

Assessment of the credibility of public websites about medicinal herbs

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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

51 *et al.* 2015). Pesticide residues have also been detected (Zhang *et al.* 2012). Herbs or herbal
52 preparations can be contaminated with mycotoxins which might cause adverse human health
53 effects (Ashiq *et al.* 2014). In some cases, even parasites have been found in herbal preparations
54 (Mazzanti *et al.* 2008). Phytochemical variability might also be an issue: chemical composition
55 and thus mode of action of the plant can be influenced by environmental factors (reviewed by
56 Dhami and Mishra 2015).

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

59 For the public, diverse information sources are available on the collection, cultivation,
60 identification, mode of action and preparation of herbs. They involve books, websites, lectures
61 (also accessible on the internet), organised excursions and/or visits to botanical gardens.
62 Electronic medium has become a more and more important tool for presenting information
63 about health-related issues, including medicinal plant databases (Ningthoujam *et al.* 2012). For
64 example, in the U.S., sixty-one percent of adults seek health information online (Kitchens *et al.*
65 2014).

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

72

73 **Methods**

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

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

82 Websites were preferred which included a list of recommended medicinal herbs with:

- 83 • description (including taxonomy, habitat or other ecological traits)
- 84 • information on collection (methods, season, etc.)
- 85 • mode of action
- 86 • suggested use, mode of preparation
- 87 • additional information (e.g. photo, potential risks, etc.).

88 Websites were evaluated based on:

- 89 • number of potentially hazardous plants per website
- 90 • number of potentially hazardous plants per website inadequately described
- 91 • number of protected species per website
- 92 • number of protected species per website inadequately described (the website did not
93 mention the protected status of the plant and did not inform the users that collection of
94 any part of the specimen was strictly forbidden by Hungarian national legislation).

95 Plants included in the list of the (Hungarian) National Institute of Pharmacy and Nutrition
96 (OÉTI 2013) were considered potentially toxic/hazardous (Table 1). In case of any doubt,
97 community herbal monographs or public statements (reviewed by Chinou 2014) were

98 consulted. In case of *Fumaria officinalis* for example, the OÉTI List states that: ‘not enough
99 data are available to assess safety’. The Community Monograph (HMPC, 2011a) gives special
100 warnings and precautions for use, such as contraindications in case of biliary diseases and
101 hepatitis.

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

106 Legal status of the species was given according to the 13/2001. (V. 9.) KöM Decree.
107

108 **Results**

109

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

115 Considering potential risk of herbs, credibility and safety of websites varied to a high
116 extent. The lowest category of safety and credibility is represented by websites where no
117 information was given about potential hazards (e.g. W1, W10 and W11). Most websites gave
118 mixed information: some medicinal herbs and their potential risks were properly described
119 while others were not (e.g. W6 which included 23 potentially hazardous species but only 3 were
120 improperly described or W12 which included 25 potentially hazardous species but gave
121 inappropriate description for approximately half of them, 13). It is interesting to note that W28
122 and W29 covered the widest range of potentially hazardous plants (38 and 32, respectively) and
123 also, number of inappropriately described plants was the highest in their case, 25 and 18,
124 respectively. Of cellphone applications, the wider database (App1) included 22 potentially
125 hazardous species but description of only 6 were found as inappropriate. The other included
126 only 6 such species, but provided correct information on the potential hazard.

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

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

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

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

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

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

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

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

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

194 However, clinical trials prove that much higher risk is posed by the plant via the
195 interaction with certain drugs, affecting their systemic bioavailability (Izzo and Ernst 2001,

196 Mills 2004). For example, reduced plasma concentration of antiretroviral and anticancer drugs
197 was reported (Borelli and Izzo 2009).

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

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

220 On the other hand, however, websites and cellphone applications are flexible in a way
221 that their content can be continuously reviewed and improved. It should be very important in
222 the case of cellphone applications which will most possibly gain wider publicity in the near
223 future.

224

225 **Acknowledgement**

226

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229

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231

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- 371

372 Table 1. List of hazardous plants which (1) were included in at least one of the websites
 373 accessed and (2) are included in the OETI List.
 374

Name of the plant	Active ingredients responsible for potential hazard
<i>Acorus calamus</i>	asarone
<i>Adonis</i> sp.	cardenolide glycoside, adonitoxin
<i>Alkanna tinctoria</i>	pyrrolizidine alkaloids, likopsamin
<i>Angelica archangelica</i>	furocoumarins
<i>Arctostaphylos uva-ursi</i>	quinone, arbutin, metlarbutin
<i>Aristolochia</i> sp.	aristolochid acid and derivatives
<i>Artemisia absinthium</i>	α -thujone
<i>Asarum europaeum</i>	β -asarone
<i>Berberis vulgaris</i>	isoquinoline alkaloids, berberine
<i>Bryonia</i> sp.	cytotoxic cucurbitacin
<i>Chelidonium majus</i>	isoquinoline alkaloids, chelidonine, protopine
<i>Cimicifuga racemosa</i>	actein, 27-deoxi-actein, cimicifugoside
<i>Colchicum</i> sp.	alkaloids, colchicine
<i>Conium maculatum</i>	alkaloids: coniine, coniceine
<i>Convallaria majalis</i>	cardenolide glycosides, convallatoxin, convallozid
<i>Datura</i> sp.	tropane alkaloids: atropine, scopolamine
<i>Digitalis</i> sp.	cardenolide glycosides, digitoxin, lanatoside
<i>Dryopteris filix-mas</i>	phloroglucin derivatives
<i>Ephedra</i> sp.	phenilalkilaminalkaloids, ephedrine, norephedrine
<i>Euonymus</i> sp.	evonine type alkaloids, evonin; cardenolide, evonoside
<i>Euphorbia</i> sp.	tiglinane, ingenane and daphnane type phorbol esters
<i>Fumaria officinalis</i>	isoquinoline alkaloids, scoulerine, protopine
<i>Genista tinctoria</i>	alkaloids: anagirin, cytisine, sparteine; izoflavone, genistein
<i>Gratiola officinalis</i>	triterpene glykoside, graciozid; cucurbitacin
<i>Hedera helix</i>	saponins, α (alpha)-hederin
<i>Helleborus</i> sp.	alkaloids, celliamine, sprintilline; cardenolide glycoside, hellebrin; toxic saponins, helleborin
<i>Hyoscyamus</i> sp.	tropane alkaloids, hyoscyamine, scopolamine
<i>Hypericum perforatum</i>	naphodiantrones, hypericin, pseudohypericin
<i>Leonorus cardiaca</i>	diterpenes of labdane skeleton lactones, leocardin; alkaloids
<i>Lycopodium clavatum</i>	alkaloids, lycopodin
<i>Melilotus officinalis</i>	coumarin
<i>Oenanthe</i> sp.	oenantotoxin, apiol, myristicin
<i>Paeonia officinalis</i>	-
<i>Petasites hybridus</i>	(un/) insaturated pyrrolizidine alkaloids
<i>Pulsatilla</i> sp.	protoanemonin, ranunculin
<i>Rhamnus frangula</i>	hydroxyanthraquinone, frangulin, glucofrangulin
<i>Scopolia</i> sp.	tropane alkaloids, atropine, scopolamine
<i>Senecio</i> sp.	(un/) insaturated pyrrolizidine alkaloids, senecionine
<i>Solanum dulcamara</i>	steroidal alkaloids and saponins
<i>Symphytum</i> sp.	pyrrolizidine alkaloids
<i>Taxus baccata</i>	diterpene pseudoalkaloids, taxine A and B
<i>Teucrium chamaedrys</i>	neo-clerodane, teucrium lactones
<i>Tussilago farfara</i>	pyrrolizidine alkaloids
<i>Veratrum album</i>	steroidal alkaloids , protoveratrin A and B
<i>Viscum album</i>	Viscum lectin I-III; viscotoxin

375

376 Table 2. Number of potentially hazardous plants per website (PH); number of potentially
 377 hazardous plants per website with missing/incorrect information on the potential hazard (PH⁻);
 378 number of protected species per website (PS); number of protected species per website with
 379 missing/incorrect information on the legal status (PS⁻); number of all taxa included; short
 380 description of the website. W1-W30: Websites 1-30; App1-App2: cellphone applications 1-2.
 381

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
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