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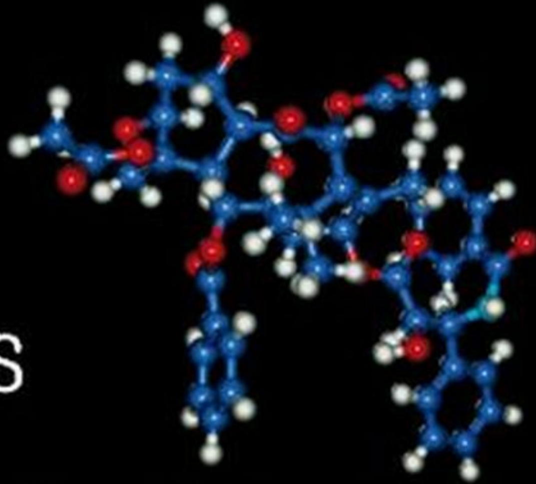

Trease and Evans

Pharmacognosy

William C Evans

SAUNDERS
ELSEVIER

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Pharmacognosy

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SIXTEENTH EDITION

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Preface

Pharmacognosy embraces a number of scientific and other disciplines providing a unified and comprehensive treatment of medicinal plants. There are constant advances and changes affecting all areas of the subject and, as in the past, this 16th edition addresses these new developments while at the same time maintaining the fundamental concepts required for the teaching of all aspects of the subject. It should continue to be of value not only to those of a pharmaceutical and medical persuasion but also to scholars of other disciplines who have an interest in natural products.

Over 60 crude drugs, recently included in editions of the European and British pharmacopoeias, have now been given separate entries in Part 3. Cognizance has been taken of the shift away from material collected in the wild, which results in the endangerment of species, towards cultivation under controlled conditions. The implementation of legal requirements for the quality control of herbal drugs and medicines has given an even greater significance to the development of additional standardization and analytical procedures; similarly for traditional Asian and Chinese medicines.

Subsequent to the publication of the 15th edition of this book, many new phytochemicals, their structures and pharmacological activities, have been reported, especially from those plant materials having current interest. In this respect, a new chapter covering plant nutraceuticals gives emphasis to the attention now being given to this diverse group of pharmacologically active food constituents. Genetic fingerprinting, now widely used by plant taxonomists, is becoming increasingly important for the characterization of closely related species of medicinal plants and for the recognition of chemical races with variable pharmacological properties; a number of examples will be found throughout the text.

As previously, I am much indebted to the contributors, who have given of their time and expertise to provide new or revised chapters on topics of current interest. It is with much regret that I record the death of my former colleague Dr Mohammed Aslam, who with characteristic enthusiasm had initiated and continued to update the chapter on Asian medicine, Thanks are due to Dr R. Hardman, Dr K. Helliwell, Dr L. W. Levy and Prof. J. D. Phillipson for aspects concerning current developments, and to Seven Seas Limited, Marfleet, for kindly updating entries on fish oils. Library facilities were made available by the Universities of Bath, Bristol, Exeter and Reading, the Royal Pharmaceutical Society of Great Britain, the Secretariat of the European Scientific Cooperative for Phytotherapy and the Taunton Public Library.

Daphne, my wife, has assisted me throughout by providing miscellaneous contributions to the text, carrying out literature searches and helping with the organization of the manuscript; without her dedicated help, this edition would not have been possible. Miscellaneous practical support afforded by other family members is also much appreciated.

I am grateful to the publishers in Edinburgh for their usual helpful assistance and understanding.

W. C. E.
2009

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PART

1 Introduction

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1

Plants in medicine: the origins of pharmacognosy

The universal role of plants in the treatment of disease is exemplified by their employment in all the major systems of medicine irrespective of the underlying philosophical premise. As examples, we have Western medicine with origins in Mesopotamia and Egypt, the Unani (Islamic) and Ayurvedic (Hindu) systems centred in western Asia and the Indian subcontinent and those of the Orient (China, Japan, Tibet, etc.). How and when such medicinal plants were first used is, in many cases, lost in pre-history, indeed animals, other than man, appear to have their own materia medica. Following the oral transmission of medical information came the use of writing (e.g. the Egyptian *Papyrus Ebers c*. 1600 BC), baked clay tablets (some 660 cuneiform tablets *c*. 650 BC from Ashurbanipal's library at Nineveh, now in the British Museum, refer to drugs well-known today), parchments and manuscript herbals, printed herbals (invention of printing 1440 AD), pharmacopoeias and other works of reference (first *London Pharmacopoeia*, 1618; first *British Pharmacopoeia*, 1864), and most recently electronic storage of data. Similar records exist for Chinese medicinal plants (texts from the 4th century BC), Ayurvedic medicine (Ayurveda 2500–600 BC) and Unani medicine (*Kitab-Al-Shifa*, the Magnum Opus of Avicenna, 980–1037 AD).

In addition to the above recorded information there is a great wealth of knowledge concerning the medicinal, narcotic and other properties of plants that is still transmitted orally from generation to generation by tribal societies, particularly those of tropical Africa, North and South America and the Pacific countries. These are areas containing the world's greatest number of plant species, not found elsewhere, and with the westernization of so many of the peoples of these zones there is a pressing need to record local knowledge before it is lost forever. In addition, with the extermination of plant species progressing at an alarming rate in certain regions, even before plants have been botanically recorded, much less studied chemically and pharmacologically, the need arises for increased efforts directed towards the conservation of gene pools.

A complete understanding of medicinal plants involves a number of disciplines including commerce, botany, horticulture, chemistry, enzymology, genetics, quality control and pharmacology. Pharmacognosy is not any one of these per se but seeks to embrace them in a unified whole for the better understanding and utilization of medicinal plants. A perusal of the monographs on crude drugs in a modern pharmacopoeia at once illustrates the necessity for a multidisciplinary approach. Unlike those who laid the foundations of pharmacognosy, no one person can now expect to be an expert in all areas and, as is illustrated in the next chapter, pharmacognosy can be independently approached from a number of viewpoints.

The word 'pharmacognosy' had its debut in the early 19th century to designate the discipline related to medicinal plants; it is derived from the Greek pharmakon, 'a drug', and gignosco, 'to acquire a knowledge of' and, as recorded by Dr K. Ganzinger (*Sci. Pharm*., 1982, **50**, 351), the terms 'pharmacognosy' and 'pharmacodynamics' were probably first coined by Johann Adam Schmidt (1759–1809) in his hand-written manuscript *Lehrbuch der Materia Medica*, which was posthumously published in Vienna in 1811. Schmidt was, until his death, professor at the medico-surgical Joseph Academy in Vienna; interestingly he was also Beethoven's physician. Shortly after the above publication, 'pharmacognosy' appears again in 1815 in a small work by Chr. Aenotheus Seydler entitled *Analecta Pharmacognostica*.

Pharmacognosy is closely related to botany and plant chemistry and, indeed, both originated from the earlier scientific studies on medicinal plants. As late as the beginning of the 20th century, the subject had developed mainly on the botanical side, being concerned with the description and identification of drugs, both in the whole state and in powder, and with their history, commerce, collection, preparation and storage. In his series *A History of British Pharmacognosy (1842–1980)*, E. J. Shellard (*Pharm. J.*, 1980, **225**, 680) wrote:

> It is a recognised fact that in the historical development of any subject the role of certain individuals is of considerable importance. This is true in pharmacognosy. The first British pharmacognosist was Jonathan Pereira (1804–1853), who as the first teacher of the subject gave it its pharmaceutical basis. He may be considered as the founder of British pharmacognosy. Daniel Hanbury (1825–1875) was the most outstanding applied pharmacognosist while the contribution made by E. M. Holmes (1843–1930) as an applied pharmacognosist stands out both in quality and quantity. H. G. Greenish (1855–1933), and T. E. Wallis (1876–1973) transformed the old academic pharmacognosy by their contribution to the elimination of adulteration from powdered drugs. Their exploitation of the microscope in pharmacognosy ensures their position as the pillars of the halcyon days (of pharmacognosy).

Such branches of pharmacognosy are still of fundamental importance, particularly for pharmacopoeial identification and quality control purposes, but rapid developments in other areas have enormously expanded the subject.

The use of modern isolation techniques and pharmacological testing procedures means that new plant drugs may find their way into medicine as purified substances rather than in the form of galenical preparations which, for various reasons, would be unsatisfactory. Preparation is usually confined to one or a few companies who process all the raw material; thus, few pharmacists have occasion to handle dried *Catharanthus roseus* although they are familiar with formulations of the isolated alkaloids vinblastine and vincristine. For these new drugs it is important that the pharmacist is cognisant of the physical, chemical and chromatographic standards applicable to the identification, purity, etc. of such products. Similar remarks apply to other anticancer drugs derived from *Taxus, Podophyllum* and *Ochrosia* spp.

When specific plants, including those used in traditional medicine, suddenly become of interest to the world at large, the local wild sources soon become exhausted. This necessitates, as in the case of *Catharanthus roseus, Coleus forskohlii, Ginkgo biloba, Arnica montana* and *Taxus brevifolia*, research into the cultivation or artificial propagation by cell culture, etc., of such species. In order to avert the type of supply crisis that arose at the clinical trial stage with the anticancer drug taxol, isolated from *T. brevifolia*, the US National Cancer Institute initiated plans for future action should a similar situation again arise (see G. M. Cragg *et al.*, *J. Nat. Prod.*, 1993, **56**, 1657). However, it was reported that as a result of the original demand for the drug galanthamine (q.v.) for the treatment of Alzheimer's disease, the native source of *Leucojum aestivum* was endangered. The situation was partially resolved following the commercial synthesis of galanthamine.

The use of single pure compounds, including synthetic drugs, is not without its limitations, and in recent years there has been an immense revival in interest in the herbal and homoeopathic systems of medicine, both of which rely heavily on plant sources. At the 9th Congress of the Italian Society of Pharmacognosy (1998) it was stated that the current return of phytotherapy was clearly reflected by the increased market of such products. In 1995 the latter, for Europe, reached a figure of $6 billion, with consumption for Germany $2.5 billion, France $1.6 billion and Italy 600 million. In the US, where the use of herbal products has never been as strong as in continental Europe, the increase in recent years has also been unprecedented with the market for all herb sales reaching a peak in 1998 approaching $700 million. Again, illustrating the same trend, the editor of *Journal of Natural Products*, 1999, wrote that in response to the increasing prominence of herbal remedies, additional contributions describing scientific investigations of a rigorous nature would be welcomed, a suggestion that appears to have been fully endorsed!

Undoubtedly, the plant kingdom still holds many species of plants containing substances of medicinal value which have yet to be discovered; large numbers of plants are constantly being screened for their possible pharmacological value (particularly for their anti-inflammatory, hypotensive, hypoglycaemic, amoebicidal, antifertility, cytotoxic, antibiotic and anti-Parkinsonism properties). Pharmacognosists with a multidisciplinary background are able to make valuable contributions to these rapidly developing fields of study and pharmacists in general need to have a knowledge of, and to give professional advice on, the many herbal preparations available to the public.

2

The scope and practice of pharmacognosy

Until relatively recently pharmacognosy was regarded, almost exclusively, as a subject in the pharmaceutical curriculum focused on those natural products employed in the allopathic system of medicine. Coincident with the increasing attractiveness of alternative (complementary) therapies and the tremendous range of herbal products now generally available to the public, regulatory requirements covering medicinal herbs have been put in place by many countries in order to control the quality of these products. Monographs are now available on a large number of such drugs giving descriptions, tests for identity and purity and assays of active constituents. These monographs are being compiled by a number of bodies (see below). In this respect recognition should be given to the pioneering production of the *British Herbal Pharmacopoeia*, first produced in 1974 with the latest volume in 1996. Pharmacognosy is also important in those countries having their own systems of medicine in which plants are important components.

Many crude drugs once generally categorized as herbal remedies are now, in accordance with Continental European practice, described in the *British Pharmacopoeia* (*BP*). Chromatographic, chemical and physical tests, together with assay procedures, are given for many drugs for which previously there was no quantitative evaluation of the chemical constituents available. The importance of quality control is paramount, as the demand and the possibility of substitution has increased. The upsurge in the marketing of Chinese and Asian traditional medicines worldwide, for which there is a need for adequate control, adds a further dimension to pharmacognosy; pharmacopoeial monographs now include Liquorice for use in Chinese medicine, Chinese angelica root and Astragalus root. It is understood that further monographs on Chinese and Indian drugs for use in traditional medicine are to be included in the *BP* 2009.

Although pharmacognosy is principally concerned with plant materials, there are a small number of animal products which are traditionally encompassed within the subject; these include such items as beeswax, gelatin, woolfat, vitamins, etc. Other natural products such as the antibiotics, hormones and others may or may not be involved, depending on the teaching practice of a particular institution. Marine organisms, both plant and animal, with potent pharmacological actions are receiving increasing attention in the search for new drugs. Materials having no pharmacological action which are of interest to pharmacognosists are natural fibres, flavouring and suspending agents, colourants, disintegrants, stabilizers and filtering and support media. Other areas that have natural associations with the subject are poisonous and hallucinogenic plants, allergens, herbicides, insecticides and molluscicides.

Vegetable drugs can be arranged for study under the following headings.

1. *Alphabetical*. Either Latin or vernacular names may be used. This arrangement is employed for dictionaries, pharmacopoeias, etc. Although suitable for quick reference it gives no indication of interrelationships between drugs.
2. *Taxonomic*. On the basis of an accepted system of botanical classification (Chapter 3), the drugs are arranged according to the plants from which they are obtained, in classes, orders, families, genera and species. It allows for a precise and ordered arrangement and accommodates any drug without ambiguity. As the basic botanical knowledge of pharmacy students decreases over the years this system is becoming less popular for teaching purposes.
3. *Morphological*. The drugs are divided into groups such as the following: leaves, flowers, fruits, seeds, herbs and entire organisms, woods, barks, rhizomes and roots (known as organized drugs), and dried latices, extracts, gums, resins, oils, fats and waxes (unorganized drugs).

These groupings have some advantages for the practical study of crude drugs; the identification of powdered drugs (see Chapter 43) is often based on micro-morphological characters.

4. *Pharmacological or Therapeutic*. This classification involves the grouping of drugs according to the pharmacological action of their most important constituent or their therapeutic use. R. Pratt and H. W. Youngken Jr. were, in 1956, the first to use this approach for an English language textbook and now, with so many plant materials being screened for specific pharmacological activity, this type of listing is found increasingly in the literature. Its use is illustrated in Chapters 27–32. However, it is important to appreciate that the constituents of any one drug may fall into different pharmacological groups.
5. *Chemical or Biogenetic*. The important constituents, e.g. alkaloids, glycosides, volatile oils, etc., or their biosynthetic pathways, form the basis of classification of the drugs. This is a popular approach when the teaching of pharmacognosy is phytochemically biased. Ambiguities arise when particular drugs possess a number of active principles belonging to different phytochemical groups, as illustrated by liquorice, ginseng, valerian, etc. The scheme is employed in Chapters 19–26 for arranging the established pharmacopoeial drugs.

The following list of works, arranged in the above five groups, will serve as examples and also provide a useful list of textbooks and works of reference; those no longer in print may be found in established pharmaceutical libraries.

1. Alphabetical

Barnes J, Anderson LA, Phillipson JD 2007 Herbal medicines, 3rd edn. Pharmaceutical Press, London
Bisset NG (ed), Wichtl M 1996 Herbal drugs, a handbook for practice on a scientific basis. Medpharm Scientific Publishers, Stuttgart
Bradley PR 1992, 2006 British herbal compendium, Vols I, II. British Herbal Medicine Association, Bournemouth, UK
British Pharmacopoeia 2008 and preceding edns
British Herbal Pharmacopoeia 1996. British Herbal Medicine Association, Exeter, UK
Duke JA 2002 Handbook of medicinal herbs, 2nd edn. CRC Press, New York
Martindale: the Complete Drug Reference, 35th edn 2007. Pharmaceutical Press, London
United States Pharmacopoeia 29/National Formulary 24 and Supplement 2006
Williamson EM 2002 Potter's herbal cyclopaedia. CW Daniel Co, Saffron Walden

The national pharmacopoeias of many countries and the European Pharmacopoeia; *the relevant crude drug monographs of the latter are included in the British Pharmacopoeia*

2. Taxonomic

Paris RR, Moyse H 1965, 1967, 1971 Matière médicale. Masson, Paris, 3 vols
Thoms H 1929 Handbuch der Pharmacie. Urban and Schwarzenberg, Berlin, Band V, 2 vols, Pharmacognosy
Trease GE, Evans WC 1972 Pharmacognosy, 10th edn. Baillière Tindall and Cassell, London

3. Morphological

Berger F Handbuch der Drogenkunde. Maudrich, Vienna, Vol I, Barks and flowers, 1949; Vol II, Leaves, 1950; Vol III, Fruits and woods, 1952; Vol IV, Herbs, 1954; Vol V, Roots, 1960; Vol VI, Resins etc and seeds, 1964; Vol VII, Index, 1967
Jackson BP, Snowdon DW 1990 Atlas of microscopy of medicinal plants, culinary herbs and spices. Belhaven Press, London
Wallis TE, 1967 Textbook of pharmacognosy, 5th edn. Churchill Livingstone, London

4. Pharmacological or Therapeutic

Der Marderosian A, Liberti LE 1988 Natural product medicine. GF Stickley, Philadelphia, PA, USA
Heinrich M, Barnes J, Gibbons S, Williamson EM 2004 Pharmacognosy and phytotherapy. Churchill Livingstone, Edinburgh
Pratt R, Youngken HW, Jr 1956 Pharmacognosy, 2nd edn. Lippincott, Philadelphia, PA, USA
Ross MSF, Brain KR 1977 An introduction to phytopharmacy. Pitman Medical, Tunbridge Wells

5. Chemical

Bruneton J 1999 Pharmacognosy, phytochemistry, medicinal plants. Intercept Scientific, Medical and Technical Publications
Dewick PM 2002 Medicinal natural products, a biosynthetic approach, 2nd edn. John Wiley, Chichester
Hänsel R, Sticher O, Steinegger E 1999 Pharmakognosie-Phytopharmazie, 6th edn. Springer, Berlin (*in German*)
Robbers JE, Speedie MK, Tyler VE 1996 Pharmacognosy and pharmacobiotechnology. Williams & Wilkins, Baltimore
Tschirch A Handbuch der Pharmakognosie. Tauchnitz, Leipzig *(two editions and numerous volumes up to 1933)*

With the increase in interest in medicinal plants world-wide there are now many publications covering regional areas of the globe. Treatment of the plants in these works may be on any of the above lines. Some examples are given following the Introduction to Part VI.

As mentioned previously, a number of bodies have implemented research and published monographs on medicinal herbs. The aim has been to set standards for quality, efficacy and safety in order that the many traditional herbs meet legal requirements. The following are of note:

German Commission E monographs. These were developed for the German Federal Health Authority between 1978–1994 and involve 324 herbs used in German traditional medicine. The monographs give sources, constituents and considerable pharmacological and clinical information. They have now been translated into English and published by the American Botanical Council in 1999 as a single work followed by expanded monographs in 2000.

ESCOP monographs. ESCOP (European Scientific Cooperative for Phytotherapy) is an affiliation of European associations which has produced 60 monographs on herbal drugs, published in loose-leaf form in six fascicules, harmonizing the standards for these drugs throughout the European Union. Information is given on approved therapeutic uses, and unlike the Commission E monographs, provides references. The second edition of *ESCOP Monographs* was published in 2003, and a third edition is in the course of preparation.

AHP monographs. The *American Herbal Pharmacopoeia* (1997–2005) has monographs on a selection of traditional indigenous herbs with some overlap with the European monographs. Treatment of individual drugs can be extensive, for example, the St John's wort monograph published in *HerbalGram* 1997, No 4 extends to 32 pages with over 150 references, colour photographs and chemical formulae.

WHO monographs. The World Health Organization published Volume 1 of its *Monographs on Selected Medicinal Plants* in 1999. It contains standards for quality of drugs together with a therapeutic section; 31 plant species, the majority of which are also included in the above lists, are considered. Volume 2 was published in 2002.

USP monographs. The United States Pharmacopoeia is also producing herbal monographs. Eleven have been published, all involving drugs treated above, and twelve more were expected during 2000.

Current awareness. Students wishing to read original research will find many references in this book and should learn how to find similar ones for themselves. As no one can hope to read all the scientific literature that is published, special journals are devoted to the publication of brief abstracts from the original papers. Such abstracts give the author's name, the subject of the research, the reference necessary to locate the paper in the original journal and usually a brief outline of the work it contains. Most pharmacy department libraries contain *Chemical Abstracts* and *Biological Abstracts*, which in the appropriate sections cover all areas of pharmacognosy. Even so, the systematic searching of the abstracts to cover a broad field of interests can itself be most time-consuming, and publications such as *Chemical Titles* and *Current Contents* can be used to give a more rapid indication of recent publications. *Phytotherapy Research* regularly includes a selected bibliography relating to plant drugs. Information storage and retrieval is now itself a science, and a glance at the shelf-space occupied by succeeding years of *Chemical Abstracts* is sufficient to indicate that before long, if not already, manual searches of the literature will become impossibly long procedures. In many libraries, hard copies of these publications and of the journals mentioned below are no longer available, but they can be accessed on-line. Inevitably it will be necessary to rely on databases for literature scanning. *Pharmacognosy Titles* is a computer abstract coverage of phytochemical research publications up to 1974 (10 vols) produced under the direction of Professor N. Farnsworth, University of Illinois. Subsequently, Farnsworth introduced NAPRALERT, a Natural Product Database which is mainly, but not entirely, post-1975 and is viewed by many as a logical and indispensable collection of pharmacognostic information. The NAPRALERT database is available on a scheduled-fee basis to scientists, industrial firms, government agencies and academic institutions. Among other useful databases having a relevance to pharmacognosy and published on the Web are MEDLINE, compiled by the US National Library of Medicine and EMBASE, produced by Excerpta Medica.

Some journals—for example, *Planta Medica, Journal of Ethnopharmacology, Phytochemistry* and *Journal of Natural Products*—periodically contain reviews on some aspect of medicinal plants. Other journals containing research papers of pharmacognostical interest are *Natural Product Research* and *Natural Product Sciences*. Periodical publications appearing in bound form and devoted to reviews on certain aspects of plant constituents are useful for updating; often the reviews cover only the advances in a particular field since the previous volume. Examples are *Natural Product Reports* (six issues per year) and *Alkaloids* (Academic Press).

A series of multi-author books *Medicinal and Aromatic Plants – Industrial Profiles* (R. Hardman, series editor, CRC Press, Boca Raton, FL) provides an in-depth coverage of major medicinal and aromatic plants for specific genera; to date (2007) forty-five volumes have been published. Individual books for appropriate drugs are cited in Part 5 under 'Further reading'. Books that are not part of a series but, like the above, multi-author and dealing with certain specialized areas (e.g. alkaloids, flavonoids, isoprenoids), continually appear and generally give up-to-date information (in so far as any book can). Symposia which cover various aspects of pharmacognosy are frequently held in various parts of the world and scientists can easily become acquainted with others having like interests. Often the informal discussions which invariably arise at such meetings can be an extremely useful means of disseminating information. In addition, the lectures presented at such meetings are often subsequently published in book form. Modern communication systems make world-wide contact between researchers much simpler.

Now available to Western scientists interested in oriental medicine is the quarterly journal *Abstracts of Chinese Medicine*, published by the Chinese University of Hong Kong. This gives abstracts in English of significant Chinese research papers from more than one hundred scientific journals not readily available outside China.

Useful dictionaries to be found in most University libraries include *Dictionary of Organic Compounds* consisting of 7 volumes and 10 supplements (to 1992), *Dictionary of Alkaloids* (2 volumes) (1989), *Dictionary of Terpenoids* (1991) and *Dictionary of Natural Products* (1994) all published by Chapman and Hall and also *Phytochemical Dictionary: A Handbook of Bioactive Compounds from Plants* (1993), published by Taylor and Francis. Some of these more expensive volumes are available on CD-ROM.

3

Plant nomenclature and taxonomy

BOTANICAL NOMENCLATURE

Before the time of Linnaeus (1707–1778) many plants were known by a double Latin title; however, it is to this great Swedish biologist that we owe the general adoption of the present binomial system, in which the first name denotes the genus, while the second (specific) name denotes the species. All specific names may be written with small initial letters although formerly capitals were used where species were named after persons. Thus the species of *Cinchona* named after Charles Ledger, who brought its seeds from Brazil in 1865, is now written *Cinchona ledgeriana* rather than *Cinchona Ledgeriana*.

The specific name is usually chosen to indicate some striking characteristic of the plant—for example, the hemlock with the spotted stem is named *Conium maculatum* (*maculatus*, *-a*, *-um*, spotted). Sometimes the reason for the name is not as obvious as in the example just mentioned, but once it is discovered it will serve as a reminder of a characteristic of the plant—for example, *Strychnos potatorum* (*potator*, *-oris*, a drinker) bears a name which is only intelligible when it is known that the seeds of this species are used in India for clearing water. A particular species can also exhibit a number of varieties; these are especially evident with cultivated plants but are also found in the wild. For a medicinal example, see *Mentha piperita* below.

The modern rules governing the terminology of plant taxonomy are laid down in the *International Code of Botanical Nomenclature*.

Unlike the names of chemical substances, which are subject to changes which conform to evolving systems of nomenclature, systematic plant names are strictly controlled by rules which give precedence to that name used by the botanist who first described the species. Nevertheless, this seemingly straightforward approach can give rise to various quirks in spelling. The following are three examples involving medicinal plants: *Rauvolfia* vis à vis *Rauwolfia*; the former name was given to this Apocynaceous genus by Plumier in 1703, honouring the botanist Leonard Rauwolf. This spelling oversight caused much contention over the years centring on whether Plumier's obvious intention should be adopted in the name *Rauwolfia*. Both spellings are commonly found but the rules dictate that *Rauvolfia* has priority. In another example the downy thornapple may be encountered as either *Datura innoxia* or *Datura inoxia*. The former, as *Datura innoxia* Miller, was used in 1768 (*Gard. Dict.*, edn. 8, *Datura* no. 5) and this spelling was invariably employed for some 200 years; however in Miller's original description, the plant was characterized as: 'Datura (*Inoxia*) pericarpiis spinosis inoxiis ovatis propendentibus foliis cordatis pubescentibus' (W. E. Safford, *J. Wash. Acad. Sci.*, 1921, **11**, 173) and taxonomists now consider *D. inoxia* Miller to have priority. Both versions are still commonly encountered. A third example concerns the genus of the coca plant which may appear as *Erythroxylum*, or in older literature as *Erythroxylon*. Uppsala Monitoring Centre (a WHO collaborating centre for International Drug Monitoring) has published 'Accepted scientific names of therapeutic plants and their synonyms'.

SUBDIVISIONS OF THE PHYLA

The branches of the genealogical tree differ so much in size that it is not easy to decide which are of equal systematic importance, and what one biologist may consider as a family another may regard as a subfamily. Similarly, the species of one botanist may be the subspecies or variety of another. The main hierarchical subdivisions of a division, arranged according to Engler's scheme, may be illustrated by the following example showing the systematic position of peppermint.

Division	Angiospermae
Class	Dicotyledoneae
Subclass	Sympetalae
Order	Tubiflorae
Suborder	Verbenineae
Family	Labiatae (Lamiaceae)
Subfamily	Stachydoideae
Tribe	Satureieae
Genus	*Mentha*
Species	*Mentha piperita* Linnaeus (Peppermint)
Varieties	*Mentha piperita* var. *officinalis* Sole (White Peppermint)
	Mentha piperita var. *vulgaris* Sole (Black Peppermint)

It will be noted that in pharmacopoeias and in research publications botanical names are followed by the names of persons or their accepted abbreviations (e.g. Linnaeus and Sole in the case of peppermint given above). These refer to the botanist who first described the species or variety. Students need not attempt to memorize these names, and in the following pages they are usually omitted except in cases where different botanical names have at different times been applied to the same plant and there is possibility of confusion. The source of cloves, for example, is now usually given as *Syzygium aromaticum* (L.) Merr. et Perry; prior to 1980 the *BP* used the name *Eugenia caryophyllus* (Spreng.) Sprague; other synonyms which may be found in the older literature are *E. caryophyllata* Thunb. and *E. aromatica* (L.) Baill. Worldwide, not all authors of research papers use the currently accepted name so caution is necessary and botanical sources should be checked.

The letters s.l. following the botanist's name refers to collective species and varieties and imply 'in the widest sense' (*sensu latiore*), e.g. *Thymus serpyllum* L.s.l.

BOTANICAL SYSTEMS OF CLASSIFICATION

Before the widespread acceptance of the principle of evolution, biologists, being convinced of the fixity of species and lacking much of the information available today, confined themselves to more or less artificial methods of classification, their systems being frequently based on one or a few characters instead of upon the organism as a whole. These earlier systems are now mainly of historic interest, but certain of their features—for example, the large division of seed plants into monocotyledons and dicotyledons as used by John Ray (1628–1705)—survive today. Linnaeus' *Species Plantarum* of 1753 is the starting point for the modern nomenclature of plants, although his actual system of classification is entirely artificial and of little significance today. The *Prodromus*, started by A. P. de Candolle (1778–1841) and completed under the editorship of his son Alphonse (1806–93), was a massive work of 17 volumes which professed to be an account of every flowering plant then known. The system of classification employed was a modification and extension of that introduced earlier by De Jussieu (1748–1836) and further demonstrated the inadequacies of the Linnaean system which were then becoming apparent. Bentham and Hooker's *Genera Plantarum* (1862–1883) was patterned on the de Candolles' work, each genus being redescribed from herbarium specimens and not consisting of a restatement of earlier literature. Although largely artificial, it was convenient to retain this system as a basis for collections such as the herbaria of Kew and the British Museum, with continuous revision based on molecular systematics.

During the last 100 years a considerable number of phylogenetic systems of classification have been propounded; these systems arrange taxa (any groups used for classification such as orders, families, genera, etc.) to indicate the possible relationship of one taxon to another. Such systems are clearly susceptible to change with increasing knowledge, and no final system acceptable to all taxonomists is in sight; indeed, for some practical purposes a stable, workable phenetic system is often preferable. A close examination of the phylogenetic systems reveals that certain taxa form precise groups, others have less well-defined boundaries and other groups are difficult to accommodate phylogenetically. The work of Engler (1844–1930) in association with other German systematists is still adhered to in this connection. Engler's scheme of classification largely embodied the fundamental concepts of Eichler (1839–87) and was exemplified in the 20-volume work (1887–89) *Die natürlichen Pflanzenfamilien*, by Engler and Prantl. Subsequent to this, there appeared many editions of Engler's *Syllabus der Pflanzenfamilien*, the eleventh by Engler and Diels in 1936. The last version of the *Syllabus*, produced by Melchoir as two volumes, was published in 1964; the plant families in Chapter 5 of this textbook are arranged in this order. The immediate popularity of Engler's works was due to their applicability to plants of the whole world; they afforded a means of identifying all known genera.

Obviously, large works such as the above are not easily compiled and many taxonomists have produced phylogenetic schemes directed at various levels of classification without the complete systematics of the Engler series. Of the schemes, those of Cronquist (1981) and Takhtajan (1959) are generally similar whereas that of Hutchinson (1992) differs in that the dicotyledons are divided into two large groups—those characteristically and primitively woody (Lignosae) and those characteristically and primitively herbaceous (Herbaceae). These schemes incorporate data often not accessible to the earlier taxonomists; thus Cronquist, while emphasizing classical morphological characters and following the strobilar theory of Angiosperm evolution also takes account of micromorphological data (e.g. embryology and pollen structure), chemical data (e.g. secondary metabolites and serology) and the fossil record.

Dahlgren's proposals (1983), which involve a taxonomic method termed cladistics, demonstrate the distribution of characters and his cladograms of the orders of Angiosperms can be conveniently used for illustrating the occurrence of secondary metabolites throughout the higher plants. In this method (cladistics), clade is a group of plants at any level sharing a common ancestor and formed by a splitting to give two new species, which themselves in the course of time may split again. Clades may be very large or small, with clades within clades; as they comprise hypothetical relationships, they are subject to change as new knowledge becomes available. Evolutionary changes as envisaged in cladistics are sudden and widespread vis à vis the continuous gradual evolution taking place by small changes over a long period of time, as postulated by Darwin. Cladistics are now widely employed by modern taxonomists.

A modern replacement for Engler's classical work, now in the course of compilation, is *The families and genera of vascular plants* [K. Kubitzki *et al*. (eds)]. So far (2007), nine volumes have been published.

TAXONOMIC CHARACTERS

All plants possess hundreds of characters of a morphological, histological, embryological, serological, chemical and genetic nature which are potentially available for building up a classification of the plant kingdom. In the artificial schemes the characters employed were those that experience had shown could be used to produce suitable groups or taxa. The eventual scheme, into which could be inserted new plants as they were discovered or in which any plant could easily be traced, resembled a catalogue with a 'telephone directory' arrangement of plants in which the groups of individuals listed together did not necessarily have any phylogenetic relationship, but merely possessed certain common features.

Phylogenetic classifications, which endeavour to indicate the relationship of one taxon to another, imply the use of characters that are capable of showing such relationships. Because some groups of plants are more primitive than others on the evolutionary scale, certain characters will also be primitive, whereas other characters will have evolved from them. Thus, woody plants are generally regarded as more primitive than herbaceous ones and flowers with few parts more advanced than those with many parts.

The difficulties facing the taxonomist are appreciable. The appearance of a particular character in certain plants does not necessarily imply a relationship between these plants, because at some time in the past, under favourable conditions, whole groups of unrelated plants could have undergone this change (e.g. the development of fused corollas from polypetalous flowers; this is known as *convergence*). Alternatively, related plants may, in some point of time, have started to diverge in their characteristics so that the modern phenotypes appear very dissimilar—this is *divergence. Parallelism* refers to the similar evolution of characters in related plants or related groups of plants. Having decided which characters are of value and how many can be used, the taxonomist then has to consider whether each character should be given equal value or whether a 'weighting' system should be employed. Computers have an obvious role in dealing with large numbers of characters applied to thousands of plants, not only from the aspect of storage and retrieval of information, but also for the science of *numerical taxonomy*, which will probably play an increasing role in the development of systematics. For a fuller discussion of this subject the reader is referred to Heywood's *Plant Taxonomy*.

CHEMICAL PLANT TAXONOMY

This subject has recently attracted much attention and has, after many years, brought the plant chemist back to systematic botany. The concept that plants can be classified on the basis of their chemical constituents is not new; for example, early workers classified the algae into green, brown and red forms, but it is only during the last 40 years that modern techniques of isolation and characterization have led to the chemical screening of many thousands of plant samples. Compared with morphological characters, chemical constituents are often more precisely definable and can be of more fundamental significance for classification purposes. Plant taxonomists, in general, hold the view that chemical characters are yet another type of character to be considered alongside those used traditionally, but it does not necessarily follow that taxa constructed on a purely chemical basis, if such were possible on the data at present available, would necessarily coincide with those arrived at by classical methods.

The characters employed in chemical taxonomy need to be those of intermediate distribution in the plant kingdom. The presence of such ubiquitous compounds as the essential amino acids and common sugars is of little diagnostic value and, at the other extreme, the occurrence of coniine in the single species *Conium maculatum* of the large family Umbelliferae is also of little taxonomic significance. Characters most studied in this connection are therefore secondary metabolites (alkaloids, isoprenoids, flavonoids, characteristic glycosides, etc.), many of which are of established pharmaceutical interest.

However, as discussed later, secondary metabolites may be subject to considerable variation in the living plant, depending on environmental and ontogenetic factors, and more stable chemical characteristics are offered by those closely associated with DNA composition of the species. Increasingly, it is becoming possible to use DNA hybridization, serotaxonomy and amino acid sequencing techniques for taxonomic purposes. One pharmacognostical application (Y. Mino *et al.*, *Phytochemistry*, 1993, **33**, 601) has been the determination of the complete amino acid sequence of one of the iron sulphur ferredoxins present in varieties of *Datura stramonium*. The results support the view that the white and purple forms are varieties of a single species and that the tree daturas (e.g. *D. arborea*) are best regarded as constituting one section of the genus *Datura* and not a separate genus (*Idem.*, *ibid.*, 1994, **37**, 429; 1995, **43**, 1186); work with *D. quercifolia* and *D. fastuosa* also suggests that the amino acid sequence depends not on the species, but on the section. Similar studies were subsequently applied to *Physalis* (Y. Mino and K. Yasuda *Phytochemistry*, 1998, **49**, 1631).

A second example (H. Mizukami *et al.*, *Biol. Pharm. Bull.*, 1993, **16**, 388) shows that restriction fragment length polymorphisms (RFLPs) can be used as a simple and efficient method for distinguishing between *Duboisia leichhardtii, D. myoporoides* and the hybrid of the two species (RFLPs are produced by digestion of DNA with restriction endonucleases and vary in number and size according to genus, species etc.) However, the same group found (*ibid.*, 1993, **16**, 611) that the technique did not distinguish between the various geographical strains of the traditional Chinese drug *Glehnia littoralis* (Umbelliferae) containing different furanocoumarin compositions but did so with *Bupleurum falcatum* (*ibid.*, p. 279).

The differentiation between samples of *Panax ginseng* (Oriental ginseng), *P. quinquefolium* (American ginseng) and adulterants can be difficult by conventional means and F. Ngan *et al*. (*Phytochemistry*, 1999, **50**, 787) have reported on the authentication and differentiation, one from another, of six species of *Panax* and also their adulterants, using RFLPs involving the DNA sequences in a selected ribosomal region; see also J. Wang *et al.*, *Planta Medica*, 2001, **67**, 781 and Z. Zhao *et al*., *Planta Medica*, 2006, **72**, 865 for the authentication of Chinese herbal medicines. *Salvia divinorum*, which contains the hallucinogenic diterpenoid salvinorin A not present in other species of *Salvia* (e.g. the sage plant), can be identified unequivocally by the combined use of analytical chemistry (HPLC-MS) and molecular DNA fingerprinting (C. M. Bertea *et al.*, *Phytochemistry*, 2006, **67**, 371).

Random amplified polymorphic DNA analysis has been used to distinguish between the various subspecies of *Melissa officinalis* common on the pharmaceutical market and now included in the *BP/EP*. Previously, samples have been classified according to the distribution pattern of compounds present in the lemon balm oil (H.-T. Wolf *et al.*, *Planta Medica*, 1999, **65**, 83).

Recent examples of the correspondence of genetic profiles and chemical constituents for the delineation of closely related plant species and chemotypes is illustrated by research on *Withania somnifera* (R. S. Dhar *et al*., *Phytochemistry*, 2006, **67**, 2269), *Zingiber officinalis* and related species (H. L. Jiang *et al.*, *Phytochemistry*, 2006, **67**, 1673), and *Hypericum* spp. (A. Smelcerovic *et al.*, *Phytochemistry*, 2006, **67**, 171).

Serotaxonomic studies of *Acacia* gum exudates have demonstrated the value of such immunological tests in the chemotaxonomic analyses of these economically important products (T. C. Baldwin *et al.*, *Phytochemistry*, 1990, **50**, 599).

A standard work on chemotaxonomy (in German) is that of Hegnauer (see 'Further reading'); it comprises 11 volumes published over nearly 40 years. A four-volume work in English is that of Darnley Gibbs, published in 1974; unfortunately, it does not appear to have been updated.

Further reading

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