

RAUWOLFIA:

Botany, Pharmacognosy, Chemistry & Pharmacology

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RAUWOLFIA SERPENTINA

apparently was first illustrated by this engraving in the *Auctuarium* of Rumphius' *Herbarium Amboinense*, published in 1755, under the name of *Radix mustelae* (Weasel-root).

GEORG EBERHARDT RUMPF

(1627–1702), sometimes called the "Pliny of India" (see title page of the *Auctuarium*), was sent to the island of Amboina by the Dutch East India Company in 1653 with a commission to write a book on the useful and otherwise remarkable plants of the Spice Islands. After many heartbreaking misadventures, Rumpf finally completed the manuscript in 1701, only a few months before his death. It was not published until about a half-century later (1741–1755); under the editorship of Burmann.



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GEORGII EVERHARDI RUMPHII,

Med. Doct. Hanavensis, Mercatoris Senioris, & in Amboina Consulis, nomine PLINII INDICI celebris, & Membri Inlustris Societatis Academiae Naturae Curiosorum Germaniae,

HERBARII AMBOINENSIS AUCTUARIUM,

Reliquas complectens Arbores, Frutices, ac Plantas,

QUAEIN AMBOINA,

ET ADJACENTIBUS DEMUM REPERTAE SUNT INSULIS,

Omnes accuratissime descriptae, & delineatae juxta earum formas, cum diversis Indicis denominationibus, cultura, usu, ac viribus;

Nunc primum in lucem editum, & in Latinum fermonem versum,

Cura & Studio

JOANNIS BURMANNI,

Med. Doct. Inlustris Athenaei, & Horti Medici Amstelaedamensis Professoris Botanici,

Academiae Caefareae Naturae curioforum Socii.

Qui varia adjecit Synonyma, fuasque Obfervationes.



AMSTELÆDAMI,

Apud

MYNARDUM UYTWERF,
&

Viduam ac Filium S. S C H O U T E N,

M. DCC. LV.

BY GEORG EBERHARDT RUMPF,

Med. Doct. of Hanau, Venerable Merchant, & Consul to Amboina, renowned as the PLINY OF INDIA, & Illustrious Member of the Academic Society of Natural Philosophers of Germany,

SUPPLEMENT TO THE HERBARIUM

AMBOINENSE,

Comprising additional Trees, Shrubs, & Herbs, Which recently have been found

IN AMBOINA.

AND IN THE ADJACENT ISLANDS,

All most accurately described, & delineated according to their kinds, with divers Indian names, culture, use, & virtues;

Now printed for the first time, & translated into the Latin tongue,

Through the Care & Learning of

JOHN BURMANN,

Illustrious Med. Doct. of the Athenaeum, & Professor of Botany of the Medicinal Garden of Amsterdam,

Fellow of the Imperial Academy of Natural Philosophers,

Who has added various Synonyms, and his own Comments.



AMSTERDAM,

1755

Foreword

Man from the earliest times has had an innate desire to find means for ameliorating the stresses of his environment. Originally many natural substances such as opium, hyoscyamus, and cannabis were administered with therapeutic intent for their effects on sensation and emotion. Later the synthetic chemist developed a variety of chemically unrelated central nervous system depressants. Although these products and compounds possessed some attributes for alleviating physical pain and mental stress, they unfortunately could produce effects which led to deterioration of the individual and even to physical dependence on the drug. No doubt the calming and hypotensive effects of Rauwolfia have been known for hundreds of years, but it was not until modern scientific methods began to elucidate the actions of depressant drugs that an effect different from sedation or hypnosis was shown to be inherent in certain drugs. This effect is one of producing a calming influence on the higher cerebral centers and is referred to as a state of tranquillity. Thus a "technological breakthrough" in the drug therapy of mental illness came about.

The unraveling of the mysteries of Rauwolfia was not the work of a single scientific discipline. This is exemplified by the experts who have assembled the data in this text. Botany, pharmacognosy, chemistry, biochemistry and pharmacology are all represented. The critical and complete review of Rauwolfia and its alkaloids as presented in this volume will undoubtedly stimulate further fundamental research. The therapy of hypertension is still based largely on empirical knowledge. The discovery of the tranquilizing action of reserpine is of such recent date that the full significance of the alterations in psychic functions is still speculative.

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Alkaloids occupy an important position in therapy. Because of the manifold pharmacological actions of the *Rauwolfia* alkaloids, this monograph should be of decided value to those seriously concerned with mechanisms of action, especially as these influence psychiatric disorders and cardiovascular pharmacology.

Arnold J. Lehman, M.D.
Chief, Division of Pharmacology
United States Food and Drug
Administration

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Pharmacognosy, Chemistry, & Pharmacology



The Botany of Rauwolfia*

SYSTEMATIC POSITION OF THE GENUS

Rauwolfia is a tropical genus of woody plants of the natural family Apocynaceae. From the morphological standpoint, the Apocynaceae are distinguished among Dicotyledones by the structure of their flowers, with their gamopetalous and predominantly pentamerous corollas prevailingly contorted in estivation, their isomerous eucyclic epipetalous stamens with introrse anthers borne upon usually enlarged sterile connectives, and their superior and typically bicarpellary ovaries surmounted by a common style and characteristically elaborate capitate stigma head. From the standpoint of anatomy the family is noteworthy in the almost universal presence of nonarticulated latex ducts which make their appearance in various tissues of the plant, and in their bicollateral stelar structure. The family is of deep interest to biochemists, particularly because of the complex alkaloid systems which have been demonstrated for nearly all genera investigated.

Following the system of K. Schumann (1895), the Apocynaceae are separable into two subfamilies, Plumeroideae and Echitoideae, which are distinguished among other respects by the essentially free and usually unappendaged anthers of the former and the closely connivent and conspicuously appendaged anthers of the latter. Contemporary pharmacological research has served to emphasize the validity of the two subfamilies, for it has found that

^{*} This study would not have been completed without the kindness of friends who provided me roots: Dr. E. Quisumbing, Dr. H. W. Youngken, Sr., E. F. Woodward, Dr. P. Campos Porto, the late Professor R. E. D. Baker, Dr O. Degener, Dr. H. St. John, E. A. Menninger, H. Keng, and very specially Dr. H. B. MacPhillamy. I must also express my appreciation to my student A. Sathyanarayana Rao for much assistance in the compilation of the text, and particularly for execution of Figures 1–4.

the alkaloids of the Plumeroideae prevailingly are sedatives and antihypertensives, while those of the Echitoideae apparently are exclusively cardiac glycosides. *Rauwolfia* is a genus of Plumeroideae.

Among other genera of Plumeroideae more or less closely related to Rauwolfia which have recently been the subject of biochemical and pharmacological study may be mentioned Holarrhena (frequently reported as an adulterant of Rauwolfia serpentina in India), Alstonia, Cameraria, Aspidosperma, Amsonia, Vinca, Tabernanthe, Vallesia, Hunteria, Cerbera, and Thevetia. For general reference to such genera, K. Schumann (1895) may be consulted, as well as the more critical and recent, if less well organized, works of Pichon (1948).

DEFINITION OF THE GENUS

RAUWOLFIA [Plum.] L. Sp. Pl. ed. 1. 208. 1753; Gen. Pl. ed. 5. 98. 1754 (as Rauvolfia). L. Gen. Pl. ed. 7 (Reichard). 118. 1778 (as Rauwolfia). L. Gen. Pl. ed. 8 (Schreber). 160. 1789; L. Sp. Pl. ed. 4 (Willdenow). 1217. 1798 (as Rauwolfia).

Ophioxylon L. Sp. Pl. ed. 1. 1043. 1753; Gen. Pl. ed. 5. 467. 1754. Dissolaena Lour. Fl. Cochinch. 137. 1790. Cyrtosiphonia Miq. Fl. Ind.-bat. 2: 401. 1856.

Laticiferous trees, shrubs, and subshrubs with mostly dichotomous to verticillate branches, the nodes with minute caducous interpetiolar stipules associated with persistent pectinate glands confined to the leaf axils or ascending the petioles. Leaves verticillate, 3-nate to 5-nate (the juvenile opposite), petiolate to sessile, simple, entire, penninerved, membranaceous to coriaceous, usually glabrous. Inflorescences interpetiolar, subterminal or lateral, usually paired at the nodes, cymose, bracteate, many- to relatively few-flowered. Flowers pedicellate to rarely sessile; calyx gamosepalous, the 5 small lobes cleft nearly to the receptacle, eglandular at the base within; corolla gamopetalous, tubular to salverform, usually white, greenish or yellowish, infrequently rose to violet, usually glabrous without, minutely villous within the throat, the limb equally 5-lobed, sinistrorsely contorted; stamens 5, antesepalous, epipetalous, the anthers free, included, with inconspicuous connectives, the thecae completely fertile, the pollen granular, mostly spherical and 3-culpate; pistil 2-carpellary, superior, the ovary apocarpous to more or less syncarpous and 2-locular, the placentation ventral and axile respectively, bearing 1-2 anatropous ovules, the style common, columnar, surmounted by the inconspicuously 2-apiculate, tympaniform stigma head. Disc hypogynous, annular or cupuliform, usually low. Fruit drupaceous, apocarpous to more or less syncarpous, frequently only 1 carpel developing, 1-seeded; seeds albuminous; embryo erect or curved, typically dicotyledonous.

Type species: Rauwolfia tetraphylla L. (Rendle, 1937).

It is a rather embarrassing position for a taxonomist of some experience to feel himself obliged to use a generic spelling clearly contrary to the International Code of Botanical Nomenclature, in strict compliance with which Linnaeus's original spelling *Rauvolfia* should be maintained. The spelling *Rauwolfia*, however, already has become so familiar to pharmaceutical practice and research that it seems futile, if not an affectation, to attempt a change, particularly in a publication designed for nonbotanical readers. The general facts of the variant orthographies may be summarized as follows.

The genus was so named in honor of a sixteenth-century traveler and botanist of Germany who, upon his return from travels to the Near East, published in 1582 a book of observations (Rauwolf[f], 1582, 1583) under the name of Leonard Rauwolff; in the following year the book was reprinted with the author cited as Leonhart Rauwolf, an inconsistency in spelling wholly consistent with individuality of practice of the times. Over a hundred years later Plumier (1703), the pioneer botanist of the Caribbean, dedicated to the early German traveler a genus of plants which he inscribed as Rauvolfia; a subsequent revision of Plumier's work, edited by Burmann (1760), however, changed the spelling of the genus to Rauwolfia. In two places in the latter text the name is abbreviated to Rawolfia.

Modern nomenclatural history of the genus begins with the first edition of Linnaeus's *Species Plantarum* (Linnaeus, 1753), in which Plumier's genus is included with his original spelling *Rauvolfia* faithfully copied. In this case Linnaeus was consistent (as was not always so, particularly with interchangeable *u*'s and *v*'s) in both texts and indices of all editions of both *Species Plantarum* and the accompanying *Genera Plantarum* as long as he himself was editor. It obviously was his intention to be so. Thus the spelling *Rauvolfia* clearly is governed by the provisions of Article 82 of the International Code of Botanical Nomenclature (1952) which conserves original spellings except typographical errors.

When the *Species* and the *Genera* came under different editorship, however, the orthography of our genus became altered. The seventh edition of the *Genera* under Reichard (Linnaeus, 1778) printed *Rauwolfia* in the index and *Ravwolfia* in the text; *Rauwolfia* was employed consistently in the eighth edition of the *Genera* under the editing of Schreber (Linnaeus, 1789), and also

in the two subsequent editions by Haenke and by Sprengel. Edition four of the *Species Plantarum*, edited by Willdenow (Linnaeus, 1798), used the "corrected" spelling *Rauwolfia*, and that form has prevailed, rightly or wrongly (evidently the latter), until very recent years. The current spelling *Rauwolfia* will be a habit difficult to break for those most concerned with the genus; I do not believe it worth trying except in a strictly taxonomic context.

THE SPECIES AND THEIR DISTRIBUTION

The *Index Kewensis* and its eleven supplements contain entries for more than 175 proposed species of *Rauwolfia*; these, of course, are exclusive of numerous infraspecific names which the *Index* does not list. No inclusive monograph of the genus exists. Consequently the exact number of natural species populations is quite conjectural. I believe that eventually there will be found to be about half that number or less.

In 1947 Pichon (1947a) published a tentative synopsis of the entire genus. In this promising study the author divides the genus into fourteen sections to which he assigns all species considered by him as probably valid. The species are not keyed individually, however, and are not described. A. Sathyanarayana Rao, late of the University of Mysore, has prepared a detailed monograph of the American species (Rao, 1956). Aside from these sources, information concerning the species of *Rauwolfia* may be obtained only through reference to such works as two inadequate treatments of the American species (Markgraf, 1924; Woodson, 1938) and various local floras.

From the works of Pichon and of Rao, however, a general notion may be obtained of the speciation of *Rauwolfia* and of its distribution. Fortunately, Pichon's sections of the genus are strongly correlated with geography, by means of which direct articulation with Rao's American treatment may be made. Unfortunately, the work of Pichon merely lists the species without regard to the involved synonymy, and as a matter of record the author actually had not examined specimens of nearly half of the species listed. Rao's, on the other hand, is the result of personal investigation of all species cited for America and consequently resolves for the American element the perplexing and ever present problem of synonymy. From these two studies an enumeration of the species