Assessment of the credibility of public websites about medicinal herbs Nora Kováts^{1*}, Katalin Hubai¹, Eszter Horváth¹, Gábor Paulovits²

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Abstract

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.

Keywords: medicinal herbs; hazardous plants; 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 2016a). Wiesner and Knöss (2014) discuss that a complete chemical profile should be given, including not only the major ingredients but all bioactive compounds.

Unexpected toxicity also occurs in case of mis-identification (Kristanc and Kreft 2016b), 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 keywords: 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 statements (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, 2011a) 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 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. Lederman *et al.* 2014, Gao *et al.* 2015).

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.* 2012a) 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, Teschke *et al.* 2012b, Stickel and Shouval 2015)

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 μ g/mL) and *Hypericum* ointment (hypericin 30 μ g/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 2004). For example, reduced plasma concentration of antiretroviral and anticancer drugs was reported (Borelli 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 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, 2011b).

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 improved. 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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N. Cal. I.				
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			
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			
	7			

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	РН	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
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