Revisiting traditional Chinese materia medica from European historical collections and perspective for current use

Yusheng Jia a, b, c, Mei Wang b, c, d, e, *, Tinde van Andel a, b, **

a Naturalis Biodiversity Center, Darwinweg 2, 2333 CR, Leiden, the Netherlands  
b Institute of Biology, Leiden University, Sylviusweg 72, 2333 BE, Leiden, the Netherlands  
c European Center for Chinese Medicine and Natural Compounds, Institute of Biology, Leiden University, Sylviusweg 72, 2333 BE, Leiden, the Netherlands  
d FL BioMedicine, Post Bus 546, 2300 AM, Leiden, the Netherlands  
e Yunnan Modern National Medicine Engineering Technology Research Center, Yunnan, China

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Abstract  

Background and aim: Chinese Materia Medica (CMM) is subject to changes over time. Investigating changes in botanical ingredients, applications, plant parts used as well as name changes over time, contribute to the understanding of the history and development of CMM.

Materials and methods: This study compares four historic collections of CMM, located in Europe, compiled between 1700 and the late 19th century, with a list of contemporary CMM marketed in Europe.

Results: More than 1700 specimens within these five collections. The dominant families are Fabaceae (5.3–7.2%) and Asteraceae (4.1–5.7%), while half of the medicinal parts are represented by roots or rhizomes and fruits and/or seeds. Their importance has been stable in a time span of 300 years. The proportion of animal and mineral drugs gradually decreased over time. 14 plant species appeared in all five collections. A total of 47 species are shared between the three more recent collections and the modern trade list. Among these common species, most medicinal parts remain unchanged, but for several species the used plant parts changed or new medicinal plant parts appeared. All common species have unanimously been used in ancient classical TCM formulae and/or Chinese patent medicines.

Conclusions: Over more than 300 years, the main body of CMM has hardly changed, with regard to plant taxa and plant parts used. The most prominent changes are related to conservation issues of threatened species, health safety and the discovery of new pharmacological applications of well-known species. Analyzing physical specimens from historic CMM collections complements literature-based research.

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1. Introduction

Chinese materia medica (CMM) has been used for thousands of years for traditional medicine in China. The nature and use of CMM have been extensively documented for centuries, with the first record dating from 1100 BC (Formulae for 52 kinds of disorders, 十二病方 wò shí ěr bǐng fāng), followed by works such as the Divine Husbandman’s Herbal Foundation Canon (神农本草经 shén nóng běn cǎo jīng) (200–250 AD), the Newly Revised Materia Medica (新修本草 xīn xiū běn cǎo) (650 AD) and the Compendium of Materia Medica (本草纲目 běn cǎo gāng mù) from 1578 AD. During the millennia of practice, most CMM have remained the same, although some changes have taken place with regard to the botanical source material and medicinal parts. Research on the historical changes in CMM reveals the development of Traditional Chinese Medicine (TCM) and the habit of drug usage, which will lead toward a better understanding of the safe and effective use of CMM. Most previous research on historical changes has focused on CMM monographs and literature, and has been well summarized in Chinese publications. With the development of textual research on the history of
CMM, the confusion of many frequently used drugs has been clarified. However, due to the excessive reliance on ancient literature, instead of on physical CMM samples, some conclusions are controversial, and confusion about botanical sources and vernacular names of medicinal plants still exist.

Early CMM collections provide valuable material evidence on historical changes, which is more intuitive and persuasive than textual research. Besides, analyzing physical specimens from pre-modern CMM collections complement literature-based research. However, few studies based on historic CMM collections are published. One of the main reasons for this is that the number of well-preserved, early CMM collections is limited, especially in China, where most of the research on TCM is carried out.

In Europe, the use of herbal medicine also has a long history and has been relatively well documented in herbals and, since the 1550s, in herbaria. From ancient Greece and Rome, the works of Theophrastus’s *Historia Plantarum* (c. 300 BC) and Dioscorides’s *De Materia Medica* (c. 65 AD), and their many translations and additions, have served for centuries as the major sources of knowledge on herbal medicine. In the Renaissance, scholars reexamined these classical works and published high-quality manuals of medicinal plants and the first book herbaria with actual specimens. Since the 16th century, the European fleet reached southeast Asia and China, after which economic, cultural, and material exchanges have increased significantly. The European interest in East Asian spices and medicine is represented by botanical voucher specimens, published works and illustrations of exotic materia medica.

CMM was regarded as an exotic novelty, a promising source of medicine and a valuable object of scientific research, and transported to Europe on these merchant ships. One famous example is the “China root”, the tuber-like rhizomes of *Smilax glabra* Roxb. (*Smilacis Glabrae Rhizoma, 广西土茯苓*). China root was described in 1535 as a wonder drug by the Dutch merchant, trader and historian Jan Linschoten, because of its effectiveness in ameliorating symptoms of syphilis. For centuries, travelers and colonial staff stationed in the East collect Chinese medicinal plant products for curiosity, which has resulted in several pre-modern CMM collections preserved in museums in Europe, such as in the Sloane Collection in Natural History Museum in London, the Westhoff Collection in the Utrecht University Museum and the Hooper Collection in Royal Botanic Gardens Kew. These valuable historical CMM collections provide the most direct physical basis for research on the historical changes and development of CMM, and can fill the gap between the body of textual research and studies on physical specimens.

In this study, we compared several historical and contemporary CMM collections located in Europe with more than a 300-year time span (three pre-modern and one modern CMM collections) to a list of currently commercialized CMM by a Chinese company in the Netherlands. We posed the following research questions:

1. Is the botanical identity of CMM products stable over time?
2. Does the medicinal part of these species change over time?
3. Which species are shared by all CMM collections and why?
4. Are there CMM species that disappeared over time?
5. Are there species that recently emerged as CMM?

By comparing the similarities and differences in the five CMM collections, our research results will contribute to a better understanding of the ‘evolution’ of Chinese herbal medicine, which will help to better evaluate the safety and effective use of CMM use.

### 2. Materials and methods

#### 2.1. Collections studied

We studied four historical CMM collections (Fig. 1) and compared these to a list of CMM from the commercial trader Zhong Hua International Trading B.V. (https://www.zhonghua-trading.com), located in Utrecht, the Netherlands. This company is one of the major players in the import and export of Chinese herbal medicine on the European market.

The oldest collection that we included in our analysis is preserved at the Natural History Museum in London, UK. It is part of the Hans Sloane Collection, and thus herein referred to as the ‘Sloane collection’, and is approximately 320 years old. This CMM collection has been studied in detail by Zhao et al., so for our analysis, we retrieved the pharmaceutical names, plant parts and scientific names from their published article. Zhao et al. counted 84 specimens in the Sloane Collection, of which 76 were plant materials, but several could not be identified to species level (Table 1, Appendices 1, tab ‘Sloane’).

The Westhoff Collection is housed by the Utrecht University Museum (Utrecht, the Netherlands). This collection was acquired from Indonesia by Dr. C.H.A. Westhoff around 1882. It contains 395 specimens, of which 314 are plant-based (Table 1, Appendices 1, tab ‘Westhoff’).

Details about the species, plant parts and Chinese names of the Westhoff Collection were published previously by Jia et al. Similar to the Sloane collection, several specimens lost their identifiable characteristics due to long-term storage.

The Hooper collection is stored in the Economic Botany Collection of the Royal Botanic Gardens Kew, UK. It was acquired from Chinese pharmacies in Malaya by the botanist Isaac Henry Burkill (1870–1965). Hooper conducted the first identifications of this collection, and therefore referred to as the Hooper Collection. Brand et al. recently revised the species identifications within the Hooper Collection, and for our analysis, we used their results with regard to plant parts and botanical taxa. Among the 619 specimens identified by Brand et al., there were many duplicates (identical taxa and plant parts, for example EBC# 69076 and EBC# 69210, see Appendices 1, tab ‘Hooper 6919’). In this study, we wanted to compare the botanical composition, so these identical specimens were counted only once. After removing 99 redundancies, 520 specimens in Hooper Collection were included in our analysis. Of these 520 specimens, 493 are plant materials (Table 1, Appendices 1, tab ‘Hooper 520’).

The Catlender Collection is a private collection held by Dr. C.M. Catlender in Leiden, the Netherlands. It is between 20 and 30 years old and contains 297 specimens, of which 247 are plant-based materials (Table 1, Appendices 1, tab ‘Catlender’). To see how many of the historically used Chinese plant taxa continue to be part of the commercialized body of CMM today, we compared the taxa in the historic collections to the 2021 species trade list obtained from Zhong Hua International Trading B.V. in Utrecht (https://www.zhonghua-trading.com), wholesaler in traditional Chinese medicine on the European market. Their product list contained 333 drug names, of which 295 represent plant-based medicine (Table 1, Appendices 1, tab ‘Zhong Hua’).

#### 2.2. Species identification

Several selection criteria were applied in our comparison of botanical species within these five collections. Excluded from our analysis were:

1. unidentified specimens;
2. CMM specimens with multiple botanical sources that could not be identified on species level based on morphological features;
3. zoological and mineral
substances. If different parts of the same plant species were used as separate medicinal products, the species itself was only counted once.

To verify the botanical identity, nomenclature and plant parts represented by the specimens, we used the specification of the Chinese Pharmacopoeia 2015 edition (ChP 2015).\(^\text{18}\) Zhong Hua Ben Cao (中華本草 zhōng huá běn cǎo)\(^\text{19}\) and Zhong Yao Da Ci Dian (中药大辞典 zhōng yào dà cí diǎn).\(^\text{20}\) For current scientific names, we followed the Plants of the World Online database (http://powo.science.kew.org/) and the Flora of China.\(^\text{21}\) To verify the use of the species shared by the five CMM collections in TCM formulae, we consulted the formulae of Chinese patent medicine\(^\text{18}\) and the ancient technical TCM formulae list issued by the Chinese National Administration of Traditional Chinese Medicine (http://kjs.satcm.gov.cn/zhengcewenjian/2018-04-16/7107.html). A Venn diagram was created to show similarities and differences among the four collections and the currently traded CMM, using the webtool Venn (http://bioinformatics.psb.ugent.be/webtools/Venn/). The UpSet plots were made with the OECloud tools (https://cloud.oebiotech.cn).

## 3. Results and discussion

### 3.1. Variation in natural origin of specimens

Our final database contained more than 1700 specimens, retrieved from the publications on the three historical CMM collections, our revision of the Catlender collection and the Zhong Hua list of currently commercialized herbal medicine (Appendix 1). Although the age and provenances of the CMM collections were quite different, the largest proportion of the specimens was always plant-based (Table 1). Some clear differences were visible in the proportion of CMM of animal and mineral origin among the collections. The Sloane collection was small (84 specimens) and contained three animal-based and one mineral specimen, while the Hooper collection did not contain animal and mineral drug.\(^\text{3}\) In the other three collections, the number of animal-based drugs decreased over time: from 9.1% of the specimens in the Westhoff collection to 6.7% in the Catlender collection and 4.8% in the Zhong Hua list (Table 1). The mineral drugs also decreased from 8.6% of the specimens in the Westhoff collection to 5.1% in the Catlender collection and 3.3% in Zhong Hua’s list. The reason for this may lie in the conservation issues concerning species of animals threatened by the trade in Chinese medicine. For example, pangolin scales (Manitits Squama, 穿山甲 chuān shān jiǎ, Manis pentadactyla L.) are commonly used in China to promote lactation in women and reduce swelling (ChP 2015). Pangolin scales were present in the Westhoff and Catlender collections, but absent from the Zhong Hua list in 2021, because pangolins are endangered and the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) transferred all eight species of pangolin from Appendix II to I in 2016.\(^\text{22}\) In 2020, the Chinese Pharmacopoeia Commission also removed pangolin scales from the Chinese Pharmacopoeia. Although pangolin scales are still illegally traded and consumed as medicine in China,\(^\text{23}\) the absence of pangolin scales in the list of commercial CMM in Europe illustrates the efforts of European environmental organizations, CITES and European law.

### 3.2. Variation in plant families

When we categorized the plant medicine on family level, the collections showed a clear tendency in botanical composition (Table 2). The most represented plant family in all five CMM collections was the Fabaceae, representing 5.3%–7.2% of the specimens. The second largest family was the Asteraceae (4.1%–5.7% of the specimens), except for the Sloane Collection, in which Rutaceae were more abundant than Asteraceae. Compared to the other four collections, the Sloane Collection was much smaller with only 84 specimens, so possible less representative of the botanical diversity in CMM used around 1700. The Asteraceae still accounted for 4.8%
of the specimens. The families Apiaceae, Rosaceae, Lamiaceae and Rutaceae were relatively abundant in all five collections (Table 2). Fabaceae and Asteraceae are among the most species-rich plant families in the world. In China, there are 1673 species of Fabaceae and 2336 species of Asteraceae. Because of their high species diversity and their known pharmacological activity, more taxa within the Fabaceae and Asteraceae are used as medicine than in other plant families. The comprehensive CMM monograph of Zhong Hua Ben Cao lists 7921 plant-based drugs, 559 belong to the Fabaceae family (7.1% of all plant-based drugs) and 420 drugs from the Asteraceae family (5.3%). These percentages are similar in the CMM collections we studied: Fabaceae and Asteraceae are major sources of medicinal plants. However, these families are not dominant and never represent more than 10% of the floristic diversity: the low percentages indicate that the plant sources of CMM are highly diverse.

3.3. Plant parts represented in CMM collections

With regard to the medicinal parts, roots and/or rhizomes, fruits and/or seeds are the dominant plant organs in all collections (Table 3). This has been stable in a time span of 300 years, as roots/rhizomes, fruits and seeds together account for about 50% of the specimens in all collections. CMM that is represented by entire herbs account for 8-11% of the specimens in each collection, except for Hooper collection, where only 2.9% of the specimens are whole herbs. This may be caused by the considerable number of unidentified specimens, which were left out of our analysis. No leaf-based drugs were found in the Sloane Collection, but this can be explained by the small size of this collection.

From an overall perspective, the composition of botanical families and medicinal parts show a remarkable continuity over a 300-year time span.

3.4. Changes and continuities in species over time

With regard to plant families and medicinal parts, the CMM collections clearly show continuity, but differences in botanical species could indicate subtle changes in Chinese herbal medicine use over time. Species that are present in all four studied collections and the modern trade list could be considered as stable elements in Chinese medicine over the past centuries. In contrast, plant taxa that only appear in one or two of the historic collections may have lost their importance in Chinese medicine today. Fig. 2 shows the number of common and unique species among the four collections and the modern trade list. As not all specimens were identified to species level in the collections, the number of species that we could compare was considerably lower than the number of specimens in each collection.

3.5. Popular CMM species over time

There are 14 plant species that appeared in all five collections (Fig. 2B, far right). Their Chinese pharmaceutical and scientific names, medicinal parts and pharmaceutical names are listed in Table 4. Although the medicines have identical botanical sources, the used parts are not always the same: the root of *Reynoutria multiflora* (Thunb.) Moldenke (*Polygoni Multi* *flor* *Radix, 韓首烏/何首烏*) is always present, but the vine with leaves of this species is only included in the modern Catlender collection and Zhong Hua trade list. The use of the root (*Polygoni Multiflori Radix*) and the stem with leaves (*Polygoni Multiflori Caulis, 夜交藤 yè jiāo téng*) of...
this species as medicine can be traced back to the 10th century (Ri Hua Zi Materia Medica, 日华子本草, ri hua zi ben cao) and the 17th century (Ben Jing Feng Yuan, 本经逢原 ben jing feng yuan). Records on the use of these roots in traditional Chinese medicine formulae also date back to the 15th century (Prescriptions for Universal Relief, 普济方 pu jì fāng, 1406). In contrast, most formulae that use the vine with leaves as an ingredient have only appeared in the 1970s–1980s. The appearance of the stem and leaves of R. multiflora in the Catlender collection demonstrates the recent changes in use of this frequently employed plant, which is again confirmed by the modern trade list. Table 4 also shows that for the species Citrus × aurantium L. and Nelumbo nucifera Gaertn., much more parts are used nowadays than in the past. For the other shared species, the plant parts employed in medicine did not change over time.

As the Sloane Collection is dissimilar to other collections due to its small sample size, we made another comparison on species overlap within the other three collections (Westhoff, Hooper and Catlender) and the Zhong Hua 2021 trade list. The number of common species increased to 47 (Table 5), but the exact uses of the species showed some variation over time. One interesting example is Dimocarpus longan Lour. In the Westhoff and Hooper collections, the flowers (Longan Flos, 龙眼花 lóng yuè huā) are used as medicine, but in the Catlender collection and Zhong Hua list, the medicinal part is the aril around the seed (Longan Arillus, 龙眼肉 lóng yuè ròu). The aril, however, has a long history of medicinal use in China, appearing as one of the main ingredients in various TCM formulae (Ji Sheng Fang, 济生方 ji shēng fāng, 1253; Jing Yue Quan Shu, 景岳全书 jǐng yuè quán shū, 1624) as well as in present Chinese patent medicine. The references on the use of the flowers as medicine are very limited and all come from local monographs of the Fujian province. These findings again support the previous conclusions that the Sloane and Westhoff collections are originally from southeast China. These differences in used plant parts among the collections reflect alterations in herbal medicine applications but also show regional variation in traditional Chinese Medicine.

Another species that all four collections have in common, Rosa laevigata Michx., also witnessed an extension of its medicinal parts. The fruit of R. laevigata (Rosae Laevigatae Fructus, 金樱子 jīn yīng zǐ) is included in the three collections, but in the Zhong Hua 2021 trade list, not only the fruit but also the root of R. laevigata (Rosae Laevigatae Radix, 金樱根 jīn yīng gén) is present. R. laevigata roots only recently appeared in TCM formulae and Chinese patent medicines, which is reflected in our comparative study as the CMM collection of the 1980s did not yet show this change.

China root, Smilax glabra Roxb. (Smilacis Glabrae Rhizoma, 土茯苓 tǔ fú líng), as we mentioned in Introduction part, was quite popular in Europe since 16th century. Unsurprisingly, it has been found in historical collections and Zhong Hua list (except Westhoff collection), which supports the conclusion drew from textual research and complement them from physical specimen aspect.
Table 4
Common species appeared in 5 collection.

| Scientific name | Sloane Collection (c. 1700) | Westhoff Collection (c. 1880) | Hooper Collection (1924) | Catlender Collection (c. 1980) | Zhong Hua trade list (2021) |
|-----------------|-----------------------------|-------------------------------|--------------------------|--------------------------------|------------------------------|
|                 | Medicinal part              | Pharmaceutical name (Chinese name) | Medicinal part         | Pharmaceutical name (Chinese name) | Medicinal part              | Pharmaceutical name (Chinese name) |
| Nelumbo nucifera Thunb. | Seed | Arecae Semen (槟榔) | Stem | Arecae Semen (槟榔) | Seed | Arecae Semen (槟榔) |
|                    | Herb | Arecae Pericarpium (大腹皮) | | | Pericarp | Arecae Pericarpium (大腹皮) |
| Citrus × aurantium L. | Fruit | Aurantii Fructus (枳壳) | Sliced peel | unknown | Fruit | Aurantii Fructus (枳壳) |
|                    | Herb | Citrus Reticulatae Pericarpium (陈皮) | | | Exocarp | Citrus Reticulatae Exocarpium (橘红) |
|                    | Perf | Citrus Reticulatae Pericarpium Viride (青皮) | | | Perf | Citrus Reticulatae Pericarpium (青皮) |
| Gardenia jasminoides J.Ellis | Fruit | Gardeniae Fructus (栀子) | Fruit | Gardeniae Fructus (栀子) | Fruit | Gardeniae Fructus (栀子) |
|                    | Perf | Gardeniae Fructus Praeparata (炙栀子) | | | Perf | Gardeniae Fructus Praeparata (炙栀子) |
| Leonurus japonicus Houtt. | Whole herb | Leonuri Herba (茯苓草) | Fruit | Leonuri Fructus (茯苓) | Whole herb | Leonuri Herba (茯苓草) |
|                    | Perf | Leonuri Fructus Praeparata (茯苓) | | | Perf | Leonuri Fructus Praeparata (茯苓) |
| Lonicera japonica Thunb. | Flower | Lonicereae Japonicae Flos (金银花) | Flower | Lonicereae Japonicae Flos (金银花) | Flower | Lonicereae Japonicae Flos (金银花) |
|                    | Perf | Lonicereae Japonicae Caulis (忍冬藤) | | | Perf | Lonicereae Japonicae Caulis (忍冬藤) |
| Nelumbo nucifera Gaertn. | Rhizome | Nelumbinis Rhizomatis Nodus (藕节) | Rhizome | Nelumbinis Rhizomatis Nodus (藕节) | Rhizome | Nelumbinis Rhizomatis Nodus (藕节) |
|                    | Perf | Nelumbinis Rhizomatis Nodus Praeparata (藕节) | | | Perf | Nelumbinis Rhizomatis Nodus Praeparata (藕节) |
|                    | Perf | Nelumbinis Stamen (藕须) | Seed | Nelumbinis Stamen (藕须) | Seed | Nelumbinis Stamen (藕须) |
|                    | Perf | Nelumbinis Semen (藕子) | Flower | Nelumbinis Semen (藕子) | Flower | Nelumbinis Semen (藕子) |
| Nepeta tenuifolia Benth. | Whole herb | Schizonepetae Herba (荆芥) | Whole herb | Schizonepetae Herba (荆芥) | Whole herb | Schizonepetae Herba (荆芥) |
|                    | Perf | Schizonepetae Praeparata (荆芥) | | | Perf | Schizonepetae Praeparata (荆芥) |
| Polygonatum odoratum (Mill.) Druce | Rhizome | Polygonatii Odorati Rhizoma (玉竹) | Rhizome | Polygonatii Odorati Rhizoma (玉竹) | Rhizome | Polygonatii Odorati Rhizoma (玉竹) |
|                    | Perf | Polygonatii Odorati Rhizoma (玉竹) | | | Perf | Polygonatii Odorati Rhizoma (玉竹) |

(continued on next page)
### Table 4 (continued)

| Scientific name | Sloane Collection (c. 1700) | Westhoff Collection (c. 1880) | Hooper Collection (1924) | Cattelender Collection (c. 1980) | Zhong Hua trade list (2021) |
|-----------------|----------------------------|-------------------------------|--------------------------|----------------------------------|------------------------------|
|                 | Medicinal part              | Pharmaceutical name (Chinese name) | Medicinal part          | Pharmaceutical name (Chinese name) | Medicinal part              | Pharmaceutical name (Chinese name) |
| **Prunus mume** (Siebold) Siebold & Zucc. | Fruit | Mume Fructus (乌梅) | Fruit | Mume Fructus (乌梅) | Fruit | Mume Fructus (乌梅) | Fruit | Mume Fructus (乌梅) |
| **Raphanus raphanistrum** subspp. sativus (L.) Domin | Seed | Raphani Semen (萊菔子) | Seed | Raphani Semen (萊菔子) | Seed | Raphani Semen (萊菔子) | Seed | Raphani Semen (萊菔子) |
| **Reynoutria multiflora** (Thunb.) Moldenke | Root | Polygony Multiflori Radix (何首烏) | Root | Polygony Multiflori Radix (何首烏) | Root | Polygony Multiflori Radix (何首烏) | Root | Polygony Multiflori Radix (何首烏) |
| **Salvia miltiorrhiza** Bunge | Root and rhizome | Salviae Miltiorrhizae Radix et Rhizoma (丹参) | Root and rhizome | Salviae Miltiorrhizae Radix et Rhizoma (丹参) | Root and rhizome | Salviae Miltiorrhizae Radix et Rhizoma (丹参) | Root and rhizome | Salviae Miltiorrhizae Radix et Rhizoma (丹参) |
| **Syringium aromatica** (L.) Merr. & L.M.Perry | Flower | Caryophylli Flos (丁香) | Flower | Caryophylli Flos (丁香) | Flower | Caryophylli Flos (丁香) | Flower | Caryophylli Flos (丁香) |

except for the common species discussed before, there are several common drugs in the five collections that are likely to come from multiple botanical sources. Glycyrrhizae Radix et Rhizoma (甘草 茯苓) can be obtained from *Glycyrrhiza uralensis* Fisch., *G. glabra* L. and *G. inflata* Batal. Ligustici Rhizoma et Radix (元胡 贡胡) has two possible botanical sources: *Ligusticum sinense* Oliv. and *L. jeholense* (Nakai & Kitag.) Nakai & Kitag. Gentianae Macrophyllae Radix (黄连 丹参) has three botanical sources: *Gentiana macrophylla* Pall., *G. stramniae* Maxim., *G. cassicaulis* Dutthie ex Burk. and *G. dahurica* Fisch. Finally, Gentianae Radix et Rhizoma (黄芩 甘草) can be harvested from *Gentiana manshurica* Kitag., *G. scabra* Bge., *G. triflora* Pall. and *G. rigescens* Franch. 18 These CMM products all appear over more than 300 years, but as the exact species from which they were harvested is not known or visible in the morphology of the product, we could not include these species in our comparative analysis.

If we focused on the large collections and exclude the smallest three collections and the modern trade list. These drugs have been used for thousands of years and are still very frequently used in China.18–20

Among the studied collections, two common drugs, Aristolochiae Fructus (木通 茯苓) and Asarum Radix et Rhizoma (细辛 芍药), both sources: *Aristolochia contorta* Bunge and *A. deblis* Siebold & Zucc.) and Asarum Radix et Rhizoma (细辛 芍药), also attracted our attention. These two products are present in four historical collections but disappeared from the list of currently commercialized CMM (Zhong Hua collection 2021). Aristolochia fruits and Asarum roots belong to the Aristolochiaceae family, well known because of its toxic aristolochic acids.27,28 These components are reported to stimulate defense mechanisms against infections and in the understanding of the toxicity of aristolochic acids, and species within the Aristolochiaceae family have been restricted or prohibited as herbal medicine in Europe.31 The recent exclusion of Aristolochiaceae species in CMM traded in Europe is also reflected in our comparative analysis.

### 3.6. Common species used in TCM formulae

In TCM, instead of single component medicines, combinations of multiple herbs are generally used for clinical treatment. These multi-herbal mixtures are known as formulae. More than 100,000 different TCM formulae have been documented over the past 2000 years.29 Many of these classic formulae of Chinese patent medicine documented in the ChP 2015 have been extensively studied for efficacy and safety, and are widely used by the general public as over-the-counter (OTC) drugs in China today. The ancient classical TCM formulae are described in well-known historical CMM monographs, such as Treatise on Febrile Diseases (伤寒论 shāng hán lùn) and Synopsis of the Golden Chamber (金匮要略 jīn kuì yào lüè) compiled by Zhang Zhongjing. Thousand Ducat Formulas for Emergencies (备急千金要方 běi jí qiān jīn yào fāng) compiled by Sun Simiao.33 Formulate from the Chinese patent medicine in the ChP 2015 and the ancient classical TCM formulae list issued by the
| Scientific name | Westhoff Collection (c. 1880) | Hooper Collection (1924) | Catlender Collection (c. 1980) | Zhong Hua trade list (2021) |
|-----------------|-------------------------------|--------------------------|-------------------------------|-------------------------------|
| Achyranthes bidentata Blume | Root Achyranthes Bidentatae Radix Praeparata (詹淮根) | Root Achyranthes Bidentatae Radix (詹淮根) | Root Achyranthes Bidentatae Radix (詹淮根) | Root Achyranthes Bidentatae Radix (詹淮根) |
| Areca catechu L. | Seed Arecae Semen (槟榔) | Seed Arecae Semen (槟榔) | Seed Arecae Semen (槟榔) | Seed Arecae Semen (槟榔) |
| Citrus × aurantiun L. | Fruit Aurantium Fructus Immaturus Praeparata (炒橘) | Sliced peel Fruit Aurantium Fructus (桔壳) | Fruit Aurantium Fructus (桔壳) | Fruit Aurantium Fructus (桔壳) |
| Exocarp | Citri Reticulatae Exocarpium (橘皮) | Flower Citri Auranti Fructus Flos (橙花) | Flower Aurantium Fructus (桔花) | Flower Aurantium Fructus (桔花) |
| Pericarp | Citri Reticulatae Pericarpium Viride (青皮) | Exocarp Citri Reticulatae Exocarpium (橘皮) | Exocarp Citri Reticulatae Exocarpium (橘皮) | Exocarp Citri Reticulatae Exocarpium (橘皮) |
| Leonurus japonicus Thunb. | Fruit Lonicerae Japonicae Flos (金花) | Whole herb Leonuri Herba Praeparata (炙草) | Whole herb Leonuri Herba (炙草) | Whole herb Leonuri Herba (炙草) |
| Nelumbo nucifera Gaertn. | Rhizome Nelumbinis Rhizomatatis Nodus (莲藕节) | Rhizome Nelumbinis Rhizomatatis Nodus (莲藕节) | Rhizome Nelumbinis Rhizomatatis Nodus (莲藕节) | Rhizome Nelumbinis Rhizomatatis Nodus (莲藕节) |
| Nepeta tenuifolia Bentth. | Whole herb Schizonepetae Herba (荆芥) | Whole herb Schizonepetae Herba (荆芥) | Whole herb Schizonepetae Herba (荆芥) | Whole herb Schizonepetae Herba (荆芥) |
| Polygonatum odoratum (Mill.) Drude | Rhizome Polygonati Odorati Rhizoma (玉竹) | Rhizome Polygonati Odorati Rhizoma (玉竹) | Rhizome Polygonati Odorati Rhizoma (玉竹) | Rhizome Polygonati Odorati Rhizoma (玉竹) |
| Reynoutria multiflora (Thunb.) Moldenke | Root Polygoni Multiflori Radix Praeparata (制首乌) | Root Polygoni Multiflori Radix (制首乌) | Root Polygoni Multiflori Radix (制首乌) | Root Polygoni Multiflori Radix (制首乌) |
| Salvia miltiorrhiza Bunge | Root and rhizome Salviae Miltiorrhizae Radix et Rhizoma Praeparata (川芎) | Root and rhizome Salviae Miltiorrhizae Radix et Rhizoma (川芎) | Root and rhizome Salviae Miltiorrhizae Radix et Rhizoma (川芎) | Root and rhizome Salviae Miltiorrhizae Radix et Rhizoma (川芎) |

(continued on next page)
| Scientific name | Westhoff Collection (c. 1880) | Hooper Collection (1924) | Carlier Collection (c. 1980) | Zhong Hua trade list (2021) |
|-----------------|-------------------------------|--------------------------|-------------------------------|-----------------------------|
|                 | Medicinal part | Pharmaceutical name (Chinese name) | Medicinal part | Pharmaceutical name (Chinese name) | Medicinal part | Pharmaceutical name (Chinese name) | Medicinal part | Pharmaceutical name (Chinese name) |
| **Myristica aromatica (L.)** | Flower | Caryophylli Flos (丁香末) | Flower | Caryophylli Flos (丁香末) | Flower | Caryophylli Flos (丁香末) | Flower | Caryophylli Flos (丁香末) |
| Acorus calamus L. | Rhizome | Acori Tatarinowii Rhizoma (石菖蒲) | Rhizome | Acori Tatarinowii Rhizoma (石菖蒲) | Rhizome | Acori Tatarinowii Rhizoma (石菖蒲) | Rhizome | Acori Tatarinowii Rhizoma (石菖蒲) |
| Alisma plantago-aquatica L. | Rhizome | Alismatis Rhizoma Praeparata (附子皮) | Rhizome | Alismatis Rhizoma Praeparata (附子皮) | Rhizome | Alismatis Rhizoma Praeparata (附子皮) | Rhizome | Alismatis Rhizoma Praeparata (附子皮) |
| Alpinia oxyphylla Miq. | Fruit | Alpiniae Oxyphyllae Fructus (豨莶仁) | Fruit | Alpiniae Oxyphyllae Fructus (豨莶仁) | Fruit | Alpiniae Oxyphyllae Fructus (豨莶仁) | Fruit | Alpiniae Oxyphyllae Fructus (豨莶仁) |
| Anemarrhena asphodeloides Bunge | Rhizome | Anemarrhenae Rhizoma Praeparata (断肠草) | Rhizome | Anemarrhenae Rhizoma Praeparata (断肠草) | Rhizome | Anemarrhenae Rhizoma Praeparata (断肠草) | Rhizome | Anemarrhenae Rhizoma Praeparata (断肠草) |
| Artemisia annua L. | Whole herb | Artemisiae Annuae Herba (青蒿) | Whole herb | Artemisiae Annuae Herba (青蒿) | Whole herb | Artemisiae Annuae Herba (青蒿) | Whole herb | Artemisiae Annuae Herba (青蒿) |
| Asparagus cochinchinensis (Lour.) Merr. | Root | Asparagi Radix (天冬) | Root | Asparagi Radix (天冬) | Root | Asparagi Radix (天冬) | Root | Asparagi Radix (天冬) |
| Carthamus tinctorius L. | Flower | Carathami Flos Praeparata (紫苏花) | Flower | Carathami Flos Praeparata (紫苏花) | Flower | Carathami Flos Praeparata (紫苏花) | Flower | Carathami Flos Praeparata (紫苏花) |
| Citrus medica L. | Pericarp | Citri Sarcodactylis Pericarpium (佛手) | Pericarp | Citri Sarcodactylis Pericarpium (佛手) | Pericarp | Citri Sarcodactylis Pericarpium (佛手) | Pericarp | Citri Sarcodactylis Pericarpium (佛手) |
| Cornus officinalis Siebold & Zucc. | Fruit | Corni Fructus (山茱萸) | Fruit | Corni Fructus (山茱萸) | Fruit | Corni Fructus (山茱萸) | Fruit | Corni Fructus (山茱萸) |
| Gleditsia pinnatifida Bunge | Fruit | Glediti Fructus (山槐) | Fruit | Glediti Fructus (山槐) | Fruit | Glediti Fructus (山槐) | Fruit | Glediti Fructus (山槐) |
| Cullen corylofolium (L.) Medik. | Fruit | Psoraleae Fructus (破故纸) | Fruit | Psoraleae Fructus (破故纸) | Fruit | Psoraleae Fructus (破故纸) | Fruit | Psoraleae Fructus (破故纸) |
| Curcuma longa L. | Rhizome | Curcumae Longae Rhizoma (姜黄) | Rhizome | Curcumae Longae Rhizoma (姜黄) | Rhizome | Curcumae Longae Rhizoma (姜黄) | Rhizome | Curcumae Longae Rhizoma (姜黄) |
| Cyperus rotundus L. | Rhizome | Cyperi Rhizoma Praeparata (香附) | Rhizome | Cyperi Rhizoma Praeparata (香附) | Rhizome | Cyperi Rhizoma Praeparata (香附) | Rhizome | Cyperi Rhizoma Praeparata (香附) |
| Dimocarpus longan Lour. | Flower | Longan Flos (龙眼花) | Flower | Longan Flos (龙眼花) | Flower | Longan Flos (龙眼花) | Flower | Longan Flos (龙眼花) |
| Eclipta prostrata (L.) L. | Whole herb | Ecliptae Herba (旱莲草) | Whole herb | Ecliptae Herba (旱莲草) | Whole herb | Ecliptae Herba (旱莲草) | Whole herb | Ecliptae Herba (旱莲草) |
| Foeniculum vulgare Mill. | Fruit | Foeniculi Fructus (小茴香) | Fruit | Foeniculi Fructus (小茴香) | Fruit | Foeniculi Fructus (小茴香) | Fruit | Foeniculi Fructus (小茴香) |
| Forsythia suspensa (Thunb.) Vahl | Fruit | Forsythiae Fructus (连翘) | Fruit | Forsythiae Fructus (连翘) | Fruit | Forsythiae Fructus (连翘) | Fruit | Forsythiae Fructus (连翘) |
| Gleditsia sinensis Lam. | Thorns | Gleditisiae Spina (翘角刺) | Thorns | Gleditisiae Spina (翘角刺) | Thorns | Gleditisiae Spina (翘角刺) | Thorns | Gleditisiae Spina (翘角刺) |
| Morus alba L. | Root bark | Mori Cortex (桑皮) | Root bark | Mori Cortex (桑皮) | Root bark | Mori Cortex (桑皮) | Root bark | Mori Cortex (桑皮) |
| Myristica fragrans Houtt. | Seed | Myristicae Semen (肉豆蔻) | Seed | Myristicae Semen (肉豆蔻) | Seed | Myristicae Semen (肉豆蔻) | Seed | Myristicae Semen (肉豆蔻) |
| Ophiopogon japonicus (Thunb.) Ker Gawl. | Root | Ophiopogonis Radix (麦冬) | Root | Ophiopogonis Radix (麦冬) | Root | Ophiopogonis Radix (麦冬) | Root | Ophiopogonis Radix (麦冬) |
| Perilla frutescens (L.) Britton | Fruit | Perillae Fructus (紫苏子) | Fruit | Perillae Fructus (紫苏子) | Fruit | Perillae Fructus (紫苏子) | Fruit | Perillae Fructus (紫苏子) |
| Pinellia ternata (Thunb.) Makino | Rhizome | Pinelliae Rhizoma (半夏) | Rhizome | Pinelliae Rhizoma (半夏) | Rhizome | Pinelliae Rhizoma (半夏) | Rhizome | Pinelliae Rhizoma (半夏) |
| Platycladus orientalis (L.) Leaf | Leaf | Platycladi Cacumen Praeparata (侧柏叶) | Leaf | Platycladi Cacumen Praeparata (侧柏叶) | Leaf | Platycladi Cacumen Praeparata (侧柏叶) | Leaf | Platycladi Cacumen Praeparata (侧柏叶) |
| Platanus acerifolia L. | Leaf | Platycladi Cacumen Praeparata (侧柏叶) | Leaf | Platycladi Cacumen Praeparata (侧柏叶) | Leaf | Platycladi Cacumen Praeparata (侧柏叶) | Leaf | Platycladi Cacumen Praeparata (侧柏叶) |
Chinese National Administration of Traditional Chinese Medicine can indicate which ingredients were commonly used in the past and present. The 14 species shared among all four studied collections and the modern trade list are all ingredients of TCM formulae that appear in both historical TCM formulae and modern Chinese patent medicine. When we exclude the Sloane collection, all 47 shared species appeared in the formulae in the two lists. The high degree of consistency indicates that the shared species as ingredients for the traditional formulae have been used with high frequency in the past and present.

What is worth mentioning is that the flowers of *Lonicera japonica* Thunb. (*Lonicerae japonicae* Flos, 金银花 jǐn yín huā), appearing in all four collections and the modern trade list, are used as a major ingredient of TCM formulae in both the classical and the modern lists. *Lonicera* flowers are included in more than 420 TCM formulae, and have always been a frequently used medicine throughout Chinese history. In 2020, Lianhua Qingwen granules, which contain *Lonicera* flowers, were widely used in the treatment of Covid-19 in China. This vivid example of continuity in CMM from ancient times to today was also shown in the physical specimens in the historic collections.

Currently, the European Union has demanded analytical and pharma-toxicological tests and clinical trials since the Directive 65/65/EEC in 1965 and the amended directive 2001/83/EC before any herbal products can be legally registered as medicines in EU member states. A systematic regulatory framework was established after the enforcement of the traditional herbal medicinal products directive (Directive 2004/24/EC), which registered herbal products with long-standing use in a simplified way, with respect to the proof of efficacy and data on safety. In the directive 2004/24/EC, any non-European herbal medicinal product is required to have at least 30 years of traditional use evidence, and evidence of 15 years of traditional use in the EU. Our current research provides new information on the traditional use of multiple species and plant parts over time, as we know that the herbal materials analyzed in this study can be traced back to China (Sloane and Catlender collections, Zhong Hua trade list) or Chinese pharmacies in the Malay peninsula (Hooper collection) or Indonesia (Westhoff collection).

### 4. Conclusion

In the four historical collections of CMM included in our analysis, we can witness great continuity but also subtle changes in traditional Chinese medicine in a time span of 300 years. In general, the proportion of plant families and medicinal plant parts remain similar. Fabaceae and Asteraceae were the most represented plant families but did not dominate the floristic diversity. A total of 14 species were present in all studied collections, and 47 were shared by all but the oldest (and least complete) Sloane collection. Still, several new medicinal parts appeared in younger collections, while some toxic CMM (Aristolochiaceae products) and endangered animals disappeared from the most recent collection and the modern trade list due to the safety issues. These four historical CMM collections have been personal showcase collections and preserved in museums or scientific institutions in Europe. These materials have not been used as medicines in Europe, however they may have indirectly influenced the European view of herbal medicine. In addition, changes of CMM in these historical collections, particularly the Westhoff and Hooper collections, which originate from outside of China, may have been influenced by local medicinal practices or the availability of certain plant resources. To prove this hypothesis, further investigation is needed on regional variation in TCM. Identification problems hindered a full comparison among all specimens in the collection. Our investigation contributes to a better understanding of time dependent changes in CMM use, either caused by safety concerns, conservation issues or innovation in traditional Chinese medicine.

### Declaration of competing interest

The authors declare that they have no conflicts of interest relevant to the publication of this document.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtcme.2021.11.001.

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