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The rise of traditional Chinese medicine and its *materia medica*: A comparison of the frequency and safety of materials and species used in Europe and China

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ABSTRACT

Ethnobotanical relevance: Due to the global rise in the use of traditional Chinese medicine (TCM), Chinese *materia medica* (medicinal materials, or CMM) are giving cause for concern over their evidence base, safety/possible toxicity, questionable quality and use of endangered species of both animals and plants. However, little if anything is actually known about the range of species used to produce CMM used in Europe and even in China. This study represents the first attempt to identify and compare the most important CMM used in both regions, to begin the process of assessing the risks to public health and possible future benefits.

Materials and methods: Data were collected from a convenience sample of TCM practitioners in the EU and mainland China, using a paper/online survey. Among other questions, respondents were asked (1) which conditions they most commonly treated using CMM and the likelihood of them using herbal manufactured products and decoctions in addition to raw herbs; (2) the perceived frequency with which they observed adverse events to CMM; (3) the frequency and reasons for use of 1 herbal formula and 6 specific individual herbs; (4) an open question about other CMM they used, including materials of non-plant origin. Data were entered into PASW statistics package and analysed using frequency tables, cross-tabulations and chi-squared tests to compare EU and Chinese results.

Results: From a total of 747 useable questionnaires (420 from China, 327 from the EU) of those responding from the EU, TCM was generally more commonly used for obstetric/gynaecological and dermatological conditions, compared to neurological and gastrointestinal diseases in China. Disorders treated by Chinese practitioners were more varied, and often more serious, than those treated by their European counterparts, and the range of materials used in China was wider. The potential for toxicity was not high in either region, but although greater in China due to the use of more potent CMM, the incidence of side effects was perceived to be higher by EU practitioners.

Conclusions: Very few of the species used to prepare CMM in the EU in this study give rise to safety concerns from what is known from the scientific and other literature, and in China only a few toxic CMM appear to be commonly used, some of them only after processing and mainly for serious disorders. The main cause for concern is likely to be interaction with prescribed medication, especially in central nervous system and cardiovascular conditions where drug interactions have previously been reported most frequently and which would currently be more applicable in China than Europe.

1. Introduction

Traditional Chinese medicine (TCM) plays an important role in healthcare in South-East Asia, and increasingly so in the West. The US spent US$7.6 billion in 2010 on TCM products from China (Cheung, 2011), and in Europe, exports of TCM products amounted to US$2 billion (Liu et al., 2009). As of May 2011, China had signed 91 TCM partnership agreements with over 70 countries, and investment in TCM research by the Chinese government reached US$770.5 million in 2010 (Cheung, 2011).

One of the mainstays of TCM is the use of herbal, animal and mineral-derived medicines, Chinese *materia medica* (or medicinal materials; CMM), and some of these are now giving cause for

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concern over their appropriate use, evidence base, possible toxicity, potential for interaction with prescription and other drugs, questionable quality and use of endangered species of both animals and plants. The MHRA (UK Medicines and Healthcare Regulatory Agency) has identified 16 areas of risk for such medicines (MHRA, 2006) but surprisingly, very little, if anything is actually known about the range of CMM used in Europe and even in China. This study represents the first modern attempt to identify the most important *materia medica* used on both continents, to begin the process of assessing their risks to public health and possible future benefits.

CMM are of mainly herbal origin but also include animal parts, giving rise to other concerns such as pathogen contamination and the use of endangered species. There are no data available on the proportions of CMM from animal sources, although animal medicines are thought likely to be less popular in Europe than in China, for cultural and legal reasons. In China, injectable products derived from herbal materials are widely used, but in the EU, parenteral preparations can only be supplied on the prescription of a medical practitioner qualified in the EU (Council Directive 2001/83/EC), and normally these would be licensed products. For these reasons, and to focus on the use of particular species, injectable products were not included in the survey, nor were decoction granules or patent formulae, with the exception of liuweidihuang (LW) which as a popular formula in both China and Europe, was surveyed specifically.

As TCM becomes ever more widely used within the European Union (EU), many high streets in the UK and elsewhere now have outlets which sell Chinese medicines, either on request or after consultation with a member of staff who may or may not have any appropriate biomedical or medical qualifications. The number of TCM practitioners in the EU, and their qualifications and range of expertise, is also unknown since TCM is currently unregulated, although plans were announced in February 2011 by the UK Department of Health to regulate all herbal practitioners (MHRA, 2011). Individual practitioners also practise very differently, depending on their training and education, with many using a variety of approaches in addition to CMM within their treatments (Robinson et al., 2012).

As a result of these concerns, the EU recently supported a programme of EU-China collaborative research, the Good Practice in traditional Chinese medicine (GP-TCM) programme, under the European Commission's Framework 7 (FP7) programme to investigate the practice of TCM in Europe and to provide recommendations for future research initiatives including the more pressing safety questions (Uzuner et al., 2012). This study is part of that networking platform and attempts to map the use of specific CMM in Europe and China by surveying practitioners in both regions. The intention is that the data will ultimately contribute to the development of clinical guidelines for TCM usage and international regulation, as well as signal areas which would be fruitful for further research.

2. Methods

Data were collected using methods described previously, as part of a larger survey also exploring the practice of acupuncture in both regions (Robinson et al., 2012). Briefly, a convenience sample of TCM practitioners in the EU (contacted via email by their professional organisations) and in mainland China (from geographically dispersed hospitals) was invited to participate in a survey conducted during 2010/2011. Practitioners' demographic details, education and training were recorded, and respondents were asked questions which included (1) which conditions they most commonly treated using CMM and the likelihood of them using herbal manufactured products and decoctions in addition to raw herbs; (2) the perceived frequency with which they observed adverse events to CMM; (3) the frequency of use of 1 herbal formula and 6 specific individual herbs (4) an open question about other CMM they used, to include materials of non-plant origin.

The formula liuweidihuang ('Six Ingredient Rehmannia') was surveyed specifically. LW is a traditional Chinese medicine containing six herbs: *Rehmannia glutinosa* (Gaertn.) DC. root; *Cornus officinalis* Siebold & Zucc. fruit; *Dioscorea opposita* Thunb. tuber; *Wolfiporia extensa* (Peck) Ginns (better known by its synonym, *Poria cocos* F.A. Wolf) fungus; *Alisma plantago-aquatica* subsp. *orientale* (Sam.) Sam. rhizome, and *Paeonia suffruticosa* bark Andr. (Huang et al., 2012). It is traditionally used to improve age-related diseases, such as impaired mobility, vision, hearing, cognition and memory, and female conditions.

The six individual herbs specified in the questionnaire were: *Ganoderma lucidum* (Curtis) P. Karst and other species (lingzhi); *Angelica pubescens* Maxim. (duhuo); *Astragalus membranaceus* Bge (huangqi); *Atractylodes macrocephala* Koidz (baizhu); *Scutellaria baicalensis* Georgi (Huang Qin); and *Tripterygium wilfordii* Hook f (leigongten).

Since no survey has yet been carried out on the use of CMM on both continents, these CMM were chosen as a starting point based on sales and popularity, using a consensus method from lists from companies trading species used in TCM in mainland China, Hong Kong and Europe, as well as lists from practitioner colleagues in China and Hong Kong and colleagues involved in the GP-TCM consortium. *Tripterygium wilfordii* was included because, although not one of the most important CMM, it has well-documented toxicity and one of the main aims of this study was to explore the use of toxic CMM in Europe compared to China. The formula liuweidihuang was included because it is widely used and available in both China and the EU. This paper reports only data from respondents using CMM in their practice. Data were coded and entered onto PASW statistics v18 to generate frequency data. Cross tabulations were generated and chi- squared tests were used to compare EU and Chinese results.

In open questions, CMM were cited by respondents under various names which were not necessarily accepted names or complete enough to identify the method of processing. Some respondents used abbreviations, including for botanical names, and some used Chinese characters only. Pinyin names were often written with a space to indicate to the non-Chinese speaker that there are 2 or more characters or words and rarely, English common names were given. To interpret these, the Chinese Pharmacopoeia 2010 English edition (Chinese Pharmacopoeia Commission, 2010) was consulted for species used and accepted pinyin names, and plant species names were authenticated using the Royal Botanical Gardens Kew data base, 'The Plant List' as is recommended good practice (Chan et al., 2012). A TCM practitioner (one of the authors, A Booker) was consulted regarding any ambiguous Chinese terms (e.g. 'shu di' for 'shudihuang') to ensure as much confidence as possible in the accuracy of the CMM cited. In this study, we have used the Chinese convention of citing the pinyin name as a single word but entries are classified in the tables under accepted species scientific name, as this is the most accurate way of identifying the origin of the material (Chan et al., 2012; Shaw et al., 2012) and in some instances the part of the plant was omitted, so the pharmaceutical drug name could not always be used. Unintelligible entries were rare: 3 from the EU, which were omitted from the analysis, and none from China.

3. Results

3.1. Responses and demographics of practitioners

A total of 1112 responses were received from TCM practitioners (including acupuncturists), with 747 useable questionnaires (relating to herbal practice) received (420 from China, 327 from the EU).

The response rate for EU practitioners could not be calculated as it was a convenience sample; however for the Chinese sample, which was purposive, there was a 98% completion rate. A total of 365 questionnaires were excluded as they were from countries not in the EU or China, incomplete, or only practised acupuncture and did not practice herbal medicine. This gave a total of 747 useable questionnaires for analysis, 420 from China, 327 from the EU (from 12 different countries: UK, Spain, Italy, Switzerland, Germany, Netherlands, Belgium, Slovenia, Portugal, Ireland, Sweden, Czech Republic). The results represent a convenience sample controlled by the logistics of the consortium and their links with practitioners, and we received no responses from Austria for example, or some other countries with a well-developed tradition of TCM. This study is intended to provide a preliminary evidence to use as a foundation for further research and cannot be considered to be representative for all of Europe Table 1.

Key points to note are that the Chinese practitioners were younger, therefore had practised for less time, and were more likely to have received biomedical training.

3.2. Comparison of commonly treated conditions by practitioners in China and the EU

Practitioners were asked their views on the conditions they normally treat using CMM. A different range of conditions were treated in China compared to the EU, as shown in Fig. 1. The most common indications for which CMM were used in the EU were, in order of prevalence, obstetric/gynaecological, dermatological, gastrointestinal, psychiatric, stress-related and allergic disorders, whereas in China they were neurological, gastrointestinal, respiratory, pain, obstetric/gynaecological and cardiovascular conditions.

In China, the conditions treated appear to be often more serious, and also generally less likely to be of psychiatric or stress-related origin than in Europe. In the survey of acupuncture use (Robinson et al., 2012), blood disorders were differentiated from cardiovascular disorders, however as can be seen here, no practitioners gave a response for 'blood disorders'.

3.3. The use of herbal manufactured products and decoctions

EU practitioners were much less likely to use herbal decoctions: 49.8% did not, compared to 11.9% of Chinese ($p < 0.001$), especially those who had trained at least partly outside China, but practitioners in both regions were equally likely to use herbal manufactured products rather than raw herbs (84% of both EU and Chinese); $p < 0.001$ with the exception of injectable products, which were not used by EU practitioners for legal reasons. Extract granules for reconstitution are becoming increasingly important products in both China and the EU (see e.g. Luo et al., 2012), but respondents did not necessarily indication the formulation used so this data could not be collated independently.

Table 1
Demographics of practitioner samples in China and the EU.

Demographics	EU N (% of sample)	China N (% of sample)
Gender		
Female	130 (40%)	224 (53%)
Male	113 (35%)	182 (43%)
Missing	84	14
Age		
18 to 29	7	154 (37%)
30 to 39	50 (15%)	169 (40%)
40 to 49	100 (31%)	68 (16%)
50 to 59	73 (22%)	12
Over 60	14	1
Missing	83	16
Biomedical training*		
Western doctor	108 (33%)	266 (63%)
Western nurse	20 (6%)	0
Physiotherapist	17	57 (14%)
Dietician	14	20 (5%)

* The remainder were TCM-trained but did not have any western conventional medical training.

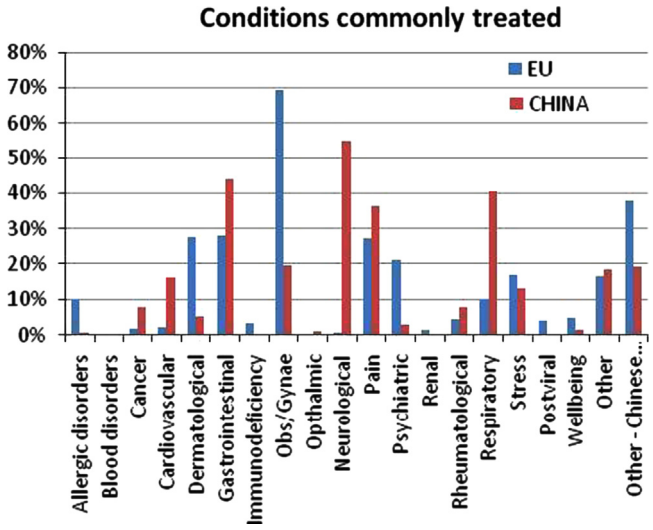

Fig. 1. Conditions commonly treated by practitioners in China and the EU.

3.4. Comparison of adverse events reported in China and the EU

Practitioners were asked about their perceptions, based on their own experience, of the incidence of adverse events to CMMs in general. Specific reactions to particular CMMs were not sought; the question was designed to find the overall impression of the safety of the materials used by practitioners.

It is noteworthy that Chinese herbalists were less likely to report seeing adverse events to CMM in practice ($p < 0.001$) and more likely to consider their incidence to be 'rare' or 'very rare'. Surprisingly however, EU respondents were more likely to say they 'never' experienced adverse events Fig. 2.

3.5. Comparison of the use of specific CMM in China and the EU

3.5.1. The formula liuweidihuang

This formula is used for a wide variety of conditions which are considered in TCM theory to be due to 'kidney yin deficiency'. These include many degenerative disorders and those of ageing, as well as menopausal symptoms and to a lesser extent, menstrual problems and infertility. Other indications were low back pain, tinnitus, arthritis, fatigue, diabetes, dry mouth, and dry skin.

Fig. 3 shows that the herbal formula liuweidihuang was more commonly used in China, with 80.3% of practitioners using it commonly or very commonly compared to 64.2% for EU practitioners ($p < 0.001$). These results confirm the popularity of the formula, justifying its inclusion in the survey.

3.5.2. The specific herbs

Five of the six named herbs (*Ganoderma lucidum*/*Gleditsia sinensis*, *Angelica pubescens*, *Astragalus membranaceus*, *Atractylodes macrocephala*, *Scutellaria baicalensis*) were used widely in both continents, confirming the validity of the consensus method by which they were selected for investigation. *Tripterygium wilfordii* was more rarely used in the EU (5%, compared to 17% in China),

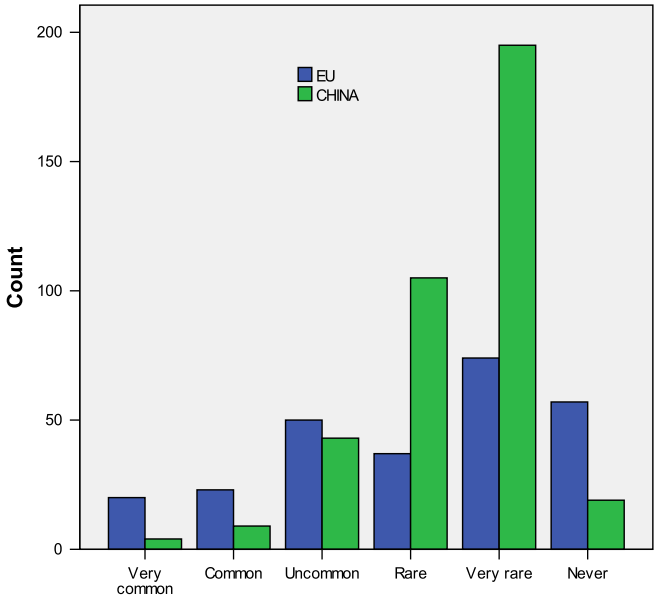

Fig. 2. Practitioners' perceptions of adverse events due to CMM.

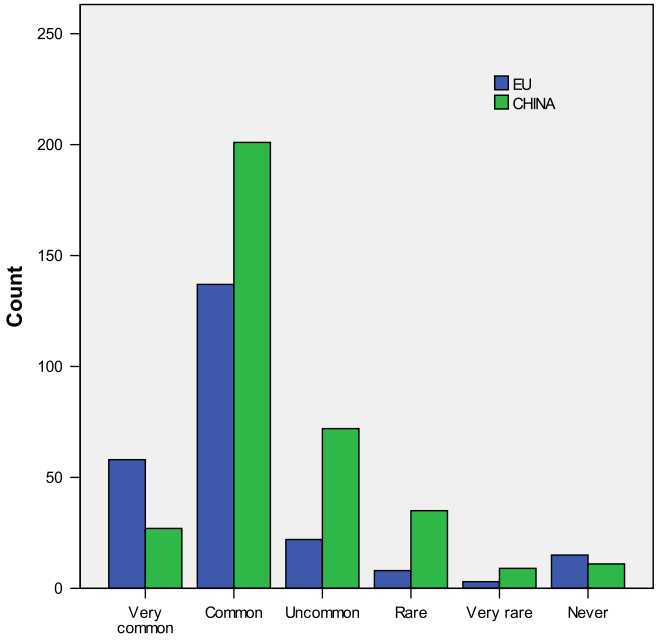

Fig. 3. Use of Liu Wei Di Huang in China and the EU.

but even this European usage was considered very high, and since response numbers were quite low, it may not be representative of the actual use. With the exception of *Ganoderma* (50% of EU compared to 35% in China), the use of these herbs was also mentioned more frequently in China than the EU. Results are shown in Table 2, with full botanical names, synonyms, pinyin and common names and parts of plants used.

Most respondents gave Chinese diagnoses for the use of the specific herbs, and many said they used them for a range of symptoms/conditions. For those that could be classified: *Angelica pubescens* was generally used for pain and rheumatism/arthritis in both areas, whereas *Astragalus membranaceus* was used for improving immune function in the EU (18.5% of all conditions) but for gastrointestinal problems in China (26.1% of conditions). *Atractylodes macrocephala* was commonly used for gastrointestinal disorders (45.2% in the EU and 24.0% in China) and *Scutellaria baicalensis* for dermatological and respiratory indications. Lingzhi (*Ganoderma*) was most commonly used for low energy, general wellbeing and improving immunity, and for chronic conditions including cancer support, allergies, respiratory, obstetric and gynecological disorders, and insomnia. Leigongteng (*Tripterygium*), a toxic herb, is used for the treatment of rheumatoid arthritis and has some anti-cancer properties. These findings are therefore consistent with the cited 'conditions most commonly treated' in each region, as shown in Fig. 1.

Those respondents who did not use the specified herbs cited 'I only use patent herbs' or 'I only use them in formulas' as their main reasons, which is entirely compatible with TCM theory where more than one herb is normally used for a particular condition. However, these herbs are likely to be constituents of such formulae, in which case their usage would not have been recorded in this survey.

3.5.3. Other herbs

The frequency of use of other herbs (in response to open questions) is also shown in Table 2. The most commonly used were: *Angelica sinensis* (Oliv.) Diels, *Paeonia lactiflora* Pall., *Rehmannia glutinosa* (Gaertn.) DC, *Glycyrrhiza glabra* L./*Glycyrrhiza uralensis* Fisch/*Glycyrrhiza inflata* Bat, *Ligusticum striatum* W.T. Aiton, *Panax ginseng* CA Meyer (and other *spp.* of *Panax*), and *Wolfiporia extensa* (syn *Poria cocos*). A wide range of herbs was used at low frequencies, but surprisingly, several important TCM drugs which were thought to be commonly used in Europe did not show up in this list, for example *Lilium brownii* (baihe) and *Corydalis yanhusuo* (yanhusuo). The reasons for this are not known, but should be investigated in future to identify any misinterpretations and unexpected limitations involved in this type of study.

3.5.4. Non-plant CMM

The use of non-plant species used to prepare CMM is given in Table 3; all were more commonly used in China. The most widely used CMM of animal origin were oyster shell, earthworm, centipede, and silkworm. Exotic and illegal materials such as rhino horn and tiger bones were not mentioned by any of the respondents either in China or the EU.

4. Discussion

To our knowledge, this is the first study to survey the range of species and materials used in TCM and compare them between China and the EU, and to assess them from a safety point of view. We have found significant differences in the conditions treated using CMM, which were in fact very similar to those found in the acupuncture survey (Robinson et al., 2012), reflecting the frequency of conditions treated in both continents, the materials used and their recorded safety. Disorders treated by Chinese practitioners were more varied, and often more serious, than those treated by their European counterparts, and the range of materials used in China was wider. The potential for toxicity was not high in either region, but although greater in China due to the use of more potent CMM, the incidence of side effects was perceived to be higher by EU practitioners. We propose further explanations for these differences: availability of specific Chinese *materia medica*, cost, regulation, and patient characteristics and/or treatment-seeking behaviour. The education of practitioners will obviously influence prescribing habits, but there is no information available about this to compare.

4.1. Availability and cost

Although no figures are available, it seems reasonable to infer that Chinese people are likely to choose a favoured over-the-counter remedy to treat minor disorders, whereas Europeans are

Table 2
Comparison of individual herb species usage by TCM practitioners in China and the EU.

Botanical species source; toxicity notes (where known, on shaded entries)	Herb: pinyin, common name(s) and plant part	EU herbalists citing herb ($n=327$)		Chinese herbalists citing herb ($n=348$)	
		N	Approx % responders	*N*	Approx % responders
Astragalus membranaceus Bge*	Huangqi; Membranous milk-vetch root	210	64	335	96
Atractylodes macrocephala Koidz*	Baizhu; Bighead or white actractylodes rhizome	204	62	329	95
Scutellaria baicalensis Georgi*	Huangqin; Baical skullcap root	190	58	300	86
Angelica pubescens Maxim.*	Duhuo; Pubescent angelica root	170	52	231	66
Ganoderma lucidum (Curtis) P. Karst and other spp.*	Lingzhi; Glossy ganoderma; Divine mushroom	163	50	122	35
Angelica sinensis (Oliv.) Diels	Danggui; Chinese angelica root	51	15	56	16
Paeonia lactiflora Pall.	Baishao/Chishao; White/red peony root	47	14	35	10
Rehmannia glutinosa (Gaertn.) DC. (prepared/raw or not stated)	Shengdihuang (raw); Shudihuang (prep). Chinese foxglove root	37	11	30	9
Glycyrrhiza glabra L., *G. uralensis* Fisch.	Gancao; Liquorice root	34	10	27	8
Ligusticum striatum DC (*L. wallichii* Franch).	Chuanxiong; Chinese/Szechuan lovage root	32	8	32	9
Panax ginseng CA Meyer and other *spp*. of *Panax*	Renshen; Ginseng root	31	9	10	3
Lycium chinensis Mill.; *L. barbarum* L. (berries/root bark).	Gouqizi (berry; *L. barbarum* only); Dìgupí (root bark). Wolfberry; goji berry	30 2	9	0 1	0 <1
Codonopsis pilosula (Franch.) Nannf./*C. tangshen* Oliv.	Dangshen; Bonnet bellflower; False or Poor man's ginseng root	25	8	54	15
Wolfiporia extensa (Peck) Ginns (syn *Poria cocos* F.A. Wolf).	Fuling; Hoelen, Poria, Tuckahoe sclerotium/fungus	23	7	60	17
Bupleurum chinense DC., *B. scorzonerifolium* Willd., *B. falcatum* L.	Chaihu; Chinese thorowax/Hare's ear root	21	6	44	37
Salvia miltiorhiza Bunge	Danshen; Chinese/Red sage root	20	6	16	5
Tripterygium wilfordii Hook.f* Triptolide is toxic and immunosuppressant	Leigongteng; Thunder-god vine root	17	5	58	17
Phellodendron amurense Rupr.; *P. chinense* C.K. Schneid.	Huangbo/Huangbai; Amur/Chinese cork tree bark	15	5	1	<1
Zingiber officinale Roscoe (dried; fresh; unspecified)	Ganjiang (dried); Shengjiang (fresh); Ginger rhizome	15	5	3	<1
Ziziphus jujube Mill. var. *spinosa* (Bunge) Hu ex H.F. Chou	Suanzaoren; Sour/spiny date seed	14	4	2	<1
Coptis chinensis Franch	Huanglian;Chinese goldthread rhizome	14	4	3	<1
Anemarrhena asphodeloides Bge.	Zhimu; Anemarrhena rhizome	12	<4	1	<1
Lonicera japonica Thunb.	Jinyinhua; Japanese honeysuckle flower	12	<4	6	<2
Chrysanthemum morifolium Ramat	Juhua; Florist's chrysanthemum	12	<4	7	2
Pinellia ternata (Thunb.) Makino Toxic unless processed (contains calcium oxalate needle crystals and lectins)	Banxia; Crow-dipper rhizome	11	3	27	8
Forsythia suspensa (Thunb.) Vahl.	Lianqiao; Forsythia fruit	11	3	5	<2
Citrus reticulata Blanco, *C. aurantium* L. Potential toxicity in excessive amounts (synephrine content)	Chenpi; Tangerine/orange ripe fruit peel. Zhiqiao; the whole sliced fruits	11	3	27	8
Paeonia suffruticosa Andr.	Mudanpi; Tree peony root	11	3	6	<2
Curcuma longa L. and related spp	Jianghuang, Yujin; Turmeric rhizome	11	3	2	<1
Cyperus rotundus L.	Xiangfu; Nut sedge tuber	11	3	1	<1
Prunus persica L. Stokes Potential toxicity (cyanide release from amygdalin)	Taoren; Peach seed kernel	10	3	19	6
Carthamus tinctorius L.	Honghua; Safflower	9	<3	29	8
Cinnamomum cassia (Nees & T. Nees) bark/twig	Rougui; guizhi; Cassia/Chinese or false cinnamon/bark or twig	9	<3	31	9
Saposhnikovia divaricata (Turcz.) Schischk (=*Ledebouriella divaricata* (Turcz.) Hiroë)	Fangfeng; Ledebouriella root	9	<3	8	2
Gardenia jasminoides Ellis	Zhizi; Cape jessamine fruit	9	<3	1	<1
Mentha canadensis L. (=*M. haplocalyx* Briq. Field) and other spp e.g. *Mentha aquatica* L.)	Bohe; Corn mint (water mint etc) herb	9	<3	1	<1
Eucommia ulmoides Oliv.	Duzhong; Chinese/hardy rubber tree bark	8	2	11	3
Fallopia multiflora (Thunb.) Haraldson (*Polygonum multiflorum* Thunb.)	Heshouwu/Shouwuteng/Foti; Fleece flower root/stem/herb	8	2	3	<1
Rheum palmatum L. and others	Dahuang; Chinese rhubarb root/rhizome	8	2	10	3
Dioscorea opposita Thunb.	Shanyao; Chinese yam tuber	7	2	15	4
Angelica dahurica (Hoffm.) Benth. & Hook.f. ex Franch. & Sav.	Baizhi; Wild/fragrant angelica root	7	2	4	1
Scrophularia ningpoensis Hemsl.	Xuanshen;Ningpo figwort root	7	2	2	<1
Citrus aurantium L., or *Citrus sinensis* (L.) Osbeck Potential toxicity (due to presence of synephrine)	Qingpi; Orange (immature fruit) peel	7	2	7	2
Albizia julibrissin Durazz.	Hehuanpi; Mimosa/Silk tree; Tree of Happiness bark	7	2	0	0
Ziziphus jujuba Mill	Dazao; Jujube fruit	7	2	2	<1
Ophiopogon japonicus (Thunb.) Ker-Gawl.	Maimendong; Mondo grass root	6	<2	11	3
Gastrodia elata Blume. †Endangered species	Tianma; Japanese orchid tuber	6	<2	13	4
Pueraria montana var. *lobata* (Willd.) Sanjappa & Pradeep	Gegen; Kudzu vine root	6	<2	10	3
Cuscuta chinensis Lam.	Tusizi; Chinese dodder seed	6	<2	7	2
Polygala tenuifolia Willd.	Yuanzhi; Chinese senega root	6	1	2	<1
Schisandra chinensis (Turcz) Baill.	Wuweizi; Magnoliavine fruit	5	<2	8	2
Uncaria rhynchophylla (Miq.) Miq. ex Havil.; *U. sinensis* (Oliv.) Havil.; *U. macrophylla* Wall.	Gouteng; Gambir stems and thorns	5	<2	7	2
Crataegus pinnatifida Bunge and other spp	Shanzha; Hawthorn fruit	5	<2	6	2
Coix lacrima-jobi L.	Yiyiren; Chinese pearl barley/Job's tears seeds	5	<2	4	1
Asparagus cochinchinensis (Lour.) Merr.	Tianmendong; Chinese asparagus tuber	5	<2	3	<1
Leonurus sibiricus L.	Yimucao; Chinese motherwort	5	<2	3	<1
Plantago depressa Willd. *P. asiatica* L. and other spp	Cheqianzi; Plantain seed	5	<2	3	<1

Table 2 (*continued*)

Botanical species source; toxicity notes (where known, on shaded entries)	Herb: pinyin, common name(s) and plant part	EU herbalists citing herb (*n*=327)		Chinese herbalists citing herb (*n*=348)	
		N	Approx % responders	*N*	Approx % responders
Aconitum spp. *A. carmichaeli* Debx.; *A. kusnezoffii* Richb. Toxic due to alkaloids; prescription only in EU	Chuanwu; Common monkshood root Kusnezoff monkshood root	4	<2	15	4
Ephedra sinica Stapf and other species. Legal restrictions in EU due to ephedrine content.	Mahuang; Ephedra herb	4	1	9	3
Ligustrum lucidum W.T. Aiton	Nuzhenzi; Glossy privet fruit	4	1	7	2
Epimedium brevicornu Maxim.; *E. sagittatum* (Siebold & Zucc.) Maxim.	Yinyanghuo; Horny goat weed; barrenwort herb	4	<2	3	<1
Trichosanthes kirilowii Maxim (fruit/root/not specified)	Gualou (fruit), Gualoupi (bark), Gualouzi (seed) Tianhuafen (root): Mongolian snakegourd)	4	<1	3	<1
Morus alba L. and other spp.	Sangshenzi (fruit); Sangye (leaf); sangbaipi (root bark); White mulberry.	4	1	3	<1
Amomum villosum Lour (=*Cardamomum villosum* (Lour.) Kuntze	Sharen; villous amomum fruit	4	1	2	<1
Viscum species. Potential toxicity due to lectin/agglutinin content	Hujisheng; Mistletoe herb/twig	3	<1	10	3
Millettia dielsiana Harms; *Spatholobus suberectus* Dunn.	Jixueteng; Diel's millettia stem	3	<1	6	<2
Alisma plantago-aquatica subsp. *Orientale* (Sam.) Sam. (=*Alisma orientale* (Sam.) Juz.)	Zexie; Oriental water plantain rhizome	3	<1	1	<1
Taraxacum officinale Webb	Pugongying; Dandelion herb	3	<1	2	<1
Pseudostellaria heterophylla (Miq.) Pax	Taizishen; False starwort root	2	<i	4	1
Platycodon grandiflorus (Jacq.) A.DC.	Jiegeng; Balloon flower	2	<1	5	1
Prunus armeniaca L. Potential toxicity (cyanide release from amygdalin)	Xingren; Apricot kernel	2	<1	7	2
Hordeum vulgare L.	Maiya; Malt; Germinated barley	2	<1	9	3
Eclipta prostrata (L.) L. (=*E. alba* (L.) Hassk.	Mohanlian, Hanliancao; Trailing/White eclipta herb	2	<1	3	<1
Dictamnus albus L. (=*Dictamnus dasycarpus* Turcz.)	Baixianpi; Dittany root bark	2	<1	2	<1
Notopterygium incisum C.T. Ting ex H.T. Chang. †Endangered species.	Qianghuo; Notopterygium root and rhizome	1	<1	12	3
Achyranthes bidentata Blume	Niuxi; Ox Knee	1	<1	12	3
Atractylodes lancea (Thunb.) DC.	Cangzhu; Lance-leaved atractylodes rhizome	1	0	9	3
Clematis chinensis Osbeck, *C. hexapetala* Pall.; etc	Weillingxian; Chinese Clematis/Traveller's Joy root	1	<1	5	1
Polygonatum odoratum and others	Yuzhu; Scented Solomon's seal rhizome	1	<1	6	<2
Commiphora myrrha (Nees) Engl. and other spp.	Moyao; Myrrh resin	1	<1	6	<2
Magnolia officinalis Rehder & E.H. Wilson.	Houpo, Magnolia bark; Xinyi, Magnolia flower.	2	<1	3	<1
Cornus officinalis Siebold & Zucc.	Shanzhuyu	2	<1	0	0
Paris polyphylla Sm.	Zaoxiu/Chonglou; Paris rhizome	1	<1	3	<1
Oldenlandia diffusa (Willd.) Roxb. and *O. corymbosa* L. (=*Hedyotis diffusa* Willd. and) and *H. corymbosa* (L.) Lam.)	Baihuasheshecao; Snake-Needle Grass, Spreading Hedyotis herb	1	<1	4	1
Aucklandia lappa Decne (=*Saussurea lappa* (Decne.) C.B. Clarke) †	Muxiang; Saussurea, Costus root	1	<1	2	<1
Glehnia littoralis F. Schmidt ex Miq.	Beishashen; Coastal glehnia root.,	1	<1	0	0
Boswellia serrata Roxb. ex Colebr.; *B. sacra* Flueck. and other species	Ruxiang; Mastic, Frankincense resin	0	0	6	<2
Eriobotrya japonica (Thunb.) Lindl. (=*Mespilus* spp). Cited as 'Medlar'; but may be Loquat	Pipaye (loquat leaf); Japanese Medlar fruit/leaf (not specified)	0	0	6	<2
Cistanche deserticola Y.C. Ma; *C. tubulosa* (Schenk) Wight†	Roucongrong; Desert broom-rape herb	0	0	4	1
Dendrobium nobile Lindl.; *D. fimbriatum* Hook, *D, chrysopterum* Schuit. & de Vogel†	Shihu; Dendrobium stem	0	0	4	1
Senna tora (L.) Roxb, *S. obtusifolia* (L.) H.S. Irwin & Barneby (=*Cassia tora* L., *C. obtusifolia* L) etc.	Juemingzi; Cassia seed	0	0	4	1
Asarum sieboldii Miq. and other spp. Toxic: banned in the EU due to aristolochic acid	Xixin; Wild ginger	0	0	3	<1
Schizonepeta tenuifolia Briq.	Jingjie; Japanese catnip/mint herb	0	0	3	<1
Daemonorops draco (Willd.) Blume and other spp.	Xuejie; Dragon's blood resin	0	0	3	<1
Carica papaya L./*Chaenomeles speciosa* (Sweet) Nak. (Species not clear).	Fanmugua; Pawpaw, Papaya/Mugua, Japanese quince (plant part not stated)	0	0	3	<1
Miscellaneous other individual herbs cited once or twice, and only by respondents in 1 region	Various	0‡	0	34	10

Notes: *These five herbs were specifically named, since they are known to be popular; the others were responses to an open question.
† Endangered species. These are more likely to adulteration or falsification if taken from the wild and may be CITES protected.
‡ No examples of herbs used by EU respondents only were found (i.e. not also cited by Chinese practitioners).
Shaded entries denote potential or real toxicity issues; but non-shaded herbs are not necessarily guaranteed safe.
Plants are listed in order of frequency of use in the EU, having been cited individually by name, by herbalists, and not as part of a set formula or patent medicine (although they are almost always used in combination). NB: all preparations and plant parts are listed under the species name, to identify frequency of use of toxic or endangered species. In some cases, the part of the plant or the method of processing was not specified by respondents. We do not imply clinical equivalence of different preparations of the same species.

probably unfamiliar with these products, unable to read Chinese, and thus more likely to get their CMM from a practitioner. Lingzhi is readily available as a food supplement in the EU (where it is also known by its Japanese name, reishi) and consequently practitioners can refer patients to buy it over the counter as well as prescribe it.

Almost certainly, the range of CMM available in China is much wider: over 10,000 medicinal plant and animal species are mentioned in the Chinese literature, and almost 1400 CMM manufacturers listed (Liu et al., 2009). Over a thousand herbs are stated to be 'commonly used' and regional variations in the use of herbs create further local differences (Weckerle et al., 2009), but availability on the markets is lower, and since TCM-hospitals use around 800 herbs (for example, see http://www.tcmtreatment.com/medications.htm), this is probably the maximum availability

Table 3
Comparison of animal species and mineral-derived CMM usage by TCM practitioners in China and the EU.

Animal species source	Pinyin and common names (and pharmaceutical name if not a direct translation)	EU data	China data
Ostrea gigas Thunb.	Muli; Oyster shell	3	4
Pheretima aspergillum Chen and other spp.	Dilong; Earthworm/Ground dragon	1	14
Scolopendra subspinipes mutilans L. Koch	Wugong; Centipede	1	4
Cervus elaphus L. and others	Lujiao Shuang; Degelatinised deer horn	1	1
Haliotis diversicolor Reeve, *H. asinina* L. and others.	Shijueming; Abalone/Sea-ear shell	1	3
Various species of fossilised large mammals	Longgu; Fossil fragments/Dragon's bones	1	3
Hyriopsis cumingii Lea, *Cristaria plicata* Leach and others	Zhenzhumu; Pearl shell; Nacre (Concha Margaritifera Usta)	1	–
Cervus elaphus L. and others	Lujaiojiao; Antler glue	1	–
Ophiocordyceps sinensis (Berk.) G.H. Sung, J.M. Sung, Hywel-Jones & Spatafora (=*Cordyceps sinensis* (Berk.) Sacc.)	Dongchongxiacao; Caterpillar fungus; 'Winter worm, summer grass'	1	–
Cryptotympana pustulata Fabricius	Chantui; Cicada moulting, cicada slough	1	–
Bombyx mori L., infected with *Beauveria bassiana*	Jiangcan; Stiffened/diseased silkworm (Bombyx Batryticatus)	–	5
Gallus gallus L.	Jineijin; Chicken gizzard-membrane	–	4
Buthus martensii Karsch (BMK) (=*Mesobuthus martensii* Karsch).	Quanxie; Scorpion (Scorpio)	–	3
Sepia esculenta Hoyle, or *Sepiella maindroni* de Rochebrune	Wuzeigu, Haipiaoxiao; Cuttle-bone	–	2
Bile (taken from ox, sheep or pig) with *Arisaema*. (*Arisaema* rhizome is toxic unless processed).	Dannanxing; Bile with Arisaema	–	2
Whitmania pigra Whitman, *Hirudo nipponica* Whitman and others	Shuizhi; Leech (Hirudo)	–	1
Bufo gargarizans Cantor and others Toxicity due to cardioactive glycosides.	Banmao; Toad skin, dried	–	1
Equus asinus L. (or *Equus africanus asinus* L.)	Ejiao; Donkey-hide gelatine (Colla Corii Asini)	–	1
Mineral	**Pinyin and common names, chemical formula (and pharmaceutical name if not a direct translation)**	**EU data**	**China data**
Hydrated magnesium silicate	Huashi; Talc; $Mg_3Si_4O_{10}(OH)_2$	–	1
Calcium sulphate dehydrate	Shigao; $CaSO_4 \cdot 2H_2O$ (Gypsum Fibrosum)	–	3

Notes: Shaded entries: toxicity suspected—may depend on processing and method of administration. This does not include possible contamination of animal tissues with pathogens.
Number of citations is absolute, not a percentage of respondents.
Listed in order of use in the EU.
These materials are all cited individually by name by practitioners; they are not part of set formula or patent medicines although they are almost always used in combination.
ALL animal product citations are included.

on the Chinese market. It is much lower in the EU and this was reflected in our results.

Another major difference is the wide use of decoctions in China compared to the EU. EU patients are accustomed to receiving their medicines in a 'ready-to-take' form, rather than having to prepare decoctions each day. Western herbalists also use alcoholic tinctures (of all kinds of herbs) routinely, which is uncommon in China (Luo et al., 2012).

4.2. Regulation

The more extensive use of TCM to treat neurological, cardiovascular and respiratory disease in China can be attributed to the fact that in EU law, it is a criminal offence for a non-medical practitioner to attempt to treat serious disease, including cancer. Also, in China, it is culturally acceptable and even routine to treat patients with a combination of TCM and Western medicine (Zhang et al., 2011).

In China, the range of legal materials used is very much broader and includes animal and mineral products unavailable in many EU countries, for example, scorpion, toad skin, chicken gizzard membrane and diseased silkworm, as well as arsenic and mercury salts. The European Directive 2004/24/EC restricted the registration of herbal products (which are allowed to make limited claims informing consumers of the conditions they are used to treat, on the basis of traditional use) to those which had a proven history of use for 30 years, of which 15 years must be in the EU (Fan et al., 2012). So there is the potential for some herbal CMM to be registered for legitimate use in the EU but not the more toxic plants, minerals or animal products. Other substances, if deemed safe, can be sold as food supplements but no claims of any kind can be made.

In China also, more animal parts were used than in the EU. Many of these are prohibited in the EU, although there is a thriving illicit global market for items such as rhino horn and tiger bones, as highlighted in the press. These items are less likely to be recorded in the EU as comprehensively as other CMM because of their illegal use, concerns from conservationists and emotive reports of animal suffering. They are also extremely expensive and most practitioners do not prescribe them (Graham-Rowe, 2011); instead they are bought by the wealthy, over (or rather, under) the counter.

4.3. Safety

Chinese herbalists were far less likely to report seeing significant adverse events in practice. There may be many reasons for this which are not obvious from our results and require further investigation. It may be that TCM is indeed safer in China, due to its long history and wide usage, although it may equally be the case that pharmacovigilance of CMMs is less comprehensive in China and events are simply not reported or collated (Zhang et al., 2012). In the EU, various organisations including the German Centre for Safety of Chinese Herbal Therapy (www.ctca.de) collect reports on side effects of TCM-pharmacotherapy and hopefully this practice may spread. Finally, as more serious diseases are treated in China with TCM, outcomes are more likely to be less beneficial, which may be attributed solely to the disease and with any role of the treatment being unrecognised.

Very few of the herbs being used in the EU in this sample of practitioners give rise to safety concerns from what is known from the scientific and other literature. The main cause for concern is likely to be interaction with prescribed medication, especially in central nervous system and cardiovascular conditions, the most likely therapeutic indications where drug interactions have been reported to occur (Williamson, 2005); however, that is outside the scope of this study. The range of substances used in China is more likely to give rise to safety concerns as it is broader and the use of certain toxic drugs is higher; however, even so, the majority of herbs commonly used do not present a serious threat of harm, and

literature reports of adverse reactions concentrate mainly on cases of *Aconitum* toxicity in China, and in both Europe and China, aristolochic acid (AA) poisoning. *Aristolochia* and *Asarum* species both contain AA and are banned in the EU. A recent report suggested that in Taiwan, the remarkably high incidence of upper urinary tract urothelial carcinoma, at nearly 4 cases per 10,000 people by 2007 (and four times higher than in the US) may be due to the very wide usage of herbal medicines containing these species (Chen et al., 2012a). No practitioners admitted to using the drug but a small number of practitioners in China reported using *Asarum sieboldii* (wild ginger). Aconite however is responsible for repeated poisoning cases in Hong Kong, and can usually be attributed to poor-quality herbs, and poor prescribing and dispensing practice (Chen et al., 2012b). *Aconitum* is toxic in its raw form (Wang et al., 2012) and also if not processed properly.

Three other herbs shown in Table 2 have potential safety issues: *Pinellia* is toxic in its raw form because it contains high levels of calcium oxalate (Liu et al., 2013) and also an agglutinin, PTA, which has pro-inflammatory activity and enhances the inflammation induced by the calcium oxalate raphides (Zhu et al., 2012). *Ephedra* has legality issues due to its potential for abuse as a CNS stimulant (due to the ephedrine content) in excessive amounts (Normile, 2003), and peach and apricot kernels (*Prunus spp.*) are toxic in large quantities as they contain amygdalin, which releases cyanide gas on hydrolysis (Haque and Bradbury, 2002). These however are most toxic if consumed in the raw state; there is less of a problem when used in decoctions, the standard application form of Chinese pharmacotherapy. Prunus is not subjected to a specific detoxification process before use and can be used peeled or unpeeled. Blanching with hot water before peeling reduces the amygdalin content by about 50%. Further details on processing methods can be obtained from the review by Zhao et al. (2010).

Tripterygium wilfordii is used only in serious disease due to its known serious side effects including infertility, dysmenorrhoea, embryo damage, cardiac damage and even death (Law et al., 2011).

Many toxic CMM are not plant-based, and include minerals e.g. cinnabar, realgar etc, as well as animals (Liu et al., 2013). The regulatory position in the EU means that many of these minerals are listed as poisons, and there are import restrictions on all animal materials, in addition to regulations governing endangered species. If Statutory Regulation for practitioners is introduced, as has been proposed, herbalists may be able to access a wider range of CMMs as 'specials', subject to the necessary approval (MHRA, 2006), but import restrictions are unlikely to be relaxed.

4.4. Patient characteristics and health conditions treated

The use of different CMM in the EU may reflect a different patient population and health conditions for those using either consulting TCM practitioners or self-medicating. For instance, liuweidihuang is commonly used for older peoples' health, which may explain its popularity in China with its rapidly increasing older population, but this equally applies to Europe and 'kidney yin deficiency' includes many female as well as degenerative disorders (Huang et al., 2012). It has been reported that age, gender and culture are indicators of complementary and alternative medicine usage (Williamson et al., 2013): therefore older people, especially women, in China will know of this herb, whereas European patients are less likely to.

Chinese practitioners cited treating neurological conditions, mainly stroke and pain, which were rarely mentioned by European herbalists, in accordance with EU law. This difference also relates to the accepted treatments for stroke: in China, stroke patients are treated with TCM immediately post-stroke with a combination of physiotherapy, acupuncture and herbs, whereas patients in the EU who elect to use TCM would not be seen by a practitioner until they are released from primary care—usually after 4–6 months, if at all (Chen et al., 1997). Pain is more commonly treated with acupuncture in the EU, which may relate to the type of pain being treated: in the EU, acute, muscular pain (which responds well to acupuncture) is the most common indication, whereas in China, pain due to serious underlying conditions such as angina pain, renal colic, and cancer is treated with both CMM as well as acupuncture (Ling et al., 2007).

EU practitioners were more likely to cite treating psychiatric conditions and stress, obstetric, gynaecological and dermatological conditions with TCM, which may be due to the differing treatment-seeking patterns and healthcare culture in the two areas. Mental health is not seen as a primarily medical issue in China, where mental disorders are more likely to be dealt with using self-management and family/peer support: one study found that 88% of individuals with non-psychotic mental disorders had never received any type of professional help for psychological problems (Phillips et al., 2009). A similar situation may be observed with obstetric and gynaecological issues: in China, girls regard questions about menstruation and potential gynaecological examination as threatening and embarrassing and most would seek advice from family members (mostly their mothers and friends) before considering seeking medical advice (Chan et al., 2009). Cancer is not commonly treated by TCM alone in China, but the practice of supporting chemotherapy with CMM is well-known in both China and the EU and a new product, PHY906 based on a traditional TCM formula, is now showing excellent promise for enhancing efficacy and attenuating side effects of many chemotherapy agents (Liu et al., 2013).

4.5. Limitations of the study

Different sample sizes and sampling procedures were used for EU and China, due to the variation in the organisation of the profession (professional bodies and registers of practitioners, geographical location, etc.), and although unavoidable, were a potential source of bias. In the case of the EU, data collection was dependent on the survey link being sent to members by the administration of the relevant professional bodies. In China, only TCM hospitals, rather than Western hospitals (who have TCM departments), were targeted, which may have influenced the results, and the Chinese sample also targeted large urban areas. The findings should therefore be interpreted and extrapolated with caution, given the relatively small sample size of practitioners surveyed and differences in sampling techniques. Furthermore, a number of Chinese practitioners said they 'did not use' these herbs, but then specified they did in fact use them within formulae, which are more common in China (Yuan and Lin, 2000). Such recipes include standard formulae from classical texts and those prepared by practitioners to their own recipes.

5. Conclusions

CMM were generally more commonly used for obstetric/gynaecological and dermatological conditions in the EU, compared to neurological and gastrointestinal disorders in China, reflecting the previous findings for acupuncture practice (Robinson et al., 2012). Of the specific herbs and formula cited in the questionnaire, although there were differences in regional use, our results confirm their universal popularity and support the consensus method of selecting them for the survey. In China, toxic herbs were more widely used, as were animal-derived CMM such as earthworm (rather more exotically known as 'ground dragon'; dilong), centipede (*Scolopendra spp.*, wugong) and 'fossil' or

'dragon' bones (longu). The range of CMM used in China was much broader, probably due to less strict regulation, wider availability and lower cost, but also greater acceptance by patients. However, the difference between the most widely used substances was less marked than anticipated.

The use of CMM appears largely safe in both areas, apart from potential safety issues with *Pinellia*, *Prunus*, *Tripterygium*, and *Aconitum* in particular. These herbs have legal restrictions in the EU and are usually subject to specific detoxification processes before use in China. The reported lower frequency of adverse effects in China needs further exploration to investigate whether TCM is actually safer in China, whether there is a cultural perception that it is, or if adverse events are simply not widely recorded. Surprisingly, some well-documented, highly toxic CMM, such as croton seed (*Croton tiglium* L.; badou), black hellebore root (*Veratrum nigrum* L.; lilu), and the animal medicine Cantharides or blister beetle (*Mylabris* spp; banmao), were not cited at all by any of the practitioners surveyed, suggesting that the use of these materials may be much less widespread than expected, and less of a public health problem than feared.

In summary, this survey, the first of its kind, suggests that in general, the species used in CMM currently most used by EU practitioners are unlikely to cause serious adverse events. In future, larger surveys are required to confirm our findings, but logistically these are very difficult to carry out. Further recommendations would be to ask practitioners to choose which herbs they use from a specified list, to avoid omissions and use of colloquial names, to explore the use of formulae and their component herbs, and preparations such as injectables and decoction granules.

As far as future benefit is concerned, traditional medicine has always supplied leads for the development of new drugs. China is very rich in medicinal plant species, and many of these are also used in other parts of the world. A recent study looking at shared phylogenetic patterns across floras showed that related plants from geographically disparate regions are used to treat medical conditions in the same therapeutic areas, indicating independent discovery of efficacy. This interpretation was corroborated by the presence of significantly more known bioactive species than in random samples (Saslis-Lagoudakis et al., 2012). Thus phylogenetic cross-cultural comparisons using herbal CMM could focus screening efforts, and revitalize the use of traditional knowledge in bioprospecting. This is in addition to the development of traditional formulae for modern use, as is the case with PHY906 as cancer adjuvant therapy (Liu and Cheng, 2012), and both suggest a bright future for TCM.

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