USEFUL PLANTS – MEDICINES

AT LEAST

28,187

PLANT SPECIES ARE CURRENTLY RECORDED AS BEING OF MEDICINAL USE

How many plant species are currently used as medicines? As traditional plant-based medicines become more widely accepted in mainstream health systems what are the mains issues and risks that need to be considered?

https://stateoftheworldsplants.com/2017/useful-plants.html

FEWER THAN 16% (4,478) OF THE SPECIES USED IN PLANT-BASED MEDICINES ARE CITED IN A MEDICINAL REGULATORY PUBLICATION.

In many regions of the world, people still rely on traditional plant-based medicines for their primary healthcare[1,2]. This is especially true for many rural communities in Africa, parts of Asia, and Central and South America, where plants and knowledge of their traditional use are accessible and affordable. In other countries, many of these traditional plant-based medicines are being integrated through regulations into mainstream health systems[3,4]. For example, in December 2016 the Chinese government announced their aim to integrate Traditional Chinese Medicine (TCM) into their healthcare system by 2020[5], recognising improved scientific understanding of the plants and their value in treating chronic conditions. In Europe, there is also a trend towards using traditional plant-based ('herbal') medicines alongside pharmaceutical drugs; in Germany, for example, it is estimated that 90% of the population use herbal medicines[2].

Precise figures for the value of international trade in medicinal plants are difficult to obtain[6,7], but it is clear that the industry is growing fast[8,9]. In 2000, US$17 billion was spent in the US on traditional herbal medicines. In 2003, the World Health Organisation estimated the annual global market for herbal medicines to be worth US$60 billion[2] and by 2012 the global industry in TCM alone was reported to be worth US$83 billion[4].

In this chapter we examine the regulation of these herbal medicines and the importance of having an accurate plant species name linked to them. The need for more research evaluating the medicinal properties of these plants is also covered, as well as their potential as new drugs.

REGULATION OF MEDICINAL PLANTS AND THEIR NAMES

Although herbal medicines are becoming increasingly popular in the West[4], not all are safe, and health regulators seek to control their sale and ensure appropriate quality control. Many countries publish 'pharmacopoeias', which are official publications providing precise detailed descriptions and tests to identify and assess the quality of plants used in herbal drugs. The number of plants covered by pharmacopoeias, however, represents only a small percentage of the diversity used in traditional plant-based medicines (see Box 1). Kew's Medicinal Plant Names Services (MPNS, see Box 2), collated information on the names of 28,187 species recorded as being used medicinally but found that only 4,478 are cited in regulatory publications[10].

AN INDICATION OF THE GROWING VALUE OF INTERNATIONAL TRADE IN HERBAL MEDICINES

Estimated value of herbal medicines in the US in 2000

Estimated global value of herbal medicines in 2003

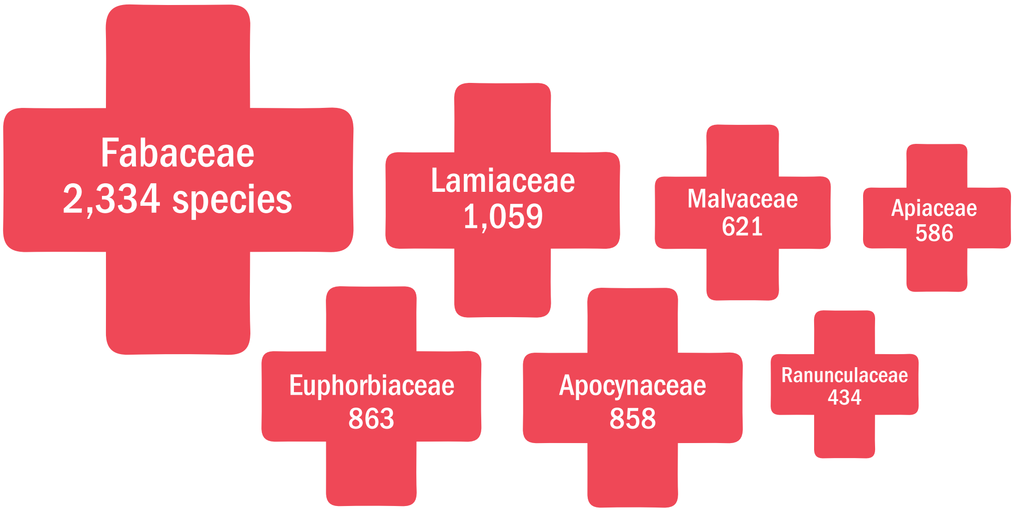
Estimated global value of TCM in 2012

BOX 1: HOW MANY MEDICINAL PLANTS ARE THERE?

The low number of plant species covered by official pharmacopoeias reflects the globalisation of a narrow range of species for use in herbal drugs. For example, in the Brazilian Pharmacopoeia the number of native Brazilian plant species decreased from 196 in the 1926 edition, to 32 in 1959, to 4 in 1977, before increasing again to 11 in 1996[11]. In addition, although the 2010 edition cites 65 species, most are European or Asian plants, with only 14 being native to Brazil[10]. A similar trend is also observed in the British Pharmacopoeia[12]. The increasing popularity of TCM and Ayurvedic medicine (a form of traditional medicine in India) in the West has led to some of the plants used in these medicines being included in pharmacopoeias[12], although globally the number of these species covered by formal monographs remains low. In China, for example, 10,000–11,250 species (c.34% of the native flora) have documented medicinal uses[13,14], but only 563 are cited in the Chinese Pharmacopoeia[10].

TABLE 1: MEDICINAL PLANT FAMILIES AND THEIR CHARACTERISTIC COMPOUNDS

Twelve of the 20 largest plant families have a significantly higher proportion of medicinal plants than would be anticipated if distribution across families were even. Here is a more detailed look at the top seven.



FAMILY	COMMON FAMILY NAME	TOTAL NUMBER OF SPECIES	NUMBER OF MEDICINAL SPECIES IN MPNS	MEDICINAL SPECIES AS % OF TOTAL	KEY CLASS OF COMPOUNDS FOUND IN MANY MEDICINAL SPECIES IN EACH FAMILY
Fabaceae	pea and bean	20,856	2,334	11.2	**alkaloids**
Lamiaceae	mint	7,756	1,059	13.7	**terpenes**
Euphorbiaceae	spurge	6,407	863	13.5	**diterpenoids**
Apocynaceae	dogbane	6,341	858	13.5	**cardiac-glycosides**
Malvaceae	mallow	5,329	621	11.7	**organic acids**
Apiaceae	parsley or carrot	4,079	586	14.4	**coumarins**
Ranunculaceae	buttercup	3,640	434	11.9	**alkaloids**

BOX 2: MEDICINAL PLANT NAMES SERVICES (MPNS)

The MPNS has collated more than 530,000 data records containing the scientific, pharmaceutical and common names used to refer to medicinal plants found in 143 sources, including pharmacopoeias, medicinal plant dictionaries, databases, publications and health regulations. The resource contains the trade forms and the plant parts cited in each of the references included (for sources see online supplementary material).

Users of the MPNS online portal can search using a herbal drug name familiar to them to find a specific medicinal plant, locate all relevant references (regardless of the names used in that reference) and discover how it is named in other references and pharmacopoeias[10].

Correct labelling is also important. Product labelling is frequently misleading, with the trade name 'ginseng', for example, referring to 15 different species of plant, each with its own particular chemistry and therapeutic properties[10]. Substitution by a Belgian clinic of one Chinese medicinal herb ('Fang Ji') with another sharing the same name, led to over 100 patients requiring kidney dialysis for the remainder of their lives[15]. For another example, see Box 3.

Robust authentication of plant ingredients included in herbal products is also vital, along with their substitutes and adulterants[16]. A recent publication of 300 internationally traded Chinese medicinal plants[17] addressed this need by presenting illustrations and detailed descriptions of source plants and trade forms, enabling comparison with their common substitutes, adulterants and counterfeits. Going forward, adulteration could be reduced by sourcing plants from sustainable resources or cultivation[18] combined with reliable traceability procedures and effective authentication and quality control[17,19].

MEDICINAL PLANTS AND DRUG DEVELOPMENT

Historically, plants have often been selected for drug development programmes because they contain specific classes of compounds, such as alkaloids and terpenoids, that are known to be biologically active, or because of their traditional medicinal uses. To what extent does family membership influence the likelihood of a species having a medicinal use? For this year's *State of the World's Plants,* we carried out an analysis of the families of 28,187 species covered by MPNS to identify the families with the highest proportion of medicinal plants (See Table 1; Figure 1). From this it is apparent that some families contain significantly more medicinal plants than might be expected. Selecting families with a high number of medicinal plants along with classes of medicinally active compounds could possibly serve as a signpost for future drug discovery programmes (see Box 4).

Plants with known medicinal uses have been a source of vital pharmaceutical drugs for the treatment of many diseases (see Boxes 5 & 6). For example, artemisinin (discovered in *Artemisia annua*) and quinine (from *Cinchona officinalis*), together with their synthetic analogues, remain among the most important weapons in our arsenal against malaria[20,21], of which 214 million cases and 400,000 deaths were recorded in 2015[22].

Will the next lead come from one or more of the 1,200 species used to treat malaria[23]? In Ghana, Nigeria, Mali and Zambia, about 60% of childhood malaria cases are first treated with herbal remedies[22]. Reviews from Cameroon and Guinea reported use of 217 and 113 species respectively[24], many proving to have antimalarial properties when tested. Of 24 species from one Latin American tree genus (*Aspidosperma*) tested in the laboratory, 19 showed activity against the *Plasmodium* malaria parasite[25]. As antimalarial drug resistance spreads[26], exploring and exploiting such under-utilised (and often under-researched) resources remains a high priority for science[27]. Success will depend both on equipping laboratories in endemic regions and establishing multidisciplinary research networks to bring together the diverse expertise necessary[28].

BOX 3: THE SIGNIFICANCE OF AMBIGUOUS LABELLING FOR PUBLIC HEALTH

Confusion about plant names may arise even in regulations intended to ensure the quality and improve the safety of herbal medicines[36,37]. A single pharmaceutical name (e.g. 'Cimicifugae Rhizoma') can be used to cover different species by different pharmacopoeias – for example, it relates to four species of *Actaea* in the *Japanese Pharmacopoeia* and one in the *European Pharmacopoeia* (see below).

MPNS enables medicine regulators to now link all these names together via an ISO standard for medicinal products[38,39].

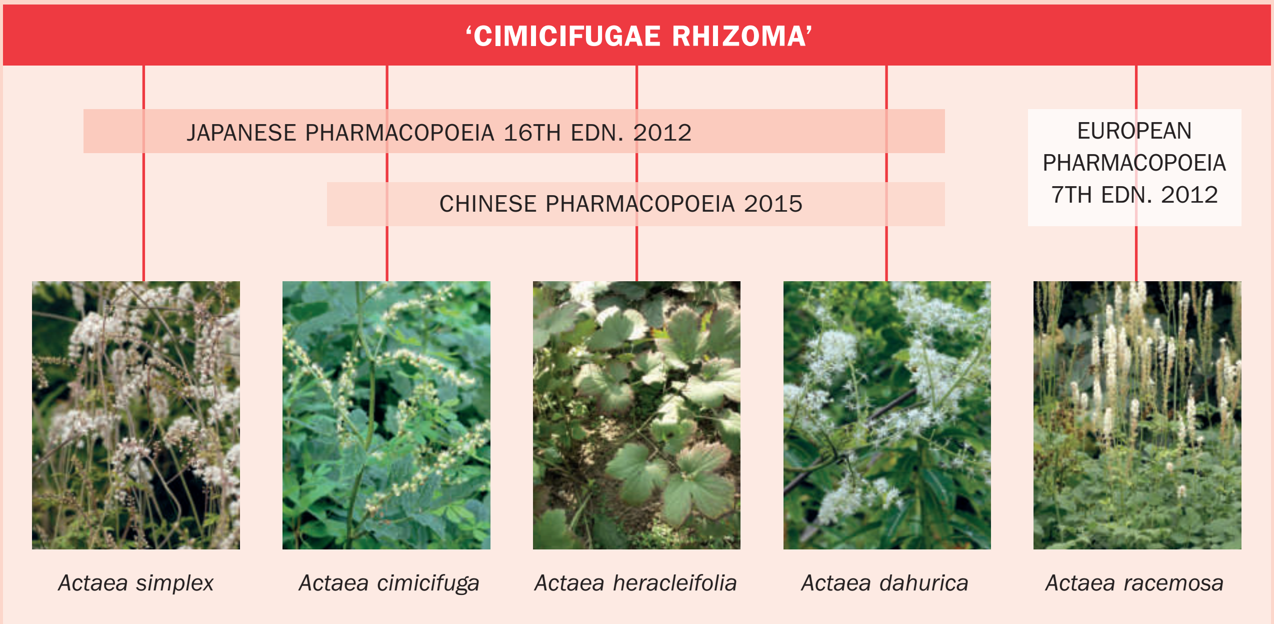
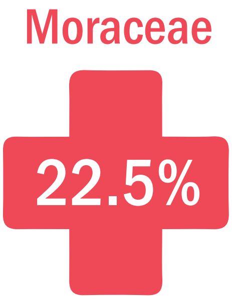
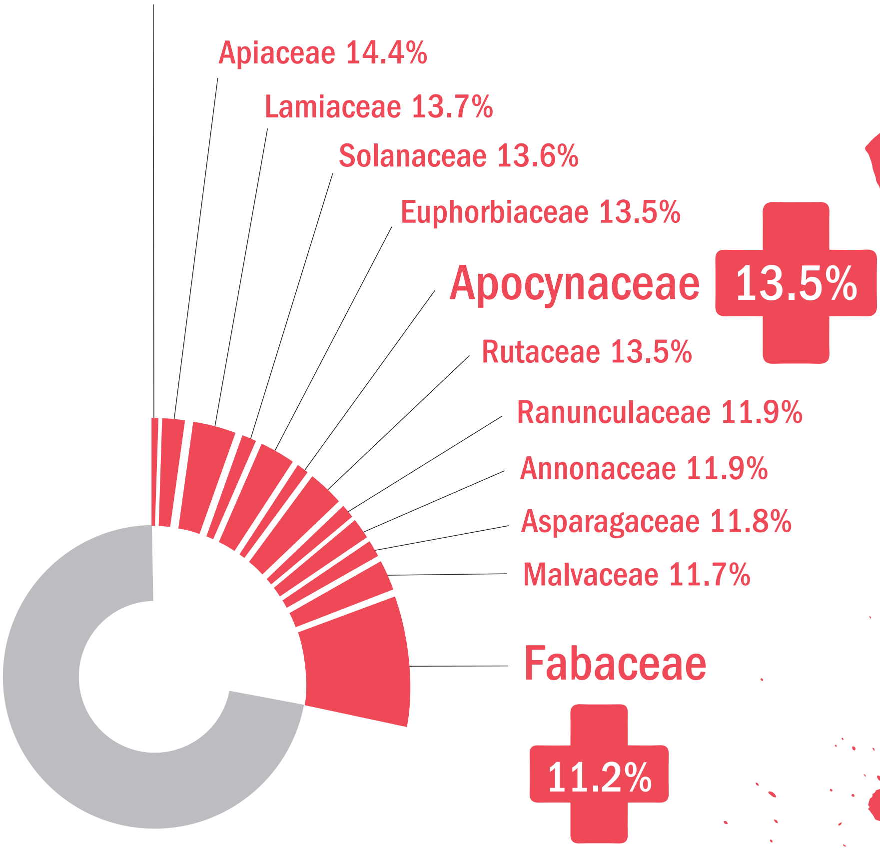


FIGURE 1: THE 12 PLANT FAMILIES WITH A SIGNIFICANTLY HIGHER PROPORTION OF MEDICINAL PLANTS THAN EXPECTED

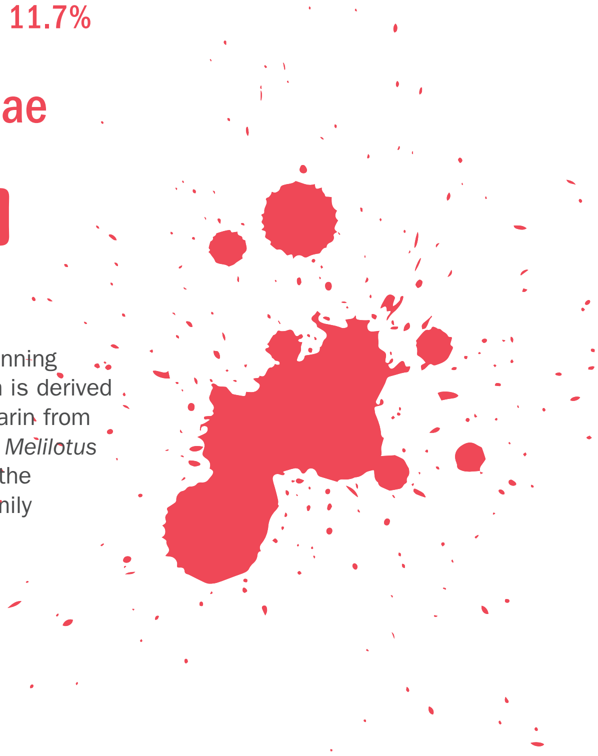


Mulberry (*Morus* spp.) in the family Moraceae, contains imino sugars used in the study of diabetes

% of species in family used for medicinal purposes



The anti-cancerous drugs **vincristine** and **vinblastine** are derived from the Madagascar periwinkle, *Catharanthus roseus* in the Apocynaceae family



The blood thinning drug **warfarin** is derived from a coumarin from sweet clover, *Melilotus officinalis,* in the Fabaceae family

There are 416 families of flowering plants (APG IV); of the 20 largest, 12 demonstrate a higher than normal percentage of species with a medicinal use. (The size of the red segment indicates the relative number of species in each family – see Table 1.)

Three noteworthy families for medicinal plants are Moraceae, Apocynaceae and Fabaceae – drugs in these families that are particularly important are shown in the schematics.

143 DATABASES AND PUBLICATIONS CITE 415,180 UNIQUE NAMES FOR PLANT-BASED MEDICINES– AN AVERAGE OF 15 ALTERNATIVE NAMES FOR EACH SPECIES

BOX 4: PLANTS AS A SOURCE OF PHARMACEUTICAL DRUGS

Since 1981, 1,130 new therapeutic agents have been approved for use as pharmaceutical drugs, of which 593 are based on compounds from natural sources. Thirty-eight are derived from medicinal plants[40,41].

Fifteen of the 56 natural drugs registered for the treatment of cancer since 1980 are derived from medicinal plants with a long history of traditional use. For example drugs based on Paclitaxel have been isolated from the yew tree (*Taxus* spp.), Camptothecin from the happy tree, (*Camptotheca acuminata*) and Podophyllotoxin from the May apple (*Podophyllum hexandrum* and *P. peltatum*).

CONSERVATION OF MEDICINAL PLANTS

Increasing demand for herbal medicines (particularly for species covered by pharmacopoeias) threatens wild populations of many of these plants[29]. Of the 28,187 species recorded in MPNS, c.1,280 are under protection according to CITES (see chapter 12)[10,30]. The commercial value of particular herbal products leads to scarcity of populations of the species used in the product. This in turn increases the frequency of species substitution – when the species is, deliberately or otherwise, substituted with a different species – and thereby threatens patient safety[17,31–34].

For example, supply shortages of *Eleutherococcus nodiflorus* (‘Wu Jia Pi’), widely used in TCM to treat musculoskeletal pain and swelling[35], frequently result in its substitution with a similar-looking adulterant from the unrelated species *Periploca sepium*, which in inappropriate dosages, is toxic[17].

In summary, the focus of world trade on relatively few species of medicinal plants leads to sustainability and conservation issues, which ultimately lead to other plants being substituted, with potential risks to human health. More effective regulation can be achieved through more precise use of scientific plant names and greater awareness of the many alternative synonyms in use. However, clarity on which plants have or have not been studied in drug discovery programmes is also needed. This is now becoming possible through the collation of global data sources on medicinal plants and ‘big data’ analytics. Such approaches will be hugely important in improving our ability to realise current and future medicinal benefits from plants.

BOX 5: PLANTS AND DEMENTIA

Dementia affects 47.5 million people worldwide, with Alzheimer’s disease causing most cases[42]. Of only five drugs developed specifically for the symptomatic treatment of Alzheimer’s disease, two are derived from plants[43]. Galantamine, from *Galanthus* (snowdrops), *Leucojum* (snowflakes) and *Narcissus* (daffodils), was the first natural product drug to treat dementia symptoms. The second was Rivastigmine, which is chemically derived from physostigmine, an alkaloid from *Physostigma venenosum* (calabar bean)[44]. A survey of 139 different plant-derived compounds with potential to target dementia symptoms, revealed the majority (43%) to be classed as alkaloids[45]. Another study documented 152 plants with traditional uses for age-related brain diseases[46]. Research continues to provide a scientific basis to explain the traditional and potential uses of medicinal plants for dementia[47].

BOX 6: PLANTS AND DIABETES

Diabetes affects an estimated 422 million adults and is a global health and economic burden[48]. One study documents 656 flowering plant species used traditionally for diabetes, representing 437 genera and 111 families[49]. When these data were superimposed onto genetic relationship data (a phylogeny), a high proportion tended to be clustered in certain closely-related plant families[49]. Of 104 plants used for diabetes in seven Central American countries, 16 showed experimental evidence that could explain their traditional use[50]. In drug discovery, *Galega officinalis* (goat’s rue) provided a useful compound for the design of the antidiabetic drug Metformin[49,50], while another plant used traditionally for diabetes, *Stevia rebaudiana* (sweetleaf), is a source of sweetener compounds used in the food industry[51].