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Botanical Nomenclature in Pharmacovigilance and a Recommendation for Standardisation

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Abstract

Nomenclature of plants in pharmacology can be presented by pharmaceutical names or scientific names in the form of Linnaean binomials. In this paper, positive and negative aspects of both systems are discussed in the context of the scientific nomenclatural framework and the systems' practical applicability. The Uppsala Monitoring Centre (UMC) runs the WHO Programme for International Drug Monitoring and is responsible for the WHO Adverse Drug Reaction (ADR) database that currently contains 3.6 million records. In order for the UMC to monitor pharmacovigilance through ADRs to herbal medicine products the following nomenclatural criteria are important: (i) the name should indicate only one species of plant; (ii) the source for this name must be authoritative; (iii) the name should indicate which part of the plant is used. Based on these criteria, the UMC investigated four options: (i) adopt main names used in recognised (inter-) national pharmacopoeias or authoritative publications; (ii) adopt option 1, but cite the publication for all names in abbreviated form; (iii) three-part pharmaceutical names consisting of Latinised part name plus Latinised genus name, plus Latinised specific epithet; (iv) scientific binomial names, optionally with author and plant part used. The UMC has chosen the latter option and will at its adoption utilise the scientific botanical nomenclature as defined by the International Code of Botanical Nomenclature. This decision satisfies all criteria set by the UMC and renders the necessity of creating a new system or upgrading an old inconsistent system obsolete. The UMC has also issued an extensive synonymy checklist of vernacular, pharmaceutical and scientific names for the herbals in the WHO ADR database. We strongly recommend the adoption of scientific names to denote plant ingredients in medicine.

Nomenclature of herbals and ingredients of plant origin in medicines is complex and can be a problem in pharmacovigilance and in medicine in general, especially when trying to collate data about the adverse responses to a species or product. This paper highlights the complications in the monitoring of herbal adverse drug reactions (ADRs). The main focus is on herbal products rather than loose, crude herbs. Lack of regulation of the ingredients of herbal medicine results in health risks: for example, confusion over identity of ingredients, lack of links to published pharmacopoeias and unscrupulous exploitation of the herbal market. The problem is aggravated by the limited number of studies on efficacy, safety and quality. Improving the monitoring of the trade of species of medicinal plants is important not just for managing the potential risk of ADRs but also to ensure that material entering the trade is not from endangered species.

The main causes for the current situation are a lack of guidelines and regulation, combined with the concept "it's natural, so it's safe". Of growing concern is that if the demand for herbals keeps increasing, there could be problems in the supply because many species are harvested from the wild. To date, very little has been done to make sure there is a sustainable supply of herbs. When the demand for a specific herb is greater than the supply, then there is an increased likelihood that adulterants and poor-quality material will be used.

Plant ingredient nomenclature lacks uniformity and various types of names are currently in use: pharmaceutical names; scientific generic names; scientific binomials; outdated scientific names (i.e.

Table I. General botanical terms essential to understand herbal nomenclature

Term	Definition
Accepted name	An accepted name is a validly published scientific name (binomial in the case of a species), which should be used to refer to a plant in preference to any other name (synonym) used to refer to this plant in the past
Vernacular name	Vernacular or common names are the names in any language that refer to certain plant species. These names will often be very local and/or refer to groups of related or unrelated species with similar properties
Pharmaceutical name	These names consist of the Latin name for the used part of the plant, plus the Latinised scientific generic name. Sometimes the name will also include the specific epithet. These names may also be referred to as pharmaceutical names or Latinised names
Scientific name	Scientific names of species are binomial names consisting of a genus name and a specific epithet, together forming the species name. Scientific binomials may be followed by the author name. Scientific binomials are often referred to as botanical names, Latin names, scientific names or binomials
Author	The author is the person who provided the species with a scientific name. Carolus Linnaeus (1707–1778) and his work Species Plantarum (1753) is the starting point of scientific botanical nomenclature. Plant names or binomials from before 1753 are not accepted as valid names according to the International Code of Botanical Nomenclature.[1] It is recommended that author names are abbreviated according to Brummitt and Powell (1992)[2] and the International Plant Names Index (2004)[3]
Genus name	The genus name has a capitalised initial letter, and is normally italicised. A genus may contain various numbers of species, ranging from one in monotypic genera, e.g. *Mellissia*, to many, i.e. *Hypericum* with >370 species
Specific epithet	The second part of a binomial name is the specific epithet. This distinguishes one species in a genus from the other. The specific epithet is italicised, but without a capitalised initial. Species may be further subdivided into subspecies, varieties, cultivars and forms
Synonym	If one plant has more than one scientific name, then these are synonyms. This can happen, for example, when seemingly different plants turn out to belong to the same species
Homonym	When the same name refers to different species, these names are homonyms. For scientific names this may happen when an author who gives a name to a plant is unaware of that this name has already been used by another author for another plant

synonyms); and vernacular names (see table I). This can become a problem if confusion arises from ambiguous vernacular and pharmaceutical names, scientific synonyms and the incorrect use of scientific names. If the incorrect species is used in an herbal prescription because there has been confusion in naming the species then this can lead to serious ADRs.

When ADRs are reported after the use of suspected prescriptions or products, such as 'oleum abietis', 'fructus oxyacanthae', or 'ginseng', it is important to know exactly what plant species these names on the prescription refer to. Only when the scientific names are known, can one look at other variables associated with the material, such as chemotype, time of harvesting, extraction method etc. For example, the names 'oleum abietis', 'fructus oxyacanthae' and 'ginseng' refer to 49, 186 and >20 species, respectively.

The Uppsala Monitoring Centre (UMC), Uppsala, Sweden, the Royal Botanic Gardens, Kew, UK, and the Department of Systematic Botany, Uppsala University, Uppsala, Sweden, collaborate on botanical nomenclature in pharmacovigilance and have set the following criteria for their work:

- the name should indicate only one species of plant;
- the source for this name must be authoritative;
- the name should indicate which part of the plant is used.

Using these criteria, four main options have been investigated:

1. Adopt main names used in recognised (inter-) national pharmacopoeias or authoritative publications, irrespective of whether the name is a scientific binomial, a pharmaceutical name or a vernacular name.

2. Adopt option 1, but cite the publication for all names (in abbreviated form) from the Approved Medicinal Plant Name Listing: Radix Rehmanniae (CE98) referring to Commission E monographs. A combination of the latter two can also be used, i.e. scientific binomial plus pharmaceutical name: *Pulsatilla vulgaris*/Pulsatillae herba.

3. Three-part pharmaceutical names, consisting of Latinised part name plus Latinised genus name, plus Latinised specific epithet (the latter is essential to conform to the criteria mentioned previously): Fructus Anisi Stellati.

4. Scientific binomial names, optionally with author, and plant part used: *Panax ginseng* C.A.Mey., root.

2. Nomenclatural Criteria

Currently, the diversity of nomenclature leads to time-consuming analyses of the different names used to describe the herbal ingredients to determine what plant species might be involved in an ADR. However, it is clear that standardisation in the process of naming the species is needed and all four proposed options have their positive and negative points.

Our experience is that in many cases it is impossible to determine what plant species were used as many pharmacopoeias include entries such as: "may be the roots of either plant A, or B, and rarely C, but less now, although D was used often in the last century". Vernacular names are not only imprecise in the sense that they may refer to more than one species in a genus, but may also refer to many unrelated species (table II and table III).

2.1 Option 1 – Adopt Main Names

To satisfy our initial criteria would require a committee to select names for plant ingredients from pharmacopoeias and publications. These would then

Table II. The variety of possible plant species that could be intended if the vernacular name 'black snakeroot' only is provided[4]

Possible intended species (accepted scientific name)
Actaea racemosa L.
Sanicula canadensis L.
Sanicula marilandica L.
Stenanthium densum (Desr.) Zomlefer & Judd

Table III. Complications that arise if a product states it contains 'aloe', without further defining the kind of aloe[4]

Vernacular name	Possibly intended species (accepted scientific names)
American aloe	*Agave americana* L.
Candelabra aloe	*Aloe arborescens* Mill.
Climbing aloe	*Aloe ciliaris* Haw.
Cape aloe	*Aloe ferox* Mill.
Broadleaf aloe, soap aloe	*Aloe maculata* All.
Socotrine aloe, Zanzibar aloe	*Aloe perryi* Baker
Coral aloe	*Aloe striata* Haw.
Kanniedood aloe, Tiger aloe	*Aloe variegata* L.
Barbados aloe, West Indian aloe	*Aloe vera* (L.) Burm. f.
Zebra-leaf aloe	*Aloe zebrina* Baker
Indian aloe wood	*Aquilaria malaccensis* Lam.
Linaloé	*Bursera aloexylon* (Schiede ex Schltdl.) Engl.
Green aloe	*Furcraea foetida* (L.) Haw.
Cobweb-aloe	*Haworthia arachnoidea* (L.) Duval
Giant hesper aloe	*Hesperaloe funifera* Trel.
Night-blooming aloe	*Hesperaloe nocturna* Gentry
Red-flower herper aloe	*Hesperaloe parviflora* (Torr.) J. M. Coult
False aloe	*Manfreda virginica* (L.) Salisb. ex Rose
Cayennelinaloe	*Ocotea cernua* (Nees) Mez
Water-aloe	*Stratiotes aloides* L.

have to be enforced to standardise the nomenclature in all future sources.

2.2 Option 2 – Cite All Names

Option 2 would require that the producers of herbal medicines include the source reference on their products. Option 1 does not require this information, but then it is not easy for the ADR reporter and recipient to know exactly which plant(s) the product contains. Adding the reference with the name (option 2) would require less bureaucracy than option 1, as only a standard list with all accepted sources would be needed. Pharmacovigilance would then require a synonymy checklist for all plant names that occur in the reference sources to be able to conduct postmarketing research focusing on specific plant species. However, there are numerous homonyms in pharmacopoeias that refer to different plant species (see example in this section). To continue with the current myriad of herbal names seems misleading and dangerous, and so neither option 1 nor 2 is feasible in the short or long term.

2.3 Option 3 – Three-Part Pharmaceutical Names

Option 3 is straightforward in that it would maintain the classical pharmaceutical nomenclature that uses Latinised scientific names. It would be necessary to add the Latinised specific epithet to reduce homonymy. For example, changing 'Herba Hyperici' to 'Herba Hyperici Perforati' reduces homonymy from about 370 species to 1 species (table IV and table V). The fact that most pharmaceutical names currently include only a Latinised genus name would make it necessary to design Latinised specific epithets for all plant species included in herbal medicine. These new three-part (Latinised part, Latinised genus plus Latinised epithet) pharmaceutical names should then be globally adopted. The enormous amount of Latinising, the artificial use of Latin, plus the inflexibility of pharmaceutical names

Table IV. Combining the current nomenclature with an authoritative herbal medicine reference source, solves confusion, but does not solve homonymy

Name	Source	Homonymy[a]
Valerian	US Herbal Pharmacopoeia, 1998	10
Radix Rehmanniae	Commission E monographs, 1998	1
Iridis Rhizome	Herbal Drugs and Phytopharmaceuticals, 1994	9
Radix Ginseng	Chinese Pharmacopoeia, English ed., 1992	23
Radix Aconiti	Chinese Pharmacopoeia, Chinese ed., Vol. 1	6
Benzoin	Japanese Pharmacopoeia, English 14th ed., 2001	5
Xinyi	Chinese herbs and compatibility, Vol. 4	28
Blue flag	British Herbal Compendium, Vol. 1	7
Gravel root	Herbal Medicines. A guide for Healthcare Professionals, 1996	2

a Based on the estimated number of different species in herbal medicine with that name.

(table V and table VI), make this a difficult option. On top of this, the lack of author names in pharmaceutical names could cause confusion.

2.4 Option 4 – Scientific Binomial Names

Option 4 is the most logical, as it requires no special committees, only the adoption of the accepted scientific binomial name for each plant species accompanied by the part of the plant that is used. In botanical nomenclature, there is only one accepted name for each plant species in a given taxonomy (table VII) with only one accepted spelling. The great advantage of accepted scientific names over pharmaceutical names is that they are unique and refer to only one species. Correct spelling of scientific names is important to prevent confusion. A drawback is that scientific names provide no information on the plant part that is used and that this has to be added separately. On the other hand, the plant-part name can be added in any language because these can be unambiguously translated to whatever language or code the pharmacovigilance researcher wishes to use.

3. Discussion

After discussion of the options, and analysis of various data resources around the world, the collaboration between the UMC and the Royal Botanic Gardens, Kew has focused mainly on accepted scientific names, whereas the Department of Systematic Botany, Uppsala University, has focused on verifying the herbal substances synonyms in the WHO

Table V. Pharmaceutical names are most often two-part names (part plus genus); using three-part names (including a Latinised specific epithet) reduces homonymy. The number of hits is an approximation of name use

Two-part[a]	Hits[b]	Homonymy[c]	Three-part	Hits[b]
Herba Hyperici	7 021	370	Herba Hyperici Perforati	817
Malvae Folium	12 878	40	Malvae Sylvestris Folium	2
Oleum Pini	391	182	Oleum Pini Sylvestris	29
Cortex Quercus	13 417	400	Cortex Quercus Robur	26
Sambuci Flos	13 442	9	Flos Sambuci Nigrae	12
Rhizoma Curcumae	1 357[d]	40	Curcumae Longae Rhizoma	3 903
Polygalae Radix	14 380	500	Radix Polygalae Senegae	2
Hippocastani Cortex	3 868	13	Aesculus Hippocastani Cortex	0

a According to Wichtl.[5]

b Based on search engine Google (27 November 2005), using entire term within double quotes, and including reverse order.

c Homonymy based on estimated genus size.[6]

d Excluding 'longae' in search.

Table VI. Examples of pharmaceutical names bearing little resemblance to the names of the plant species to which they apparently refer. The number of hits is an approximation of name use

Pharmaceutical name[a]	Hits[b]	Intended scientific binomial
Caryophylli Flos	13 497	*Syzygium aromaticum* (L.) Merr. & L.M. Perry
Graminis Rhizoma	12 437	*Elytrigia repens* (L.) Desv. ex Nevski
Maidis Stigma	73	*Zea mays* L.
Semen Pulicariae	9	*Plantago afra* L., or *P. arenaria* Waldst. & Kit.
Ratanhiae Radix	15 740	*Krameria lappacea* (Dombey) Burdet & B. B. Simpson
Bardanae Radix	12 609	*Arctium lappa* L., *Arctium minus* (Hill) Bernh., or *Arctium tomentosum* Mill.

a According to Wichtl.[6]

b Based on search engine Google (27 November 2005), using entire term within double quotes and including reverse order.

ADR database[8] and WHO Drug Dictionary;[9] together they have resulted in the creation of a synonymised checklist of vernacular, pharmaceutical and scientific names.[10] This checklist comprises 500 of the most common herbals and approximately 7500 synonyms to these.

Other resources to find accepted scientific names for plants are, for example, the websites of the US Department of Agriculture's Agricultural Research Service Germplasm Resources Information Network (USDA-ARS-GRIN) Taxonomy database,[4] the World Checklist of Selected Plant Families,[11] and the International Seed Testing Association (ISTA) List of Stabilized Plant Names. In addition, the International Plant Names Index (IPNI)[3] is a database of published names and basic bibliographical details of seed plants, ferns and fern allies. It is a key resource for checking the authors associated with individual names and, hence, is an invaluable tool for resolving homonyms. However, it is not intended to be used as a guide for determining synonymy nor for identifying accepted names.

4. Conclusions

The UMC/Kew/Uppsala University collaboration will continue into the future. The practical application of the work has already resulted in the development of a WHO Herbal Dictionary[9] and a database structure for the WHO Programme for International Drug Monitoring, which allows for the reporting and analysis of herbal ADRs. The work has also resulted in two publications,[12,13] promoting the idea of option 4 becoming a WHO standard classification based on the existing Anatomical Therapeutic Chemical (ATC) classification. Overall, the work of the collaboration has been reflected in the 'WHO Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems',[12,14] and a book, *Accepted Botanical names of Therapeutic Herbs and their Synonyms*, has recently been published.[10] This international collaboration is open to any group that has the ambition to link herbal-product information to the global botanical standardisation process.

Table VII. Some examples to illustrate that synonyms may be more commonly used than accepted scientific names. The number of hits indicates the popularity of the name

Scientific synonym	Hits[a]	Accepted scientific name	Hits[a]
Anthemis nobilis L.	125 000	*Chamaemelum nobile* (L.) All.	61 400
Cephaelis ipecacuanha (Brot.) A. Rich.	102 000	*Psychotria ipecacuanha* (Brot.) Stokes[b]	1 550

a Based on search engine Google (27 November 2005), using binomial within double quotes.

b Psychotria ipecacuanha was placed in the genus Carapichea by Andersson in 2002.[7]

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