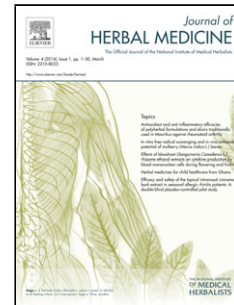


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Macroscopic authentication of Chinese *materia medica* (CMM): a UK market study of seeds and fruits

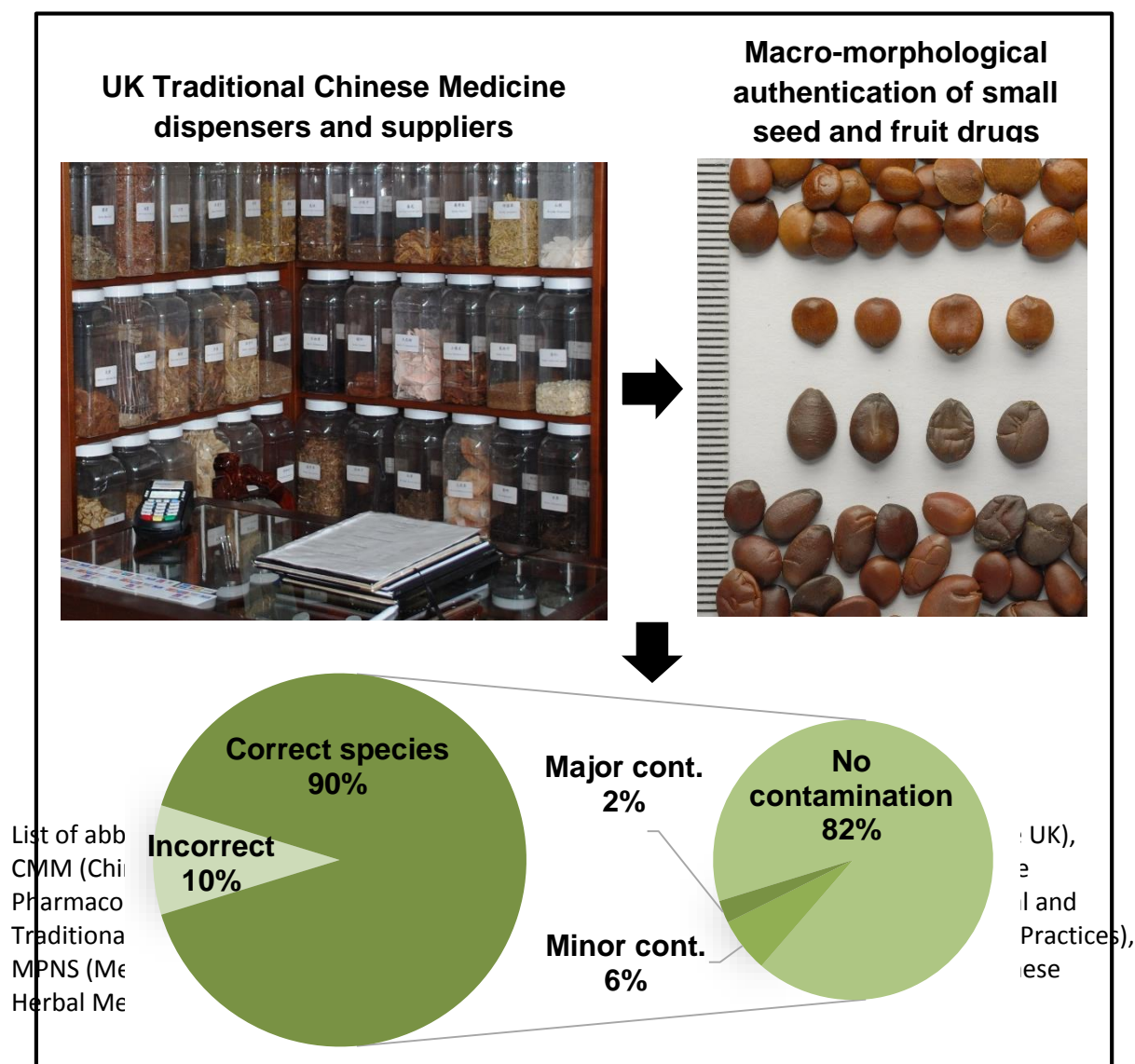
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Graphical abstract



Abstract

This small-scale macroscopic and quantitative authentication study, the first of its kind in the UK and elsewhere, assesses the identity and purity (excluding pesticides and heavy metals) of a selection of Chinese *materia medica* (CMM) seeds and fruits on the UK market. 25 fruit and seed CMM were chosen based on their inclusion in the Chinese Pharmacopoeia (2010, referred hereafter as 'official species'), maximum dimension of 10 mm, and regular use in Traditional Chinese Medicine (TCM) practice in the UK according to UK practitioners. In 2012 samples were obtained from six TCM wholesale traders and eight retail dispensaries in southeast England. Macroscopic identity and purity testing was undertaken drawing on expertise at the Royal Botanic Gardens, Kew and its collection of vouchered CMM reference drugs, herbarium specimens and published identification texts. Of the 25 CMM requested from suppliers, 23 were obtained, represented by 211 samples. 191 samples were identified as being sourced from the correct drug; 20 were identified as sourced from unofficial species. Of the 191 correct samples, 5 displayed major contamination by other plant material, stones, earth, etc. (defined as >5% of sample volume), and 12 had minor contamination (2-5%). 95% of samples derived from medicinally cultivated plants were sourced from an official species, 5% were contaminated; in contrast, 78% of wild-sourced CMM samples were sourced from an official species, and 14% showed contamination. These results aim to guide the further development of good practice in TCM herbal drug quality control, for which suggestions are provided.

List of abbreviations: ATCM (Association for Traditional Chinese Medicine and Acupuncture UK), CMM (Chinese *materia medica*), CMIR (Chinese Medical Institute and Register), CP (Chinese Pharmacopoeia), EBC (Economic Botany Collection, Kew Gardens), EHTPA (European Herbal and Traditional Medicine Practitioners Association), GA(C)P (Good Agricultural (and Collection) Practices), MPNS (Medicinal Plant Names Services), QA (Quality Assessment), RCHM (Register for Chinese Herbal Medicine), TCM (Traditional Chinese Medicine).

Keywords: quality control; market survey; Chinese herbal medicine; morphology; medicinal plant trade

1. Introduction

The rise in global trade and use of Chinese *materia medica* (CMM) as part of Traditional Chinese Medicine (TCM) practice has become increasingly evident in the West during the last 30 years (Liu et al. 2009); in the UK alone 400-500 CMM raw herbs are now regularly traded and dispensed through many TCM suppliers and clinics – at least 60 in London alone (Teng et al. 2008). The lack of regulation governing the quality of these herbs has meant that many escape routine quality assessment (QA) checks, raising concerns about the efficacy of some TCM practices as well as public safety (Teng et al. 2015).

Shortly following this increase in popularity, two Chinese medicinal herbs were proven to be the cause of over 100 high-profile cases in western Europe of serious adverse reactions, some fatal. These were due primarily to renal failure (McRae et al. 2002, Perharic et al. 1995), and linked to what has been termed “aristolochic acid nephritis” (Vanherweghem et al. 1993).

These events raised awareness of the importance of correct botanical identification, nomenclature and labelling of CMM, both for assessing safety and, for scientific research into their efficacy and mechanisms of action (Atherton et al. 1993, Chan et al. 2012, Farah et al. 2006). Many identification manuals, studies of individual CMM ingredients as well as pharmacopoeia QA monographs have been published. However, many of these are not readily accessible to traders and dispensaries, others require technical expertise (often laboratory-based) to interpret and others may be misleading if lookalike substitutes and contaminants are not included for comparison. Furthermore, systematic surveys of the extent of confusion in herbs being traded or being dispensed are rare, and it is therefore hard to judge the extent of the problem. In one of the few market surveys published, in Hong Kong, Zhao et al. (2006) identified 86 pairs of commonly confused species found in TCM retail outlets.

For this study, a market survey and authentication exercise was carried out in 2012, based in part on systematic purchasing of selected CMM from retail dispensaries in London and Canterbury, and in part on voluntary provision of samples by UK-based wholesale suppliers. Small seeds and fruits (maximum dimension 10 mm) were chosen for the study because these were considered to be among those CMM whose identity and purity are most challenging to assess by traders and retailers, given their small size and vulnerability to accidental or intentional contamination; furthermore seeds were chosen because of the first author's research training in seed identification.

A wide range number of methods can be used for CMM authentication, notably macroscopic and microscopic observation, (physico)chemical or genetic analyses (Zhao et al. 2007a), and most recently, those based on advances in systems biology and “omic techniques” (Buriani et al. 2012). For this study we relied solely on macroscopic and to some extent organoleptic authentication, using a hand lens and stereomicroscope, to examine gross characteristics of seeds and fruits. The characteristics used include: shape, size, colour, surface ornamentation, texture, fracture, cross-section, smell and taste. These features arguably provide the cheapest and fastest means to check CMM quality (Zhao et al. 2011; Leon and Lin 2017).

2. Materials and Methods

2.1 Sampling

A list of 25 CMM sourced from small seeds and fruits was generated according to four criteria: 1) CMM officially recognised either as seed or fruit in the 2005 and/or 2010 editions of the Chinese Pharmacopoeia; 2) seeds and fruits with maximum dimension <10 mm (excludes nearly unmistakable seeds such as *Ginkgo biloba* (Bai Guo) and *Litchi chinensis* (Li Zhi He); 3) presence of macroscopic characters enabling robust identification (sometimes to

species level) and 4) CMM widely available in the UK. To determine the last criterion we consulted with seven experienced, UK-based TCM practitioners (> 10 years of practice), asking them to categorise by frequency of use a list of 50 herbs as “common”, “average”, “rare”, or “don’t know”, and we also referred to the EHTPA (European Herbal and Traditional Medicine Practitioners Association) Core Curriculum listing the most clinically important Chinese herbs (EHTPA 2014).

A combination of sampling strategies was used to source the samples. Suppliers were contacted via three TCM practitioner associations in the UK: the Register of Chinese Herbal Medicine (RCHM), Association for Traditional Chinese Medicine and Acupuncture UK (ATCM) and the Chinese Medical Institute and Register (CMIR). Herbal trade suppliers were sent a written invitation, a short questionnaire and the list of study herbs using Chinese, English, pharmacopoeia names. Two suppliers were the source of only 1-2 samples; these were excluded from the analysis, leaving 99 samples from 6 suppliers for inclusion in the analysis (see Supplementary File 1). Clinics with Chinese herbal dispensaries not affiliated to any practitioner association were found using Google. A subset of these, in London and Canterbury, were visited based on location and variation in clinic characteristics (size, affiliation, part of TCM clinic chain). The list of selected seed and fruit drugs (as in Supplementary File 1) was shown to the dispensing staff, but excluding scientific names, and a small sample (20–30 grams) of each available CMM was bought. Two dispensaries could only supply 1-2 samples, so were excluded from the analysis, which is based on 112 samples collected from 8 dispensaries.

Two of the CMM sought were not available from any of the sources and were therefore excluded from further analysis: Qing Ma Zi (Abutili Semen, seed of *Abutilon theophrasti*

Medik.) and Tian Xian Zi (Hyoscyami Semen, seed of *Hyoscyamus niger* L.). *H. niger* is a restricted herbal ingredient only to be sold in the UK under supervision of a registered pharmacist (MHRA 2016), so its absence was not surprising.

2.2 Authentication

Macroscopic authentication was carried out using the naked eye, a hand lens (x10 magnification) or a stereomicroscope with light source (Olympus SZ 40, magnification x10–60) as diagnostic tools. To complement the identification expertise of the authors each sample was also compared with Kew's vouchered TCM *materia medica* reference collection and wider herbarium collections, TCM identification guides (Applequist 2006; Cappers et al. 2006, 2009; Chen et al. 2010; Forestry Administration 2000; Guan 2000; Guo 1998, 2011; Leon and Lin 2017; Medicinal Biological Products Department 2011; USDA 2016), three key Chinese trade authentication studies (Ho et al. 2006, Zhang 2002, Zhao et al. 2007b) and a core reference text on the practice of Chinese herbal medicine in Western countries (Bensky et al. 2004). Detailed identification criteria are given for some difficult cases in the discussion below.

When the appearance of sample seeds and fruits matched descriptions and reference material of an official species for the drug in question, the identification was considered 'correct'. Identification of unknown species, in the case of incorrect material, is more difficult. In some cases it may be possible to species level; in others only to genus or above. These cases are discussed on a drug-by-drug basis in section 4.2.

Latin scientific names for the medicinal species discussed follow the Kew Medicinal Plant Names Services database (MPNS 2016); names of other species follow the *Flora of China*

(Wu et al. 1994-). Author names for official CMM species are given in Supplementary File 1; for other species at first mention in the text.

The purity of each herb sample was assessed, with contamination described as ‘acceptable’ (< 2%), ‘minor’ (2–5%) or ‘major’ (> 5%). The threshold of 2% is based on that set in the British Pharmacopoeia (2015), CP2010 and WHO (2011). Each sample was spread out in a thin layer on a Petri dish and the level of contamination estimated by sight. Our assessment of contamination excludes that due to pesticides, heavy metals and micro-organisms and only includes material visible under a x10 hand lens, comprising other plant matter, soil or stones.

After authentication each sample was retained for reference as part of the Economic Botany Collection (EBC) at the Royal Botanic Gardens, Kew.

2.3 Definitions

We use the term ‘correct drug’ in this paper to refer to the correct botanical source of a drug as specified in the Chinese Pharmacopoeia (CP) (2010 edition). Where the CP2010 defines a single drug as being sourced from more than one species or infra-specific taxa these are all described as ‘correct drugs’ within the context of this paper. We use the term ‘incorrect’ to refer to an entity which is *not* one of these alternative CP2010 sources; note that such an ‘incorrect’ entity may be a different CP drug, a look-alike entity (but not a CP drug) or a completely different entity that looks quite dissimilar but perhaps which shares the same Chinese name as an official CP drug. We emphasise such definitions here because they may differ from those of many TCM texts and how such terms may be used in clinical settings. For example, in a clinical setting it is normal practice for a TCM practitioner sometimes to exchange (in effect substitute) one ingredient (CMM) in a prescription for another with

similar or slightly different clinical properties according to the pathology of the patient's condition, the price of the ingredient or the presence of certain other CMM in the prescription etc. Therein lies one of the skills of an expert TCM practitioner but such 'clinical substitutions' arise from intentional prescribing and not from accidental use of an 'incorrect entity'. Essentially, because the focus of this paper is botanical identity and not clinical substitution our definitions may differ from those used in dispensary or clinical settings.

We use the term 'adulterant' when the occurrence of an 'incorrect entity' appears to have been intentional; such adulterants are often look-alike substances or bulking agents (plant or other) and may easily go undetected along a supply chain where rigorous quality control is absent.

'Cultivated': refers to a drug cultivated as a medicinal crop (regardless of scale) as opposed to one grown for ornamental or other purposes, or harvested from the wild.

Of the 23 drugs studied here, five have multiple plant species sources according to the CP2010; therefore all these species are correct (in the context of their specific CP drug): Jue Ming Zi (Cassiae Semen) can officially be sourced from *Senna obtusifolia* or *S. tora*; Che Qian Zi (Plantaginis Semen) from *Plantago asiatica* or *P. depressa*; Chi Xiao Dou (Vignae Semen) from *Vigna umbellata* or *V. angularis*; Man Jing Zi (Viticis Fructus) from *Vitex trifolia* subsp. *litoralis* or subsp. *trifolia*; and Ting Li Zi (Descurainiae Semen/Lepidii Semen) from *Descurainia sophia* or *Lepidium apetalum*.

2.4 Nomenclature

The CP2010 uses various types of drug name for the title of each drug entry: Latinised pharmacopoeia name, scientific name, Pin Yin, Chinese and English names, e.g. Astragali Complanati Semen, *Phyllolobium chinense*, Sha Yuan Zi, 沙苑子, flatstem milkvetch seed. However, for reasons of economy of space as well as botanical clarity, the first reference to a CP2010 drug name in this paper uses the Pin Yin name followed by the pharmacopoeia name plus currently accepted scientific name sourced from MPNS (2016), e.g. Sha Yuan Zi (Astragali Complanati Semen, *Phyllolobium chinense*).

3. Results

The main authentication results are summarised in Figure 1, and are based on the data presented in Supplementary File 1. Identification and authentication comments for each sample are provided in Supplementary File 2.

3.1 Overall patterns

Although authentication is the priority focus for this study (i.e. determining if the correct drug has been supplied), the process of authentication inevitably sheds light on other aspects of herbal quality too: processing, freshness, purity (i.e. levels of contamination) and the identification and safety of incorrect entities. Where notable these herbal quality aspects are included our findings below.

Of the 23 drugs investigated, 13 (57%) had at least one sample substituted by an unofficial plant species (i.e. an incorrect entity) or that was contaminated with organic or inorganic material above an acceptable level. Overall, of the 211 samples investigated, 191 (91%) were sourced from the correct CP2010 plant species.

Of the 20 samples sourced from incorrect species, 14 were identified as closely related species or genera: 5 samples named by the trade as Sha Yuan Zi (seed of *Phyllolobium chinense*) were substituted with *Astragalus* spp.; 7 named as Suan Zao Ren (seed of *Ziziphus jujuba* var. *spinosa*) were substituted with that of *Z. mauritiana*, and 2 named as Bei Wu Wei Zi (fruit of *Schisandra chinensis*) were substituted with that of *S. sphenanthera*. For 6 samples, entirely unrelated species were supplied: 1 sample of Che Qian Zi (seed of *Plantago asiatica*, *P. depressa*) was substituted by *Bupleurum* sp.; 2 of He Shi (fruit of *Carpesium abrotanoides*) substituted by *Torilis japonica*; 2 of Man Jing Zi (fruit of *Vitex trifolia* subsp. *litoralis* and subsp. *trifolia*), one substituted by fruit of *Ligustrum lucidum* and the other by that of *Vitex negundo*; and one of Bu Gu Zhi (*Cullen corylifolium*) substituted by an unidentified seed. In this last case the same supplier also provided a correctly sourced sample of Bu Gu Zhi, the only case where the same drug was supplied twice from one supplier.

Contamination is only quantified in Supplementary File 1 for samples identified as the correct CP2010 drug. Of these samples, 5 showed major contamination and 12 showed minor contamination. Hence 17 samples displayed unacceptable levels of contamination. Overall, 174 samples (82%) were of good quality, defined here as being both sourced from the correct drugs *and* with low levels of contamination.

Other quality concerns not included in Supplementary File 1 range from non-standard processing, mixing of 2 official species within one sample (e.g. two official *Senna* species for Jue Ming Zi (Cassiae Semen), atypical odour (one rancid Chong Wei Zi (Leonuri Fructus) sample, one Niu Bang Zi (Arctii Fructus) sample smelling like fennel) and suspected counterfeiting by means of a dye (in three Wu Wei Zi (Schisandrae Fructus) samples). Insect remains (particularly of beetles, Coleoptera) were found in 4 samples.

The availability of the 23 drugs from all 14 suppliers varied considerably. No single supplier was able to provide samples of all the drugs requested. 14 suppliers were able to provide somewhere between 11 to 13 drugs, and a further 7 to 10 suppliers were able to provide at least 6 drugs.

(Insert Figure 1 here)

3.2 Drug sample analysis

Two drugs were supplied by a high proportion (>50%) of suppliers and demonstrated high levels of substitution (>50% of samples): Sha Yuan Zi (Astragali Complanati Semen, *Phyllobium chinense*) and Suan Zao Ren (Ziziphi Spinosae Semen, *Ziziphus jujuba* var. *spinosa*). Three drugs exhibited high levels of substitution (33-100% of samples) but relatively few samples were supplied, meaning that these figures must be treated as less robust indicators of a widespread problem: Man Jing Zi (Viticis Fructus, *Vitex trifolia* subsp. *litoralis*), Bei/Wu Wei Zi (Schisandrae Chinensis Fructus, *Schisandra chinensis*) and He Shi (Carpesii Fructus, *Carpesium abrotanoides*).

One drug was widely available and had frequent occurrence of minor or major contamination (42% of 12 samples): She Chuang Zi (Cnidii Fructus, *Cnidium monnieri*). Other drugs showing 25% or more of contaminated samples were Che Qian Zi (Plantaginis Semen, *Plantago* spp.), Chong Wei Zi (Leonuri Fructus, *Leonurus japonicus*) and Di Fu Zi (Kochiae Fructus, *Bassia scoparia*).

Several of the substitutes identified have previously been reported in the TCM trade authentication literature (see below); these are *Astragalus* spp. for Sha Yuan Zi (Astragali Semen), *Zizyphus mauritiana* for Suan Zao Ren (Ziziphi Semen) and *Torilis japonica* for He Shi (Carpesii Fructus). However, one case of substitution is reported here for the first time: *Bupleurum* sp. fruits for Che Qian Zi (Plantaginis Semen).

3.3 Suppliers

There was a small but consistent difference in herbal quality between the wholesalers and retail dispensaries. 92% of samples from wholesalers (n = 99) were of the correct CP2010 drug, while those from dispensaries (n = 112) were 89% correct; 5% of samples from wholesalers had minor or major contamination; in contrast, 11% of samples from dispensaries were contaminated.

3.4 Wild versus cultivated source

The cultivation status of most TCM herbs is well documented; nonetheless, absolute certainty is difficult as a species may be wild or cultivated or both according to its local provenance. The designations in Supplementary File 1 should be regarded as indicative, for the purpose of data analysis. Where taxa are known to be both wild harvested and cultivated they were excluded from the analysis: Niu Bang Zi (Arctii Fructus), Yi Yi Ren (Coicis Semen), Nan Ting Li Zi (Descurainiae Semen) and Che Qian Zi (Plantaginis Semen). Plants considered 'mainly cultivated' were treated as 'cultivated' for the analysis.

There was a major difference between wild and cultivated plant sources. 95% of samples derived from cultivated plants (n = 103) were identified as sourced from a correct species, and

5% showed minor or major contamination. 78% of samples from wild plants (n = 64) were identified as sourced from of a correct species, and 14% showed contamination.

4. Discussion

4.1 Limitations of the study

The results of this pilot study must be interpreted with caution. The 23 drugs studied represent a small proportion of the 400-500 Chinese herbal drugs currently on the market in the UK, and the wholesalers and dispensaries are again an incomplete sample: for example, there are estimated to be 60+ TCM retail dispensaries in London alone (Teng et al. 2008, 2015). In some cases only a few samples of a TCM drug were supplied by our sources. Furthermore, these results cannot be regarded as applicable to manufactured herbal products, which are produced in a factory setting with the potential for greater control of quality. Occurrence of heavy metals and pesticides (both known to be a problem in Chinese herbal drugs) or other micro-biological contamination, was not assessed.

4.2 Herb-by-herb authentication of selected trade samples

Sha Yuan Zi (沙苑子) - *Astragali Complanati Semen*

Of the eight trade samples of Sha Yuan Zi examined, only three were consistent with Kew's seed reference specimens of *Phyllobium chinense*, the CP2010 source species for this drug (most TCM literature including the CP2010 refers to it by its synonym *Astragalus complanatus* R. Br. ex Bunge). The species is a perennial herb with pinnate leaves and yellow to pinkish-red flowers borne in tightly clustered vertical heads and is endemic to W, C, E and NE China. Its seeds are somewhat kidney-shaped and slightly flattened (2-2.5 mm x 1.5-2 mm); the testa is brownish-green or greenish-brown and slightly paler around the small, round hilum which is situated at the centre of a distinct ventral indentation.

The seeds in the remaining five samples bear some resemblance to *P. chinense* but are a better match with seed of other species in the genus *Astragalus*; the latter is a taxonomically challenging genus closely related to *Phyllobium*, comprising 400 species in China and requires specialist botanical knowledge for identification to species level (even when whole plants are available). In contrast to *P. chinense* seed these seeds (as observed by the first author) have a dull greenish-brown testa, often mottled with dark brown spots, and a faint reticulate pattern of small surface cells (Figure 2A, B). Given that *Phyllobium chinense* is wild-harvested in many Chinese provinces and its source plants as well as seed are easily confused with those of species in the ubiquitous genus *Astragalus* (Figure 2C), identification confusion at source is likely to account for the high levels of seed contamination.

Inorganic contamination, mainly in the form of small stones, along with smaller soil particles, was found in six samples. These stones are of a similar size, shape and colour to the seeds of Sha Yuan Zi, suggesting probable intentional bulking up.

Che Qian Zi (车前子) - Plantaginis Semen

Che Qian Zi is officially sourced (CP2010) from seed of either *Plantago asiatica* or *P. depressa*. (see Figure 2D). Both species are short, perennial herbs with leaves in a basal rosette and tiny flowers densely packed into long, cylindrical upright heads. The majority of Che Qian Zi in trade is reported to be sourced from *P. asiatica*, which is widely cultivated on medicinal plant farms; *P. depressa* is entirely wild harvested. There is no commercial need to distinguish the seed of the two official species since they are considered to have very similar clinical actions, however macroscopic differentiation is possible under an x10 hand lens: *P. depressa* seed is smaller (0.9-1.7 mm long; 0.6-0.9 mm diam.) than that of *P. asiatica* (1.2- 2

mm long; 1 mm wide) and is less angular. But identification of *P. depressa* seed in this study is indicative only because, being wild harvested, seed cannot be differentiated from the other 20 wild Chinese species of *Plantago* using macroscopic characters alone.

Of the 12 trade samples studied here, 11 were consistent with Kew's authentic reference seed of *P. asiatica*. Two samples appeared to have been processed with salt; this a traditional processing method described in CP2010. The main contaminant common to all three samples closely resembled fruits of *Bassia* (synonym *Kochia*) in the Amaranthaceae family of which *B. scoparia* is the most widespread by far, growing wild throughout China. Its fruits are the source of a separate CP2010 drug 'Di Fu Zi' (*Kochiae Fructus*). One sample was almost completely substituted by fruit material resembling the fruit mericarps of a member of the Apiaceae family, possibly in the genus *Bupleurum*.

Suan Zao Ren (酸枣仁) - *Ziziphi Spinosae Semen*

Suan Zao Ren is officially sourced from the seed of wild *Ziziphus jujuba* var. *spinosa* and is a widespread, spiny and deciduous shrub (up to 10 m) endemic to northern China and producing, in late summer, red-purplish fruit with a distinctively spongy, sour-tasting flesh. It is widely used for hedging in China owing to its sharp spines. A different variety, *Z. jujuba* Mill. var. *jujuba*, is widely cultivated for its sweet, spongy fruit and is the source of a separate TCM drug called Da Zao (*Jujubae Fructus*).

Of the 12 trade samples examined, 5 were consistent with Kew's authentic reference seed of Suan Zao Ren (i.e. the official CP2010 species) of which two had undergone dry-frying, a traditional TCM processing method which typically slightly inflates and darkens the seed.

Contamination levels by other plant materials (in this case in endocarp fragments) in these 5 correctly sourced samples were considered to be within acceptable limits (i.e. < 2%).

Seven samples were substituted in their entirety by seeds resembling those of *Z. mauritiana* Lam. The latter species is widely cultivated in China for its edible fruit (Hu 2005) and it is plausible that its seed (normally discarded) has been used here as a cheap look-alike substitute for the official drug. Whole plants of the two species are easily distinguished as are their seeds (Figure 2E). Although superficially similar, *Z. mauritiana* seeds are more rounded and thinner (6-7 mm long; 5-6 mm wide; 2 mm thick), while seed of the official species is ellipsoidal or oblate (5-9 mm long; 5-7 mm diam.; ca. 3 mm thick); the testa of *Z. mauritiana* is usually lustrous and yellowish- or reddish-brown (as opposed to slightly lustrous and reddish- or purplish-brown in the official species) and the ventral surface is smooth while the official species usually has a longitudinal ridge or furrow, or is randomly fissured (Leon and Lin 2017: 722-723).

He Shi (鹤虱) - *Carpesii Fructus*

He Shi is officially sourced from the fruit of *Carpesium abrotanoides*, a much branched, perennial herb in the Asteraceae family. The species has simple, alternate, elliptic leaves with small branching clusters of flowerheads (capitula) arising from the leaf axils; each capitulum contains 130-300 tiny, yellow, densely packed florets which develop into cylindrical and longitudinally ribbed achenes (ca. 3.5 mm long x 1 mm diam.), the source of He Shi. The plant is widely distributed as a ruderal throughout China except in the North.

Although only two samples were supplied, neither were the correct drug. Instead, they were identified as the spiny and much larger fruits of *Torilis japonica* (Houtt.) DC. (Apiaceae

family) a widespread species in China, whose fruits are used in local medicine. Their occurrence as an adulterant of He Shi is widely reported (Bensky et al. 2004, Zhao and Xiao 2010) and it is likely this is due to confusion about their similar Chinese names (Hua Nan He Shi and He Shi) rather than mistaken identity; *Torilis* fruits are easily distinguishable from those of He Shi (Figure 2F; for identification criteria, see Table 2).

She Chuang Zi (蛇床子) - *Cnidii Fructus*

She Chuang Zi is officially sourced from the fruit of *Cnidium monnieri* (family Apiaceae). The species is an annual herb with 1-3 pinnate leaves and tiny, white, 5-petalled flowers borne in compound, 15-20-flowered umbels (ca 2-4 cm diam.). Fruits are dry, brittle and ovoid-ellipsoid (1.5-3 mm long; 1-2 mm diam.) with a persistent swollen style base (stylopodium) at the apex and occasionally with 2 recurved styles. At maturity fruits split into 2 mericarps; each mericarp has a flat ventral surface with 2 brown longitudinal oil ducts (vittae) and a dorsal surface with 5 distinctive cork-like wings. The trade item, She Chuang Zi, mostly consists of these separated mericarps and which, when crushed, are distinctly aromatic.

All 12 samples were consistent with Kew's reference material of *C. monnieri* (Leon and Lin 2017: 717). Four samples showed minor contamination and one showed major contamination; the contaminant in all these samples resembled fruits in the Amaranthaceae family (probably the genus *Bassia* (synonym *Kochia*; see also Che Qian Zi above).

Zi Su Zi (紫苏子) - *Perillae Fructus*

Zi Su Zi is officially sourced from the fruit of *Perilla frutescens* (Lamiaceae family). The species is an annual herb (0.3-2 m tall) with ovate leaves varying in colour according to variety. Tiny white to purplish-red flowers are borne in short cylindrical heads and develop into greyish-brown, almost spherical, 1-seeded nutlets (1- 1.5 mm diam.) with a distinctive and slightly raised reticulated surface. The species has long been cultivated in east-central China for its medicinal fruit (Zi Su Zi), leaves (Zi Su Ye) and stems (Zi Su Geng), each recognised as a separate medicinal ‘herb’ in the CP2010. The species is also widely cultivated in China for its leaves and flowerheads as a culinary ingredient, and the seed oil is used as a waterproofing agent (Yu 1997). In addition to the three wild varieties of this species (Wu et al. 1994-), the diverse uses outlined above have also led to the development of many cultivars which exhibit considerable variation in leaf and fruit morphology. The CP2010 does not mention any cultivar(s) by name as the specific source of Zi Su Zi so it would appear that any can be used; its description of the fruits reads (translated from the Chinese) ‘*about 1.5 mm diameter, externally greyish-brown, with dark purple and slightly raised reticulate striations*’.

In the eight samples obtained the seed morphology was broadly consistent with the CP2010 description and Kew’s reference material of *Perilla frutescens* (Leon and Lin 2017: 768-769). However, seeds in five samples were markedly larger than the size stated in the CP2010 (ca 1.5 mm diam.) with most falling in the range 1.9-2.7 mm and another two samples were markedly smaller (0.6-1.3 mm diam.). These are significant size differences. Considerable variation in colour (greyish-brown, pale creamy-yellow, yellowish-brown and purplish-brown) and variation in the prominence of the reticulated fruit surfaces was also noticed between samples (Figure 2G, H). It is possible that these samples were harvested from cultivars which exhibit a more variable fruit morphology than those forms of *P. frutescens* that are officially recognised as acceptable sources of Zi Su Zi. It is also possible that the fruit

having been dry-fried, a traditional processing procedure that slightly darkens the fruit surface and which may even cause the fruits to swell. However the samples in this study did not have the appearance of having been dry-fried. To bring clarity to these UK market findings, further research is recommended into which cultivars of *P. frutescens* are considered suitable for sourcing Zi Su Zi, and whether amendment to the current CP2010 macroscopic description is required.

The variability in seed appearance makes detection of contaminants in these samples difficult. Two samples, at least, were possibly contaminated by fruits of another species, with different reticulation leading to an almost sculpted surface, small size (0.6-1.3 mm diam.) and the virtual absence of an areola at one end. These may be fruits of species in the genus *Mosla* (closely related to *Perilla*) which have been reported as contaminants or adulterants of Zi Su Zi on the Chinese market (NICPBP 1997-2002, Bensky et al. 2004). It is not possible to discriminate between the fruits of all 13 Chinese *Mosla* species solely on the basis of macroscopic characters, and for reliable detection, laboratory-based authentication methods are advised.

Bu Gu Zhi (补骨脂) - Psoraleae Fructus

The official source of Bu Gu Zhi is the fruit of *Cullen corylifolium* (family Fabaceae). This is an annual herb (0.6-1.5 m tall) with leaves, and especially calyx, dotted with black glands and flowers yellow or blue and borne in dense, axillary flowerheads. The crude drug is made from the fruits, which are dry, ovoid and often reniform (ca. 5 mm long) with a blackish-brown or greyish-brown, brittle and densely reticulated periderm; with an apical end with a small prominence and the basal end slightly depressed with a tiny fruit-stalk scar; each fruit contains one seed.

Examination of the 12 trade samples obtained, revealed that 11 were completely consistent with the fruit of Kew's reference material of the *Cullen corylifolium* (as described above). Two or three samples showed some (albeit negligible) evidence of sub-standard processing owing to the persistence of the distinctive membranous, black gland-dotted calyx still attached at the base; calices are normally removed when traditionally processed. Another sample showed evidence of having been dry-fried with salt (a traditional TCM processing method), recognised by the slightly different appearance of the pericarp: pale brown and slightly inflated or cracked. The one sample that did not comply with the reference material was very heavily adulterated (ca 90%) with an unpleasant-smelling sub-ovoid seed (3-4 x 2-3 mm) with a thin, mat and brittle testa (not reticulated), frequently dented and sometimes cracked to reveal two blackened cotyledons within (Figure 2I). Its identity has not been established; dry-fried radish seed (*Raphanus sativus* L.) was considered as a possibility (this is the source of a separate TCM herb 'Lai Fu Zi' 莱菔子 (Raphani Semen), but we have been unable to confirm this. To the naked eye the unknown seeds superficially resemble fruits of *Cullen corylifolium*; whole plants are very different in appearance, suggesting intentional adulteration but for reasons unknown.

Care was taken when examining all these trade samples to ensure the absence of seed of *Datura* spp. (Solanaceae), notably *D. stramonium* L. and *D. inoxia* Mill.; these are toxic, bear a close resemblance to Bu Gu Zi and both have been reported as contaminants of Bu Gu Zi (Bensky et al. 2004; NICPBP 1997-2002, vol. 3). No such contamination was found in any of the samples.

(Bei) Wu Wei Zi (北)五味子 - *Schisandrae Chinensis Fructus*

(Nan) Wu Wei Zi (南)五味子 - *Schisandrae Sphenantherae Fructus*

Bei Wu Wei Zi (also known as Wu Wei Zi) is officially sourced from the fruits of *Schisandra chinensis* and Nan Wu Wei Zi from *S. sphenanthera* (family Schisandraceae). The two species are discussed together here because although officially recognised as the source of two separate TCM drugs (from the CP2000 onwards), they are often used interchangeably in a clinical setting due to their similar pharmacological actions, and because they are difficult to distinguish macroscopically. Clinical preference exists for *S. chinensis* however and this is reflected in trade prices. Owing to increasing demand, especially in overseas markets where it is marketed as a health food, *S. chinensis* has recently been brought into commercial cultivation in parts of north-east China, and Good Agricultural Practice (GAP) certification awarded at some production sites in Jilin province (Zhang et al. 2010). *S. sphenanthera* continues to be sourced only from wild populations.

The two species are deciduous climbers with *S. chinensis* found wild in slightly more northerly parts of China compared to *S. sphenanthera*, hence their prefixes ‘Bei’ [north] and ‘Nan’ [south]. Both have elliptical leaves, solitary 5-9 ‘petalled’ flowers and pinkish-red ovoid fruits developing in pendant clusters. The main differences are to be found in their flower colour (white or whitish-yellow in *S. chinensis*; yellow, orange or red in *S. sphenanthera*) and in the number of their stamens.

The macroscopic identification of Wu Wei Zi to species level can be challenging, especially when the fruits are dried. A pure, good quality sample of Bei Wu Wei Zi is usually straightforward but a lower quality and less homogeneous sample is often problematic especially where mixed species samples are suspected. Accordingly, samples in trade are easily confused, accidentally or intentionally for the reasons outlined above. The main

distinguishing characters of Nan Wu Wei Zi are: fruits less fleshy and often smaller (c. 5-5.5 mm diam.); fruit wall dull, brownish-red to dark brown with seed difficult to remove cleanly; seed slightly smaller and more rounded (3-3.5 x 3.5-4 mm; Bei Wu Wei Zi 3.2-3.8 x 4.4-4.8 mm); seed coat dark greyish-brown, mat, somewhat verrucose (warty) (Upton 1999; Leon and Lin 2017: 687, 742-743; authors' personal observations).

13 samples were obtained, requested under each name: Bei Wu Wei Zi and Nan Wu Wei Zi. 5 suppliers did not attempt to distinguish the two species and simply supplied their samples as Wu Wei Zi; these were identified as *S. sphenanthera*. The other 8 samples were supplied with the more precise prefixes Bei (北, Northern) or Nan (南, Southern). In this group, two samples named by the supplier as Bei Wu Wei Zi were identified as *S. sphenanthera*. Whether such mis-naming was intentional or accidental is unclear; possibly a mix of the two is most likely given the price differential between the 2 species.

Three samples (2 supplied under the name 'Wu Wei Zi' and one as 'Nan Wu Wei Zi') were found to be adulterated with a red dye. This was detected when the fruits were immersed in water and a strong pinkish-red colour was instantly released (Figure 3). In the dry material of these samples we had noted that contaminant pieces of stem in each of these samples were unusually dark and vivid red suggesting adulteration. Bei Wu Wei Zi are typically a strong red colour compared to duller Nan Wu Wei Zi, so the use of a red dye in the latter is plausible as an attempt to pass them off in trade as fruit of the former more expensive herb. Our research indicates confusion in the UK market in respect of which species are being traded as Wu Wei Zi.

(Insert Figure 3 here)

Man Jing Zi (蔓荆子) - *Viticis Fructus*

Man Jing Zi is sourced from the small, hard round fruits of *Vitex trifolia* (Lamiaceae family), mostly from subspecies *litoralis* (appears under the synonym *V. trifolia* var. *simplicifolia* Cham. in CP2010). This subspecies is a prostrate shrub with small purplish-mauve flowers, widely cultivated near lakes and along coastal areas in central and south-eastern China.

Subspecies *trifolia* is an alternative official source whose fruits are virtually indistinguishable from those of the above (the scientific nomenclature for this in the CP2010 is ambiguous but it is assumed that this type subspecies is intended since the other subspecies is named in full).

Of the ten UK trade samples acquired as Man Jing Zi, eight were identified as consistent with Kew's reference samples of *V. trifolia* fruit (i.e. official Man Jing Zi); these could be further separated into subsp. *trifolia* (6 samples) and subsp. *litoralis* (2 samples) (Leon and Lin 2017: 680-681). One of the subsp. *trifolia* samples was typical of the Hong Kong trade style of Man Jing Zi where fruit calyces are removed and another was significantly contaminated (15%) with *V. negundo* fruits (see below). The two remaining samples were totally incorrect. One was identified as fruit of *V. negundo* L. easily identified as smaller (3-4 x 2-3 mm, as opposed to 4-5 x 4-6 mm) with a shallowly- (as opposed to deeply-) toothed persistent calyx enclosing at least half (as opposed to one-third) of the fruit (Figure 2J). *V. negundo* fruits are a commonly reported substitute or adulterant of Man Jing Zi. They are used in Chinese folk medicine (albeit for different clinical conditions) and the leaves of the species are also widely used for large-scale extraction to produce the separate TCM herb 'Mu Jing Ye' (*Viticis Negundo Folium*); as such the fruits may be readily available as a cheap look-alike for official Man Jing Zi. An accidental cause of substitution may also arise due to potential confusion of

the similar Chinese trade names of these two herbs; *V. negundo* fruit is often called Huang Jing Zi (黄荆子) and when this and Man Jing Zi (蔓荆子) are shortened in trade circles to Jing Zi (荆子) confusion may ensue.

The other incorrect sample was considered a straightforward dispensing error since although the supplier's jar was labelled 'Man Jing Zi' its contents were easily identified as *Ligustrum lucidum* fruit which is a separate and easily distinguished TCM herb (Nu Zhen Zi 女贞子).

4.3 Possible causes of substitution, adulteration and contamination

Chinese herbal drugs present a special challenge in documentation and authentication, in part simply because of the number of species involved (500+) and the size of the country in which they are produced and used (Zhao et al. 2006; Leon and Lin 2017)). Many *materia medica* can be sourced from more than one official species, or from unofficial substitutes, both of which may reflect supply shortages or price differentials. In addition, the choice of plant part and processing technique are further variables (Zhao et al. 2010). We have drawn on two approaches to clarify the patterns observed here: Zhao et al.'s (2007a) analysis of deliberate and accidental forms of substitution in Chinese *materia medica*, as modified in our Table 3, and Booker et al.'s (2012) study of value chains in the supply of herbal medicines, which highlights the many loci and individuals involved in the typical supply chain. Although existing studies on value chains focus on their influence on village-level livelihoods, there is obvious potential for study of their effect on medicinal plant quality.

The marked difference in quality between drugs harvested from the wild, of which 36% of samples were either of the incorrect species or with minor or major contamination, and those from cultivation, with the corresponding figure of 10%, points to the origin of the drugs as a

crucial factor. In the case of Sha Yuan Zi (*Astragali Complanati Semen*), *Phyllolobium chinense* is substituted by one or more species from a very closely related genus, *Astragalus*, with plants and seeds that are very similar in morphology, to the extent that *P. chinense* was until recently classified as an *Astragalus* species. These seed contaminants are most likely to be entering trade through accidental confusion during wild harvesting. In contrast, the occurrence of the sample substituted with an Apiaceae fruit (not known as a TCM drug) is more likely to be due to intentional adulteration owing to its superficial resemblance. The other wild-harvested drug to show a high incidence of substitution (probably intentional) is Suan Zao Ren (*Ziziphi Spinosae Semen*) where the seeds of *Ziziphus jujuba* var. *spinosa* have been substituted with those of the widely cultivated *Z. mauritiana*.

Higher levels of contamination in wild-harvested species doubtless reflect the inadvertent harvesting of nearby plants. Of the contaminant species, *Bassia* (synonym *Kochia*) fruit is clearly the most significant, turning up in three samples of She Chuang Zi (*Cnidii Fructus*), three samples of Che Qian Zi (*Plantaginis Semen*) and one sample of Chong Wei Zi (*Leonuri Fructus*). *Cnidium monnieri* fruit (i.e. She Chuang Zi) is a close second, and was found in 4 samples of Chong Wei Zi (*Leonuri Fructus*) and 1 of Di Fu Zi (*Kochiae Fructus*). *Bassia*, *Cnidium* and *Leonurus* fruits were all present as contaminants in several samples of each of the respective herbs. *Cnidium* and *Leonurus* especially have been found to contaminate each other repeatedly. The three last-mentioned taxa are all ruderals, occurring as weeds, in field margins and on roadsides and therefore are likely to be accidental contaminants. Other weedy species occurring commonly as contaminants are *Echinochloa* sp. awns and caryopses (in at least 11 samples of six different herbs, especially *Kochiae Fructus*), and Amaranthaceae seeds (probably *Chenopodium* spp.).

The higher quality (i.e. use of the correct species and absence of contamination) of cultivated samples is not surprising, given the greater degree of control over plant and habitat (e.g. through weeding) during production and harvesting. It may also reflect the increasingly widespread implementation of Good Agricultural Practice (GAP) in China.

Chinese *materia medica* reach UK sources through a complex chain of suppliers, and it is difficult to point to the exact point that a problem affecting quality is introduced. Our data suggest that some errors occur at the end point. The difference in quality between drugs available from wholesale suppliers, with 87% of samples supplied as the correct species and without contamination, compared to 79% from retail dispensaries, suggests that some errors are introduced in handling within shops. Cases that are not otherwise explicable, and probably thus represent simple matters of mislabelling or careless handling, were *Ligustrum lucidum* supplied in place of *Vitex trifolia* for Viticis Fructus (Man Jing Zi), from a dispensary, and two samples of Psoraleae Fructus (Bu Gu Zhi) obtained from a trader, one correct and containing *Cullen corylifolium* seeds; the other incorrect but the identity of which has not been possible to establish.

Confusion about similar Chinese names could have occurred in the UK or at an earlier point in the supply chain. Two examples of substitution were possibly due to this: replacement of He Shi (Carpesii Fructus) by Nan He Shi (Carotae Fructus), and replacement of one sample of Viticis Fructus (Man Jing Zi) by Huang Jing Zi (*Vitex negundo*).

Three cases of deliberate adulteration were found; these most likely occurred close to the point of origin, probably while the crude drugs were being processed. These cases are an unidentified seed instead of Bu Gu Zhi (Psoraleae Fructus) referred to above; the stones

mixed in with seeds of Sha Yuan Zi (*Astragali Complanati Semen*), and the dyeing red of fruits of Nan Wu Wei Zi (*Schisandrae Sphenantherae Fructus*) in three samples.

4.4 Suggested solutions

The presence of many individuals in the supply chain means that the question of whose responsibility it is to ensure safe, high-quality herbs is complex. Although some quality issues are best resolved at the point of production in China or of sale in London, most will benefit from increased East-West dialogue which can help to initiate, accelerate and shape outcomes as well as promote take-up of good practice protocols. Two such protocols, GAP for cultivated and FairWild for wild-sourced plants, are discussed here; the WHO (2003) *Guidelines on Good Agricultural and Collection Practices (GACP) for medicinal plants* are also relevant.

Chinese Good Agricultural Practice (GAP) certification for TCM herbs provides documented assurance of identity, purity and standard quality, and also indicates traceability and compliance with heavy metal limits set by the *Chinese Pharmacopoeia*. By guaranteeing cultivated origin, such certification also ensures production will not have damaged wild populations through over-harvesting. The three downsides of GAP-certified herbs are that their prices are higher, coverage is confined to only 58 TCM herbal drugs, and current supply falls far short of demand (Zhang et al. 2010, Guo et al. 2014). A full list of producers of GAP-certified TCM drugs is available from the China Food and Drug Administration website (CFDA 2016); as GAP certification is issued to named producers for named species for a limited 5-year period, this site needs to be checked regularly for updates. A scaled-up GAP

production system would help address some of the quality issues presented in the UK study described here.

For TCM drugs yet to be covered by GAP (i.e. by far the bulk in international trade) the greatest variability in quality inevitably occurs among wild-harvested species; this is due not only to the natural variability of wild species, but also to the increased likelihood of contamination with easily-confused species at the point of harvest. Trying to avoid the use of wild-sourced herbs, however, is difficult since 70-80% of CMM species in world trade continue to be wild sourced (Zhang et al. 2010). Fortunately, recent international medicinal plant initiatives designed primarily as tools for sustainable wild-harvesting and good collection practices also include species identification and traceability procedures that can help address herbal quality issues (WHO 2003, FairWild Foundation 2010). For example, the FairWild Standard aims ‘to identify and facilitate socially responsible business practices for sustainable wild plant collection’ and has recently been field-trialled on a selection of TCM drugs in 3 Chinese provinces as part of a recent EU-China funded project, led by TRAFFIC International (Timoshyna et al. 2015). This project reflects changing attitudes within China about the sustainable sourcing of TCM raw materials and is a promising model that could be expanded to other CMM. As such it deserves close evaluation by Western suppliers.

A growing understanding of medicinal plant value chains, aimed at resolving socio-ecological impacts of complex and poorly managed TCM supply routes, also provides many opportunities for East-West dialogue that may help to hasten quality improvement of CMM in world trade (Booker et al. 2012).

Further research is also required to identify the full range of CMM sold in the UK, and in other areas outside China, so as to identify which have the greatest quality problems. The results of this work will then enable efforts to be most effectively directed. Such work could not only seek to improve quality at the point of production, but also promote more responsible attitudes and good practice protocols in the supply of TCM herbs and even consider whether some commonly used, closely related substitutes are in fact suitable candidates for recognition as official substitutes. Methodical data collection, as demonstrated in this paper but covering all *materia medica* and a larger number of sources, will generate valuable data for other purposes too. The popularity of wild-harvested plants, and instances of large-scale substitution of these, will indicate where conservation efforts should be directed to wild plant populations. Differences between European and Chinese prescribing practice are also likely to be found (Williamson et al. 2013), and these will be of interest to historians and anthropologists of medicine interested in the transformation of TCM in overseas contexts. Such market surveys are most effectively undertaken on the basis of collaboration between researchers, traders and the professional TCM practitioner bodies, of the kind demonstrated in this paper as well as by the pioneering work of the now well-established Approved Suppliers Scheme initiated and managed by the RCHM.

The occasional use by suppliers of species-specific prefixes for certain drugs (e.g. those for Wu Wei Zi – *Schisandra*) suggest there is supplier confidence in precisely which species is being traded; this study however has revealed that such apparent precision is not reliable and authentication is required to be certain of the species' identity.

5. Conclusions

According to readers' perspectives, the headline results of this survey can be presented either as encouraging (91% of samples were of the correct species) or discouraging (18% of samples were of incorrect species or had major or minor levels of contamination). Of these incorrect species and contaminants none were considered to pose direct health problems (i.e. none were considered to be toxic). Most significant, however, is that the above quality issues were found in some of the most popular herbs (i.e. those that were sold by the greatest number of sources), including three of the six EHTPA-listed herbs in this study, which had, respectively, 8, 25 and 33% of samples either incorrect or contaminated.

The clinical impact of including herbs with such quality issues in TCM prescriptions is not known. At the very least the efficacy (and possibly safety) of such a prescription will be compromised owing to an imbalance in the ratio and assemblage (and hence pharmacological profile) of the prescription's ingredients but it is outside the scope of this study and its authors' expertise to comment on possible clinical implications. The findings of a recent and large-scale questionnaire survey of TCM practitioners in China and the EU state that 'The use of CMM appears largely safe in both areas [EU and China]' (Williamson et al. 2013)].

Although physical CMM samples were not examined in the latter study, the overall findings of the present UK-based paper support this view. Equivalent market studies covering more CMM over a wider geographical area would provide further corroboration. In the meantime, greater vigilance is needed to improve the quality of CMM on the UK market specifically.

While resolving quality issues depends in part on the action of suppliers and dispensers, their full resolution will depend on collaboration with producers and regulators in and outside China to ensure consistent standards of production (Fan et al. 2012). Market surveys with a

focus on authentication will have an important role to play in detecting problem herbs and enabling efforts at improvement to be focused.

(Insert Figure 2 here)

Supplementary Materials

Supplementary File 1 (.xlsx). Summary authentication table listing the various *materia medica* names, their cultivation status, and the actual authentication results for dispensers and suppliers. Botanical names are given for those correct species found in the samples; other plant species that are correct for a drug, but which were not found, are given in section 2.3.

Supplementary File 2 (.xlsx). Sample-by-sample authentication table. The first column indicates the source of each sample included in this study, listing all suppliers (wholesale traders and retail dispensaries) who provided a sample from the study herb list. The numbers in the second column refer to the list of 23 study herbs (see Supplementary File 1). Other names that were supplied by providers that are not mentioned in CP2010 are in column three. The actual authentication result consists of the main component and comments on herbal purity, processing and quality. Each plant part identification should be read as being preceded by ‘good match with Kew reference materials for X’. Acceptable contamination (cont.) generally stands for < 2% foreign matter, minor contamination for 2-5% and major > 5%. Incorrect entities are marked in dark grey, unacceptable contamination in light grey, and other significant authenticity issues are underlined. When no taxonomic identification is given together with a plant part contaminant then it is most likely from the main component. 211 samples were studied in total.

Declarations

Ethics approval and consent to participate

This project was approved by the Ethics Committee of the School of Anthropology and Conservation, University of Kent. Prior informed consent was obtained from each of the three collaborating UK TCM practitioner associations, and from individual practitioners participating in the study. No further permissions or licenses were required or appropriate for obtaining and studying the plant materials. The authors adhered to Kew's biodiversity policies.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files. However, UK TCM suppliers and clinics have been anonymised.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

This article is based on JMAVDV's Ethnobotany MSc dissertation project carried out at the School of Anthropology and Conservation (University of Kent) and the Royal Botanic Gardens, Kew. JMAVDV organised and undertook the sampling and macroscopic

identification. CL and JMAVDV designed the research study. All three authors participated equally in data analysis and interpretation.

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Figure 1. A graphical overview of the main authentication results. The asterisk (*) indicates EHTPA-listed herbs.

Figure 2. Photographic grid of noteworthy trade issues. The small scale bars are 1 mm, the large scale bars 1 cm. **A.** Sample traded as ‘Sha Yuan Zi’ (Astragali Complanati Semen, seed of *Phyllolobium chinense*, EBC 83804 (dispenser 1) heavily contaminated with unidentified seed of closely related genera (possibly *Astragalus* and *Crotalaria*). **B.** detail of 83804 showing range of seed contaminants. **C.** Kew reference drug (top left) of Sha Yuan Zi (Astragali Complanati Semen, seed of *Phyllolobium chinense*, EBC 82195) and five reference seeds from the Kew Legume Seed Collection of closely related genera: *Astragalus sinicus* L. (top right), *A. sinensis* Turrill (centre left), *Aeschynomene indica* L. (centre right), *Crotalaria pallida* Aiton (bottom left), and *Abutilon indicum* (L.) Sweet (bottom right). **D.** Kew reference drug of Che Qian Zi (Plantaginis Semen) showing seed of the two official source species: *Plantago asiatica* (left, EBC 82352) and *P. depressa* (right, EBC 83240). **E.** *Left:* Kew reference drug of Suan Zao Ren (Ziziphi Spinosae Semen, seed of *Ziziphus jujuba* var. *spinosa*, EBC 81794). *Right:* sample traded as ‘Suan Zao Ren’ but identified as seed of the unofficial substitute *Z. mauritiana* (EBC 83929, supplier 5). **F.** *Top:* reference drug of He Shi (Carpesii Fructus, fruit of *Carpesium arbotanoides*, C-Standard-3966). *Lower left:* reference fruit of *Daucus carota* ‘Nan He Shi’, EBC 83081). *Lower right:* sample traded as ‘He Shi’ fruit but identified as fruit of *Torilis japonica* (sold by supplier 5, EBC 83828). **G.** Sample traded as ‘Zi Su Zi’ (Perillae Fructus, fruit of *Perilla frutescens*, EBC 83983, dispenser 8) but heavily contaminated by fruit of other species, possibly *Mosla*. **H.** Kew reference drug Zi Su Zi (fruit of *P. frutescens*, EBC 81840, top left) and Kew reference fruit of three species of *Mosla* (*M. dianthera*, bottom left; *M. scabra*, bottom right; *M. chinensis*, top right). N.B. the slightly larger and paler fruits of *P. frutescens* in the top photo, compared to those of the Kew reference drug, are probably a well-known cultivar of *P. frutescens* called ‘Bai Su Zi’. **I.** *Left:* Kew reference drug of Bu Gu Zhi (Psoraleae Fructus, fruit of *Cullen corylifolium*, EBC 82989). *Right:* sample traded as ‘Bu Gu Zhi’ but heavily contaminated with black seed of an unidentified species (EBC 83939, supplier 5). **J.** *Left:* Kew reference drug of Man Jing Zi (Viticis Fructus, fruit of *Vitex trifolia* subsp. *trifolia* EBC 80016). *Right:* sample traded as ‘Man Jing Zi’ (EBC 83939, supplier 5) but identified as *V. negundo* fruit, an unofficial substitute.

Figure 3. *Left:* Kew reference drug of Nan Wu Wei Zi (fruit of *Schisandra sphenanthera*, EBC 80419). *Middle:* sample traded as ‘Wu Wei Zi’ (EBC 83897, dispenser 7), identified as Nan Wu Wei Zi (*S. sphenanthera*) and dyed (middle petri dish). *Right:* Kew reference drug of Bei Wu Wei Zi (fruit of *S. chinensis*, EBC 80572). *Top row:* the 3 samples after brief immersion in water. The ruler indicates 1 mm.

Fig 1

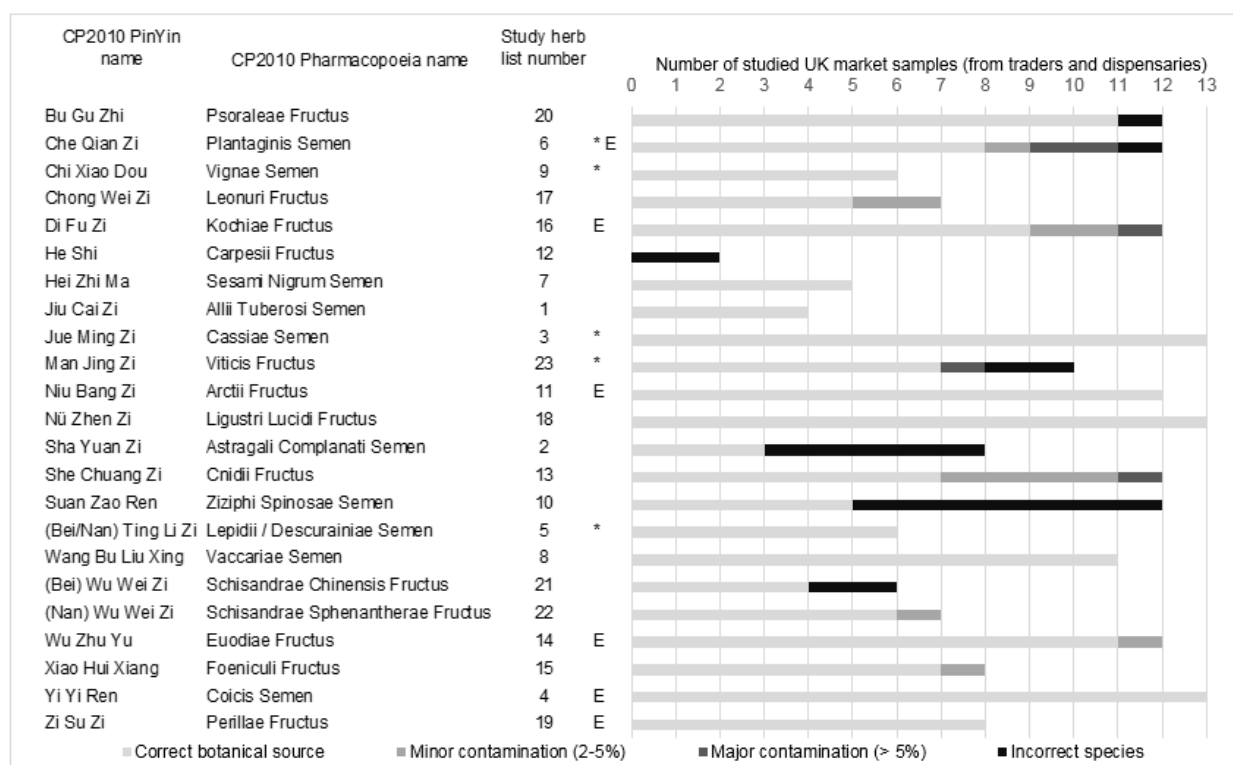


Fig 2



Fig 3



Table 2. Identification criteria for seeds of *Carpesium abrotanoides*, *Torilis japonica* and *Daucus carota*.

Character	<i>Carpesium abrotanoides</i>	<i>Torilis japonica</i>	<i>Daucus carota</i>
size (without spines)	3.5-4 mm long; 0.5 mm diam.	2.0-3.8 mm long; 1.2-1.5 mm diam.	2.2-4.0 mm long; 1.2-1.9 mm diam.
shape	narrowly cylindrical	ovoid-ellipsoid	ovoid-ellipsoid
dorsal surface	several shallow longitudinal ribs; bristles absent	3 broad dorsal ribs, covered densely in spines (0.5-0.8 mm long) with spines curving towards apex	4 broad dorsal ribs, covered densely in straight spines ca 1 mm long
stylopodium	spreading like a beak (0.7 mm long) to form an apical cartilaginous ring	conical, not spreading	conical, not spreading

Table 3. Possible reasons for identification and purity issues of single, loose dried herbs (cf. Zhao et al. 2006a, b). The table does not incorporate chemical and microbiological contamination as these often cannot be detected macroscopically.

1 Sourcing	
1a multiple official sources	(different versions of) CP, other (inter)national pharmacopoeias listed in provincial publications (e.g. Guangdong pharmacopoeia) used locally as a substitute
1b regional source	
1c local source	
2 Naming	
2a botanical nomenclature	lack of authority, synonyms, unresolved names
2b other names	Chinese, Pinyin, Pharmacopoeia, and English names, etc.
3 Morphological similarity	
3a whole plant	entire plants look alike
3b plant part	targeted plant parts of different plants look alike
3c counterfeiting	artificially manufactured to look alike
4 Plant part	wrong plant part(s)
5 Processing	processing not mentioned, non-standard processing
6 Dispensing error	wrong label on batch or sample
7 Contamination	

7a field contamination	collected/harvested together with drug source
7b cross- contamination	adhering to processing equipment, container, during transport
7c intentional	added to artificially increase the amount of product