herbal hepatotoxicity are the most often discussed and reviewed (Ernst 2003, Stickel and Shouval 2015, Teschke *et al*. 2012*b*).

Another example is St. John's wort (*Hypericum perforatum*), which was included in most of the websites, 25. Roughly 50% (13) gave proper safety instructions. The plant is most valued for treating depression and other mood disorders; exact modes of action are reviewed by Klemow *et al.* (2011). The main active compound is the photodynamic active plant pigment hypericin. Phototoxic symptoms ("hypericism") have been observed in grazing animals consuming large amounts of St. John's wort, however, standard dosage used in case of mood disorders does not produce phototoxic symptoms in humans (Schempp *et al.* 2002).

In addition to its antidepressant capacity, St. John's wort is used for the topical treatment of superficial wounds such as scars and burns. Schempp *et al*. (2000) assessed the photosensitizing capacity of topical application of *Hypericum* oil (hypericin 110 μg/mL) and *Hypericum* ointment (hypericin 30 μg/mL) on volunteers. While no severe phototoxic potential was demonstrated, an increase of the erythema-index could be detected following the treatment with the *Hypericum* oil.

However, clinical trials prove that much higher risk is posed by the plant via the interaction with certain drugs, affecting their systemic bioavailability (Izzo and Ernst 2001, Mills *et al*. 2004). For example, reduced plasma concentration of antiretroviral and anticancer drugs was reported (Borrelli and Izzo 2009).

Recognising the potential risks associated with the use of herbal medicinal products (HMPs), Directive 2004/24/EC was issued in the European Union (Knöss and Chinou 2012). Naturally, its main field is the regulation of the market of such products. The public can be informed about the safe use or potential risk of herbs and herbal products by Community herbal monographs, Community list entries or public statements (PS) (reviewed by Chinou 2014). Community monographs are issued by the Committee on Herbal Medicinal Products, while Community list entries are published by the European Commission. Both Monographs and List entries provide a final and complete assessment of the safety and traditional use, but Community list entries are regarded as legally binding (Peschel 2014). Public statements have been published when the assessment could not be completed due to lack of data or safety issues emerged. For example, the PS on *C. majus* formulates the problems: gives chemical description of alkaloid content and also summarises reported adverse drug reactions. It also gives a conclusion, including the following statements: "the benefit-risk assessment of oral use of *Chelidonium majus* is considered negative with respect to the establishment of a community monograph" and "safer herbal medicinal products are available in the indication in question" (HMPC 2011*b*).

As a conclusion, it has been revealed by our study that the websites evaluated showed very diverse credibility, so in case of any doubt it is strongly recommended for potential users to consult more than one sources of information. Elvin-Lewis (2001) in an excellent work (Should we be concerned about herbal remedies) summarises all potential risks and formulates some useful guidelines. These include, among others, the following points: "be informed, seek out unbiased, scientific sources" and "know benefits and risks and potential side effects".

On the other hand, however, websites and cellphone applications are flexible in a way that their content can be continuously reviewed and im-

proved. It should be very important in the case of cellphone applications, which will most possibly gain wider publicity in the near future.

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