Chemical Authentication of Botanical Ingredients: A Review of Commercial Herbal Products

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Chemical methods are the most important and widely used traditional plant identification techniques recommended by national and international pharmacopoeias. We have reviewed the successful use of different chemical methods for the botanical authentication of 2,386 commercial herbal products, sold in 37 countries spread over six continents. The majority of the analyzed products were reported to be authentic (73%) but more than a quarter proved to be adulterated (27%). At a national level, the number of products and the adulteration proportions varied very widely. Yet, the adulteration reported for the four countries, from which more than 100 commercial products were purchased and their botanical ingredients chemically authenticated, was 37% (United Kingdom), 31% (Italy), 27% (United States), and 21% (China). Simple or hyphenated chemical analytical techniques have identified the total absence of labeled botanical ingredients, substitution with closely related or unrelated species, the use of biological filler material, and the hidden presence of regulated, forbidden or allergenic species. Additionally, affecting the safety and efficacy of the commercial herbal products, other low quality aspects were reported: considerable variability of the labeled metabolic profile and/or phytochemical content, significant product-to-product variation of botanical ingredients or even between batches by the same manufacturer, and misleading quality and quantity label claims. Choosing an appropriate chemical technique can be the only possibility for assessing the botanical authenticity of samples which have lost their diagnostic microscopic characteristics or were processed so that DNA cannot be adequately recovered.

Keywords: chemical marker, natural product, herbal product, food supplement, herbal medicine, authentication, adulteration, contamination

INTRODUCTION

Herbal products are being sold under many and diverse commercial descriptions in the international marketplace, including herbal drugs, botanical drugs, botanicals, phytomedicines, traditional medicines (TMs), herbal medicines (HMs), traditional herbal medicines products (THMPs), natural health products (NHPs), dietary supplements (DSs), plant food supplements (PFSs), nutraceuticals (NCs) and food supplements (FSs) (Ichim, 2019), the differences being mainly due to the prevailing national legislation under which they are marketed (Simmller et al., 2018). Herbal products are commercialized as medicines or foods, according to their officially declared
intended final use by their manufacturers operating under various regulatory frameworks, and they are purchased, and subsequently used and consumed, for their medicinal claims (herbal medicines) or their expected health benefits (food supplements) (Thakkar et al., 2020). In the United Kingdom, for example, plant products are regulated under two main criteria, the first being what is claimed, i.e. if a manufacturer claims a medicinal effect, the product will automatically fall under medicines legislation; the second consideration being the activity of the plant in vivo, if it has shown to have a strong medicinal or pharmacological action then it is deemed a medicine regardless of the claims, the most notable plant in this category being Hypericum perforatum L. (St John’s Wort). Whereas in the United States most plant products are regulated as food supplements (botanicals) and in Germany the majority are considered medicines. Unfortunately, these marketing differences, due to significant differences between the regulatory approaches across jurisdictions (Low et al., 2017), are further contributing to their poor regulation on the international market.

Accidental contamination or the deliberate use of filler or substitute species (Shanmughanandhan et al., 2016) leads inherently to non-authentic, adulterated products (Simmier et al., 2018). The adulteration of commercial herbal products is an internationally widespread problem, as it has been reported for many countries from all inhabited continents (Ichim, 2019; Ichim et al., 2020). Moreover, large percentages of adulterated products have been reviewed, irrespective of the formal category of herbal products, being affected food and dietary supplements and medicines altogether (Ichim and de Boer, 2021), including products used in centuries or even millennia-old Ayurveda (Revathy et al., 2012; Seethapathy et al., 2019) and Asian traditional medicine systems (Masada, 2016; Xu et al., 2019).

The substantial proportion of adulterated commercial herbal products described appears to be independent of the methods used for their analysis, traditional pharmacopoeial methods being employed, such as macroscopic inspection (van der Valk et al., 2017), microscopy (Ichim et al., 2020), chemical techniques (Li et al., 2008; Upton et al., 2020), or even the more recently developed DNA-based ones, such as the rapidly technologically evolving DNA barcoding and metabarcoding (Ichim, 2019; Grazina et al., 2020).

On the global market, herbal products are sold in an extremely diverse variety of forms, from single ingredient, unprocessed, raw, whole plants to multi-species, highly processed extracts. Therefore, the successful authentication of commercial herbal products reported by peer reviewed studies are a valuable and useful source of information which provide the necessary practicalities, including their strengths and the limitations, of employing the right methods for a specific type of product along the length of its value chain (Booker et al., 2012). Such analyses of peer-reviewed authentication reports focused exclusively on commercial herbal products have concluded that, microscopy, a traditional pharmacopoeial identification method, is cost-efficient and can cope with mixtures and impurities but it has limited applicability for highly processed commercial samples e.g. extracts (Ichim et al., 2020). On the other hand, DNA-based identification, only recently adopted by the first two national Pharmacopoeias (Pharmacopoeia Committee of P. R. China, 2015; British Pharmacopoeia Commission, 2018), facilitate simultaneous multi-taxa identification by using the DNA of different origins extracted from complex mixtures and matrices but false-negatives can be expected if the DNA has been degraded or lost during post-harvest processing or manufacturing (Raclariu et al., 2018a; Ichim, 2019; Grazina et al., 2020). In this respect, our review adds the much needed peer-reviewed, systematically searched information, about the successful use of chemical identification for the authentication of commercial herbal products. While doing so, our review also provides some missing pieces of the commercial herbal products’ authenticity puzzle.

**METHODS**

**Databases**

**Search Strategy**

Four databases were systematically searched for peer reviewed records following the PRISMA guidelines (Moher et al., 2009) using combinations of relevant keywords, Boolean operators and wildcards: [(“herbal product” OR “herbal medicine” OR “traditional medicine” OR “food supplement” OR “dietary supplement” OR “herbal supplement” OR nutraceutical) AND (authentic* OR contaminat* OR substitut*)] for Web of Science, PubMed, Scopus, and [(“herbal product” OR “herbal medicine” OR “food supplement” OR “dietary supplement” OR “herbal supplement” OR nutraceutical) AND (authentication OR contamination OR substitution)] for ScienceDirect. The option “search alert” was activated for all four databases, to receive weekly updates after the literature search was performed. Furthermore, we used cross-referencing to identify additional peer-reviewed publications.

**Selection Process and Criteria**

**Identification:** 10,497 records were identified through database searching (WoS = 1,317, PubMed = 3,253, Scopus = 5,446, and ScienceDirect = 481), and 196 additional records from cross-referencing and the weekly updates from the four databases. Screening: after the duplicates had been removed, 2,326 records were collected and their abstracts screened. After screening, 1,745 records were excluded for not reporting data relevant for the chemical authentication of herbal products. Eligibility: 581 full-text articles were assessed and screened based on the following eligibility criteria: 1) The reported products had to be “herbal products”; the full wide range of commercial names was searched for and accepted for being included in our analysis. 2) The analyzed products had to be “commercial”; keywords such as “purchased”, “bought”, were accepted. Our analysis excluded samples which were obtained “cost-free”, a “gift” or “donated” by a person, institution or company. 3) The products had to be clearly allocated to a “country” or “territory” (e.g., European Union). 4) The conclusion “authentic”/”adulterated” had to be drawn by the authors of the analyzed studies. 5) The products had to be analyzed with a “chemical” method or techniques.
### Table 1: The authenticity of the chemically authenticated commercial herbal products at global level.

| No. | Country / territory | Products (details) / authenticated species | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/chemical reference materials/standards | Bibliographic reference |
|-----|---------------------|--------------------------------------------|-----------------------|---------------------------------------------|-----------------------------------|-------------------------------------------------|-------------------------|
| 1   | Australia           | grape seed extract products (capsules) from retail pharmacies, health stores / Vitis vinifera | 9 4 5 | complete substitution or heavy adulteration, possibly with peanut skin extract, Pinus massoniana (or other A-type procyanidin-containing species) | not reported | V. vinifera (seeds, seed extracts), A. hypogaea, P. massoniana, P. pinaster, V. macrocarpon, T. cacao (extracts) | Govindaraghavan (2019) |
|     |                     |                                           |                       | RP HPLC-UV-MS / catechin, epicatechin, procyanidin B2, procyanidin A2, rape seed oligomeric proanthocyanidins |                       |                                                 |                         |
|     |                     |                                           |                       |                                            |                                   | V. vinifera (seeds, seed extracts), A. hypogaea, P. massoniana, P. pinaster, V. macrocarpon, T. cacao (extracts) | Govindaraghavan (2019) |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
| 2   | New Zealand         | gingko products (capsule, tablets) from retail stores / Ginkgo biloba | 6 6 0 | n/a | adulteration with flavonol aglycones, likely with Styphnolobium japonicum | contained genistein, an isoflavone that does not occur in ginkgo leaf | authentic samples of dried Ginkgo biloba leaf from commercial suppliers |
|     |                     |                                           |                       | RP HPLC, LC-MS / flavonol aglycones (quercetin, kaempferol, isorhamnetin) | contaminate |                                                 |                         |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
| 3   | Belgium             | products (tablets and capsules) containing regulated plants / Aristolochia fangchi, Ilex paraguariensis, Epimedium spp., Pausinystalia johimbe, Tribulus terrestris | 69 48 21 | adulteration / contamination with unlabeled ingredients: A. fangchi (forbidden), I. paraguariensis, Epimedium spp., T. terrestris (all should be notified to authorities), P. johimbe | not identified in some products although claimed on the label | P. yohimbe or T. terrestris | Deconinck et al. (2019) |
|     |                     |                                           |                       | FT-Mid-IR, HPLC-DAD, LC-MS | authentic samples of five plant species (leaves, bark, fruits) |                                                 |                         |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
| 4   | Belgium             | herbal products (capsules, tablets) from local pharmacy / Passi flora edulis | 3 3 0 | n/a | HPLC-DAD, HPLC-MS | not reported | commercial P. edulis (dry extract) (European Pharmacopoeia) | Deconinck et al. (2015) |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
| 5   | Belgium             | products containing three non-regulated herbs (capsule, tablets) from local pharmacy / Frangula purshiana, Passi flora edulis, Crataegus monogyna | 3 3 0 | n/a | HPLC-DAD-ELSD, HPLC-MS | not reported | commercial plant extracts of F. purshiana, P. edulis, C. monogyna (European Pharmacopoeia) | Deconinck et al. (2013) |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
| 6   | Belgium             | illegal products (tablets, capsules) containing regulated plant species / Epimedium spp., Tribulus terrestris | 2 2 0 | n/a | HPLC-PDA, HPLC-MS | adulteration with sildenafil | self-made triturations in three different botanical matrices from reference standards of Epimedium spp. leaves, P. johimbe bark, T. terrestris fruit authenticated samples of B. trimera (aerial parts, leaves) / standard oil of B. trimera (extracted) | Custers et al. (2017) |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |
| 7   | Brazil              | "carqueja" products (bags with pulverized plant material or parts of the plant) from commercial shops / Baccharis trimera | 15 11 4 | non-authentic | GC-RID / essential oil | intensity of the peaks in most of cases was different | authenticated samples of dried Ginkgo biloba leaf from commercial suppliers |
|     |                     |                                           |                       |                                            |                                   |                                                 |                         |

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| No. | Country / territory | Products (details) / authenticated species | Products total / authenticated/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|--------------------------------------------|------------------------------------------|-----------------------|---------------------------------------------|--------------------------------|---------------------------------------------|-------------------------|
| 8   | Brazil              | "sarsaparilla" products from drugstores / Smilax goyazana, S. rufescens, S. brasiliensis, S. campestris, S. cissoides, S. fluminensis, S. oblongifolia, S. polyantha | 15 0 15 different from the reference Smilax sp. | TLC / flavonoids, saponins, terpenoids, steroids, catechins | n/a authenticated reference material (roots) of S. brasiliensis, S. campestris, S. cissoides, S. fluminensis, S. goyazana, S. oblongifolia, S. rufescens, S. polyantha | Martins et al. (2014) |
| 9   | Brazil              | "copaiba" oil-resin products from local markets / Copaifera multijuga | 12 3 9 substitution and adulteration with soybean oil | TLC not reported | reference C. multijuga oil-resins, prepared mixtures of soybean oil and copaiba oil resin | Barbosa et al. (2009) |
| 10  | Brazil              | "carqueja" products from herbal shops, pharmacies / Baccharis trimera | 12 12 0 n/a | TLC / 3-o-methyl-quercetin | large variations in the percentage of flavonoids (quercetin) | B. trimera reference samples / Brazilian Pharmacopoeia (BP) | Beltrame et al. (2009) |
| 11  | Brazil              | "janaguba" milk products from local market / Himatanthus drasticus | 10 4 6 complete substitution or adulteration with Hancornia speciosa | TLC | not reported | authentic samples of "janaguba" latex, mango tree latex sample | Soares et al. (2016) |
| 12  | Brazil              | "Bauhinia spp." products (ground dry leaves) from drugstores, local market / Bauhinia forficata spp. | 9 2 7 not containing claimed B. forficata | HPLC-UV/PDA, MCR-ALS/PCA | not reported | B. forficata, B. f. var. longifolia authenticated leaves | Arêla et al. (2015) |
| 13  | Brazil              | "jatoba" sap products / Hymenaea stigonocarpa, Hymenaea martiana | 6 0 6 probably achieved by a decoction of the stem bark or other sources | HPLC-MS / flavonoids, procyanidins | n/a | H. stigonocarpa, H. martiana authenticated sap and stem bark samples | De Souza Farias et al. (2017) |
| 14  | Brazil              | herbal products from commercial shops / Maytenus ilicifolia | 3 1 2 possible substitution with plants from the same family and/or contamination due to addition of similar other plants parts to the commercial one | FTIR, 1H NMR | not reported | M. ilicifolia control sample from the open market, in the selected natural form, recognized by "herbal trackers" | Preto et al. (2013) |
| 15  | Brazil              | herbal products (raw material) from different suppliers / Echinodorus grandiflorus | 3 3 0 n/a | TLC / caffeic acid, isoorientin and swertiajaponin, o-hydroxycinnamic acid derivatives | variable quantity of some marker compounds | Brazilian Pharmacopoeia (BP) 5th edition | Dias et al. (2013) |

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### Table 1: The Authenticity of the Chemically Authenticated Commercial Herbal Products at Global Level (Continued)

| No. crt. | Country / territory | Products (details) / authenticated species | Products Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/chemical reference materials/standards | Bibliographic reference |
|----------|---------------------|-------------------------------------------|--------------------------------|---------------------------------------------|----------------------------------|-----------------------------------------------|-------------------------|
| 16       | Canada              | Smilax ornata, organic Sarsaparilla root, Hemidesmus indicus products from online store / Hemidesmus indicus, Periploca indicus | 3 0 3 adulteration with Decalepis hamiltonii and Pteridium aquilinum | 1H-NMR/HCA | not reported | reference samples of known provenance of P. aquilinum, Smilax aristolochiifolia, D. hamiltoni, H. indicus | Kesnakurti et al. (2020) |
| 17       | China               | "Tong-guanteng" products from medicine markets, drug stores / Marsdenia tenacissima ginseng products (pills, bag, injections, capsules, tablets, powders, dripping pills) from drugstores / Panax ginseng, P. quinquefolius, P. notoginseng | 62 61 1 substitution with Tinospora sinensis | TLC, HPLC / tenacissoside H | TS-H contents (0.39-1.09%) larger than that regulated in the Chinese Pharmacopoeia (0.12%) in few products markers for PG not detected, signals for PN (ginsenoside Rf) very weak | genuine M. tenacissima herb | Yu et al. (2018) |
| 18       | China               | ginseng products (pills, bag, injections, capsules, tablets, powders, dripping pills) from drugstores / Panax ginseng, P. quinquefolius, P. notoginseng | 40 38 2 P. ginseng products adulterated (weak chromatographic peaks, and several marker compounds were not detected) | LC–MS / ginsenosides | | | Yang et al. (2016) |
| 19       | China               | Pinelliae rhizoma products from herbal medicine markets / Pinellia ternata | 39 12 27 substitution with Pinellia pedatisecta | HPLC-DAD, HPLC-MS, LC-MS / triglochinic acid | not reported | | Jing et al. (2019) |
| 20       | China               | "Wuweizi" (Schisandrae Chinensis Fructus) and "Nan-wuweizi" (Schisandrae Sphenantherae Fructus) products from pharmaceutical manufacturers, pharmacies / Schisandra chinensis, S. sphenanthera | 36 34 2 substitution with S. sphenanthera | LC-DAD-MS, TLC, HPLC / schisandrin, anwulignan | not reported | | Jiang et al. (2016) |
| 21       | China               | American or Asian ginseng root products from stores / Panax ginseng, P. quinquefolius | 31 28 3 adulteration and substitution of wild with cultivated ginseng | 1H NMR-PCA / sucrose, glucose, arginine, choline, 2-oxoglutarate, malate, ginsenosides | not reported | | Zhao et al. (2015) |

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## TABLE 1  (Continued) The authenticity of the chemically authenticated commercial herbal products at global level.

| No. crt. | Country / territory | Products (details) / authenticated species | Products / authentic/ adulterated species | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|----------|---------------------|-------------------------------------------|------------------------------------------|-----------------------|-------------------------------------------|---------------------------------|---------------------------------|-------------------------|
| 22       | China               | "Chaihu" (Bupleuri Radix) products from major herbal distribution centres / Bupleurum chinense, B. scorzonerifolium | 31 20 11 | substitution with B. longiradiatum, B. bicaule, B. falcatum, B. marginatum var. stenophyllum | HPLC-ELSD, HPTLC / saikosaponins | great variation in the content of the major saikosaponins | n/a | Tian et al. (2009) |
| 23       | China               | red yeast rice (RYR) commercial raw materials from supplement manufacturers / Monascus purpureus - fermented rice | 31 21 10 | did not show the presence of any monacolins analyzed | UHPLC-DAD–QToF-MS / monacolins, citrinin | n/a | RYR authenticated samples | Avula et al. (2014) |
|          | United States      | RYR-containing products from online retailers / Monascus purpureus - fermented rice | 14 14 0 | n/a | n/a | large variations (20-40 fold) in quantity and quality of monacolin K | n/a | |
| 24       | China               | Asian and American ginseng products from local drug stores / Panax ginseng, P. quinquenetus | 31 23 8 | adulteration with P. ginseng | UPLC/Q-TOF-MS / ginsenoside Rf, 24 (R)-pseudoginsenoside F11 | not reported | self-prepared samples with different contents (spiking the Asian ginseng powder into the American ginseng powder) | Li et al. (2010) |
|          | United States      | Asian and American ginseng products from local drug stores / Panax ginseng, P. quinquenetus | 4 4 0 | n/a | n/a | self-prepared samples with different contents (spiking the Asian ginseng powder into the American ginseng powder) | n/a | |
| 25       | China               | "Gou-Teng" batches of (Uncariae Rammulus Cum Uncis) from markets / Uncaria macrophylla, U. hirsuta, U. sinensis, U. sesatifructus | 20 16 4 | substitution with other Uncaria sp. or unlabelled mixtures with the five officially accepted Uncaria sp. | UPLC/Q-TOF MS / alkaloids | not reported | authenticated batches of five Uncaria sp. (stems with hooks) / isolated and identified alkaloids | Pan et al. (2020) |
| 26       | China               | Chaenomelis Fructus (raw) products from manufacturers, herbal markets / Chaenomeles speciosa | 20 19 1 | the source plant is not C. speciosa | HPLC-DAD / quinic acid, malic acid, protocatechic acid, shikimic acid, chlorogenic acid | the relative contents of each component may vary in some of the samples | n/a | Zhu et al. (2019) |

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### TABLE 1 | The authenticity of the chemically authenticated commercial herbal products at global level.

| No. | Country / territory | Products (details) / authenticated species | Products total | Products authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|---------------------------------------------|---------------|---------------------------------|-----------------------|--------------------------------------------|----------------------------------|---------------------------------|-------------------------|
| 27  | China               | “Beimu” (Fritillariae Bulbus) products from drugstores / Fritillaria tajaeaeis, F. unibracteata var, wabuensis, F. delavayi, F. unibracteata, F. przewalski, F. cirnosa, F. ussuriensis, F. thunbergi | 16            | 11                              | 5 substitution or adulteration with unlabeled F. ussuriensis | UPLC-QTOF-MS / steroidal alkaloids | loss of specific features, possibly resulted from different processes of different manufacturers | authenticated batches of Fritillaria sp. | Liu et al. (2020) |
| 28  | China               | Menispermi Rhizoma products (dried rhizomes, pills, capsules) from drug stores / Menispermum dauricum | 16            | 15                              | 1 counterfeit (most of the important marker alkaloids could not be detected) | UPLC-DAD-MS / alkaloids | discrepancies among the samples of different origins (the contents of the nine alkaloids varied greatly) | authenticated MR batches from various drug stores / separated and purified (from MR) alkaloids | Liu et al. (2013a) |
| 29  | China               | batches of “Shuxiong” tablets from manufacturers, drugstores / Panax notoginseng, Carthamus tinctorius, Ligusticum striatum | 12            | 12                              | 0 n/a | UPLC/ODa-SiM / (saponins, quinonolalones C-glycosides, 16 O-glycoside, phenolic acid, pathalides | low content of some markers in a few products possibly caused by different preparation process or use of poor-quality drug materials | crude drug reference materials Notoginseng Radix et Rhizoma, Carthami Flos, Chuanxiong Rhizoma | Yao et al. (2016) |
| 30  | China               | “Huangqi” (Radix Astragali) products from wholesale TCM markets, city pharmacies / Astragalus prompquius | 12            | 11                              | 1 substitution with Astragalus tongonlensis | HPLC-UV / isoflavonoids | total isoflavonoids content varies considerably | n/a | Wu et al. (2005) |
| 31  | China               | “ci-wu-jia” tea products (leaf, leaf powder) from local stores / Eleutherococcus senticosus | 11            | 8                               | 3 adulteration with green tea (Camellia sinensis) | UHPLC-UV/MS / organic acid derivatives, flavonoids, triterpene saponins | not reported | E. senticosus leaf samples collected from China / in-house UNIFI library of Eleutherococcus genus and green tea extracts | Wang et al. (2019) |
| 32  | China               | Panax ginseng and P. quinquefolius products (bolus, tea, tablet, drink) from local pharmacies / P. ginseng, P. quinquefolius | 11            | 10                              | 1 substitution or adulteration with P. ginseng | UHPLC-TOF/MS / OPLS-DA / ginsenosides | n/a | 34 white ginsengs, 23 red ginsengs, 30 P. notoginseng and 21 P. quinquefolius collected samples | Wu et al. (2020) |

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TABLE 1 | (Continued) The authenticity of the chemically authenticated commercial herbal products at global level.

| No. | Country / territory | Products (details) / authenticated species | Products total | Products authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|-------------------------------------------|----------------|-------------------------------|-----------------------|-------------------------------------------|----------------------------------|---------------------------------|-------------------------|
| 33  | China               | Panax notoginseng powder products from drug stores, CHM manufacturers / P. notoginseng | 10             | 9                             | 1                     | UPLC/Qtof MS/ PCA / notoginsenosides, ginsenosides, 20S-ginsenoside R1, gypenoside XVII | not reported                      | authenticated P. notoginseng powder samples | Liu et al. (2015)        |
| 34  | China               | “Xihuangcao” (Isodonis lophanthoidis herba) from herbal markets / Isodon lophanthoides | 9              | 7                             | 2                     | HPTLC / 2α-O-β-D-glucoside-12-en-28-ursolic acid, 2α,19α-dihydroxy-12-en-28-ursolic acid, 2α-hydroxy-12-en-28-ursolic acid, ursolic acid | not reported                      | collected batches of I. lophanthoides | Lin et al. (2019)        |
| 35  | China               | Panax ginseng products from local drug stores / P. ginseng | 8              | 5                             | 3                     | FT-NIR                                    | not reported                      | authenticated P. ginseng samples | Dong et al. (2020)       |
| 36  | China               | “Xihuangcao” products (tea bags) from retail stores / Isodon lophanthoides, I. serra | 8              | 0                             | 8                     | UPLC-ESI-QTOF-MS                           | n/a                             | authenticated I. lophanthoides and I. serra plant material / reference teas of many plant species | Wan et al. (2016)       |
| 37  | China               | gingko leaf product and health foods (tea, tablets, soft gels) from drug store, local stores / Gingko biloba | 6              | 5                             | 1                     | HPLC/EIS/MS / flavonol glycosides, terpene trilactones, flavonol aglycones, biflavones | not reported                      | G. biloba leaves collected from different habitats | Song et al. (2010)       |
| 38  | China               | St. John’s Worth products (loose) | 5              | 5                             | 0                     | HPTLC, 1H-NMR/PCA                         | low content of typical H.p. compounds apparently due to higher amount of woody material | authenticated Hypericum sp. samples | Scotti et al. (2019)   |
| Bulgaria |                           | material from herbal markets, pharmacies and producer’s cultivation / Hypericum perforatum | 2              | 2                             | 0                     |                                          |                                  |                                  |                         |
| Greece |                           |                                | 2              | 2                             | 0                     |                                          |                                  |                                  |                         |
| Chile |                           |                                | 1              | 1                             | 0                     |                                          |                                  |                                  |                         |
| United Kingdom |                           |                                | 1              | 1                             | 0                     |                                          |                                  |                                  |                         |
| 39  | China               | Aquilariae Lignum Resinatum (ALR) products from market / Aquilaria sinensis | 3              | 0                             | 3                     | FT-IR, SD-IR, 2D-IR                       | not reported                      | standard ALR (the resin-rich wood of A. sinensis) | Qu et al. (2016)       |
| 40  | China               | Aquilariae Lignum Resinatum (ALR) products from market / Aquilaria sinensis | 3              | 0                             | 3                     | FT-IR, 2D-IR                             | n/a                             | reference A. sinensis samples, no-resin wood of A. sinensis, authentic ALR samples | Qu et al. (2017)       |

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| No. | Country / territory | Products (details) / authenticated species | Products / authentic / adulterated species | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical / chemical reference materials / standards | Bibliographic reference |
|-----|---------------------|---------------------------------------------|-------------------------------------------|----------------------|-----------------------------------------|-------------------------------|---------------------------------|--------------------------|
| 41  | China               | Ophiocordyceps sinensis products from TCM market / O. sinensis | 2 / 1 / 1 | substitution with lepidopteran larvae infected by Metacordyceps taii | HPLC / cordycepin, adenosine and other nucleosides | not reported | authenticated O. sinensis specimens collected in Tibet | Wen et al. (2016) |
| 42  | Croatia             | Ginkgo products (GBEs, food supplements / capsules, tablets, powder) / Ginkgo biloba | 10 / 8 / 2 | substitution with Sophora japonica extracts | HPLC / quercetin/ kaempferol ratio, ginkgo flavone glycosides (quercetin, kaempferol, isorhamnetin) | not reported | n/a | Budeč et al. (2019) |
| 43  | Denmark             | St. John’s Worth products (tablets, capsules) from commercial suppliers / Hypericum perforatum | 10 / 10 / 0 | n/a | 1H-NMR/PCA | considerable differences in the products composition (e.g. flavonoids), inter-product and inter-batch variation | n/a | Rasmussen et al. (2006) |
| 44  | Egypt               | Herbal products (tea) from market / chamomile, marjoram, licorice, fennel, dill, caraway, basil, lemon grass, anise, chicory, achillea, verbascum, hibiscus, vine | 3 / 0 / 3 | adulterated with other species, some labeled species missing those of the formula | GC-MS, HPLC / essential oil, polyphenols, flavonoids | some of the herbs used are exhausted | reference herbal teas prepared from herbs purchased from the market | Kamal et al. (2017) |
| 45  | Egypt               | Herbal products (tea) / chicory, marjoram, nettle and senna leaves, liquorice roots, celery fruits, calendula flowers and fennel, senna and chicory | 2 / 2 / 0 | n/a | HPLC, GC-MS / sennoside A, esculetin, scopoletin, volatile oil | not reported | prepared standard herbal mixtures | Abdel Kawy et al. (2012) |
| 46  | European Union      | Panax ginseng products (herb, root extracts, stem/leaf extracts) / P. ginseng leaf or other plant parts, P. quinquefolius roots | 12 / 6 / 6 | P. ginseng leaf or other plant parts, P. quinquefolius roots | HPTLC, HPLC / ginsenosides | not reported | bulk crude P. ginseng dried root samples, P. ginseng leaf and stem | Govindaraghavan (2017) |
|     | Australia           | Extract, berry extract (capsules, tablets) / P. ginseng | 4 / 1 / 3 | P. ginseng leaf or other plant parts | n/a | | | |
|     | China               | Food supplements containing ginkgo dry extract or ginkgo leaf (tablets, soft and hard capsules) from local community pharmacies / Ginkgo biloba | 10 / 2 / 8 | adulteration | HPLC-UV, LC-MS/MS / flavonoids and terpenes lactones (ginkgolides, bilobalide) | n/a | G. biloba herbal medicinal product (control) | Czigle et al. (2018) |
| 47  | European Union      | G. biloba herbal medicinal product (control) | 1 / 0 / 1 | n/a | | | | |
| No. | Country / territory | Products (details) / authenticated species | Products total (no. no. no.) | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical / chemical reference materials / standards | Bibliographic reference |
|-----|---------------------|--------------------------------------------|-----------------------------|----------------------|---------------------------------------------|---------------------------------|-----------------------------------------------|------------------------|
| 48  | India               | "Asoka" raw herbal products from shops / Saraca asoca | 25 3 22 substitution | 1D/2D NMR/PCA | not reported | taxonomically authenticated samples of S. asoca bark, flower, stem | Urumudappa et al. (2016) |
| 49  | Norway, Romania, Sweden, United States | Garcinia products (capsules, tablets) from pharmacies, internet / Garcinia guinna-gutta, G. indica | 5 5 0 n/a | 1H NMR / (-)-hydroxycitric acid, (-)-hydroxycitric acid lactone | large variation in the content of (-)-hydroxycitric acid; only one product contained quantifiable amounts of (-)-hydroxycitric acid lactone | | Seethapathy et al. (2018) |
| 50  | India               | licorice products (raw material) from local shops / Glycyrrhiza glabra, G. uralensis, G. inflata | 2 2 0 HPTLC, HPLC / 18β-glycyrrhizic acid | not reported | voucher, botanically confirmed sample, raw materials (whole, chopped, or powdered) of licorice root / United States Pharmacopeia (USP) refined and standardized dry extract from the bilberry fruit | Frommenwiler et al. (2017) |
| 51  | Italy               | bilberry products (extracts) from different producers / Vaccinium myrtillus | 71 65 6 adulteration with anthocyanins extracted from other berries (black mulberry, chokeberry, blackberry) | HPLC-DAD, FT-NIR/PCA / anthocyanins and the respective aglycones | the amount of anthocyanins in the bilberry extracts in the range 18-34% | European Pharmacopeia | Gardana et al. (2018) |
| 52  | Italy               | cranberry products (extracts) from herbal shops, local markets / Vaccinium macrocarpon | 24 5 19 misidentification of the raw material | HPLC-UV/Vis, Orbitrap LC-MS / anthocyanins | only one product complied the criteria of good preparation, respected their uniformity of dosage, and contained V. macrocarpon | European Pharmacopeia | Mannino et al. (2020) |
| 53  | Italy               | cranberry products (extracts) from herbal shops, local markets / Vaccinium macrocarpon | 10 4 6 adulteration with Morus nigra extract | UPLC-DAD-Orbitrap-MS-PCA / anthocyanin, epicatechin/catechin, procyanidin A2/total procyanidin, procyanidin/anthocyanin ratios | only one product provided the daily dose deemed effective for treating a urinary tract infection | fruits and extract of possible adulterants | Gardana et al. (2020) |
| 54  | Italy               | sweet fenel pre-packaged teabags and instant tea products (freeze-dried powders) from local pharmacies, grocery stores / Foeniculum vulgare | 5 5 0 n/a | GC-MS / constituents of volatile oil | possible presence of bitter fennel or, for the powdered material, the presence of other parts of fennel | commercial reference samples of fruits of F. vulgare / European Pharmacopoeia (1997) monograph | Billa et al. (2002) |

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| No. | Country / territory | Products (details) / authenticated species | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/chemical reference materials/standards | Bibliographic reference |
|-----|---------------------|------------------------------------------|-----------------------|------------------------------------------|----------------------------------|-----------------------------------------------|-------------------------|
| 55  | Italy               | herbal product (liquid preparations containing four species) from herbalist shop / Olea europaea, Crataegus rhipidophylla, Fumaria officinalis, Capsella bursa-pastoris | 2                      | adulteration with a root extract from a Rauvolfia sp. (indole alkaloids) | HPLC-DAD–MS, HPLC–MS, NMR | n/a               | purchased herbal products and collected plant material | Karioti et al. (2014) |
| 56  | Italy               | herbal product (liquid preparations containing five species) / Olea europaea, Crataegus rhipidophylla, Fumaria officinalis, Capsella bursa-pastoris | 1                      | adulteration with an extract from a Rauvolfia sp (indole alkaloids) | HPLC-ESI-ITMS, NMR | n/a               | n/a         | Gallo et al. (2012) |
| 57  | Japan               | bilberry products (extracts) from the marketplace (tablets, hard and soft gel caps) / Vaccinium myrtillus | 20                     | n/a                                  | LC-MS / anthocyanins           | marked composition differences | V. myrtillus reference dry extract | Cassinese et al. (2007) |
|     | United States       |                                          | 15                     | substitution with berries             |                                  |                                |                          |                          |
|     | Italy               |                                          | 4                      | different from V. myrtillus           |                                  |                                |                          |                          |
|     | Malaysia            |                                          | 1                      |                                      |                                  |                                |                          |                          |
| 58  | Japan               | herbal products (crude drug extracts) (soft capsules, hard capsules, sugared coated tablets) from internet / Poria sclerotium, Ophiopogonis tuber, Rheum emodi | 14                     | mislabeling, adulteration            | HPLC-PDA / sennoside A, aloe-emodin, emodin, rhein, chrysophanol | illegal adulteration with sibutramine | authenticated rhubarb rhizome | Yoshida et al. (2015) |
| 59  | Japan               | chasteberry extracts (granules, tablets, soft and hard capsules) purchased via internet / Vitex agnus-castus | 11                     | adulteration, contaminated with V. negundo | HPLC-PCA, quantitative determination of chemical marker compounds / agnuside, castion | poor formulation quality | reference standard of V. agnus-castus fruit dry extract | Sogame et al. (2019) |
| 60  | Japan               | herbal products (tea bags, granules, tablets) containing senna stems / Cassia alexandrina | 8                      | adulteration with senna leaves and midribs | TLC, HPLC / sennoside A, sennoside B | the amount of sennosides ranged from 0.2-11 mg | reference raw senna materials (stems, leaves) | Kojima et al. (2000) |

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| No. | Country / territory | Products (details) / authenticated species | Products Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/chemical reference materials/standards | Bibliographic reference |
|-----|---------------------|-------------------------------------------|-------------------------------|-------------------------------------------|-----------------------------------|-----------------------------------------------|-------------------------|
| 61  | Japan               | Siberian ginseng products (capsules, teas) from internet / Eleutherococcus senticosus | 4 3 1 substitution with Panax ginseng | HPLC-DAD / eleutheroside B, eleutheroside E, isofraxidin | not reported | specimens of E. senticosus, E. sessiliflorus and congeneric species, crude drugs from markets / chemical standards isolated from an authenticated commercial SG sample purified E. longifolia crude extract | Zhu et al. (2011) |
| 62  | Malaysia            | “Tongkat Ali” products from pharmacies, night markets, jamu shops, food courts, on-line stores / Eurycoma longifolia | 46 20 26 substitution | HPLC, 2DE / protein marker (A), eurycomanone | the amount of the markers detected varies among the products | standardized E. longifolia root extracts | Vejayan et al. (2018) |
| 63  | Malaysia            | ‘Tongkat Ali’ products (capsules, spherical tablets) from pharmacies, drug stores / Eurycoma longifolia | 29 18 11 substitution | 2DE / protein markers (A, B) (~14kDa) | not reported | authenticated E. longifolia root extracts | Vejayan et al. (2013) |
| 64  | Malaysia            | “Tongkat Ali” products (capsules, tea, tablet) from retail shops / Eurycoma longifolia | 7 3 4 substitution | HPLC-DAD / eurycomanone | none of the products met the officially required minimum concentration of eurycomanone | authenticated E. longifolia plant and five-year-old root sample | Abubakar et al. (2018) |
| 65  | Mexic               | “Damiana” botanical products (extracts) from local markets / Tumera diffusa | 6 3 3 substitution, adulteration | 1H-NMR/PCA / hepatodamianol | differences in the chemical components | authenticated T. diffusa specimens / purified chemical reference standard (hepatodamianol) n/a | Lucio-Gutiérrez et al. (2019) |
| 66  | Pakistan            | crude drugs from local market / Foeniculum vulgare, Curcuma longa, Aloe vera, Plantago ovata, Zingiber officinale, Glycyrrhiza glabra | 6 6 0 n/a | TLC, spectrophotometry, FTIR / anethole, barbaloin, xylose, galactose, gingerol-1, gingerol-2, 6-gingerol, glycercirhilic acid, curcumin | all the samples of Plantago ovata do not comply with the pharmacopoeial standard | authenticated gum resin samples of C. wightii and M. indica | Fatima et al. (2020) |
| 67  | Pakistan            | “guggul” gum resin product from herbal market / Commiphora wightii | 1 0 1 adulteration with Mangifera indica gum | NMR | n/a | authenticated gum resin | Ahmed et al. (2011) |

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| No. | Country / territory | Products (details) / authenticated species | Products authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|---------------------------------------------|---------------------------------|-----------------------|---------------------------------------------|----------------------------------|-----------------------------------------------|------------------------|
| 68  | Poland              | chamomile samples (fragmented, granulated) from different manufacturers / Matricaria chamomilla | 19 19 0 n/a                      | HPLC / phenolic acids (gallic, caffeic, syringic, p-coumaric, ferulic), flavonoids (rutin, myricetin, quercetin, kaempferol) | not reported | n/a | Vlapiana et al. (2016) |
| 69  | Poland              | ginkgo products (leaf extracts) (capsules, tablets) from local pharmacies, markets, online pharmacies / Ginkgo biloba | 16 9 7 adulteration probably with Sophora japonica (fruit or flower extracts) | ATR-FTIR, iPLS-DA / rutin, quercetin, kaempferol | large amounts of quercetin and kaempferol | standardized (24/48) ginkgo extracts | Walkowiak et al. (2019) |
| 70  | Poland              | herbal products containing sage ethanolic extract (capsules, tablets, ointments, tincture, finished product) / Salvia officinalis | 6 5 1 substitution | TLC / rosmarinic acid | not reported | S. officinalis authenticated botanical extracts | Cieśla and Waks mundzka-Hajnos (2010) |
| 71  | Romania             | St. John’s Wort products (herbal teas, capsules, tablets, extracts) from pharmacies, herbal shops, supermarkets, internet / Hypericum perforatum | 50 34 16 substitution with other Hypericum sp. or did not contain Hypericum species in detectable amounts | TLC, HPLC-MS / rutin, hyperoside, hyperforin, hypericin | not reported | authenticated reference plant material of H. elegans, H. maculatum, H. olympicum, H. patulum, H. perforatum, H. polyphyllum | Raclariu et al. (2017) |
|     | Slovakia            |                                          |                                  |                       |                                             |                                  |                                               |
|     | Turkey              |                                          |                                  |                       |                                             |                                  |                                               |
|     | Austria             |                                          |                                  |                       |                                             |                                  |                                               |
|     | Czech Republic      |                                          |                                  |                       |                                             |                                  |                                               |
|     | Germany             |                                          |                                  |                       |                                             |                                  |                                               |
|     | Italy               |                                          |                                  |                       |                                             |                                  |                                               |
|     | Netherlands         |                                          |                                  |                       |                                             |                                  |                                               |
|     | Poland              |                                          |                                  |                       |                                             |                                  |                                               |
|     | Spain               |                                          |                                  |                       |                                             |                                  |                                               |
|     | Switzerland         |                                          |                                  |                       |                                             |                                  |                                               |
|     | Norway              |                                          |                                  |                       |                                             |                                  |                                               |
| 72  | Romania             | Echinacea products (teas, capsules, tablets, extracts) from retail stores, e-commerce / Echinacea purpurea, E. angustifolia, E. pallida | 34 30 4 substitution or adulteration with unlabeled Echinacea sp. | HPTLC / echinacoside, cynarin, cichoric acid, chlorogenic acid, caffeic acid, caftaric acid | products totally devoided of any Echinacea sp. material | reference botanical standards: E. purpurea, E. angustifolia, E. pallida (UPS) | Raclariu et al. (2018b) |
|     | Czech Republic      |                                          |                                  |                       |                                             |                                  |                                               |
|     | Germany             |                                          |                                  |                       |                                             |                                  |                                               |
|     | Italy               |                                          |                                  |                       |                                             |                                  |                                               |
|     | Poland              |                                          |                                  |                       |                                             |                                  |                                               |
|     | Spain               |                                          |                                  |                       |                                             |                                  |                                               |
|     | Austria             |                                          |                                  |                       |                                             |                                  |                                               |
|     | France              |                                          |                                  |                       |                                             |                                  |                                               |
|     | Norway              |                                          |                                  |                       |                                             |                                  |                                               |

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| No. crt. | Country / territory | Products (details) / authenticated species | Products authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|----------|---------------------|-------------------------------------------|--------------------------------|-----------------------|---------------------------------------------|----------------------------------|-----------------------------------------------|--------------------------|
| 73       | South Korea         | Panax ginseng (decoctions, beverages, capsules, tablets), Platycodon grandiflorus (decoctions, beverages), Codonopsis lanceolata (decoctions, beverages), Pueraria montana var. lobata (beverages) from local markets / P. ginseng, P. grandiflorum, C. lanceolata, P. montana var. lobata | 81 81 0 n/a | HPLC, UPLC-DAD-ESI-IT-TOF-MS / lobetyolin, ononin | not reported | raw plant material of P. ginseng, P. grandiflorum, C. lanceolata, P. montana var. lobata | Choi et al. (2018) |
| 74       | South Korea         | *Malabar tamarind* products from local market / Garcinia gummi-gutta | 11 11 0 n/a | HPLC / cyanidin-3-O-sambubioside, cyanidin-3-O-glucoside | not reported | collected fruit rinds of G. gummi-gutta, purchased G. indica fruit samples reference standards, including some isolated previously from T. chebula | Jamila et al. (2016) |
| 75       | Taiwan              | *myrobalan* (Fructus Chebulae) products from local herbal markets / Terminalia chebula, Terminalia chebula var. tomentella | 28 20 8 substitution with T. chebula var. parviflora | HPLC / tannin-related constituents | not reported | | Juang and Sheu (2005) |
| 76       | Taiwan              | herbal materials of Fritillariae Thunbergii Bulbus from local markets / Fritillaria thunbergii | 12 12 0 n/a | HPLC-UV / peimine, peiminine | product with low total content of peimine (not to be used clinically) | n/a | (Lin et al., 2015) |
| 77       | Taiwan              | white ginseng products (radix sliced material, powder, capsules) / Panax ginseng | 8 7 1 not composed of 6 years old ginseng radix only | 1H-NMR/PCA/CA | not reported | authenticated, one to six year-old, fresh white ginseng radix (P. ginseng) | Lin et al. (2010) |
| 78       | Taiwan              | 5:1 concentrated extract products (prepared from dried roots) from different companies / Scutellaria baicalensis | 6 6 0 n/a | HPLC / baicalin, baicalein | significant product-to-product and batch-to-batch variation of the marker compounds | n/a | Ye et al. (2004) |
| 79       | Thailand            | white *Kwao Krua* products from Thai local markets, drugstores / Pueraria candollei | 7 7 0 n/a | HPLC / isoflavone glycosides (puerarin, daidzin, genistin), isoflavones (daidzein, genistein) | not reported | authenticated P. candollei, Mucuna macrocarpa, Butea superba plant material, Kwao Krua crude drugs | Intharuksa et al. (2020) |

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| No. | Country / territory | Products (details) / authenticated species | Products total | Products authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|-------------------------------------------|---------------|-------------------------------|-----------------------|---------------------------------------------|---------------------------------|---------------------------------------------|--------------------------|
| 80  | Thailand            | Garcinia atroviridis products (capsules) from market / G. atroviridis | 5             | 4,1 substitution               | CZE / hydroxycitric acid and hydroxycitric acid lactone | not reported                        | n/a                             | Muensritharam et al. (2008)              |
| 81  | Thailand            | "Ya dok khao" smoking cessation tea product from local market / Cyanthillium cinereum | 1             | 1,0 n/a                       | HPTLC / triterpenoid compounds (ß-amyrin, taraxasterol, lupeol, betulin) | not reported                        | C. cinereum, E. sonchifolia collected samples, raw C. cinereum materials wild and cultivated varieties of chamomiles, chamomile-like flowers (Anthemis L., Bellis L., Tanacetum L., Ohrysanthemum L.) | Thongkhao et al. (2020)             |
| 82  | Turkey              | chamomile products (tea bags, bulk or packaged crude flowers) from food stores, bazaar / Matricaria chamomilla | 16            | 5,11 adulteration (possibly with Anthemis spp., Tanacetum sp. and Chrysanthemum sp.) | HPLC, HPTLC - PCA, HCA / apigenin 7-O-glucoside | A7G content in different tea brands ranged from 0.43-0.80 mg/g | Demirezer et al. (2014)                          |
| 83  | Turkey              | Ginkgo products (extracts) from local pharmacy, local markets / Ginkgo biloba | 13            | 13,0 n/a                      | LC-MS, HPLC-DAD / ginkgolides, flavonoid aglycones | total flavonoids and ginkgolides higher in medicinal products, no or very little flavonoids in food supplements | Guzelmeric et al. (2017)                        |
| 84  | Turkey              | "okaliptus" products (leaves, essential oils) from herbal shops / Eucalyptus globulus | 13            | 0,13 substitution with E. camaldulensis | TLC / essential oils | n/a                                      | E. camaldulensis, E. globulus, E. grandis reference plant material / essential oils extracted from the reference plant material | Tombul et al. (2012)                  |
| 85  | United Kingdom  | turmeric products (capsules, tablets, soft gels, powder, extracts) from stores, internet / Curcuma longa | 50            | 48,2 absence of C. longa      | 1H-NMR/ PCA, HPTLC / curcumin , pipeline, (S)-ar-Turmerone | significant quality variation between samples | Chatzinasiou et al. (2019)                   |
| 86  | United Kingdom  | St John’s Wort products (tablets, capsules, powder) from internet, pharmacies, stores / Hypericum perforatum | 22            | 14,8 adulteration (possibly with other Hypericum sp. obtained from China or use of chemically distinct H. perforatum cultivars or chemotypes) | HPTLC, 1H-NMR/ PCA | significant compositional variation among commercial finished products, adulteration with food dyes | S. roseum crude drug material, R. crenulata aqueous extracts | Booker et al. (2018)                   |
| 87  | United Kingdom  | Sedum roseum products (root and rhizome powder) (hard capsules, soft gel capsules, tablets) from retail outlets, internet / S. roseum | 39            | 32,7 substitution, adulteration with other Rhodiola sp. (e.g. R. crenulata) | HPTLC, MS, 1H NMR / rosavin, salidroside | lower rosavin content, substitution with 5-hydroxytryptophan | S. roseum crude drug material, R. crenulata aqueous extracts | Booker et al. (2016b)                   |

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| No. | Country / territory | Products (details) / authenticated species | Products total | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/chemical reference materials/standards | Bibliographic reference |
|-----|---------------------|----------------------------------------|----------------|-----------------------|------------------------------------------|---------------------------------|-----------------------------------------------|------------------------|
| 88  | United Kingdom      | Ginkgo food supplements (tablets, hard capsules, caplets) from health food stores, supermarkets, pharmacies, internet/ Ginkgo biloba | 33 5 28         | adulteration (not in compliance with their label specification) | 1H NMR/ PCA, HPTLC / flavonoids, terpene lactones | variable quality (different from that described in pharmacopoeias) | quantified and licensed Ginkgo extracts, G. biloba leaf samples | Booker et al. (2016a)  |
| 89  | United Kingdom      | American ginseng, white Asian ginseng, sanchi ginseng samples from importing companies / Panax ginseng, P. quinquefolius, P. notoginseng | 8 8 0 n/a        | n/a                   | LC/MS/MS / malonyl-ginsenosides            | not reported | authentic root samples of P. ginseng, P. quinquefolius, P. notoginseng | Kite et al. (2003)  |
| 90  | United Kingdom      | herbal tinctures from health shop / Echinacea purpurea, Hypericum perforatum, Ginkgo biloba, Valériana officinalis | 4 4 0 n/a        | n/a                   | 1H-NMR, MS / hyperforin, hypericin, ginkgolic acids, terpene lactones ginkgolides A, B, and C | not reported | n/a                             | Politi et al. (2009)  |
| 91  | United Kingdom      | herbal product (capsules) / Equisetum arvense | 3 1 2 no Equisetum sp. material (no TLC chromatogram) | n/a                   | TLC / kaempferol glucosides               | not reported | material deposited in herbarium / characters used in the European Pharmacopoeia to identify Equisetum sp. | Saslis-Lagoudakis et al. (2015)  |
|     | Bulgaria            | herbal product (tea) / E. arvense        | 1 0 1 adulterated with E. palustre | n/a                   | n/a                                      | n/a                             |                                 | Pawar et al. (2020)  |
|     | Germany             | herbal product (tea) / E. arvense        | 1 1 0 n/a         | n/a                   | n/a                                      | n/a                             |                                 | Pawar et al. (2020)  |
| 92  | United States       | bitter orange products (tablets, capsules, gel-containing capsules, drink powders) from online / Citrus aurantium | 59 59 0 n/a      | n/a                   | LC–MS/MS / phenethylamines (sympathomimetic amine) | very few appear to meet claims for their label concentration declarations | n/a                             | Gilroy et al. (2003)  |
| 93  | United States       | Echinacea preparations (tablet, caplet, capsule, liquid, powder, granule) from health food, drug, and grocery stores / E. purpurea, E. angustifolia, E. pallida | 49 31 18 adulteration, substitution with unlabeled Echinacea sp., no measurable Echinacea | n/a                   | TLC / cichoric acid, echinacoside             | variability in chemical composition | n/a                             | Gilroy et al. (2003)  |

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| No. | Country / territory | Products (details) / authenticated species | Products total | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/chemical reference materials/standards | Bibliographic reference |
|-----|---------------------|------------------------------------------|----------------|----------------------|-----------------------------------------------|---------------------------------|-----------------------------------------------|------------------------|
| 94  | United States       | herbal supplements (loose powders, capsules, tablets, liquid extracts, dried fruit forms) to contain cranberry, lingonberry, bilberry, or blueberry from local stores or internet / Vaccinium macrocarpon, V. vitis-idaea, V. myrtillus, V. corymbosum | 41 | 27 | adulteration and substitution with Vaccinium sp. | HPLC/DAD / anthocyanins (cyanidin-3-glucoside) | wide variation of the anthocyanin content | verified authentic fruit with known anthocyanin profiles, anthocyanin profiles of small authenticated fruit samples | Lee (2016) |
| 95  | United States       | goldenseal products (dried material, extract, freeze-dried material) (capsules, tinctures, powdered bulk materials, tea bags) from online / Hydrastis canadensis | 35 | 32 | adulteration with Berberis. vulgaris, B. aquifolium, Coptis. chinensis | LC-MS/PCA / berberine, hydrastine, canadine | not reported | reference materials (H. canadensis, C. chinensis, B. aquifolium, B. vulgaris) / canadine reference (isolated and purified from H. canadensis) | Wallace et al. (2018) |
| 96  | United States       | black cohosh products (powder, dried extract, liquid extract) (capsules, tablets, soft gels, drops) from local stores or Internet / Actaea racemosa | 33 | 19 | not containing A. racemosa material | UPLC-PDA, UPLC-MRM / V9c and V9a markers, caffeic acid, ferulic acid, isofurulic acid | not containing the full spectrum of plant chemicals after preparation process | authenticated rhizome/root materials from different Actaea sp. | Geng et al. (2019) |
| 97  | United States       | ginkgo products (tablets, capsules, caplet) from health food stores, supermarkets / Ginkgo biloba | 27 | 27 | n/a | HPLC / flavone glycosides, terpene lactones, ginkgolic acids | relevant compositional differences, particularly with regard to the content of ginkgolic acids | EGb 761 extract | Kressmann et al. (2002) |
| 98  | United States       | “buchu” products (whole leaves, powders, capsules, tea bag) / Agathosma betulina | 27 | 16 | not containing labeled A. betulina or A. crenulata | HPTLC / rutin, chlorogenic acid, kaempferol | not reported | A. betulina, A. crenulata plant reference material | Raman et al. (2015) |
| 99  | United States       | yohimbe products (powder, caplet, capsules, liquid, powdered drink mix) from retail health food outlets / Pausinystalia johimbe | 26 | 17 | not containing yohimbe material | GC/MS / yohimbine HCl, ajmaline, corynanthine | containing only trace amounts of yohimbine, largely devoid of the other alkaloids, possible presence of undeclared diluents | authenticated johimbe bark | Betz et al. (1995) |

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|---------|---------------------|--------------------------------------------|----------------|----------------------|---------------------------------------------|----------------------------------|-----------------------------------------------|------------------------|
| 100     | United States       | ginseng preparations from the genera Panax or Eleutherococcus from local health food store / P. ginseng, P. quinquefolius, P. notoginseng, E. senticosus | 25 25 0 n/a | LC-MS, HPLC / ginsenoside (Rb1, Rb2, Rc, Rd, Re, Rf, Rg1), eleutheroside (B and E) | product-to-product variability in the amount of ginsenosides or eleutherosides present | n/a | Harkey et al. (2001) |
| 101     | United States       | German chamomile, Roman chamomile and Juhua products (crude drugs, capsules, tea bags, crude drugs mixed with other plant materials, powder, extracts) from supermarkets, local retail pharmacies, online / Matricaria chamomilla, Chamaemelum nobile, Chrysanthemum morifolium | 24 20 4 | substitution (not containing the labeled chamomile species) did not contain any detectable volatile components | GC/MS, PLS-DA / volatile compounds (b-Farnesene, a-bisabolol oxide A, B) | not reported | authenticated C. nobile, M. chamomilla, C. morifolium samples / essential oil samples obtained from the authenticated plant materials | Wang et al. (2014a) |
|         | China               |                                            | 11 11 0 n/a | HPLC/U/MS, LC-MS, TLC / proanthocyanidin B-type dimers | wide degree of variability in chemical composition | authenticated grape seed extract, peanut skin extract, pine bark extract | Villani et al. (2015) |
| 102     | United States       | grape seed powder products (capsules) from vitamin supplement retailers, supermarkets, online / Vitis vinifera | 21 12 9 | adulteration with peanut skin extract | GC/MS, LC/MS, UHPLC/MS / ginkgolic acids, terpene tri lactones, flavonol glycosides | not reported | G. biloba authenticated and commercial plant samples (leaves, seeds, leaf extracts, sarcotesta) | Wang et al. (2014b) |
| 103     | United States       | gingko products (leaf extracts) from food supermarkets, local retail pharmacies, online / Ginkgo biloba | 21 21 0 n/a | GC/MS, LC/MS, UHPLC/MS / ginkgolic acids, terpene tri lactones, flavonol glycosides | not reported | G. biloba authenticated and commercial plant samples (leaves, seeds, leaf extracts, sarcotesta) | Wang et al. (2014b) |
| 104     | United States       | American and Korean ginseng products (fresh or dried roots) (powders, capsules, tablets) from local and national herbal health care stores / Panax ginseng, P. quinquefolius | 20 18 2 | devoid of ginseng material | RP-HPLC / ginsenosides (Rf, Rb1, Rc) | not reported | n/a | Mihalov et al. (2000) |

(Continued on following page)
| No. | Country / territory | Products (details) / authenticated species | Products total | Authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|--------------------------------------------|----------------|------------------------|-----------------------|---------------------------------------------|-----------------------------------|-----------------------------------------------|---------------------------|
| 105 | United States       | black raspberry products (freeze-dried whole and pre-ground powders) (capsules, extract, liquid form internet / Rubus occidentalis) | 19             | 12                     | 7                     | possible substitution with blackberry (Rubus spp.) | HPLC/DAD/MS / anthocyanins (cyanidin-3-glucoside) | wide range of anthocyanin concentration | n/a                       | Lee (2014)                |
| 106 | United States       | milk thistle products (capsules with dried, oil-based extracts) from market / Silybum marianum | 19             | 19                     | 0                     | n/a                          | U-HPLC-HRMS / silymarin flavonoids, flavonolignans | marked differences in the content of individual flavonoids/ flavonolignans, even within different batches by the same manufacturers | n/a                       | Fenclova et al. (2019)   |
| 107 | United States       | black cohosh products (dry extracts, powdered plant material) from pharmacies, internet / Cimicifuga Racemosa | 19             | 7                      | 12                    | substitution and adulteration with C. churca, C. foetida | LC-MS/MS / actein, 23-epi-26-deoxyactein | not reported | Czech Rep                     | masada-atsumi et al. (2014) |
| 108 | United States       | Aloe vera products / Aloe vera              | 18             | 18                     | 0 | n/a                          | 1H-NMR / nicotinamide | differences among products (possible deacetylation) | n/a                       | Jiao et al. (2010)        |
| 109 | United States       | Tinospora products from internet (capsules, caplets, granule, powder) / T. crispa, T. sinensis | 17             | 15                     | 2 | substitution with T. shenensis | UHPLC-PDA-MS / flavonoid, alkaloids, amid, diterpenoids | not reported | Germany                        | Parveen et al. (2020)     |
| 110 | United States       | skullcap and Chinese skullcap based dietary supplements from internet / Scutellaria lateriflora, S. baicalensis | 15             | 6                      | 9 | substitution with S. baicalensis or Teucrium canadense | FI/MS/PCA / baicalin, verbascoside | very low S. lateriflora concentration | n/a                       | Sun and Chen (2011)       |
| 111 | United States       | “guarana” products (dried seeds, dried paste, seed powders, tablets, capsule) from local health food outlets, manufacturers, internet / Paullinia cupana | 14             | 7                      | 7 | substitution (devoid of P. cupana material) | LC / theobromine, theophylline, caffeine, catechin, epicatechin | possible fortification with synthetic caffeine and dilution with inert ingredients | n/a                       | Carlson and Thompson (1998) |

(Continued on following page)
| No. | Country / territory | Products (details) / authenticated species | Products total | Products authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|-------------------------------------------|---------------|---------------------------------|----------------------|-------------------------------------------|----------------------------------|-----------------------------------------------|--------------------------|
| 112 | United States       | Hoodia gordonii products (gels, capsules, tablets, sprays, teas, snacks, bars, powders, juices) / H. gordonii | 13            | 2 11                            | substitution (no H. gordonii detected, other botanicals present) | HPTLC / pregnane glycosides (hoodigosides, P57) | not reported | various Hoodia sp. / isolated chemical reference standards | Rumalla et al. (2008) |
| 113 | United States       | saw palmetto products (soft and hard gel capsules, tablets, tinctures) from retail | 13            | 13 0                            | n/a                  | GC, 1H-NMR/PCA / quantification of fatty acids | inaccurate labeling of fatty acid content | n/a               | Booker et al. (2014) |
|     | United Kingdom      |                                          | 11            | 11 0                            |                      |                                          |                                  |                                |                          |
|     | Canada              |                                          | 7             | 7 0                             |                      |                                          |                                  |                                |                          |
|     | Switzerland         |                                          | 6             | 6 0                             |                      |                                          |                                  |                                |                          |
|     | Spain               | Serenoa repens                           | 5             | 5 0                             |                      |                                          |                                  |                                |                          |
|     | South Korea         |                                          | 4             | 4 0                             |                      |                                          |                                  |                                |                          |
|     | Finland             |                                          | 1             | 1 0                             |                      |                                          |                                  |                                |                          |
|     | Germany             |                                          | 1             | 1 0                             |                      |                                          |                                  |                                |                          |
| 114 | United States       | St. John’s Wort (herb/aerial parts, extracts) products from market, online / Hypericum perforatum | 12            | 6 6                             | adulteration (possible mixtures with H. undulatum) | HPTLC / rutin, hypericin, pseudohypericin | not reported | H. perforatum extract standard, H. undulatum, H. montanum, H. tetrapterum, and H. hirsutum samples authenticated crude goldenseal powder | Frommenwiler et al. (2016) |
|     | United States       | goldenseal products (capsules, raw, tea bag, liquid extract) from local retailers or internet / Hydrastis canadensis | 12            | 12 0                            | n/a                  | HPLC / berberine chloride, (β)-b-hydrastine | wide range of content variation for hydrastine (0.00–2.51%) and berberine (0.00–4.35%) | Authoredashed and Khan (2001) |
| 115 | United States       | “yohimbe” products (bark cut and sifted pieces, powders) from online / Pausinystalia johimbe | 12            | 8 4                             | adulterated, yohimbine not detected | UPLC-UV-MS / yohimbine | products range widely in yohimbine content (0.1–0.91%) | authenticated P. johimbe bark samples | Raman et al. (2013) |
| 116 | United States       | black cohosh products (extracts, powdered plant material (tablets, capsules) from stores / Actaea racemosa | 11            | 7 4                             | substitution and contamination with Asian Actaea species | TLC, HPLC, LC-MS / triterpene glycosides, phenolics | significant product-to-product variability in the amounts of the selected triterpene glycosides and phenolic constituents not reported | authenticated plant material of Actaea cimicifuga, Actaea dahurica, Actaea yunnanensis | Jiang et al. (2006) |
| 117 | United States       | pure Hoodia gordonii products from the market / H. gordonii | 10            | 1 9                             | substitution with H. parviflora, contamination | 1H NMR / P57, hoodigoside L | not reported | authenticated samples of H. gordonii, H. parviflora, H. raschii, H. currori / isolated chemical reference standards | Zhao et al. (2011) |

(Continued on following page)
| No. crt. | Country / territory | Products (details) / authenticated species | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/chemical reference materials/standards | Bibliographic reference |
|---------|---------------------|------------------------------------------|----------------------|---------------------------------------------|----------------------------------|-----------------------------------------------|------------------------|
| 119     | United States       | goldenseal products (root/rhizome) (capsules) from internet / Hydrastis canadensis | 10 10 0 n/a          | LC-UV, LC-MS / berberine, canadine, hydrastine, coptisine, palmatine, jatrorrhizine, dihydcoptisine | not reported                      | reference samples (dried powders) of H. canadensis (root), Coptis chinensis (root) | Wallace et al. (2020) |
| 120     | United States       | cranberry products (powders, concentrate, fruit solids) from common vendors or internet / Vaccinium macrocarpon | 9 3 6 adulteration (with extracts from other plant species) | 1H-NMR / triterpenoids, organic acids, total proanthocyanidins and anthocyanins | substantially variation of the metabolic profile, slightly lower PAC content may be caused by removal during manufacturing | unsubstantially variation of the nutritional profile, slightly lower PAC content may be caused by removal during manufacturing | Turbitt et al. (2020) |
| 121     | United States       | "ma-huang" products from local retailers, internet / Ephedra sinica | 9 9 0 n/a             | HPLC / ephedrine-type alkaloids | not reported                      | unprocessed E. lematolepis | Gurley (1998) |
| 122     | United States       | standardized (24/6) ginkgo products (leaf extracts) from suppliers / Ginkgo biloba | 8 5 3 adulteration (possibly with sophora extracts) | HPLC-DAD / flavone glycosides | high levels of quercetin and kaempferol | certified ginkgo extract (24/6, commercial extracts of Styrphobium japonicum) | Chandra et al. (2011) |
| 123     | United States       | Vangueria agrestis products (extracts) / V. agrestis | 7 4 3 adulteration | HPTLC / saponins, flavonoids, phenolics, iridoid | not reported                     | unprocessed V. agrestis samples (twigs with intact leaves, stems, roots) | Raman et al. (2018) |
| 124     | United States       | American ginseng products from supermarkets / Panax quinquefolius | 6 4 2 substitution with P. ginseng | HPLC-HCA/PCA / ginseng saponins | not reported                      | certified ginkgo extract standard P. ginseng, P. notoginseng samples (24/6, commercial extracts of Styrphobium japonicum) | Yu et al. (2014) |
| 125     | United States       | African mango products from internet / Irvingia gabonensis | 5 1 4 substitution (do not contain detectable amount of authentic material) | UHPLC-PDA-HRMS / ellagic acid, mono-, di-, tri-O-methyl-ellagic acids and their glycosides | trace constituents of regular mango seeds | certified ginkgo extract standard P. ginseng, P. notoginseng samples (24/6, commercial extracts of Styrphobium japonicum) | Sun and Chen (2012) |
| 126     | United States       | Echinacea products (tablets, capsules, powders) / Echinacea purpurea | 5 1 4 adulteration | HPLC-CAD | not reported                      | Echinacea sp. (extracts, root, herb) | Waidyanatha et al. (2020) |
| 127     | United States       | plantain products (tablets) / Plantago major | 5 4 1 contamination with Digitalis lanata | Kedde reaction, TLC, LC-MS / cardiac glycosides (lanatosides A, B, C, digoxin, digitoxin) | not reported                      | n/a | Silfman et al. (1998) |
| No. | Country / territory | Products (details) / authenticated species | Products authentic/ adulterated | Adulteration reported | Authentication method / marker (if reported) | Additional quality issues detected | Botanical/ chemical reference materials/ standards | Bibliographic reference |
|-----|---------------------|------------------------------------------|---------------------------------|-----------------------|---------------------------------------------|----------------------------------|-----------------------------------------------|------------------------|
| 128 | United States       | black cohosh products from health store, marketplace / Actaea racemosa | 4 3 1 substitution with Cimicifuga foetida | HPLC-PDA/MS/ELSD / (triterpene glycosides, phenolic compounds) | product inadequately manufactured (overheating) | Actaea sp. plant material / authentic Cimicifuga chemical reference standards authenticated aerial parts of P. edulis, P. violacea, P. suberosa, P. montala, P. quadrangularis, seeds of Peganum harmala | He et al. (2006) |
| 129 | United States       | passion flower products (capsules) from online / Passiflora edulis | 4 4 0 n/a UPLC-UV-MS, HPTLC / flavonoids, harmame-carboline alkaloids | not reported |  | | Avula et al. (2012) |
| 130 | United States       | feverfew extracts (capsules, drops) / Tanacetum parthenium herbal products (tea, capsules) / Equisetum arvense | 3 3 0 n/a | LC-UV/LC-MS / parthenolide | not reported | authenticated ginseng roots (P. quinquefolius, P. ginseng, P. notoginseng) | Avula et al. (2006) |
| 131 | United States       | goldenseal products (root powder) from bulk suppliers / Hydrastis canadensis | 3 2 1 adulteration, possibly with Coptis root or barberry bark | LC-MS / alkaloids (berberine, hydrastine, canadine) | not reported | material deposited in herbarium / characters used in the European Pharmacopoeia to identify Equisetum sp. Coptis japonica root powder, Berberis aquifolium root powder, Chelidonium majus herb, Berberis vulgaris bark powder authenticated ginseng roots (P. quinquefolius, P. ginseng, P. notoginseng) | Saslis-Lagoudakis et al. (2015) |
| 132 | United States       | ginseng products (liquid extract, capsules) from a local nutritional store / Panax quinquefolius, P. ginseng, P. notoginseng | 2 2 0 n/a UPLC/QTOF-MS/PCA / (ginsenosides, pseudoginsenosides, gypenosides, notoginsenosides) | not reported |  | | Yuk et al. (2016) |
| 133 | United States       | African mango sample (powdered seeds) / Irvingia gabonensis | 1 0 1 contamination or adulteration with goji berry (Lyocum barbarum) | HPLC-PDA, LC-IT-MS, 1H NMR / pymole alkaloid | not reported | authentic sample of African mango seed powder, goji berries | Li et al. (2014) |
| 134 | United States       | American skullcap (freeze-dried) product / Scutellaria lateriflora | 1 1 0 | HPLC / flavonoids (baicalin, baicalein, wogonin) | not reported | S. lateriflora (aerial parts) reference material | Brock et al. (2013) |
| Total | 2,386 | 1,734 | 652 |

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The set of retrieved full-text articles was further reduced by 446 that did not meet all eligibility criteria. Included: 135 records.

RESULTS

Different chemical methods have been successfully employed for the botanical authentication of 2,386 commercial herbal products, sold in 37 countries spread on six continents. The majority of the analyzed products were reported to be authentic (73%) but more than a quarter proved to be adulterated (27%), when the botanical identity of their content was compared with the label stated ingredients (Table 1).

The herbal products were purchased from 37 countries scattered over six continents: Europe (n = 20), Asia (n = 9), North America (n = 3), Australia (n = 2), South America (n = 2), and Africa (n = 1) (Supplementary Table S1). The numbers of reported samples were geographically heterogeneous, at continental level the highest number of commercial herbal products was reported for Asia (n = 877), North America (n = 767), Europe (n = 573), followed distantly by South America (n = 86), Australia (n = 25) and Africa (n = 5). The proportion of adulterated products varies significantly among continents, being highest in Africa (60%), South America (57%), Australia (44%), and lower in Europe (28%), North America (27%), and Asia (25%). The adulteration percentage of the last three continents enumerated is close to the global one (27%) which can be influenced also by the significantly higher number of commercial products analyzed and reported, compared with the samples analyzed from the other three continents.

The distribution of commercial samples among the 37 countries is highly heterogeneous as well (Table 2). More than 100 commercial products were reported for four countries, i.e. United States (n = 746), China (n = 491) followed distantly by

| Country/Territory | Products | Authentic products | Adulterated products |
|------------------|----------|--------------------|----------------------|
| United States    | 746      | 548                | 198                  |
| China            | 491      | 388                | 103                  |
| United Kingdom   | 123      | 78                 | 45                   |
| Italy            | 119      | 82                 | 37                   |
| South Korea      | 96       | 96                 | 0                    |
| Brazil           | 85       | 36                 | 49                   |
| Romania          | 85       | 65                 | 20                   |
| Malaysia         | 83       | 41                 | 42                   |
| Belgium          | 77       | 56                 | 21                   |
| Japan            | 57       | 37                 | 20                   |
| Taiwan           | 54       | 45                 | 9                    |
| Poland           | 47       | 38                 | 9                    |
| Turkey           | 44       | 19                 | 25                   |
| India            | 32       | 10                 | 22                   |
| Germany          | 22       | 18                 | 4                    |
| European Union a | 22       | 8                  | 14                   |
| Australia        | 19       | 8                  | 11                   |
| Canada           | 15       | 12                 | 3                    |
| Thailand         | 13       | 12                 | 1                    |
| Denmark          | 12       | 12                 | 0                    |
| Croatia          | 10       | 8                  | 2                    |
| Czech Republic   | 10       | 8                  | 2                    |
| Spain            | 9        | 7                  | 2                    |
| Netherlands      | 8        | 8                  | 0                    |
| Pakistan         | 7        | 6                  | 1                    |
| Switzerland      | 7        | 7                  | 0                    |
| Mexico           | 6        | 3                  | 3                    |
| New Zealand      | 6        | 6                  | 0                    |
| Egypt            | 5        | 2                  | 3                    |
| Norway           | 5        | 5                  | 0                    |
| Austria          | 3        | 3                  | 0                    |
| Bulgaria         | 3        | 2                  | 1                    |
| Greece           | 3        | 2                  | 1                    |
| Slovakia         | 3        | 1                  | 2                    |
| France           | 2        | 2                  | 0                    |
| Sweden           | 2        | 2                  | 0                    |
| Chile            | 1        | 1                  | 0                    |
| Finland          | 1        | 1                  | 0                    |

a The percentage values were rounded to the nearest whole number.

b Not reported by the authors the exact EU country.
United Kingdom ($n = 123$) and Italy ($n = 119$). Another seventeen countries are well represented ($n \geq 10$) by the successfully analyzed samples, while the other sixteen countries have even fewer ($n < 10$) products reported.

In twelve countries, out of the total of thirty-seven, all the analyzed commercial herbal products (100%) were reported as authentic, albeit, for eight of them, less than 10 samples were reported. Notably, the botanical identity of the samples purchased from South Korea ($n = 96$) and Denmark ($n = 12$) matched the labeled information. The adulterated proportion in the remaining twenty-five countries varied widely, from 8% up to as much as 80%. From the countries where more than 10 samples from their marketplace have been chemically authenticated and non-authenticated products have been reported, the majority of the commercial products was adulterated, being the highest in India (69%), followed closely by Australia (58%), Brazil (58%), Turkey (57%) and Malaysia (51%). Noticeably, the adulteration percentage of the four countries with more than 100 commercial products reported is 37% (United Kingdom), 31% (Italy), 27% (United States) and the lowest is reported for China (21%).

**Sampling Heterogeneity and Unavoidable Bias**

The authentication raw data were all retrieved from peer-reviewed articles, the vast majority of them after they were indexed in the four major international databases which were systematically searched for while some other few articles were identified after cross-referencing. Although no limiting criteria (e.g., publication year, or language) was used, the authentication data reported in journals with limited-impact and international visibility might be underrepresented in the retrieved data. Moreover, the access of researchers from the economically depressed economies to high-impact journals, and especially to the OA journals, is a further limiting factor for publicly communicating the authentication results relevant for a certain country. On the other hand, as it was previously mentioned as possible bias, also the countries with a functional consumer safety system might be underrepresented as the authentication results of the commercial samples screened by the respective institutions will be published in internal bulletins or protocols, rather than in peer-reviewed journals (Ichim et al., 2020).

**DISCUSSION**

The chemical identification methods have confirmed that a substantial proportion (27%) of herbal products from the international market place is adulterated: on average, more than one in each four products sold in the 37 countries included in our analysis was proved to be non-authentic regarding their botanical identity. This adulteration percentage, revealed by employing many and very diverse chemical analytical methods, almost matches the figure obtained after the use of DNA-based techniques were assessed for their use for the authentication of commercial herbal products in a comparable number of countries: 27% (Ichim, 2019). Indeed, this percentage was obtained after almost a triple number of commercial herbal products ($n = 5,957$) were analyzed and their results reviewed recently. Notably, the microscopic authentication of commercial herbal products have reported a much higher adulteration rate (41%) but the number of analyzed samples was considerably much smaller ($n = 508$) which can be a possible bias of this finding (Ichim et al., 2020).

As it was previously reported by many peer-reviewed reports (Hoban et al., 2018; Seethapathy et al., 2019; Amritha et al., 2020; Anthoons et al., 2021; Palhares et al., 2021), irrespective of the authentication method, adulterated commercial HPs are geographically present across all continents (Supplementary Table S1). Moreover, this highly relevant category of commercial products was found to not comply with the labeled botanical ingredients in proportions almost identical (26 ± 2%), irrespective if they are traditionally used as herbal medicines, as commonly found in Asia, or overwhelmingly consumed as food supplements as in Europe or North America. These two main categories of herbal products commercialized in the global marketplace have many types of value chains (Booker et al., 2012), with some different stakeholders and entities along their shorter or more complex trade chains. Nevertheless, the end-users of both systems seem to be equally affected by non-authentic, accidental contamination or fraudulent substitution of labeled botanical ingredients and even the addition of compounds in an attempt to fool quality control testing e.g. as in adding food dyes to *H. perforatum* in order to achieve higher UV spectroscopy readings (Booker et al., 2018). Indeed, although monographs for herbal raw materials (e.g., Ph. Eur, USP) allow a minor presence of foreign organic matter (Parveen et al., 2016), the adulteration patters documented by employing different chemical methods, are very diverse and most of them are made possible only by the intentional, economically motivated and fraudulent actions of onerous producers or traders.

The total absence of labeled botanical ingredients and/or their extracts from the commercial herbal products tested was detected by using chemical methods. Commercial samples devoid of labeled botanical ingredient species (Carlson and Thompson, 1998; Ardila et al., 2015; Geng et al., 2019; Zhu et al., 2019) or not even substituted with their related species (Wan et al., 2016). An easy way to increase the profit margin of the products was the use of cheaper plant material as it was the use of other plant parts than the ones recommended, labeled and expected by the product’s users, *senna* (*Senna alexandrina* Mill.) stems substituted with leaves and midribs (Kojima et al., 2000), *Panax ginseng* C.A.Mey roots with other plant parts (leaf or stem) (Govindaraghan, 2017), or *Panax notoginseng* Burkill F.H.Chen roots with flowers (Liu et al., 2015). Another similar deceptive adulteration strategy was the reported use of extracts obtained from plant parts other than the recommended ones, such as the decoction of the stem bark to substitute the genuine “jatoba” sap products (*Hymenaea stigonocarpa* Hayne, *Hymenaea martiana* Hayne) and the adulteration of *Aquilaria Lignum Resinatum* (*Aquilaria sinensis* (Lour.) Spreng) products with cheap resin (e.g. rosin) (Qu et al., 2017).
The economically motivated adulteration includes also the use of unlabeled filler species as the DNA of species such as rice (Oryza sativa L.), soybean (Glycine max (L) Merr.) and wheat (Triticum spp.) was previously identified in commercial herbal products (Newmaster et al., 2013; Ivanova et al., 2016). Yet, the TLC alone was able to detect the fraudulent use of soybean oil as filler in “copaiba” (Copaifera multijuga Hayne) oil-resin products (Barbosa et al., 2009).

The detection of unlabeled species with allergenic potential and known or suspected toxicity was previously reported by the use of DNA-based authentication techniques (Newmaster et al., 2013; Speranskaya et al., 2018). The same potential was shown by the phytochemical analyses which have been able to unmask the presence of unwanted and hazardous botanic ingredients, such as species that should have been notified to authorities (e.g. Ilex paraguariensis A. St-Hil., Epimedium spp., Tribulus terrestris L.), or forbidden toxic plants (e.g. Aristolochia fangchi Y.C.Wu ex L.D-Chow and S.M.Hwang) (Deconinck et al., 2019) or even health hazardous contaminations, with Digitalis lanata Ehrh. added to plantain (Plantago major L.) products (Slifman et al., 1998). Moreover, as peanut allergy is a major public health concern and can be severe or even life-threatening (Gray, 2020), chemical methods have proved able to detect adulteration with the peanut skin extract of grape seed-containing herbal products (Vitis vinifera L.) from Australia (Govindaraghan, 2019) and United States (Villani et al., 2015).

All the intentional adulteration practices documented and reported repeatedly till now (Li et al., 2008; Ichim, 2019; Xu et al., 2019; Ichim et al., 2020; Upton et al., 2020) can be evidenced by peer-reviewed reports referring to the top selling herbal products containing highly valued or widely used medicinal species across countries and cultures. The prices of ginseng herbal medicines and supplements vary widely based on the species, quality, and purity of the ginseng, and this provides a strong driver for intentional adulteration (Ichim and de Boer, 2021). Indeed, several chemical methods were able to identify ginseng plant material or partially devoid of the labeled Panax ginseng plant material (Mihalov et al., 2000; Yang et al., 2016) and prove that, in most cases, labeled Panax species were substituted with other Panax species (Li et al., 2010; Yu et al., 2014; Dong et al., 2020), but also the substitution of ginseng root with leaves, stems or flowers (Liu et al., 2015; Govindaraghan, 2017). Notably, chemical analysis was even able to detect the adulteration and substitution of wild with cultivated ginseng (Zhao et al., 2015) as well as a white ginseng products (P. ginseng) not composed of 6 years old ginseng radix only (Li et al., 2010).

Studies carried out at UCL School of Pharmacy, London have consistently shown that product adulteration is commonplace, with 25–40% of products typically being found to be of poor quality or adulterated, and especially with products obtained via the internet. Although with products that have been registered as Traditional Herbal Medicines under the Traditional Herbal Medicinal Products Directive (THMPD), no adulteration has so far been found and these products have shown to be of acceptable quality (Booker et al., 2016a; Booker et al., 2016b; Booker et al., 2018). This does not necessarily mean that all non-registered products (e.g. food supplements) are of poor quality but the problem being that it is difficult for the general public to be able to reliably discern high quality products from inferior ones. Organic certification provides some assurances regarding traceability, including origin, cultivation methods and manufacturing practices and so until more formal regulations are introduced for these food supplement products, buying organic may be the best option.

The many cases of substituted or adulterated herbal products purchased from a very high number of national marketplaces, where the labeled botanical ingredients did not match the chemically identified ones are, unfortunately, accompanied by other low-quality issues which additionally affect the safety and potential efficacy of commercial herbal products. As many as forty-one peer reviewed research articles, which have reported a case of adulteration among analyzed commercial samples, have also reported other quality issues which further lower the overall quality expected by their users and consumers. Additionally, another nineteen studies reported quality issues of the tested products without identifying any proof for their botanical identity adulteration. For the majority of herbal products reported, considerable variability of their labeled metabolic profile and/or content, such as the alkaloid content of “ma-huang” (Ephedra sinica Stapf) products (Gurley, 1998) or Menispermi Rhizoma (Menispernum dauricum DC) products (Liu et al., 2013b), selected triterpene glycosides and phenolic constituents in black cohosh (A. racemosa) products (jiang et al., 2006) or the PAC content of cranberry products (Turbitt et al., 2020). Furthermore, aside of significant product-to-product variability, the marked differences of the content of individual flavonoids/flavanolignans in milk thistle (Silybum marianum (L.) Gaertn.) products have revealed quality difference also between different batches by the same manufacturers (Fenclova et al., 2019).

The peer-reviewed authentication results and the methods which were successfully employed to analyze commercial herbal products and significantly contribute to a better understanding of authenticity issues affecting the herbal industry and provides an as close-to-reality possible picture of the commercial herbal products’ authenticity as well as examples of techniques to be efficiently and accurately used for their authentication.

It is clear that chemical analysis alone can only identify existing problems. In order to prevent these problems from arising in the first place, better governance needs to be implemented along all stages of the supply chain. Regulation can help with this process but resources are scarce and real progress on quality is more achievable through having closer and more focused co-operation between the regulators and the producers, manufacturers and retailers of herbal products.

**AUTHOR CONTRIBUTIONS**

MI performed the literature systematic search and analyzed the results. MI and AB wrote the manuscript together.
**SUPPLEMENTARY MATERIAL**

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphar.2021.666850/full#supplementary-material.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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