THE CINCHONA BARKS.

FLÜCKIGER.

THE CINCHONA BARKS:

Pharmacognostically Considered.

BY

FRIEDRICH A. FLÜCKIGER, PH.D.,

PROFESSOR IN THE UNIVERSITY OF STRASBURG, GERMANY, AND AUTHOR OF PHARMACEUTICAL CHEMISTRY.

TRANSLATED FROM THE ORIGINAL TEXT, WITH SOME ADDITIONAL NOTES.

BY

FREDERICK B. POWER, PH.D.,

PROFESSOR OF PHARMACY AND MATERIA MEDICA IN THE UNIVERSITY OF WISCONSIN.

WITH EIGHT LITHOGRAPHIC PLATES AND ONE WOOD-CUT.

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AUTHOR'S PREFACE.

In accordance with the progress of human development, the most important vegetable remedies are, or were, to a large degree, of Oriental or South European origin. America contributed at first but few products; and that which has now acquired such extraordinary significance in the National economy—tobacco—is without importance from a medicinal point of view, although Nicotiana was first introduced into Europe for the sake of its medicinal virtues. A century later there appeared a remedy from the American vegetable kingdom in the form of Cinchona bark, the value of which has received ever increasing recognition, even under the severest criticism of the present day. With reference to the sums of money which it sets in motion, the world's market may designate this bark as the most important medicinal remedy, although its value at the present time depends much more upon the fact of its affording the crude material for manufacturing industries. Since the discovery of quinine, and the immediate subsequent preparation of the same on a manufacturing scale, the pharmacognostical importance of Cinchona barks has correspondingly changed; the greater certitude in the quantitative estimation of the alkaloids also has the effect of forcing a knowledge of the external characters of the barks, as such, in the background. The revolution is slowly effected, and until within a short period the chapter of Cinchona barks still flourished in pharmaceutical literature, with all of its original and extreme luxuriance.

The advances in the cultivation of the Cinchonas now render necessary a different comprehension of the subject of "Chinchonology" (Chinology or Quinology), as, with scarcely justifiable emphasis, this section of pharmacognosy has been named.

Unfortunately, there is still altogether too much wanting to produce satisfactory and complete symmetry. Even from a systematical consideration, the botanical knowledge of the respective

Besides the above noted and a few minor additions, I have been kindly favored by the author with numerous notes, comprising the results of more recent observations or research, which are distributed throughout the work.

With these brief statements, the translator ventures to express the hope that the work of his honored friend and master may also be received in America, as in Europe, with the favor it so richly merits, and, while aiding in the dissemination of general knowledge, may likewise incite to the further substantial development of true pharmacognostical science.

MADISON, WIS., March, 1884.

SYNOPSIS OF CONTENTS.

THE

CINCHONA BARKS;

THEIR

HISTORY, BOTANICAL AND CHEMICAL CHARACTERS.

SECTION I.

BOTANICAL ORIGIN.

By the expressions *Cinchona barks* or *Peruvian barks*, Latin *cortices cinchonæ* or *cortices chinæ*, German *chinarinden*, French *écorces de quinquina*, Spanish *quina*, are designated such barks as contain alkaloids of a particular group, which may directly be denoted as the cinchona bases. These anti-febrile alkaloids have, as yet, been met with only in the barks of the cinchoneæ.

In the very numerous family of the Rubiaceæ the *Cinchoneæ* belong to the series of those having dry, many-seeded, capsular fruits, and scale-like, deciduous stipules; and within this circle they form one of those groups which are characterized by an expanded, branched, not contracted or capitate inflorescence. Both valves of the capsule contain a large number of small seeds, winged all around by a broad membrane, which is very irregularly toothed or lacerated at the edge (Plate III); the embryo is embedded in richly developed endosperm.

The division of the Eucinchoneæ presents a valvate, not reflexed or imbricated corolla (Plate II), and angular funiculi in the middle of the partition of the capsule. The genus *Cinchona* is distinguished finally by a tolerably long, cylindrical, or only very slightly contracted or expanded corolla tube. The five flatly expanded lobes of the corolla, which are small in dimensions, are of delicate texture, fringed at the margin (Plate II), and of a whitish, purple, bright red or somewhat violet color. The period of flowering of the Cinchonas continues, at least in India, through the greater part of the year, so that fruits and flowers are usually present at the same time. The styles of the latter sometimes project beyond the corolla tube (Plate II, c), and are sometimes enclosed (Plate II, b); a third form of the flower with almost sessile stigmas and longer stamens may also be observed. While the

fertilization of other heterostylous plants is usually effected by insects, this appears not to be applicable to the Cinchonas, but is accomplished rather through the agency of the wind.

The flowers are arranged in the form of abundant terminal panicles or cymes (Plate VI). The valves of the ovate or somewhat lengthened, but usually not particularly slender capsules, dehisce from the base in consequence of the splitting of the partition; but the two halves of the capsule remain connected at the apex by the five-toothed, permanent calyx, without, however, thus preventing the detachment of the funiculi (Plate I, III, IV).

The most closely related members of the Eucinchoneæ differ in the following respects from the genus Cinchona:[1]—

The species of *Cascarilla*, including *Buena* and *Cosmibuena*, have larger, firm, often even leathery corolla lobes, which are not fringed, but beset with coarse, club-shaped hairs. The capsules dehisce first from the apex (Plate V, left).[2]

The genus *Remijia* (Plate VI), otherwise differing but slightly from Cinchona, is distinguished by the long-stalked, interrupted racemes, cymes or panicles, situated in the axils of the leaves. The edge of the calyx is furthermore extended, often cup-shaped, the capsules cylindrically compressed, ovate or nearly spherical, and, as a rule, dehiscing first from the apex. The Remijia species have on the contrary, in common with the Cinchonas, the slightly attractive, red or white flowers, and even the pleasant odor of the latter. The Remijia does not represent large trees; the leaves of the smaller forms are occasionally arranged in whorls of three.

In the *Pimentelia* the inflorescence forms compact panicles projecting from the axils of the leaves.[3] *Ladenbergia* and *Macrocnemum* are separated in the most striking manner from Cinchona by their entire appearance.[4]

To what extent the barks of these plants show corresponding distinctions in regard to their anatomical structure, has been but slightly investigated. The *Condaminea*, mentioned on page

[1] Bentham et Hooker. *Genera Plantarum* II (1873–1876), 33. Baillon. *Histoire des Plantes*, VII (1880), 479.

[2] The following drawings of Karsten's in the *Floræ Columbiæ specim. select*, give a good representation of Cascarilla: C. barbacoënsis, tab. xxiii; C. Henleana, tab. xxvii; C. heterocarpa, tab. vi; C. macrocarpa, tab. xxi.

[3] Weddell, in *Hist. nat. des Quinquinas*, tab. 27, B., gives a figure of the Pimentelia glomerata.

[4] Compare, for example, Karsten's figure of Joosia (Ladenbergia) umbellifera, in *Flor. Columb. specim. sel.*, Tab. V, and Lasionema (Macrocnemum) cinchonoïdes, in Weddell's Plate 27 B.

49, approaches the Cinchoneæ to some extent in this respect, from which, however, it must be excluded for morphological reasons.

Cascarilla, the Remijias, Pimentelia, the Ladenbergias, and the Macrocnemum species, in opposition to the Cinchonas, are much more widely distributed through the tropical and a portion of the sub-tropical countries of South America, and by no means confined to the mountains. Among the Spanish and Portuguese population they are all comprehended under the name of *Cascarillos bobos*,[1] spurious or false cinchonas. The barks of many of the trees belonging to this class are considered in their native country to possess medicinal properties, and occasionally found their way to Europe, particularly before the discovery of quinine. After this period, however, it was ascertained that the so-called *spurious cinchona barks*, which had already been regarded in Europe as dubitable, contained either no alkaloid at all, or at least no anti-febrile alkaloid, and a general inclination to the view was adopted that only such barks contain cinchona alkaloids which possess the structure described on page 35. This conception was corrected in the year 1871 by an acquaintance with the Cinchona cuprea, which occupies an intermediate position, in that it belongs anatomically to the false, but chemically to the good cinchona barks, which contain alkaloid. It is probable that in the course of time other useful barks of this class will be brought to light from the above-mentioned genera of Cascarilla, Remijia and Pimentelia. The bark collectors, who are familiar with the appearance of the true Cinchonas, will therefore presumably in future restrict themselves less from a closer acquaintance with other Cinchonas, since the Cinchona cuprea has proved itself valuable.

The Cinchonas or fever-bark trees, *Cascarillos finos*, are evergreen, with mostly leathery, shining leaves, which are traversed by a strong mid-rib and finely veined by delicate lateral nerves. The thick leaf-stalk, which is often of a fine purple color, attains at the most one-third the length of the leaf, but usually remains shorter. In outline the leaves are ovate, obovate, or nearly circular, in some species lanceolate, seldom somewhat cordate (as in C. cordifolia

[1] *Bobo* signifies in Spanish, stupid or foolish. In a pamphlet printed at Lisbon in 1799, *Quinographia portugueza ou collecçâo de varias memorias sobre 22 especies de Quinas, etc.* (64 pages and 17 plates, or, in another edition, 192 pages and 14 plates), the minorite José mariano de la concepcion velloso, from the province of Rio de Janeiro, has described 22 Cinchonas, which all belong to the "spurious" class. It will be interesting to determine whether the bark of some of these does not indeed contain the cinchona alkaloids. How very improbable this is, is shown by the cinchona rosa from Tucuman, mentioned on page 50, Note 6, and also possibly the Tolima bark (page 52.)

Mutis,[1] and also possibly in part in C. hirsuta, C. Mutisii, and C. pubescens); they are smooth, or at the most slightly revolute, always entire, and besides often very variable on the same tree, (as, *e. g.*, in C. heterophylla). With regard to size, the leaves also vary considerably. Occasionally the young leaves are of a purple or purplish-violet color (in Spanish *morado*) on the under surface; and the fully developed leaves of several species assume quite regularly, directly before falling, this often very rich, dark color, which is strongly marked, *e. g.* in C. purpurescens, *Wedd.*

The Cinchonas present themselves as handsome, even though not precisely extraordinarily remarkable, shrubs or trees of the tropical primeval forest, of about the appearance of the Syringa.

The genus Cinchona is one so uniform, and whose members agree so closely, that a satisfactory definition of the latter is not readily accomplished. The individual species are connected with each other by intermediate forms, and form a continuous series, the terminal members of which are moreover scarcely more sharply separated from the above-mentioned allied genera than from plants of their own series. In the systematic botany of the Cinchonas the limit of the species is therefore often dependent upon very insignificant characters, for the justification of which doubt prevails in many cases. According to the diversity of view in the conception of the species, the number of species of cinchona accepted by botanists has consequently varied. In the year 1830, for example, the *Prodromus* of De Candolle accepted 18 species. Howard's handsome work, "Nueva Quinologia," contains 38 species, which are represented also for the most part by figures; but which on the one hand must be considerably increased, and, on the other, modified by the combination of evident sub-species. Without consideration of the fact that some botanists have connected plants with the genus Cinchona, which, according to the above outlined diagnosis of the genus (page 10), are positively distinct therefrom, the number of good species of Cinchona which has been gradually described has increased to about 50. A complete review of the same is given in Weddell's "Notes sur les Quinquinas," where indeed 33 species[2] are still represented, while 18 others are mentioned only as sub-species, with varieties and sub-varieties. According to Weddell's representation there is, however, also in those species no

[1] Figures in *Histoire naturelle des Quinquinas*, 17, by Weddell; *Flor. Columb.* I, tab. VIII, by Karsten; and in *Medicinal Plants* by Bentley and Trimen, London, 1880, 143.

[2] Enumerated in *Pharmacographia* by Flückiger and Hanbury, 1879, p. 355, with the exception of Cinchona Chomeliana and C. barbacöensis, which must be separated from Cinchona.

strict separation observable, but rather gives thereby to his views the particular expression that he refers all the Cinchonas to 5 stems (souches, stirpes). To these fundamental forms, from which all others radiate, Weddell assigns the name of the Cinchona which, for the respective stem, is the most striking or the best known, namely: 1. Stirps of *Cinchona officinalis*, 2. Stirps *Cinchonæ rugosæ*. 3. Stirps *Cinchonæ micranthæ*. 4. Stirps *Cinchonæ Calisayæ*. 5. Stirps *Cinchonæ ovatæ*. The last forms accepted by Weddell approach already very closely to Cascarillos bobos, or to the spurious cinchonas, namely, on account of the slender capsules, which dehisce from the apex.

Kuntze[1] desires to have all the cinchona trees referred to four species, and declares the numerous species represented by other botanists, with the exception of Howard's Cinchona Pahudiana, as hybrids of the four species, which have been described by him in sharply discriminating diagnoses and in light outlines.

From Kuntze's disquisition the following review is obtained:—

A. Cinchonas with coarse, not very large leaves; the capsules so contracted longitudinally in the centre that both halves of the fruit appear plainly evident. Each of the latter is provided with from 4 to 6 ribs, but both are held together by the widely expanded funnel-shaped calyx of the fruit.

(1) Cinchona Weddelliana is provided with leaf-pits, *scrobiculi*, and is distinguished by the only slightly lengthened, nearly spherical capsule, which is crowned by a very small fruit calyx.

(2) Cinchona Pahudiana, in distinction from the above, is pubescent, the corolla tube is pentagonal, and the fruit calyx almost as wide as the fruit itself.

B. Cinchonas with less coarse or thin, often very large leaves. The capsule is somewhat dilated, almost cylindrically beaked, scarcely contracted longitudinally, without ribs, and terminating without contraction in the small unexpanded calyx.

(3) Cinchona Howardiana is remarkable for the not pure green color and the significant size of the leaves, which, even in the inflorescence, are still quite prominent, and are always devoid of pits; and also for the remarkable width of the pale wing of the seeds.

(4) Cinchona Pavoniana deviates therefrom in possessing, at least on the flowing branches, leaves of a beautiful green color, which are provided with leaf-pits; but, on the contrary, only yellowish-white, not bright flowers.

[1] Title under section 18. See Kuntze's remarks in the *Pharmaceut. Zeitung*, December 2d, 1882, p. 730, and in the London *Journal of Botany*, January, 1883.

The distinctions between A and B are very definite and based upon good observations. As a progressive step may be prominently noted the consideration of the ribs, which are represented by the fruits of the division A; other good points of observation are afforded by the edges of the corolla in C. Pahudiana, as also the widely expanded form of the fruit-calyx in A. The credit is due to Kuntze for having discovered these characteristics, which, as it appears, on the living plant are very sharply defined. The flowers and capsules suffer changes by drying which lead to deception, and half-ripe fruits of the division B may, in an herbarium, for example, present ribs which, during life at least, do not pertain to the ripe fruit.

Between 1 and 2, as may be seen, there is no deficiency of very positive distinctions; the species 3 and 4, to judge from the descriptions and figures of Kuntze, are less widely separated.

These 4 chief species of Kuntze correspond but slightly to the 5 fundamental forms (stirpes) of Weddell. The former has observed living Cinchonas on the Indian plantations, Weddell, the species growing wild in Bolivia and Peru; both botanists have moreover compared dried specimens of forms which were not seen by them in nature. It must remain the task of a third systematic botanist to determine anew which method of comprehension best corresponds to the totality of the forms. Kuntze arranges the stems of Weddell in the following order:—

(1) The forms of Weddell combined under *C. officinalis* he declares as hybrids of C. Weddelliana with C. Pavoniana and C. Howardiana.

(2) In the *rugosæ* he recognizes C. Pahudiana and related hybrids.

(3) Weddell's *C. micranthæ* Kuntze declares as C. Pavoniana and derivatives belonging thereto.

(4) The *Calisayæ* as C. Weddelliana and hybrids.

(5) The *C. ovatæ* of Weddell are, according to Kuntze, to be referred to C. Howardiana.

It remains questionable whether anything is gained by exchanging the 51 species and sub-species of Weddell for the 44 species and hybrids of Kuntze.

If, however, it be admitted that the origin of the forms which were met with by Kuntze in British India and Java have been correctly recognized by him, it is still not evident why the wild-growing Cinchonas of South America should be embraced, collectively and individually, with the hybrids accepted by Kuntze.

The observations on the plantations have indeed proved that

hybridization between the Cinchonas, which, among themselves, are so closely related, may very easily be accomplished; but in nature it would be scarcely possible to distinguish whether such a mixed derivative is in question, or a form of a definite species which has originated through other influences.

The view of Baillon,[1] which is moreover not based upon thorough observation, that about 20 species of Cinchona are to be accepted, may possibly be the most correct.

SECTION II.

THE MOST IMPORTANT CINCHONAS.

As Cinchonas of most prominent importance, the following are at the present time to be designated :—

(1) CINCHONA SUCCIRUBRA Pavon, Plate I. This beautiful tree, which attains a height of 25 meters (82 feet), bears ovate or somewhat oblong, scarcely acuminate, thin leaves, which attain nearly half a meter (20 inches) in length, and often 35 centimeters (13.5 inches) in width; they are somewhat reflexed on the margin, and pubescent on the netted veins of the dull lower surface. The panicle of flowers is but slightly attractive. The distribution of C. succirubra in its native country is confined; it descends from the western declivity of the Chimborazo (S. Antonio de Huaranda) southward through Riobamba, Alausi and Cuenca, to northern Peru (province of Jaén in the department of Caxamarca) deep into the valleys.

In Ceylon it flourishes admirably between 2000 and 5000 feet above the level of the sea; in the south-Indian Nilagiris between 5000 and 7000 feet. C. succirubra is therefore well adapted for improvement by means of grafting or hybridization. Such a valuable form, occurring in Ceylon as the product of Cinchona officinalis and C. succirubra, is designated by Trimen[2] as Cinchona robusta.

After Weddell for a short time had presumed the C. succirubra to be the mother-plant of the red cinchona bark, which, however, as C. ovata (γ. erythroderma) he had not recognized with sufficient precision, Howard and Klotzsch furnished the proof of the independent character of the plant and its importance (page 46). The

[1] *Histoire des Plantes.* VII (1879), 342.

[2] *Pharm. Journ.* XII (1882), 352, 801, 1018. The cinchona designated there, *loc. cit.* VIII (1878), pp. 638, 805 and 825, as "pubescens" or also as "lanosa," is not to be confused with C. pubescens *vahl.* Of the former Bidie gives a tolerably good figure in the pamphlet mentioned under No. 3 in section 18.

colorless juice which exudes upon wounding the bark of this tree becomes, by exposure to the air, first milky, and then immediately red, in consequence of the active absorption of oxygen by the cincho-tannic acid.

Other figures of C. succirubra are contained in Howard's *Nueva Quinologia*, tab. 8; Bentley and Trimen's *Medicinal Plants*, 142; and Baillon *loc. cit.* 342 (uncolored).

(2) CINCHONA CALISAYA Weddell, Plates II and III. Occurs in part as a high tree, and in part shrub-like, as the variety β. Josephiana. It is distinguished by the ovate capsule, which attains scarcely the length of the flower. Weddell discovered this species in the year 1847, near Apolobamba in Bolivia, northeast of lake Titicaca; it extends beyond the Peruvian boundary, and is distributed through the Province of Carabaya (in the department of Puno), but not further northward. The Calisaya is also on Bolivian territory confined to the hot, wooded, elevated valleys (*Yungas* in the language of Aymara) of La Paz, to the seventeenth degree of southern latitude, between 1500 and 1800 meters (4875 and 5850 feet) above the level of the sea. In the grass regions, about 300 meters (975 feet) higher, it remains shrub-like, and only a few meters in height.

The native designation of Calisaya is deducted by Weddell from *colli*, signifying red in the Quichua language, and *saya*, imitated or shaped, with reference to the bark or perhaps to the leaf. Pöppig[1] explains it as *calla*, signifying a remedy, and *salla*, a rocky foundation. Markham interprets it as a small chief's family, Calisaya, which, about the year 1780, is said to have played a part in the Province of Carabaya.

Other figures of the plant are contained in: Weddell, tab. 3; Berg and Schmidt, *Offizin. Gewächse*, XIV; Bentley and Trimen, 141; Baillon, *loc. cit.* 338 (uncolored); and Howard, *East Indian Plantations*, VII to X.

As *C. boliviana*, Weddell has described and figured a variety of Calisaya which is more confined to Bolivia, and which is principally distinguished by the almost invariable purple color of the lower side of the leaves. It appears that the characters scarcely suffice to retain the plant as a variety, and certainly not to elevate it to a particular species.

The English merchant, Charles Ledger, who, since the year 1845, has resided at Puno, the chief city of the Peruvian department of Caravaya, westward from lake Titicaca, and, among other things, also engaged in the export of cinchona barks, was directed by the

[1] *Travels in Peru, Chili, and on the Amazon River*, II (1836), 218.

natives, in his repeated endeavors to discover the best bark, to the "Rojo,"[1] as the choicest sort. In the year 1851 Ledger met with the respective cinchona trees on the Mamoré, a tributary of the Madeira on the left, which has its origin in the northeast chain of the Bolivian cordilleras, in the Province of Caupolican. It was, however, first in the year 1865 that Ledger's servant, Manuel Incra Mamani, succeeded in collecting seeds of this cinchona in the same province, 120 leguas (about 780 kilometers or 480 miles) from Pelechuco, in about the fifteenth degree of southern latitude and 68 degrees west of Greenwich, and to deliver the same to his master. The servant, who was imprisoned in consequence by the Corregidor of Coroico, died shortly afterward, from the result of the mistreatment which he was forced to suffer. The seeds, which Ledger offered for sale in London without success, were bought by the Dutch Government for Java, and then furnished plants whose large percentage of alkaloid was in the year 1874 definitely determined.[2]

Howard has described this cinchona as a variety of the Calisaya, and figured the same very handsomely in the "Quinology of the East India Plantations," Part III, Plates IV, V and VI.[3] The external peculiarities of the *Cinchona Calisaya Var. Ledgeriana* (compare our plates II and III) are unimportant, and consist chiefly in the small size of the usually pure white, very fragrant flowers, which remind of those of *Cinchona micrantha* Ruiz et Pavon.[4] The tube of the corolla is not contracted as in many other cinchonas; the inflorescence is very compactly crowded, often nodding. The capsules of Calisaya Ledgeriana are furthermore not tomentose.

Calisaya Ledgeriana, according to Kuntze's comprehension, which is disputed by Howard, is a form of his Cinchona Pavoniani-Weddelliana. Experience must first demonstrate whether by cultivation this cinchona, which at the present time is indeed the most valuable of all, can be retained in such a degree of excellence.

[1] *Rojo* signifies in Spanish, red or reddish-yellow.

[2] Howard, *East Indian Plantations*, II, 46; *Pharm. Journ.* X (1880), 730.

[3] The diagnosis delineated by Weddell in Howard's "Quinology of the East Indian Plantations," fol. 85, is, in concurrence with the latter, as follows: "*Cinchona Calisaya, var. Ledgeriana* How. Foliis elliptico-oblongis vel fere oblongis obtusis obtusissimisve, haud raro ante apicem nonnihil angustis s. constrictis membranaceis, utriusque viridibus vel subtus pallide purpurascentibus nervis simul rubico, axillis vulgo sat distinctis scrobiculatis; panicula florifera ovata, corollis albis, antheris subexsertis (saltem in spec. obviis), panicula fructifera subcorymbosa, densa, capsulis ellipticis (9 ad 12 millimetr. longis), puberulis. From this, indeed, no striking characteristic can be observed. Bernelot Moens as well as Trimen consider Ledger's plant as a peculiar species: Cinchona Ledgeriana Moens; see *Journal of Botany*, London, 1881, p. 321, with figure. In Darjeeling the best "Calisayas" are stated by King, Report of May 28, 1881, to be nothing else than C. Ledgeriana.

[4] Figured in Howard's *Nueva Quinologia*, 5; Weddell, 14.

It would be extremely remarkable to see the permanency in richness of alkaloid attained here by cultivation, which otherwise does not occur.

(3) CINCHONA LANCIFOLIA Mutis, *Tuna* or *Tunita* of the Bogotians, Plate IV. More than 25 meters (80 feet) in height, leaves sharply lanceolate, leathery, mostly 12 centimeters (nearly 5 inches), on the luxuriant sprigs as much as 36 centimeters (about 14 inches) in length, although very variable.

This species, which has been known since 1776, is confined to Columbia (New Granada), and grows admirably in the south, from Bogota to Popayan, at an elevation of from 2500 to 3000 meters (8125 to 9750 feet) above the level of the sea, but also northwards in the mountains of the Magdalena near Chiquinquira, Velez, Socorro, and from Pamplona to Ocanna, and, according to Howard, also in Uchubamba, not far from Loxa.

It is very handsomely represented in Karsten's *Flor. Columb.*, tab. xi; Var. discolor. tab. xii.

(4) CINCHONA OFFICINALIS, the earliest named species.

In the year 1742 Linnæus established the genus Cinchona in accordance with the notes published by Ch. M. De La Condamine, and in 1753 named the tree discovered by the latter Cinchona officinalis, but in 1766 he gave a different diagnosis, which was based upon the communications received by him from Mutis in the year 1764. These related, however, according to Triana (fol. 10 of the work mentioned in section XVIII), to the C. cordifolia of the present day. It follows therefrom that the designation Cinchona officinalis, as established by Linnæus, is capable of a double interpretation. In his writings from 1742 to 1766 it related to the species which Hooker in 1863 again named Cinchona officinalis, but in 1766 Linnæus included in the diagnosis the present C. cordifolia (not C. pubescens as has been generally believed). Furthermore Triana, as well as his predecessors, did not find in the herbarium of Linnæus in London specimens of a "Cinchona officinalis," but on the contrary, only fragments of C. cordifolia, Cascarilla nitida and Exostemma coriaceum, which were designated as Cinchona peruviana. With propriety, therefore, C. officinalis passed into oblivion; and it was first in the year 1863 that Sir Joseph Hooker was induced to establish a new diagnosis of Cinchona officinalis, and to complete the same by a good figure.

Cinchona officinalis Hooker, Plate V, is therefore to be regarded as a new species, which is indigenous to Ecuador and Peru. It does not possess any very striking characteristics; the flowers are small, of a beautiful carmine-red, and downy, and the oblong cap-

sules sometimes more than 12 millimeters (half an inch) in length. Weddell combines under the name of C. officinalis the Cinchona Chahuarguera, C. Condaminea, C. Bonplandiana, C. crispa and C. Uritusinga of former systematic botanists.

A prominent distinction between C. officinalis and C. lancifolia is not plainly observable.

Those different forms of C. officinalis probably furnished chiefly in the seventeenth and eighteenth centuries and to the present time the so-called *Loxa Cinchona*. According to Wellcome, the region of Loxa, from the fourth to the fifth degree of southern latitude, on the boundary of Ecuador and Peru, is now exhausted.

Other figures of C. officinalis are to be found in Hooker's *Bot. Magazine*, 5364; Howard's *N. Quinol*, I, 19; Howard's *East India Pl.*, IX; Bentley and Trimen's *Medic. Plants*, 140; and in Baillon's *Hist. des Plantes*, 340-341 (uncolored, but elegant).

SECTION III.

REMIJIA.

Of the most closely connected allies of the Cinchonas mentioned on page 10 only two species of the genus Remijia have as yet attained actual significance. The shrubs belonging to this genus were recommended to the Brazilians first from the environs of Ouro Preto, the chief city of Minas geraes, by a surgeon Remijo, as *Quina de Serra* or mountain cinchona,[1] in that they are distributed as far as the rough, dry, mountainous regions of the Province Minas geraes. Velloso, the Brazilian botanist, who has already been mentioned on page 11, had described such *Quina de Remijio*, as it was also called, under the name of Macrocnemum.[2] Saint-Hilaire[3] placed these plants in the series of the genus Cinchona, which at that time was much more broadly comprehended than at present. De Candolle[4] was the first to separate the genus Remijia, which, according to Triana, at present embraces the following species:[5]

[1] C. F. Ph. Von Martius, "Die Fieber-Rinde, der Chinabaum, etc." in Buchner's *Repertorium für Pharm.* XII (1863), p. 358.

[2] In Vandelli, *Floræ lusitanæ et brasiliensis specimen. Conimbricæ*, 1788.

[3] *Plantes usuelles des Brésiliens.* 1824.

[4] *Bibliothèque universelle de Genève* II (1829), 185. *Prodromus*, IV, 357.

[5] Bentham et Hooker, *Genera Plantarum*, II (1873), 33, accept 13 species of Remijia, and enumerate therewith, among others, the Cinchona prismatostylis (Tab. VII) and C. macrophylla (Tab. XXXV), which have been handsomely figured by Karsten. The former corresponds to the character of the Remijia evidently on account of its bell-shaped calyx, the glandular disk, and the terminal panicles. In both of the latter respects, on the contrary, the cinchona (Remijia) macrophylla is again separated. According to Triana (*Nouvelles Etudes*, 72), this is nothing else than Remijia ferruginea *D. C., Prodr.* IV, 357.

(1) Remijia Hilarii *D. C.*, in the Province of Minas geraes. (2) R. paniculata *D. C.*, in Brazil. (3) R. cujabensis *Weddell* (Ladenbergia *Klotzsch*), Bahia. (4) R. Bergeniana *Wedd.* (Ladenbergia *Kl.*). (5) R. firmula *Wedd.* (Ladenbergia *Kl.*), in Brazil. (6) R. macrocnemia *Wedd.* (Ladenbergia *Kl.*), on the Amazon. (7) R. densiflora *Benth. et Hooker*, in British Guiana. (8) R. hispida *Triana*, on the Orinoco. (9) R. tenuiflora *Bentham*, between Barra and Barcelos on the Rio Negro, about 65° of western longitude. (10) Remijia Purdieana *Wedd.*, in the Columbian provinces of Antioquia and Santander, in the district of the Magdalena river and the Cauca. (11) Remijia Pedunculata *Triana*, in the mountainous declivities southward from Bogota and eastward to the Orinoco, between 1000 and 2000 meters (3250 and 6500 feet) above the sea, in the region of the Rio Mesa, Rio Negro, Guaviare, Papamene, Zarapote, and other rivers within the domain of the upper Orinoco and the Amazon.

Remijia Purdieana was discovered near Cauvas, in the province of Antioquia, by Purdie, the director of the garden at Trinidad (†1837), and was described by Weddell.[1] It is characterized by the long-stalked opposite panicles, which are located in the axils of the leaves, and whose ramifications bear a rust-colored felt; the corolla is of a firm consistence, tomentose on the exterior, and the corolla tube narrow.

Remijia Pedunculata, plate VI, has been met with, both by Karsten and Triana, as a small tree 3 meters (about 10 feet) in height on the eastern slope of the Cordillera of Bogota, on the road in the plains of the Orinoco, near the village of Susumuco,[2] at an elevation of 1000 meters (3250 feet). Karsten gives prominence to the silky lustre of the hairs which envelop the young shoots, and are also not wanting on the younger leaves. In the fully developed leaves, the leathery lamina, which is sharply lanceolate above and below, attains a length of 2 decimeters (8 inches), and is smooth, with the exception of isolated small bristles on the lower surface. The inflorescence is an axillary, long-stalked cyme, the border of the calyx bell-shaped, the ovary covered with a glandular ring, and the capsule dehisces through the partition from the apex to the base, more rarely from the base to the apex.

[1] *Annales des Sciences naturelles*, Bot. XI (1849), 272. The diagnosis is as follows: "foliis oblongis, basi attenuatis, abrupta acuminatis, planis, demum glabratis; panicula subcorymbosa, bracteis foliaceis integris, bi-tridentatis; floribus subcapitatis. Paniculæ axillares, oppositæ, longe pedunculatæ, subcorymbosae pedunculis ramulisque ferrugineo-tomentosis. Corolla membranacea, extrorsum puberula, tubo angusto 1 centim. longo. . . ." (The capsule was not at Weddell's command.)

[2] Between this village and Villavicencio (Triana).

Of the most closely related species, Cascarilla heterocarpa,[1] C. magnifolia,[2] and C. Riveroana,[3] the Remijia pedunculata is distinguished by the axillary inflorescence, by smaller capsules,[4] and the leather-like leaves. In plate XXVI of the *Floræ Columbiæ Specim. select.*, mentioned in section XVIII, Karsten completes the above description[5] of R. pedunculata (still designated by him as Cinchona) by a handsome figure of the same.

According to Triana[6] the two last named species are very positively distinguished from each other. The calyx teeth of Remijia Purdieana are much longer than the calyx tube, and nearly linear, the stipules sharply lanceolate, and the capsules more slender than in Remijia pedunculata. The short calyx teeth of the latter are roundish triangular, and the broad stipules obtusely ovate.

Both species of Remijia afford the barks described below as Cinchona cuprea, and must therefore, at least the Remijia pedunculata, occur abundantly in the wide domain from the Magdalena river to the eastern declivities of the Cordilleras, southeastward from Bogota.

SECTION IV.

HABITAT OF THE CINCHONAS.

The Cinchonas are confined to the Cordilleras, whereas the other Cinchoneæ inhabit a far more extended area under the most diverse climatic relations. In other districts of South America, which apparently fulfill the same physical conditions as the cinchona belt of the Cordilleras, no true cinchona trees have indeed as yet been met with.

[1] Karsten, tab. VI.

[2] Howard, *N. Quinol.*, tab. X; presumably not different from C. heterocarpa.

[3] Figured under the incorrect name of C. Ruizii in Weddell's *Hist. nat. des Quinquinas*, tab. XXIII.

[4] The pear-shaped capsules of Remijia pedunculata, dehiscing from the apex, for which I am indebted to Dr. Triana, are 8 millimeters (about three-tenths of an inch) in length, with a maximum diameter of 5 millimeters (one-fifth of an inch).

[5] *Flor. Columb. Specim. sel.* 54, where the diagnosis is embraced in the following words: "Cinchona foliis *coriaceis*, *lanceolatis* vel *ellipticis*, calvis, subtus in costa nervisque paullum pilosulis; stipulis magnis obovatis quam petioli longioribus; in *basi connatis*, extus pilosis, intus ad basin *area triquetra imo serie villorum tectis;* cymis *axillaribus* foliis longioribus, corymbiformibus, pedunculo communi longissimo, ramis minute bracteolatis; corollis *membranaceis*, extus sericeis, limbi laciniis supra barbatis; staminibus tubo corollæ medio insertis, inclusis; filamentis glabris, brevibus; *antherarum rimis* ciliatis; capsulis compressis, sublignosis, lanceolatis, 15 ad 18 millimetr. longis, ab apice ad basin, rarius a basi ad apicem, septicide dehiscentibus, pilis minutis adpressis; seminum alæ ciliato fimbriatæ, imperforatæ."

[6] *Pharm. Journ.* XII (1882), 862; also *Journ. de Pharm.* V, 567.

However much the latter are confined in a vertical direction, yet they accompany the chief South American mountain range through the greater portion of the northern half, for a distance of about 30 degrees of latitude.

The most northerly locality of the Cinchonas, which is approximately below the tenth degree of latitude, is designated by the occurrence of C. cordifolia in the district S.S.W. from Caracas, with which species C. tucujensis Karsten is also here associated.

Weddell, who penetrated the cinchona zone from the southeast, met at about the nineteenth degree of southern latitude, far in the interior of Bolivia, with the most southerly species, which he accordingly designated as C. australis. The country west of Chuquisaca (Sucre), the chief city of Bolivia, would form, according to Weddell, the southern boundary of the Cinchonas. It appears, however, that this must be still further extended, and about to the twenty-second degree of southern latitude, for Scherzer[1] relates of a clergyman in Tarija (on the Argentine boundary, in the south of Bolivia), who is said to have offered for sale 3000 hundred weight of excellent bark, *sucupira* of the Indians, which was procured from the forests between Tarija and Cochabamba, thus from the water-shed between the Marannon and the La Plata.

Between these extreme points in the south, and the mountains of Caracas, not far from the Caribbean sea in the north, the belt of the Cinchonas, following the crests of the mighty mountain chain, describes a crescent, opened toward the east, of about 500 geographical miles in length.

The conditions under which the Cinchonas live may be deducted already in part from the above intimations with regard to the occurrence of the most important species, and, in indited form, have been elaborately elucidated by Martius,[2] and still more accurately, on the spot itself, by those English travelers who have distinguished themselves by the removal of the cinchona trees to India and the Colonies.[3] Only the variable, sunny climate of the tropical mountain regions, which is interrupted by frequent showers, storms, thick fog and mist, with very changeable but not widely digressing ranges of temperature, is adapted to the Cinchonas. A transient depression of temperature to the freezing point, and not unfrequent showers of hail, may indeed be borne by strong plants; yet the mean temperature most favorable to them should be estimated at not less than from 12 to 20° C. (54 to 68° F.). According to the

[1] *Voyage of the Austrian frigate Novara*, III (1859), 366.

[2] Buchner's *Repertorium für Pharmacie*, XII (1863), 362, 373.

[3] Complete reports in the Blue Books cited under section 18.

opinion of the bark collectors, however, a proportionately cooler location, extending to the uppermost boundary of forest vegetation, favors the formation of alkaloid. A considerable exposure to direct sunlight appears to be injurious to young plants, but decidedly favorable to strongly developed trees, and particularly also to increase the brightness of color of the bark, which in commerce is so highly prized.

As the precise habitat of the Cascarilla fina, the best cinchona bark, Karsten[1] unhesitatingly designates the foggy region of the Andes chain, which is intercepted by deep valleys, with a mean temperature of 12 to 13° C. (53.6 to 55.4 F.), where, through nine months of the year, rain prevails, and an actual alternation of seasons occurs to so slight an extent that the Cinchonas continually bear flowers and fruits. The lower region, in which already a dry season may be distinguished, contains chiefly large-leaved cinchona trees of less medicinal power, together with the worthless "Cascarillos bobos."

From the dimensions already stated it is manifest that the Cinchonas belong to the medium and higher forms of the tropical primeval forest, but are, however, overtopped by the far more mighty representatives of the Artocarpeæ, Lecythideæ, Sapindaceæ, Terebinthaceæ, the palms, and many others.

The richness of the tropical flora excludes a uniform constituency of the forest, and accordingly the Cinchonas also live mostly dispersed, at the most, forming here and there smaller groups, which in the distance are discriminated more by a particular color than by a striking arrangement of the complete picture of the primitive forest. Such spots (*manchas*) in the variegated carpet of the crowns of foliage are espied by the disciplined eye of the bark collector (*cascarillero*) at the remotest distances,[2] even at a time when they are not decorated by the rich flower clusters.

Extended groups of C. corymbosa, which almost deserve the name of cinchona forests, were met with by Karsten[3] on the boundary of New Granada and Ecuador, on the western declivity of the volcanoes Cumbal and Chiles.

The Cinchonas may always be designated as a very remarkable member in the vegetative dress of their surroundings, so that the portion of the South American mountain regions inhabited by

[1] *Medicinische Chinarinden Neu-Granadas*, p. 12-13.

[2] Weddell, *Hist. nat.* fol. 9. 10; also Wellcome: "A visit to the native Cinchona forests of South America," *Proceedings of the American Pharm. Association* (1879), 814-830; reprinted in the *Pharm. Journ.* X (1879), 980, and abstracted in Just's *Botan. Jahresberichte*, 1880.

[3] *Medic. Chinarinden*, p. 20.

them, at an elevation of 700 to 2900 meters (2275 to 9425 feet), was prominently noted by Humboldt as the region of the tropical oaks and Cinchonas.

Weddell excluded the cinchoneæ which generally inhabit lower altitudes and do not contain alkaloid, and drew for the zone of the true cinchona trees the boundaries of elevation at 1600 and 2400 meters (5200 and 7800 feet). The lowest altitude at which the true Cinchonas occur in their native country is at an elevation of 1200 meters (3900 feet), and the uppermost line is to be accepted as 3270 meters (10,630 feet), or, in accordance with KARSTEN, as 3500 meters (11,375 feet). With the distance from the equator the average altitude of the Cinchona zone becomes considerably decreased, although the Cascarillos finos do not readily descend lower than 2000 meters (6500 feet). C. succirubra occurs exceptionally as low as 800 meters (2600 feet); but by its very large, not precisely leathery, leaves, as also by the slender fruits, likewise does not agree with most of the other species of valuable Cinchona.

SECTION V.

THE CULTURE OF THE CINCHONAS.

The earnest desire to subject the Cinchonas to the careful attention of forest husbandry, in more conveniently located districts, must have excited activity as soon as some scientific information had been obtained regarding these trees. Even Condamine, to whom we are indebted for the first description of a Cinchona, had sought to transport young cinchona plants to Europe, but lost them by the waves at the mouth of the Amazon river.[1] Mutis was probably the first who, in Mariquita (see section 17), occupied himself with the cultivation of the Cinchonas.[2] In earlier times the Jesuits in Bolivia had also already imposed upon the Cascarilleros the obligation to plant 5 seedlings in the form of a cross ⁘ for each cinchona tree that was felled.[3]

The idea of transferring the cinchona trees to the old world was ever newly revived,[4] and experiments relating thereto were also not completely wanting. Such an one, for example, emanated, in

[1] H. von Bergen, *Monogr. der China*, 117, after Condamine's *Relation d' un voyage*, etc.

[2] A von Humboldt. "Ueber die Chinawälder in Südamerica." *Der Gesellschaft Naturforschender Freunde zu Berlin Magazin für die neusten Entdeckungen in der Naturkunde*, I (1807), 57–68.

[3] Howard. *East Indian Plantations*, III, 49.

[4] Compare the English *Blue Book* of 1863, fol. I; Delondre et Soubeiran (Title under section 18); Oudemans *Handleiding tot de Pharmocognosie*, Amsterdam 1880, p. 146.

1849, from the Jesuits in Cuzco, in central Peru, who sent Cinchonas to their settlements in Algeria.[1] These endeavors in Algeria remained unsuccessful, but attracted the attention of the Dutch, so that finally, in 1851, Miquel's repeated impulsions received the approbation of the Colonial Minister Pahud, who now realized the excellent idea, and later, in 1855, being advanced to the position of Governor-General of the Dutch East Indies, actively assisted in its accomplishment. Pahud accordingly effected the despatch of the German botanist Hasskarl to South America, which took place in December, 1852, from Southampton; in 1853 he traveled from Lima, through the district of Cuzco, as far as Sandia, on the Bolivian boundary, and finally, after a repeated visit to Bolivia, the collections, contained in 21 Wardian cases, were, on the 21st of August, 1854, successfully brought on board of a frigate which the government had sent to Islay for this express purpose. Hasskarl brought the young plants in December, 1854, to Batavia, and cared for their settlement in Java;[2] the seeds collected by him were at the same time transferred to the University gardens in Holland. But the Dutch had also been otherwise active. In 1848 Weddell brought seeds of Cinchona Calisaya to Paris, which there developed well, in the commercial garden of Thibaut and Keteleer.[2] In 1852 the Dutch Government sent young Calisaya plants of this firm to Java, and likewise in 1854 the seeds of Cinchona lancifolia, obtained through Karsten from Columbia. The gardens in Holland furthermore soon furnished from Hasskarl's seeds strong plants for Java; the first results there from all these endeavors corresponded, however, but little to the expectations.

On the part of the English, a report from Royle in June, 1852, addressed to the East India Company, gave an impulse for the energetic pursuance of the planting of Cinchona trees. The learned botanist recommended for the settlements in India the Blue Hills (Nilagiris, Neilgherries) of the Malabar coast and the southern promontories of the Himalaya.[3]

After the but slightly satisfactory attempts of the Government, through the intervention of the English agents, to attain the purpose in view, Markham finally came forward, in April, 1859, with an offer to accept the matter, for which he was rendered capable by a thorough acquaintance with the land and people of the domains on

[1] *Journ. de Pharm.* XX (1851), 286; compare also Weddell, "Sur la culture des Quinquinas, communication faite au Congrés international de Botanique tenu à Paris en Août 1867."

[2] A most complete description is given by Oudemans, *loc. cit.* 146, and following; also by Gorkom (Title under section XVIII).

[3] *Blue Book* of 1863.

the borders of Bolivia and Peru, as also by a knowledge of the Spanish and Quichua languages, and also already with the most important Cinchona trees. Being well aware, from the nature of things, of the underlying difficulties, Markham earnestly insisted that nothing should be neglected which could ensure success. It was of great value that he effected the appointment of the distinguished botanist, Spruce, who was at that time traveling in Ecuador, for the obtainment of the C. succirubra, as also the services of Prichett, likewise resident in South America, for the region of Huánuco in central Peru, 10° S. latitude. A very competent gardener was afterward (1861) secured, in Cross, an original companion of Spruce, who collected still more of the seeds and young plants of the best species, and placed them with his own hands in India. Markham reserved for himself the border-lands of Peru and Bolivia, in order to obtain C. Calisaya, and for this purpose started from Islay in March 1860. Having arrived in the middle of April, by way of Arequipa and Puno, at Crucero, the chief city of Caravaya, he met, not far from Sandia, with the first thickets of C. Josephiana, then also C. boliviana, C. Calisaya and others. Markham thus secured for himself 456 young plants, which were successfully shipped at Islay, toward the end of June. The ripening of the seeds of the Calisaya, which takes place in the month of August, could not be waited for, in consequence of the hostile disposition of the people of the country with regard to the enterprise; and in general very great difficulties were required to be overcome, of which the leader of the entire expedition has projected a picture which is as instructive as it is interesting.[1]

Further settlements of the precious plants were begun in 1861, at Hakgalla, in the central mountain districts of Ceylon, at an elevation of 5000 feet; in 1862 at Dardschiling (Darjeeling), in the southern part of Sikkim, in the southeastern Himalaya; in 1865, in New Zealand and upon the Australian continent, for example, in 1866, in part through private citizens, at Brisbane (Queensland, on the eastern coast of Australia). As the primary central point of the entire undertaking, however, Utacamand (Ootacamund), between 11 and 12° N. lat., is prominent, together with its branches, extending as far as the southern point of the Indian peninsula, in part at elevations of about 8000 feet above the sea. Before the arrival of Markham with the first young Cinchonas from Bolivia, the most careful examinations, from a meteorological and geological standpoint, had led to the selection of this locality. In addition thereto, occurred the fortunate circumstance that the plantations

[1] Markham's Reports in the *Blue Books*, and his monograph "Peruvian Bark."

here were placed in charge of the experienced gardener, William Graham Mac Ivor (died June 8, 1876), who applied to his task the greatest zeal, and also discovered methods for the rapid multiplication of the Cinchonas.

The plantations of Java, which in the beginning were not in a perfectly satisfactory condition, flourished to such an extent after the year 1856, under Junghuhn's management, that in December, 1862, there were already, at 10 different places 1,360,000 seedlings and young trees, of which, however, the most valuable species were in the minority. The experiences in Java led to active and in part very bitter discussions, which were terminated on the one hand by the death of Junghuhn (April 20, 1864), and on the other by the highly meritorious analytical investigations of J. E. De Vrij. In the year 1857 the latter chemist[1] was despatched by the Government of Holland to Java, in order to follow the entire cinchona question in its chemical considerations. In 1864, K. W. Van Gorkom was appointed superintendent of the cinchona plantations in Java, which at the present time are successfully directed, also in their chemical considerations, by J. C. Bernelot Moens.

In September, 1866, John Broughton was appointed by the English Government for the chemical superintendence and direction of the plantations at Ootacamund, and rendered very important service until December, 1874, when, in consequence of disagreement with the authorities, he resigned his position. The vacancy thus incurred has recently been filled by the appointment of M. A. Lawson, professor of botany at Oxford, as superintendent of the government cinchona plantations.[2]

The success of the great exertions, which in the main are delineated in the above outlines, finds a living expression in the following facts. On March 16, 1859 De Vrij laid before the resident Governor-General Pahud of Java the first crystals of sulphate of quinine, which he had prepared in his laboratory at Bandong, from bark grown by himself upon the island.[3] Howard, of London, likewise reported to Markham, in May, 1863, that he had obtained from 500 grains (about 30 grams) of the bark of Cinchona succirubra grown in India the sulphates of quinine, cinchonidine and cinchonine.[4] Furthermore, in August, 1867, the importation of Indian barks into London commenced; and of the first supplies, the bark

[1] Dr. De Vrij was appointed May 6, 1857, and resigned, on account of his health, in September 1863.

[2] London *Journal of Botany*. Jan. 1883, p. 32.

[3] Written and verbal communications of my friend Dr. De Vrij.

[4] *Blue Book*, 1866, p. 14.

of Cinchona succirubra from the Denison plantation near Ootacamund, I have preserved a specimen.[1]

In October, 1870, the first 750 kilograms (about 1650 pounds) of cinchona bark from Java arrived at the Amsterdam market; a second portion followed in March, 1872, and since that time increasing consignments of Javanese barks arrive regularly, from year to year, in Holland. In the second quarter of the year 1882 the Government plantations in Java consisted principally of Calisaya Ledgeriana, comprising in the aggregate nearly 1½ million plants.[2]

Among the very numerous points of the old and new world in which plantations of Cinchonas are now in progress of rich development, the following, with relation to the world's market, come now particularly into consideration: the plantations of the English Government near Hakgalle in Ceylon, in the Nilagiri Hills near Ootacamund, as also in the promontories of the Himalaya in British Sikkim near Darjeeling,[3] Mungpoo, Sitting and Rungbee. In the second place, the numerous cinchona forests of the Dutch Administration at Java. Independent of these State enterprises, an incentive has thus been given to the establishment of a large number of private plantations, for the condition and productions of which, however, no similar reports are at hand as are regularly deposited by the English and Dutch Administrations in their most instructive publications, and communicated in a liberal manner.

Jamaica, in 1880, also began to bring cinchona barks into the market.

Finally, in the native country of the Cinchonas itself, plantations are in progress; for example, on the Mapiri, in the Bolivian province of Larecaya, and also in the Yungas (see p. 16).

There is no deficiency of guides for the establishment and management of the cinchona plantations; some of the publications relating thereto from India are mentioned in Section XVIII, under the names of Bidie, Gorkom, King, Mac Ivor, and Owen, and in addition to these, such information has also been recently received from Jamaica.[4]

In India the Cinchonas have at an early date become injured by beetles (*Melolontha*) and caterpillars,[5] and recently a critical enemy

[1] *Pharmacographia*, 2 edition, p. 351, Note 2.

[2] The recent volcanic eruptions in Java (August, 1883) are reported to have produced great destruction among the cinchona plantations. (F. B. P).

[3] At an elevation of 2113 meters (6930 feet) above the sea, and since 1882 in railroad communication with Calcutta.

[4] *Pharm. Journ.* XII (1882), 748.

[5] *Blue Book*, 1866, p. 170.

of the cinchona plantations has revealed itself there, in the form of the small hemiptera, *Helopeltis Antonii* Sigm., or the so-called "tea-bug" of the English planters. The female of this insect, which also produces damage in the tea plantations, deposits its eggs, from 8 to 14 in number, in the tops of the cinchona branches and in the leaf-stalks, and causes thereby the disease of the trees known by the name of *kinarœst*, in that the young wingless insects nourish themselves at the expense of the young leaves.[1]

The barks containing alkaloid which, under the name of Cinchona cuprea, have recently attained such prominent significance, belong to the genus *Remijia*,[2] which grows under climatic conditions quite different from most Cinchonas. If the forest husbandry will now also assume control of the valuable Remijias, the cultivation of the febrifuge trees may be extended in wide domains of territory from which they have hitherto been excluded. In distinction to the Cinchonas, the Remijias are not confined to the mountain regions, but are capable of enduring dryness and higher temperatures, which, for example, prevail in the climate of the Llanos, in the domain of the Orinoco and the Amazon. It is easily possible that among these or other related trees still more may be discovered with barks containing quinine, which would repay cultivation.

SECTION VI.

COLLECTION OF THE BARKS.

The hardships of bark collecting in the slightly accessible primeval forests of South America are undertaken only by the half-civilized Indians and people of mixed race, in the pay of larger or smaller speculators or companies located in the towns. All who are engaged in the business, especially the collectors themselves, are called *Cascarilleros practicos*, or also *Cascadores*, from the Spanish word *Cascara*, bark. A major-domo, placed at the head of the collectors, directs and superintends the proceedings of the several bands in the forest itself, where, in huts of light construction, the provisions and afterwards the produce are deposited. Weddell, as also Karsten and Wellcome,[3] have given in a striking manner, as eye-witnesses, a picture of these operations.

The cascarillero, by means of a sabre-like knife, *Machete* (*machiar*

[1] Bernelot Moens, also K. W. Van Gorkom, in the writings mentioned in Just's *Botan. Jahresbericht*, 1879, pp. 314 and 319.

[2] Compare pages 16 and 54.

[3] In the writings previously mentioned, p. 23, and in Section XVIII. I am recently also indebted to Dr. Chas. Robbins, of New York, for such reports.

= to become bare), first deprives the exterior of the stem of the often luxuriant climbing and parasitic plants, and begins immediately also in most cases to scrape off the sapless layer of bark, after the same has been rendered soft by beating. In order to detach the valuable inner bark, longitudinal and transverse incisions are made with chisels, as far as can be reached on the stem. The tree is then felled, and, together with the branches, divided, and the stripping finally completed. In most cases, especially after previous beating with a mallet, the bark, notwithstanding its slight coherence in many species, separates easily from the wood.

Any considerable quantities of the barks must, at least in many districts, be quickly dried by a fire, which is usually built upon the floor of lightly constructed huts. By means of the stems of palm leaves, bamboo stalks, or other suitable parts of plants, large hurdles are constructed over the fire, upon which the barks are from time to time rearranged. The walls of the huts are also constructed of the same lattice-work, and likewise receive large pieces of the bark. In New Granada the drying of the bark is effected almost exclusively over a fire.

The process of drying, however, is not permitted to be conducted too hastily, even when it is required to immediately protect the barks from mould, as but slightly excessive heat destroys the alkaloids. With this imperfect arrangement, which is the only one possible under the described conditions, the article apparently only then assumes a salable appearance when the drying has been continued for three or four weeks.

In Southern Peru and Bolivia, however, according to Weddell's representation, even the thickest Calisaya barks are dried only by exposure to the sun, without requiring the aid of a fire.

That the bark of the branches is not deprived of the corky layer, requires no explanation. With regard to the barks of the stem, it depends in part upon the commercial use, whether they are furnished unaltered or peeled; but in part the anatomical conditions also probably have some influence. Where an abundant and deeply penetrating formation of bork occurs, as in C. Calisaya, the removal of the worthless cork is very easily and completely effected; in other species, on the contrary, such a natural separation of the corky layer does not take place to the same degree, and the altogether too circumstantial process of peeling is omitted.

From the report of the personal observations of Wellcome in Ecuador, a Cascarillero, after having espied from some higher point a tract of forest that indicates sufficient value, procures, by the payment of a small fee, a title from the Government. The

forest district which is thereby allotted to him, for whatever of profit it may yield, he names after some holy person—for example, Bosque (forest) of San Miguel. In consideration of titles of this kind for several such Bosques the master Cascarillero may receive from a commercial house advancements of money, in order to engage the services of occasionally from 300 to 400 laborers, *Peons*, which, in October or November, he guides into the forest. The men begin their activities by the erection of bamboo huts, and are then divided into sections, at the head of which a *Jefe*, Captain, is usually placed. For the search of the trees, felling them, cleaning and peeling the trunks, digging up the roots, and drying the bark, a proper division of work is assigned to the several sections. The peons transport the bundles of bark, weighing about 150 pounds, to large depositories, whereby many succumb to their immoderate exertions and often insufficient nourishment; others are carried away by malarial fever, so that not unfrequently one-fourth of the men suffer destruction. The final sorting and packing in serons[1] (heavy sacking is at the present time meeting with increased use), as also the admixture of inferior barks, takes place mostly in the magazines, "bodegas," of the seaports. It is said that only a few bark dealers are ultimately successful in accumulating wealth.

The thinner bark of the less developed portions of the stem rolls up, upon drying, into quills (*canutos*, *canutillos*), while the pieces stripped from the stronger stems are very often made to receive their flat form (*plancha*, *tabla*) by placing them for a short time one upon another and loading with weights,[2] then exposing to the sun, and repeating this treatment several times.

After drying, the barks are either sorted, chiefly according to their size, or all are packed together, without distinction, in sacks of manilla-hemp (the bast of the agave-like Fourcroya), or in linen or cotton material, in the form of bales, containing about 100 pounds. In some places, as at Popayan, the bark is even stamped, in order to reduce it to the smallest possible bulk. The large dealers of the seaport towns then enclose the bark in raw bullock hide (*zurron*), which, having been previously moistened, compresses the contents most firmly upon drying. In many places, particularly in the neighborhood of Loxa, wooden chests are also employed for the transportation of the bark.

In the domain of the Cordilleras the transportation of the barks

[1] *Zurron* signifies in Spanish a pouch or bag made from cowhide, or also the hide itself.

[2] The handsome frontispiece in Weddell's *Hist. nat. des Quinquinas* represents this occupation in the forest of San Juan del Ora, province of Carabaya.

over the pathless mountains is attended with great difficulties, which frequently forbid the employment of direct routes; in most cases also serving to prevent the exportation of bad barks, which would not repay collection. Karsten, as also Wellcome, thus explains the reasons which occasionally compel the bark dealers of the upper Cauca valley, in the districts of Popayan, Pitayo, Almaguer, and Pasto, not to take the route to the nearest seaport of Buenaventura, and not directly to descend the Cauca, with its numerous cataracts, but rather the elevated passes of Quindiu (nearly 4000 meters = 1300 feet above the level of the sea) and Huanacas in the valley of the Magdalena river. But also upon the latter a relading must take place near Honda, before the barks can continue their voyage to Baranquilla, at the mouth of the river, and reach the near seaports of Sabanilla and Carthagena. The export from these Columbian places has recently become very significant.

It is only exceptionally that cinchona barks, for instance those from Huanuco on the Ucayali and other tributaries of the Amazon, have been conveyed to the Atlantic coast, to Para.[1]

In the year 1819 Calisaya bark was conveyed by land along the Paraguay and its tributaries, or down the stream, to Buenos Ayres.[2]

For Ecuador the ports of Esmeraldas and Guayaquil are of importance, while the export from the more central ports of Peru is less considerable. The southern ports, Islay, Iquique, and especially Arica, receive the barks from Carabaya and the high valleys (*Yungas*) of Bolivia.

The regular settlements of Cinchonas, which are now in a state of progressive development in many lands, especially in India, admit of much more rational management, and a planless felling and stripping of the trees is there out of the question.

With regard to the collection of the barks, two methods are competitive in their claims for superiority—the treatment with moss, or "mossing," and the felling system, or "coppicing." The former consists in separating from the stem vertical strips of bark, only about 4 centimeters (1½ inches) in width, and afterwards enveloping the stem in moss. The bark renews itself very speedily on the denuded places, becomes stronger than before, and even richer in alkaloid. In India, clay is now beginning to be employed instead

[1] Compare Howard's description of such a direct importation of cinchona bark into England, Seeman's *Journal of Botany*, VI (1868), p. 323; also my essay in Vorwerk's *Neues Jahrbuch für Pharmacie*, XXXI (1869), p. 15.

[2] H. von Bergen, *Monogr. der China*, p. 287.

of moss, and in Java the Alang-Alang grass (Imperata Konigii) is applied to this purpose. When the covering of the peeled stems is effected by either of these methods, there is to be distinguished: 1, the unaltered bark, which is first removed; 2, the strips of bark which are allowed to remain, and afterward subjected to treatment with moss—the so-called "mossed bark;" and 3, the "renewed bark." If it is indeed possible through a long series of years to separate the bark of the Cinchona trees in strips, as above described, and even to effect an increase of alkaloid, at least in the renewed bark, this method would possess much that is alluring. It remains, however, questionable whether the trees are thereby capable of regaining strength. The mossing process was discovered and very strongly recommended by Mac Ivor, the meritorious director of the Cinchona plantations at Ootacamund.[1]

Greater security for the maintenance of the trees is perhaps presented in the procedure suggested by Bernelot Moens, in Java, in the year 1880, according to which the bark is not removed to the extent of its full development, but only "scraped." Much more care also is taken to leave a sufficient coating of bark on the entire circumference of the stem.

The idea readily suggested itself, in the case of the Cinchonas, to employ that form of utilization which admits of application with woody plants, as far as this relates to the most abundant obtainment of a constituent or a definite amount of such, entirely without consideration of the further development of the plant itself. This is the method of stripping, which is in use in Europe, especially in the case of the oaks,[2] also in Sicily, with regard to the manna-ash,[3] and in Ceylon with cinnamon.[4] The Cinchonas are subjected to a similar treatment the more willingly, since the root barks, which fall off by the occasional clearing of the cinchona plantations, have proved themselves very valuable. According to this method of procedure, or coppicing, which is now customary, especially in Java and Ceylon, the stem, at the age of about 8 years, is felled 15 centimeters (6 inches) above the ground, and stripped, whereupon side-shoots develop, which, after another 8 years, furnish bark rich in alkaloid. By this stripping process the roots may also be obtained in proportionate amount; an operation especially related to this is distinguished as "uprooting." The root barks, which were formerly

[1] *Blue Book;* more completely described in the illustrated publications of Mac Ivor, mentioned in Section XVIII. With relation to Java, compare the annual reports of Bernelot Moens, also Oudemans, *Pharmakognosie*, p. 163.

[2] Compare Flückiger, *Pharmakognosie*, p. 473.

[3] Ibid, p. 21.

[4] Ibid, p. 565.

neglected, have uniformly revealed themselves to be remarkably rich in alkaloid.

It can only be conclusively decided by longer experience whether coppicing or mossing is permanently entitled to preference. Further information on this subject is contained, among others, in the English Blue Book on the Indian Cinchona plantations of 1877.

Broughton has shown that the amount of alkaloids appears to diminish somewhat upon drying. He finds it most advisable to dry the bark without delay, but at the lowest possible temperature.[1] In Java the employment of artificial heat has been considered. The moisture contained in fresh Indian barks may easily amount to over 70 per cent.; the bark which is used for exportation, compared with the powdered bark dried at 120°C. (248°F.), retains on an average, according to the determinations of Bernelot Moens, 13.5 per cent. of water.

SECTION VII.

APPEARANCE AND ANATOMICAL STRUCTURE OF THE CINCHONA BARKS.

With regard to the development of the bark, the Cinchonas show some distinctions. Many are distinguished from an early age by an abundant exfoliation of the outer surface. This is especially the case in C. Calisaya, with its bork scales attaining as much as 1 centimeter (⅜-inch) in thickness, and also in C. micrantha, while in others a voluntary ejection of the cork or bork takes place to a less extent, and in these it is not so readily removed, even by beating.

Other species succumb to the peculiar bork formation only at an advanced age, and only on the lower portions of the stem and on the root.

In the barks of younger stems or branches, a grayish, sometimes light, sometimes blackish color predominates; the outer surface of thicker stems, on the contrary, displays a more characteristic brown, yellow or reddish color, which is particularly prominent after the removal of the corky layers. Although differences in the tint of the bark may be produced by the locality, and especially by the manner of drying, yet Karsten nevertheless gives prominence to the permanency of their inner fundamental color on the stem, and on the branches and twigs of the same species.

In the fresh condition, however, these colors are very pale, and it is only after peeling, and especially upon drying, that they fully

[1] *Blue Book*, 1870, p. 239.

acquire their peculiar tint. The light grayish-yellow or yellowish-red bark of C. micrantha begins to assume a blood-red color immediately after its separation; the white bark of C. australis changes to a rust color, as soon as the external layer which has been beaten soft is removed. In C. Calisaya the fresh bark is externally of a light greenish-yellow color; in C. pubescens, of a dirty white or green.

These colors are indeed subject to some final variation, according to whether the drying of the bark is effected more or less quickly by a fire, or by allowing it to remain exposed to the air and sun, whereby, frequently through rain and dew, the barks again become moist. The remarkable change of color of the fresh bark always remains a noteworthy characteristic of the true Cinchonas.

In the color of the bark a serviceable means is presented for the characterization of the barks individually, or at least for forming the varieties into groups. The older investigators of this subject, as also the bark collectors themselves, have, therefore, not improperly referred to these distinctions as: Quina *amarilla* (yellow), *blanca* (white), *colorada* or *roja* (red), *naranjada* (orange), *negrilla* (brown), etc. The plates of the works mentioned under numbers 2, 6 and 37 in section XVIII give a very good representation of the colors of most Cinchona barks.

The Cinchona barks in their structure do not display any more remarkable peculiarities than many other barks; and that which imparts to them particular features may be comprised in the following statements.

The formation of cork (*periderm*) takes place in the primary bark in the zone of tissue located nearest to the inner surface of the epidermis. The cork cells of the barks of the true Cinchonas which occur in commerce are thin-walled, and show the usual tabular form and radial arrangement (Plate VII, A. C. e). The younger barks are usually still covered with cork, but in older ones this is not always the case. Even the older barks of Cinchona succirubra, for example, still occur in commerce with the cork adhering, while the equally strong stem-barks of C. Calisaya yield to the formation of bork and do not present the uninjured cork, which, in consequence of the formation of corky bands in the inner tissue, is thrown off together with the outer bark. The cascarilleros appropriately designate the shallow trough-shaped bork cavities which are thus formed as *Conchas*, on account of their resemblance to flat mussels. Where they are longitudinally extended and also possibly coalesce, they present an appearance as though having been formed by impressions of the fingers. These conchas are present to the most striking extent in the stem-barks of C. Calisaya.

The originally collenchymatous outer bark, situated beneath the cork, is built up of cells of considerable size, which are more or less extended in a tangential direction (Plate VII, A. C. o). The uniformity of this tissue (without considering the interior cork formation) is thereby interrupted, in that its often coarse, porous cells become, either singly or in large numbers, sclerotic. Such stone-cells (Plate VII, C. k) are, in the dried bark, either empty or filled with a crystalline powder of calcium oxalate, or contain a reddish-brown, solid, occasionally granular substance, which, without sufficient foundation, has been designated as resin. The stone-cells (sclerotic cells) vary in their form without regularity, so that it must be regarded as superfluous to distinguish them as cubical cells, as spherical, or upon the transverse section tangentially extended stone-cells. A discrimination according to their contents, as crystal-cells and resin-cells, is likewise of no greater importance. In the direction of the axis, the stone-cells of the Cinchona barks exhibit no considerable extension. They appear in the bark, either scattered singly or united in groups, but never representing actually closed circles of large dimensions, as in so many other barks: *e. g.*, that of Guaiacum officinale,[1] Quassia amara,[2] and Strychnos Nux vomica.[3] In many Cinchona barks, the stone-cells are uniformly wanting: *e. g.*, in the Calisaya and the red bark; in others they occur sparingly, and in many they are found abundantly, and also in the bast, as, for instance, in Cinchona latifolia.

On the boundary of the bast, but always only on the inner side of the parenchyma of the outer bark, isolated ducts of very considerable size are frequently observable, which, upon a transverse section (Plate VII, A. p), present a circular or tangentially extended outline, and in circumference, but not in the thickness of the walls, surpass the neighboring parenchyma cells. In the larger diameter they frequently attain over 200 micromillimeters (C. succirubra), in C. boliviana, even more than 500, but are also often diminished to less than from 40 to 50 micromillimeters.

On a longitudinal section, these *milk tubes* or *lacticiferous ducts* do not appear extended in length; their obtuse ends are closed, and they are usually isolated, or from two to three arranged in a row before the last bast-wedges, without, however, having any definite relation to the latter. On a transverse section, the lacticiferous ducts therefore form a but slightly regular, sometimes repeated,

[1] Compare Flückiger, *Pharmakognosie*, second edition, 1882, p. 453.

[2] *Ibid*, p. 459.

[3] The same work, first edition, 1867, p. 427. Möller, *Anatomie der Baumrinden*, 1882, pp. 162, 419.

and often approximately closed circle. In cases where they remain small, they may be easily overlooked when the sections are softened with potassa instead of the less destructive alkali ammonia.

According to Karsten the lacticiferous ducts occur in the youngest branches of all or nearly all Cinchonas and their nearest allies, but in individual species they remain very narrow and soon become quite insignificant; a change which is also in part thereby effected, that in their interior a new formation of parenchymatous cells takes place.[1]

Although these lacticiferous ducts can scarcely be considered as a peculiarity of individual Cinchonas, they are, indeed, wanting in some commercial barks, and are retained in a state of preservation in others, in so far as the entire outer bark has not become completely destroyed by the formation of bork.

The lacticiferous ducts may, moreover, according to Weddell,[2] be best traced in the medulla of living branches, especially near the nodes of young axes.

More important points of discrimination are afforded by the bast of the Cinchona barks (Plate VII, B. C. v), which, in consequence of the removal of the bork, represents exclusively some varieties of commercial bark (Plate VII, B). It is intersected by medullary rays (Plate VII, v), which radiate from the wood in 3, or at most 4 parallel rows (large medullary rays, chief medullary rays). The cells of the medullary rays are almost invariably larger than those of the bast parenchyma, and increase toward the exterior in width as also in the number of the individual rows. In the tissue of the medullary rays, especially in the outermost layers, isolated cells often become thickened to stone-cells (Plate VII, C); still more frequently many contain a crystalline powder, and also without becoming lignified.

The bast contains as its most prominent constituent spindle-shaped fibres (Plate VII, s c), which are extended in the direction of the axis, and whose walls become thickened at a very early period. When the cells become thickened to a less extent, and do not terminate in a point, they are distinguished as *staff-cells*, or staff-shaped stone-cells.

In the younger barks of most species the bast-fibres are found sparingly scattered, but with increased age they multiply considerably in number, lose their cavity almost completely, and press back the surrounding bast-parenchyma quite strongly. On a transverse

[1] Compare Vogl, *Chinarinden des Wiener Grosshandels*, p. 12; De Bary, *Anatomie*, p. 558.

[2] *Hist. nat. des Quinquinas*, Tab. I. Fig. 26.

section the fibres appear in distinct and very neatly arranged layers, which are traversed by fine canal-like pores;[1] in outline they are spherical or angular, frequently somewhat extended in a radial direction, and the cavity mostly confined to a dark fissure or a point. Since the bast-fibres terminate at the ends in a point, which, however, is not actually sharp, the dimensions of a transverse section at different heights is subject to variation. The larger diameter of the strongest fibres attains to about 200 micromillimeters, but is usually only one-half or one-third of this size.

On a longitudinal section the bast-fibres of the Cinchonas are seen to be proportionately shorter than the corresponding cells of many other barks, although their length is within the limits of ordinary measurements, and easily amounts to from 2 to 3 millimeters. They present themselves, in so far as they do not stand completely isolated, with their pointed ends wedged above and between each other, and never transversely connected, but rather always either simply curved, or at the most, sabre-shaped; they are, however, mostly spindle-shaped. In consequence also of their shining yellow or yellowish-red color they may readily be observed in the other tissue.

The transverse sections of strong bast-fibres are very handsome objects in polarized light, in that they display a black cross, and besides, with only slightly thicker sections, vivid colors in the quadrants.

The finer spiral rudiments of their structure can only be observed when the bast-fibres have first been boiled in hydrochloric acid, and subsequently placed in an ammoniacal solution of oxide of copper.[2]

The bast-fibres of the true Cinchonas are characterized by their considerable thickness and lignification, as also by their simple form and pointed ends. Although in the beginning making their appearance in an isolated form in the youngest axes, they afterward arrange themselves in various ways, so that the individual species of Cinchona are also to a certain extent characterized by their peculiarities in this respect.

The bast of the Cinchona barks, *i. e.*, that of the true Cinchonas, does not appear distinctly reticulated. Even where lignified bast-fibres occur in large numbers, they do not form groups of large dimensions, nor branched, long and compact bundles;[3] and espe-

[1] De Bary, *Vergleichende Anatomie der Vegetationsorgane*, 1877, p. 139.

[2] Compare Hofmeister, *Verhandlungen der sächs. Gesellschaft der Wissenschaften zu Leipzig*, X (1858), p. 32; Flückiger, *Grundlagen der pharm. Waarenkunde*, 1873, p. 36, Fig. 11, 12.

[3] Compare De Bary, *Anatomie*, p. 544.

cially at the point of the bast-wedges, on the boundary of the outer bark, they occur only very much scattered (Plate VII, A).

The *sieve-tubes* in the Cinchona barks of commerce are usually very much collapsed, and therefore can only be isolated with considerable difficulty.[1]

While in the young barks the soft bast predominates, this proportion becomes gradually changed in favor of the greater or less development of the sclerotic fibres. The bark of the same species must, therefore, in accordance with its age, present a very dissimilar appearance, and consequently afford but a deceptive criterion for the purpose of diagnosis, even when within certain boundaries the specific peculiarity is maintained.

The barks of the individual Cinchonas present some prominent distinctions, especially with regard to the more or less considerable number of stone-cells, as in some barks such sclerotic cells are entirely wanting. The barks furthermore differ from each other with relation to the arrangement of the bast-fibres. The considerable thickness, the simple, spindle-shaped, compact form, and the not very large number of these bast-fibres, impart to the Cinchona barks a definite character, which is not possessed by the barks of the most closely related species that have as yet been examined. That, however, intermediate representatives are not wanting, is illustrated by the "Cinchona rosa," as described on page 49. Among themselves the Cinchona barks display, indeed, great uniformity; and in many figures, such as are given by Berg[2], for example, no decided characteristics are rendered prominent, when they are compared with each other.

SECTION VIII.

CONTENTS OF THE TISSUE. LOCATION OF THE ALKALOIDS.

Most of the cells of the true, as also of the false Cinchona barks which are not lignified, or not completely so, with the exception of those of the cork cambium and the crystal ducts, are so abundantly filled with coloring matter, which also penetrates the walls, that their other constituents, as also their structure, is only plainly perceptible when the coloring matters are to some extent removed, an operation which is best effected by ammoniacal alcohol. Even the cork frequently contains Cinchona-red, and in the innermost,

[1] A description of them is given by Möller, *Baumrinden*, pp. 132, 138.

[2] In the work mentioned under Section XVIII. With regard to the peculiarities of structure of the Cinchona barks in comparison with other Rubiaceæ, see Möller, *Baumrinden*, pp. 132, 138.

still living layers, small starch granules. The same are also found in the parenchyma of the bark itself, although not very abundantly. The outermost layers of young barks contain, moreover, also chlorophyll granules.

The already mentioned, extremely small and slightly developed crystals of calcium oxalate, are deposited here and there in the parenchyma of the true Cinchonas, so that all the cells containing crystals by no means possess lignified or even only thickened walls; the stone-cells enclosing oxalate are altogether of even less frequent occurrence. Larger, often well developed crystals, are contained in the barks of those trees which are related to the Cinchonas, as in the Cinchona cuprea, and, as it appears, also usually in greater abundance. In others, vertical rows of cells containing crystals are found in the bast, while in the Cinchona barks these only occur isolated.

In addition to these universally distributed substances, the peculiar constituents of the Cinchona barks do not admit of direct observation by means of the microscope.

Oudemans (*Aanteekeningen*, etc., of the Pharmacopœia Neerlandica, 1854 to 1856, p. 221) had already observed the occurrence of crystals in Cinchona Calisaya and Cinchona rubra. Howard, in 1862, in the Nueva Quinologia of Pavon (Plate II of the microscopic figures), and in 1870, in the first part of the "East Indian Plantations," figured crystals which exhibit themselves in the parenchyma of Cinchona barks when thin sections of the same are warmed for a moment with caustic alkali, and the latter removed as speedily as possible. Howard declares these crystals to be the chinovates of the cinchona bases, and considers that they are already deposited in a crystalline form[1] in the respective barks, as, for instance, in Ledger's Calisaya bark, where these crystals are said to be already visible without further treatment of the section. By the examination of a bark kindly furnished me by Howard, I was unable to convince myself that such crystals were originally present therein; they presumably consist of the alkaloids which have been liberated by the action of the alkali.

Through my investigation,[2] as also that of Müller,[3] it is known that the alkaloids are located in the parenchyma of the Cinchona barks and not in the bast-fibres. Carles[4] has likewise confirmed these observations.

[1] Kerner finds the chinovates of the cinchona bases to be uncrystallizable.

[2] Wiggers-Husemann's *Jahresbericht der Pharmakognosie, etc.*, 1866, p. 82; Howard, *Quinology of the East Indian Plantations*, 1869, p. 33.

[3] In Pringsheim's *Jahrbücher für wissenschaftliche Botanik*, 1866, p. 238.

[4] *Journal de Pharmacie*, 16, (1873), p. 22.

SECTION IX.

VARIETIES OF CINCHONA BARK.

If the anatomical relations of the true Cinchona barks are summarized, it is manifest that they owe their peculiar character as well to the totality of the former as also particularly to the nature and position of their lignified bast-fibres. This appears very prominent in distinction to the other Cinchoneæ which are so closely connected in the system, the structure of which, however, has as yet only been described in a few instances.[1] In many of the latter, the lacticiferous ducts are much more perfectly developed, and the sclerenchyma forms likewise, even in the outer bark, large and often vertically extended bundles; the bast, however, deviates most from the above-described type of the Cinchonas, as has already been shown on page 38. The bast-fibres of many of the false Cinchonas are thin, by far not completely lignified, on a transverse section exhibiting a significant cavity, and usually roundish. On a longitudinal section they display considerable length, and as strong, often net-like, transversely connected fibres, impart to the entire tissue a coherence which the short, simple fibres of the Cinchonas are not able to give.

In many of the false barks, the parenchyma of the bast also performs a more significant part, whether it be that its regularly arranged tangential zones, alternating with fibre-bundles, cause a reticulated appearance, or whether the inner half of the bast is built up, to a largely predominating extent, of parenchyma. The tissue of these barks also receives hereby far greater firmness and tenacity than the Cinchona barks.

These distinctions are then also perfectly adequate to discriminate between the barks of the Cinchonas and those of the other allied genera.

As in many barks, the transverse fracture of the Cinchona barks is also subject to variation in the inner and the outer portions. The latter, consisting of the cork and the parenchyma of the outer bark, break uniformly and short, in so far as dead portions of the bast are not, through the formation of bork, drawn into the external coating or periderma.

In opposition to this uniform, quite smooth, so-called corky fracture, the inner layer of stronger barks does not present an even fractured surface, but there project therefrom isolated, compact bundles of fibres, which are extended in the direction of the axis.

[1] Compare Berg, *Chinarinden der pharmakognost. Sammlung in Berlin*, 1865, p. 39; Flückiger, *Jahresbericht der Pharmacie*, 1871, p. 95; Vogl, *Falsche Chinarinden*, 1876,

Weddell was the first to emphasize that the appearance of the fracture of the Cinchona barks is subject to variation, according to the size and the arrangement of the bast-fibres. To these short, not interlaced fibres, the Cinchona barks owe particularly the great brittleness.

The root-bark of the true Cinchonas appears to possess in general the structure of the bark of the stem or branches, and particularly to be much inclined to the formation of bork.

Among the chief varieties which hitherto came from South America, and which received the preference for pharmaceutical applications, the following are to be particularly mentioned:—

I. CINCHONA CALISAYA.

After Jussieu had already traversed the region of the Cinchona Calisaya, Rubin de Celis,[1] in 1776, and Thaddäus Hänke,[2] in 1791, called attention to the value of their bark, so that the latter, since about the year 1789, acquired ever increasing significance, although the tree itself was first made known by Weddell (see page 16). In commerce there is found the entire bark of the branches, in the form of quills, as also the flat stem bark deprived of the bork, and indeed:—

(a) The former under the names of *Cortex Cinchonæ* (*Chinæ*) *regius, convolutus, Cinchona* (*China*) *calisaya cum epidermide, Calisaya tecta s. tubulata; Quill Calisaya;* Ger., *Gerollte* or *bedeckte Königschina;* Fr., *Quinquina Calisaya roulé.* It forms quills 3 to 4 centimeters (1¼ to 1½ inches) in thickness, which are mostly rolled inward at both edges (double quills), of a dark grayish-brown color, or whitish, and having coarse, irregular, longitudinal channels and furrows, which, however, in general are to a certain extent uniformly arranged, and intersected by deep transverse fissures, which frequently extend over the entire periphery. Reticulations with elevated edges and a usually somewhat more finely furrowed surface are hereby formed, which readily become detached, and still permit the recognition of their outlines on the outer surface of the cinnamon-brown inner bark. The inner surface is of a brownish-yellow color, and accurately striped in a vertical direction by the bright bast-fibres; the fracture is purely fibrous, but externally darker and shorter.

[1] A Spanish marine officer.

[2] Hänke was born in the year 1761 at Kreibitz in Bohemia, and in 1790 went to South America with the Spanish expedition under Malaspina. He located, in 1796, at Cochabamba in Bolivia, repeatedly visited the districts where Cinchona bark is collected, and died in 1817, upon his estate at Buxacaxey, in the province of Cochabamba. Petermann, *Geogr. Mittheilungen*, VII (1867), 264.

The outer bark exhibits practically no stone-cells or only a few isolated ones, but contains a single or double circle of lacticiferous ducts, which, however, soon disappear.

The bark of the Indian Calisaya Ledgeriana (see page 17), in consequence of its much higher percentage of alkaloid, now furnishes a complete substitute for the American bark. Many of the varieties formerly known as *Loxa Bark*, and derived from different Cinchonas, are especially distinguished from the bark of the twigs of Calisaya by the less reticulated outer surface.

(b) The bast of the stem as *Cinchona (China) regia plana, Cinchona (China) regia sine epidermide; Flat Calisaya;* Ger., *Flache, platte, unbedeckte Königschina;* Fr., *Calisaya plat.*

Flat pieces, of a foot or several feet in length, often nearly 2 decimeters (8 inches) in width and from 5 to 15 millimeters (¼ to ⅝ inch) in thickness, and of that particularly handsome pure color which is designated as a type of the yellow varieties of Cinchona; indeed, the approach to a reddish-yellow tint is often scarcely perceptible. The outer surface, by the action of the air, is frequently darker, at least in spots, and in consequence of the conchas (see page 35) more or less, often to the highest degree, irregular; the inner surface does not always exhibit parallel stripes, as in the barks of the branches, but is often wavy. In this case, the bast bundles of the different layers occasionally separate from the fractured surface in a diverging direction. This variety of bark is highly characterized by its soft tissue; even with the finger-nail one can, without effort, separate the pointed fibres, which readily penetrate the skin.

On the edges of the conchas there are, as a rule, only a few easily detached bork-scales. The bast, of which, without consideration of the interior cork bands, the bark alone consists, displays sometimes more and sometimes less plainly radial, occasionally also almost tangential, rows of fibres. Here and there from 2 to 4 of these rows come in direct contact, but otherwise they always occur separated by the abundant parenchyma.

The flat Calisaya bark from Bolivia, which until within a few years maintained a high character, has latterly occurred in commerce with a very much diminished percentage of alkaloid. It was occasionally confused with the bark of a south Peruvian species,[1] *Cinchona scrobiculata* Humboldt et Bonpland. Their uncovered bast-plates resemble to a high degree those of the flat Calisaya, but are distinguished, however, especially upon being moist-

[1] Figure in Humb. et Bonp., *Plantes équinoct,* t. 47; also Weddell's *Hist. nat. des Quinquinas,* Plate VII.

ened, by their plainly reddish and often fiery color, and by greater compactness and fibrous fracture. The parenchyma of the outer bark is rich in stone-cells, and contains also in younger pieces lacticiferous ducts. No other cinchona shows a so plainly radially arranged bast. The fibres of the latter form upon a transverse section, long, mostly one-lined radial rows, in which often upon large spaces only here and there a small parenchyma-cell occurs. The bast-fibres are present in such large numbers that in the inner layers they predominate to a considerable extent.

This bark, which appears to contain regularly only a small percentage of alkaloid, finds its way into commerce under many designations in the pure state, as also mixed with Calisaya. Thus in Cusco it is commonly termed *Cascarilla colorada* or *Cascarilla de Santa Ana;* in Europe it is known as light Calisaya, reddish Calisaya, Carabaya, or red Cusco bark, Cinchona (China) peruviana, and Calisaya fibrosa.

In the illustrations of the bark, the coloring by Delondre and Bouchardat, Plate 3, although not absolutely accurate, is much more correctly reproduced than in Weddell's Plate XXVIII, where the color agrees altogether too closely with that of Calisaya.

II. BARKS OF CINCHONA LANCIFOLIA.

The cork is at first grayish, afterwards whitish or yellowish, glistening, soft and readily exfoliating. The bast is yellow or reddish-yellow; the bark parenchyma is still in part retained, even in the quite strong, flat trunk barks of as much as 1 centimeter (⅜ inch) in thickness, as they usually occur in commerce; for it is only at a late period that the true formation of bork takes place. The outer bark is distinguished by a number of tangentially extended stone-cells, which often form a nearly connected layer (Plate VII, C). The moderately thick bast-fibres are in single or double radial rows, connected at intervals, and having an occasional tendency to a tangential grouping in the interior. In the bast there are numerous staff-cells, and not unfrequently there are also the same stone-cells as in the outer bark; the latter form of cells occurs quite as frequently in the medullary rays.

The bark breaks with a fine splintery, sometimes short and sometimes long fracture, and is found in different varieties, which, by subordinate characteristics, deviate somewhat in appearance and structure. It is nevertheless possible that they may be referred to several Cinchonas.

In this place belong the varieties of cinchona designated as *flava fibrosa*, then the *Calisaya of Santa Fe de Bogotá, Quina anaranjada*

of Mutis, the *Caqueta bark* of the English, more correctly Caqueza (after the place of this name not far from Bogotá), the *Carthagène ligneux* of the French, etc. Many barks of *Cinchona rubiginosa* of former times were derived likewise from C. lancifolia.

Karsten, as also the Consul Rampon,[1] whose opinions are based upon personal observations at the place itself, give prominence to the fact that C. lancifolia, which is botanically so variable, furnishes also, indeed, barks of very different appearance. The best varieties are called in New Granada, *columbian;* the less valuable bear the name of *Carthagena Barks.*

III. RED CINCHONA BARKS, FROM CINCHONA SUCCIRUBRA.

The bark of small, one and-a-half year old trees, which in its moist condition is only 1 millimeter ($\frac{1}{24}$ inch) in thickness, *e. g.*, from Hakgalle in Ceylon, consists only to the extent of $\frac{1}{3}$ of the bast layer, wherein entirely isolated or groups of from 2 to 3 bast fibres occur, which are mostly already lignified. The boundary of the outer bark is designated by wide lacticiferous ducts, which, occurring usually to the number of two before a bast ray, represent a very interrupted circle.

Even by a thickness of about 5 millimeters ($\frac{1}{5}$ inch) the relation of the two layers of bark becomes so altered that the bast begins to predominate, and deposits its beautiful dark red fibres in very large numbers. The latter are in interrupted radial rows, separated by narrow strips of quite small-celled parenchyma, and toward the interior by a tangential arrangement, affording also at the same time, in places, an almost reticulated appearance.

A multiplication of the lacticiferous ducts is not prominent, but they become gradually enlarged, and by the development of the bark remain for a long time intact, as it is only at a late period that the formation of bork occurs. Pieces of bark over 12 millimeters ($\frac{1}{2}$ inch) in thickness (in their dry condition), still display lacticiferous ducts.

The ejection of the peridermis takes place with much greater difficulty than with C. Calisaya, so that even strong trunk barks of the red cinchona still bear a firmly adhering, more grayish-black than red external coating, even by a well defined development of the interior cork.

According to Von Bergen, the Red Cinchona was already distributed in North Germany at the beginning of the eighteenth century, and Condamine makes mention of it, in the year 1737, as the best Cinchona; it may, *e. g.*, with reference to the description

[1] In Planchon (Title under section xviii) 95.

of Mutis (p. 48), remain undecided whether it was always really the bark of C. succirubra.[1] The formerly quite extensive exports of fine trunk barks of this Cinchona from Guayaquil have long since considerably decreased. On the other hand, branch barks of the same from Ceylon and from the peninsula of India, as also from the other Cinchona plantations, are brought in ever increasing amounts into commerce.

The American Red Cinchona, in accordance with Howard's proposition, was referred in 1857 by Klotzsch and H. Schacht[2] to C. succirubra.

For the classification of the Cinchona barks the color was adopted as a principal characteristic, until the study of their anatomical structure appeared in the foreground. It may be accepted that the fundamental color of the barks of one species does not remain the same at all periods of life; C. succirubra, *e. g.*, shows that the special color first appears with absolute definiteness at an advanced age. Younger barks of most species are, as a rule, covered with a grayish-white or sometimes brownish or nearly blackish cork, which only in the extremes of its color or in the form of its outer surface is able to afford points of discrimination. Still more indefinite and predominatingly brownish is the color of the inner tissue, so that mixtures of the most different quill barks taken from the twigs or younger trunks bear the general name of *Cortex Cinchonæ* (*Chinæ*) *fuscus*. As of equal signification the usually less appropriate designation of *Cortex Cinchonæ* (*Chinæ*) *griseus seu pallidus* is applied, with reference to the external coating, as also the appellations, quite common with the French, of *Quinquinas gris ou brun*, and the English expressions, *Pale Cinchona Bark, Gray Bark.*

As the most important of the brown varieties, is to be mentioned the Cinchona from the district of Huánuco, in central Peru, which is exported by way of Lima, and named after these two cities. It usually consists of quills, which, after being moistened, are from 1 to 2 centimeters ($\frac{3}{8}$ to $\frac{3}{4}$ inch) in circumference and from 2 to 5 millimeters ($\frac{1}{10}$ to $\frac{1}{5}$ inch) in diameter. Its grayish-brown, and in general quite bright external surface, is somewhat furrowed longitudinally, provided with transverse fissures, which are mostly not very deep and do not extend over the entire periphery, and often still covered with whitish cork. The inner surface is of a bright

[1] Compare also therewith, Murray, *Apparatus medicaminum*, VI (1792), 44.

[2] "On the Origin of the Red Cinchona Bark of Commerce," *Abhandlungen der Akademie der Wissensch, zu Berlin*, 1858, pp. 51-78.

cinnamon color, and frequently finely sprinkled with white, in consequence of the cells of the medullary rays, which contain oxalate. A transverse section shows directly beneath the outer bark a so-called resin ring.

A species belonging in this category, namely, the bark of *Cinchona nitida* Ruiz et Pavon, which is designated as *Pata de gallinazo*, affords an excellent example of the fantastic names with which the Cascarilleros provide the Cinchona Barks. In consequence of the corky warts (lenticels?), as also of the Sphæriaceæ, which are found upon this bark as well as upon many others, there is formed a peculiar delineation of the outer surface, which in Peru is designated as "vulture claws," *pata de gallinazo*. Gallinazo refers in Lima to the carrion vulture, Cathartes fœtens.[1] Such names are now best cleared away by the innovation of the Dutch Government, which consists in attaching to the larger packages of Javanese barks the results of the analysis and the designation of the mother plant.

In former times the Huánuco variety consisted chiefly of barks of the *Cinchona nitida*,[2] which grows in large amounts by San Cristoval de Cuchero or Cocheros, not far from Huánuco. The barks of this district were made known since 1776, by Francisco Renquifo and Manuel Alcarraz, and then by Ruiz, Pavon and Dombey,[3] and finally toward the end of the century introduced into commerce by merchants from Lima, as gray bark of Huánuco.

As *Loxa* or *Loja Cinchona*, barks are or were exported, which, in distinction to the preceding variety, are predominatingly of a dark brownish color, have a more gray than whitish coating, and, beside longitudinal wrinkles, exhibit numerous, somewhat distant, transverse fissures. The Loxa bark consists mostly of quills having a maximum circumference of 1 centimeter ($\frac{3}{8}$ inch), and only 1 to 2 millimeters ($\frac{1}{24}$ to $\frac{1}{12}$ inch) in diameter, and is frequently abundantly beset with lichens. A sharp transverse section of the better sorts of Loxa bark exhibits the glistening "resin ring."

As has been previously mentioned (p 19), the district of Loxa furnished the first Cinchona barks. At the time of the Spanish sovereignty the most select specimens of the same, a yellowish and a reddish variety, *Cascarilla amarilla del Rey* and *Cascarilla colorada del Rey*, were retained for the Spanish Court, and bore for

[1] Markham, Pritchett, *Blue Book* 1863, 120, 125. I was told, however, by Mr. Spruce, in August 1867, that the expression *Pata de gallinazo* refers to the fracture of the bark.

[2] Figure in Weddell, T. 10; Howard, *N. Quinologia*, T. 20.

[3] Joseph Dombey was born in the year 1742, at Mâcon, and went to Peru with Ruiz and Pavon in 1777; he returned to France in 1785, but departed again for America in 1793, and died in 1794 at Montserrat.—Cap. *Études biogr. pour servir à l'hist. des Sciences*, II (1864); compare also my *Pharm. Chemie*, pp. 611, 890.

a long time the name of *Cinchona* (*China*) *coronalis*, which is still retained in the English "Brown Bark," Ger., Königschina, while the adjective *regius* or *regia* has been transferred to Calisaya. To obtain this original Brown Cinchona, at the time of Humboldt's residence in South America, very young trees were stripped, of which from 800 to 900 were required in order to furnish the small amount of 110 hundred-weight of bark, which the Court required.

This entire class of the predominatingly brown South American barks comprised several sorts, the discrimination of which reposes upon such external characteristics as deprive them of exact scientific definition.

The circle of the officinal Cinchona barks was confined therewith, on the one hand, to the medium or younger quills of a few species, in that, for the accustomed sorts, as above shown, in the course of time the same Cinchonas were not always collected, and on the other hand to the red-trunk barks and the bast-plates of Calisaya.

All the remaining sorts which occur in commerce, of which here also mention is occasionally made, and still others, are of interest only for their applications in chemical industry, and not for pharmacy.

The plantations of the Cinchonas in India, Jamacia and other districts furnish meanwhile mostly still younger barks, in which very decided peculiarities are wanting. At the present day more importance must be attached to the determination of the amount of alkaloid of these barks than to their external appearance.

SECTION X.

THE SO-CALLED SPURIOUS CINCHONA BARKS.

Before the alkaloids were known, various other barks found their way into commerce, in part without disguise, as a pretended substitute for the medicinally active Cinchona barks, and in part mixed with the latter, although their inferior value was perceived at an early period. Among these false or spurious Cinchona barks the only one until recently of any importance was the hard bark of *Cascarilla magnifolia*,[1] Endlicher (*Cinchona oblongifolia* Mutis, *C. magnifolia* Pavon, *Ladenbergia magnifolia* Klotzsch, *Buena magnifolia* Weddell; it is also probable that Karsten's *Cinchona heterocarpa* was nothing else than this tree.) Mutis, in the year 1780,

[1] Figured in Howard's *N. Quinol.*, Tab. 10; Karsten's *Fl. Colomb.* Tab. VI.

erroneously described the same as *Cascarilla roja*,[1] and later, particularly at the beginning of this century, it was brought in enormous quantities into commerce as *Cinchona* (*China*) *nova surinamensis*, although probably for the most part not from Surinam,[2] but from New Granada. This stately tree is distributed through Columbia and Ecuador, presumably also still more widely, and is known as *Cascarilla flor de Azahar*. Its small white flowers, scarcely tinted with red, which indeed by their downy pubescence approximately resemble the Cinchonas, diffuse a fine orange-like fragrance. (*Azahar* designating in Spanish, orange and lemon).

This Cinchona nova also occurred from 20 to 30 years ago under the name of *Cinchona rosea* or *Cinchona Savanilla*,[3] and even as *Cinchona Valparaiso*. It contains no cinchona alkaloid, as one may easily become convinced by means of Grahe's test (see p. 68), and is altogether free from alkaloid.[4] At the present time it is not found in commerce.

From an anatomical point of view this bark is positively distinguished from the barks of the Cinchonas, especially with regard to the obtuse ends of the bast-fibres and the remarkable abundance of sieve tubes. The bast-fibres of the "Cinchona (China) nova" are much more numerous, thinner, longer, and not so completely lignefied. The figure of the transverse section[5] agrees very nearly with that of Cinchona cuprea (see Plate VIII). When, however, at some time the barks of numerous other Cinchoneæ shall be compared therewith, there is no doubt but that intermediate forms will be found. Such an one, *e. g.*, is to be observed to a certain extent in the beautiful rose-red, feebly bitter bark of *Condaminea tinctoria* D. C.,[6] which contains not a very large number of strong bast-fibres,

[1] See page 17, by Calisaya Ledgeriana.

[2] Murray, *Apparatus Medicaminum*, VI, 181, 222, was indeed, in 1790, in possession of a specimen of this bark from Surinam. It was known that it did not possess the medicinal power of the true Cinchona. Later communications relating to this worthless bark are contained in the *Jahresbericht der Pharm.*, 1857, p. 40, and 1862, p. 42.

[3] *Archiv. der Pharm.* 116 (1851) 374, and therefrom in the *Jahresbericht*, 1851, 52. It is very remarkable that this bark was named by some drug dealers *Cinchona from Valparaiso.*

[4] Hesse in Fehling's *Neues Handwörterbuch der Chemie.*, II (1875), 531.

[5] Berg, *Chinarinden*, Plate X, 27.

[6] Synonyms: *Cinchona laccifera* Pavon, *Macrocnemum tinctorium* Humboldt, Bonpland et Kunth. The genus *Condaminea*, establisned by De Candolle, is distinguished from the Cinchoneæ by the fleshy corolla, the conical capsule and the wingless seeds. Tafalla (section 17), had already called attention to the bark of this tree, which, in the domain of the upper Orinoco or Paragua furnishes to the natives a red color. It is also probably with regard to this that it has received by the natives the popular designation of *Paraguatan bark*. After the bark, through Humboldt, had become known to a certain extent in Europe, small quantities of it appear occasionally to have been brought into commerce. Virey, *e. g.*, stated in the *Journal de Pharmacie*, XIX, (1833) p 199,

reminding of those of Cinchona bark. The fibres of the Condaminea are, however, thicker, less brittle, of very unequal length and thickness, and mostly provided with a considerable cavity. As much as this bark[1] is separated from the true Cinchona barks in its appearance, it nevertheless, by reason of these bast-fibres, approximates more closely to the latter than, *e. g.*, to the Cinchona cuprea.

SECTION XI.

CINCHONA CUPREA.

The remarkable bark, which I designated in the year 1871 as *Cinchona* (*China*) *cuprea*,[2] has received much consideration. It is characterized by a peculiar color, which, on the outer surface, reminds of somewhat rusty copper utensils. It was emphatically set forth that I did not compare the appearance of this copper-colored bark to the color of the bright metal.

After the communications of Hesse and myself in regard to the Cinchona cuprea (1871), nothing was heard again for a time of this bark. It was first at the end of February, 1880, that Mr. J. E. Howard informed me that it began to appear, unmixed, in larger

that Paraguatan bark had been received at Cadiz; O. Henry (ibid, p 201) found it to be free from cinchona alkaloids. It is furthermore described in Guibourt's *Histoire naturelle des Drogues simples*, III (1869), p 185. Condaminea tinctoria, moreover, grows not only in the northeastern part of South America, but also in Chili and in the Argentine Republic. Mr. Stuckert, an apothecary of Basel, brought the bark of the same from Tucuman in 1880, under the name of *Cinchona* (*China*) *rosa*.

[1] The longitudinal section shows, however, great distinctions in comparison with Cinchona barks; the fibres of the Condaminea bark are much less regularly spindle shaped. In the beautiful red decoction which fresh "Cinchona rosa" affords, the coloring matter is only suspended, not properly dissolved. When this is removed by filtration through bole or charcoal, a fluorescent filtrate is obtained, the bluish reflex of which is not destroyed by hydrochloric acid, and therefore cannot proceed from quinine. This remarkable bark also does not afford the red tar (p 68); nevertheless it is said to contain a trace of alkaloid.

Very similar to the "Cinchona rosa," and perhaps identical therewith, is also the so-called *Arariba bark*, which Rieth describes in Liebig's *Annalen*, 120 (1861), p. 247, and, in accordance with the statement of Martius, refers it to *Arariba rubra*, which is entirely unknown to me. Its diagnosis will be found in C. Fr. Ph. von Martius' paper, entitled "Zur Kritik des Gattungscharacters von Cinchona," as contained in the *Sitzungsberichte der Münchener Akademie*, III (1860), p. 323. Rieth found in the bark the crystallizable Arabine, $C_{23}H_{20}N_4$, the only solid base which is free fron oxygen. Vogl, on page 17 of the commemorative essay mentioned under section 18, No. 35 of this work, describes the same bark as *Cinchona* (*China*) *von Cantagallo*, and Möller, *Baumrinden*, 1882, gives on page 142 a good figure of a magnified transverse section of the same.

[2] Vorwerk's *Neues Jahrbuch für Pharmacie und verwandte Fächer*, XXXVI (Speier, 1871), p 296, and therefrom in Wiggers-Husemann's *Jahresberichte* der Pharm, 1872, p 132. Mr. J. E. Howard forwarded to me at that time a good specimen of Cinchona cuprea, which, as early as 1857, had come under his observation among other barks in the London market. He had also already found it to contain quinine, although he had not published anything concerning it. Vogl has likewise considered the Cinchona cuprea in his commemorative essay, p 98, mentioned under section 18 of this work.

quantities in the London market, and was eagerly purchased. The first imports, according to Paul,[1] occurred as early as June 1879, and soon thereafter, notwithstanding the unusual appearance of the "Cuprea," its value was determined to the effect that it contained about 2 per cent. of sulphate of quinine and only a small amount of the associate alkaloids. De Vrij obtained from the same altogether as much even as 5.9 per cent. of alkaloids (Letter of September 23, 1882). In May, 1880, large supplies of this bark were already to be seen in London,[2] and the subsequent imports directly assumed unsuspected dimensions.

Cinchona cuprea occurs in quite flat or channeled pieces, more rarely in quills of scarcely half a meter (20 inches) in length, and at the most from 5 to 7 millimeters ($\frac{1}{5}$ to $\frac{1}{4}$ inch) in thickness; but by far the predominating amount consists of small fragments, and conveys altogether the impression that it can only be derived from a tree of small dimensions. The light brown, longitudinally wrinkled or warty cork is usually scraped off, so that the smooth outer surface is formed of the tissue of the outer bark, to which pertains the previously mentioned color of copper vessels. The outer surface also often shows impressions of the incisions of a sharp knife, which are occasionally but a few millimeters distant from each other, and extend in a parallel direction, probably for the purpose of removing the cork, and presumably in order to render prominent the more pleasing color of the inner tissue. This is indeed so peculiar, in distinction to former Cinchona barks, that it must attract the attention of any one who has made himself familiar with the appearance of true Cinchona barks; the copper-colored bark deviates to a still greater degree from all true Cinchona barks by its great hardness. It is also impossible to confuse it with the Cinchona nova surinamensis, for the reason that the Cinchona cuprea yields the red tar of Grahe's test (p. 68).

Specimens of this Cinchona cuprea were furnished, in 1879, to a German house (Lengerke & Co.) in Bucaramanga, in the Columbian state of Santander, and were sent by them to New York and London for the purpose of examination. The favorable result of the analyses then led to the collection of this bark on a large scale in the forests of the mountains which, above Bucaramanga, ascend from the main valley of the Magdalena river to the chain of La Paz, and form the water-shed between this stream and its tributary, the Suarez.

The tree which furnishes the Cinchona cuprea begins to make

[1] *Pharm. Journ.* XI (September, 1880) 259.

[2] *Pharm. Journ* X (1880), 954.

its appearance at elevations of 1600 feet, and the best bark is only stripped at elevations of from 2200 and 3200, or even as much as 4200 feet, as was reported to me in November, 1881 and in February, 1882 by Dr. Chas. A. Robbins of New York, from personal observations. Only a small portion of the root-bark is collected with the other; and in the wide surroundings of Bucaramanga the trees of this variety of Cinchona are now quite completely felled. A to some extent similar bark from other districts, *e. g.*, from Tolima, in about 5° N. lat., in the upper Magdalena valley, has been proved to contain but little alkaloid. 20,000 *colli* (serons) of the same, which were thrown upon the market in 1882, afforded either extremely little, or at the most from 0.8 to 1.5 per cent. of quinine. The derivation of this *Tolima* bark has not been determined. From an anatomical point of view, I find it to agree with common Cuprea bark; it yielded to Dr. Kerner (1882) 1.778 per cent. of crystallized sulphate of quinine.

Of late years, and especially until August 1881, the copper-colored Cinchona has been brought to Europe in ever increasing amounts. Among the 100,000 *colli* (serons), of South American product, which were imported into London in 1881, there were over 60,000 *colli* of "Cuprea," of which, moreover, more than 5500 *colli* found their way to France. Cinchona cuprea, according to its structure (Plate VIII), belongs to the previously considered false Cinchona barks, but, in consequence of the alkaloids which it contains, forms a very remarkable exception. The cork is formed of thick-walled cells (Plate VIII, e. f.), which are distinguished in the most striking manner from the much wider, and always delicate-walled, tabular cells of the cork of true Cinchonas (Plate VIII, A. C. e.) This fact is the more remarkable, since the bark of Remijia Hilarii, for example, appears to possess delicate-walled cork cells.[1] Furthermore, the largest part of the tissue of Cinchona cuprea is seen to have become converted into sclerenchyma. In the outer bark (o) already, there are numerous groups of unelongated sclerotic cells (k) interspersed; and on the boundary of the bast there are found isolated lacticiferous ducts (p), which, indeed, are wanting in very many pieces. The bast consists to a predominating extent of thickened, simple, somewhat short, unpointed fibres (s), which, therefore, when observed longitudinally (Plate VII, sr). deviate entirely from the bast fibres of true Cinchona barks. Only the staff cells, mentioned on p. 37, are similar to the fibres of Cinchona cuprea. The bast of the latter contains, moreover, shortened sclerenchyma cells, as well as the outer bark. It is only in the

[1] Möller, *Baumrinden* p. 137 (Remijia Vellozii).

youngest bast layers that sieve-tubes and parenchyma predominate; and here particularly, although also in the outer bast, crystal-cells (x) are present, in which finely crystallized oxalate is deposited. The bast shows accordingly (Plate VIII) a distinct separation into an outer zone, rich in sclerenchyma, and an inner parenchymatic zone, containing fewer fibres, and particularly a less number of stone cells. The medullary rays of the bast are but narrow. The by far predominating sclerenchyma is the cause of the remarkable hardness of this bark, which, therefore, in London, was also named "hard bark." It is, furthermore, characterized by the red coloring matter, which penetrates the entire tissue so abundantly that it is almost impossible to decolorize it, *e. g.*, by means of ammoniacal alcohol.

The bark of the Cascarilla magnifolia, mentioned on pages 10 and 48, agrees very nearly, in regard to its structure,[1] with the Cinchona cuprea. The cork cells of the former, however, are thin-walled, as in the Cinchonas, and its bast-fibres do not form such long, straight rows as in Cinchona cuprea, where they may be followed uninterruptedly from the youngest portion of the bast even into the outer bark.

Hesse has shown[2] that in this Cinchona cuprea, which I saw for the first time in his collection, the same alkaloids are present as in the Cinchona barks. Since the Cinchona cuprea, independent of the other bases, affords uniformly from 1 to 2 per cent. of quinine, it is the more willingly worked by the manufacturers, as in consequence of the absence of cinchonidine[3] the preparation of pure sulphate of quinine from this bark is rendered much easier.

The tannic acid of the Cinchona cuprea, according to Hesse, is not the same which exists in the Cinchona barks, although the former likewise produces a dark-green precipitate with ferric salts. Hlasiwetz, in 1867, ascertained that the tannic acid of coffee, by boiling with caustic alkali, may be split into sugar and *caffeeic acid*, $C_9H_8O_4$, one of the hydro-cinnamic acids $C_6H_3{<}^{(OH)_2}_{CH=CH\text{-}CO\text{-}OH}$. Kerner, in 1882, treated an alcoholic extract of Cuprea bark in the same manner, supersaturated the liquid with sulphuric acid, and agitated it with ether, which then furnished crystals of caffeeic acid. The yield amounted to about ½ per cent. of the bark employed.

[1] This is well figured in Berg's *Chinarinden der pharmakognostichen Sammlung zu Berlin*, 1865, Plate X, Fig. 27. In the innermost portion of the bast there are many more fibres than here—compare our Plate VIII.

[2] *Berichte der Deutschen Chemischen Gesellschaft*, 1871, p. 818.

[3] According to Hesse, *Berichte der Deutsch Chem. Ges.* 1883, pp. 59, 60, homocinchonidine, dicinchonine, quinamine and conquinamine have also never been met with in cuprea bark. (F. B. P.)

The extracts of other Cinchona barks afforded by the same treatment no caffeeic acid. This investigation was instituted in consequence of crystals of caffeeate of quinine having been found in the mother liquids obtained from Cinchona cuprea in the quinine manufactory at Milan.

All the Cinchona cuprea which I have obtained from London and New York, as also from Jobst's manufactory, near Stuttgart, and, furthermore, *e. g.*, that which I have inspected in large amounts in Zimmer's manufactory at Frankfort, always represented one and the same product. Triana states that the districts southeast of Bogota, mentioned on page 20, also furnish the same bark; the latter he derives with precision from the there described *Remijia pedunculata*, to which thus the bark from Bucaramanga may probably also belong.[1]

Among the Cinchona cuprea which reached France, small amounts of a bark have, however, been found by Von Arnaud,[2] which, according to Planchon, is essentially distinct from my Cinchona cuprea. As Arnaud has discovered in that a new alkaloid, *cinchonamine*,[3] the respective variety may here be designated as *Cinchonamine bark*. It is, as stated by Planchon,[4] mostly deprived of the warty cork, and displays upon a transverse section about 10 rows of small, isodiametrical or polygonal cells, which, toward the interior, gradually become extended in a tangential direction, and thereby impart to the transverse section a peculiar delineation. In the bast there are very numerous, densely crowded fibres with considerable cavities, in radial rows, which are separated by medullary rays of from 4 to 5 cells in width. On a longitudinal section the fibres appear slightly elongated, and short sclerenchyma cells and lacticiferous ducts are wanting, while my Cinchona cuprea is particularly characterized by the abundant development of groups of sclerenchyma.[5] The bast of Cinchona cuprea displays, as may be observed in Plate VIII, two distinct strata; according to Planchon's intimation this is not the case in the bast of the Cinchonamine bark, although, indeed, here also the fibres in the outermost bast layers occur somewhat more numerously than in the inner.

[1] *Journ. de Pharm.*, V (1882), p. 567; also *Pharm. Journ.* XII (1882), p. 861.

[2] *Répertoire de Pharm.* 1881, p. 507.

[3] The name *cinchonamine* was already bestowed by A. C. Oudemans, in 1879, to another alkaloid, which has not been met with again since it was discovered.

[4] *Journ. de Pharm.* V (1882), p. 354, "Quinquina à cinchonamine;" and VI, p. 89, "Note sur les Écorces de Remijia."

[5] I unfortunately did not succeed in obtaining the Cinchonamine bark. It is presumably the same bark which, according to the *Pharm. Journ.* XI, p. 895, also appeared once in 1881, in London.

Of the tree, which in the valley of the Magdalena (probably more correctly in the central district, between the Cauca and Magdalena?) furnishes the Cinchonamine bark, Triana[1] procured the required organs, in order to be able to determine that it is the *Remijia Purdieana*, mentioned on p. 20. By a comparison of this material with the Cuprea barks occurring in commerce, Planchon has definitely established the derivation here given of my Cinchona cuprea, as well as that of the Cinchonamine bark.

SECTION XII.

COMMERCIAL STATISTICS.

A conception of the large dimensions of the commerce in Cinchona barks is given by the following figures:[2]—

According to an estimate in the London *Pharmaceutical Journal* of September 18, 1880, there are annually more than 6 million kilograms[3] of Cinchona bark (considered in the dry state) peeled and brought into commerce. The following statements indicate that this figure is well founded. If one may accept that the average value of one kilogram of Cinchona bark is from 4 to 5 *marks*,[4] the annual cinchona harvest would be worth, at the present time, nearly 30 million marks (nearly 7½ million dollars).

Among all the drugs, only Opium attains to still larger sums; by far the smallest part of which, however, serves for medicinal purposes. Indeed, in the case of the Cinchona barks also, only a small and not easily estimated portion finds direct application in pharmacy.

In the year 1880 there were exported from the northern part of South America, in Ciudad Bolivar, 29,650 kilograms (in 1881 only 6,650), from Puerto Cabello 24,107 kilograms, and in Barranquilla (Sabanilla) 3,797,861 kilograms of Cinchona; in 1881, the latter figure, consisting chiefly of Cinchona cuprea, was increased to 6,838,920 kilograms.

Ecuador, presumably inclusive of the neighboring districts of Peru, furnished in 1880, via Guayaquil, 1,516,102 kilograms of bark; in 1881 only about half so much.

[1] *Pharm. Journ.* XII, p. 861; *Journ. de Pharm.* V, p. 567.

[2] For a part of these figures I am indebted to the obliging communications of Dr. G. Kerner (Zimmer's quinine manufactory), of Frankfort, Mr. David Howard, of Stratford, and Mr. Gehe, of Dresden, while the remainder were obtained from official reports compared by myself.

[3] 1 kilogram = 2 lbs, 3¼ ozs, nearly, avoirdupois.

[4] 1 mark = about 23 cents, U. S. currency.

In 1877 there were exported from Bolivia 56,620 kilograms by water to Pará, 254,009 kilograms to Arica, and 374,309 kilograms to Molendo (south of Islay and Arequipa).

The export from Ceylon amounted, in 1870, to 86,000, in 1880, to 186,000, in 1881, to 600,000 kilograms, and for 1882 it is estimated at about 1 million kilograms.[1] It may be presumed that in 1885 the export will amount to at least 4 million kilograms.

The plantations of the Dutch Government, in Java, had furnished, in 1879, but 35,000 kilograms, in 1880 more than 55,000 kilograms, in 1881 already 81,043 kilograms, and at the principal auction at Amsterdam, May 23, 1882, 81,000 kilograms were offered for sale. There are, moreover, also noteworthy plantations of private owners upon the island, which, in 1881, had already furnished 522 bales and 64 chests of Cinchona bark to the Amsterdam market.

In May, 1880, the first supplies from Jamaica came to London, which, in March, 1882, had already attained to more than 15,000 kilograms.

In 1878 the import of France amounted to somewhat more than 1,600,000 kilograms of Cinchona bark, at a value of 11,201,988 francs, and in 1881 nearly as much. The United States received, between 1874 and 1877, an annual average of 3,853,662 pounds, and in 1881 nearly the same amount.

London is the princial point for the commerce in Cinchona barks. The import of this place, which amounted to 1,140,000 kilograms in the year 1876, has since regularly increased, to a particular extent in the year 1881, and exceeded in the past year 6 million kilograms. If there be added thereto that which is imported into Paris, New York, Hamburg and Amsterdam, the total harvest of Cinchona bark for 1876 may be estimated at 3¼ million, for 1881, however, at 9 million kilograms. Hamburg, with an annual importation of about 30,000 to 80,000 kilograms of Cinchona bark, comes scarcely more into consideration than Amsterdam, where are brought the barks which are grown almost exclusively in Java.

Since 1876 the greatest increase is to be seen in the imports from India and Columbia (New Granada). From the latter country 4,797,000 kilograms were received in London in 1881, which, indeed, includes the Cinchona cuprea, the occurrence of which, however, is probably but transitory. On April 1, 1881, there were stored in London 26,805 *colli* of Cinchona bark, thus at least

[1] The export from Ceylon has already attained to more than 1¼ million kilograms; that of Java, in 1881, 165,000 kilograms.

1,340,000 kilograms.[1] At the beginning of July, 1882, the supply there amounted to 3½ million, and in Paris to about ½ million kilograms.

If one attempt to estimate the amount of sulphate of quinine[2] (including the other salts of quinine and the remaining Cinchona bases) which is annually manufactured in recent years, there results, with some degree of probability, the figure of 120,000 kilograms, which presupposes nearly 86,400 kilograms of alkaloid. If it then be assumed that the barks contain, on an average, but two per cent. of alkaloids, the manufactories must annually work up about 4⅓ million kilograms of Cinchona bark; at the present day, however, it may be presumed to be considerable more.

The commercial reports are accustomed to calculate according to *colli* (serons, bales), which contain from 50 to 55 kilograms of bark.

If one will assume that for each of the nearly 5000 pharmacies[3] of Germany there is a daily consumption of 100 grams of Cinchona bark, this figure, which is undoubtedly too highly estimated, would correspond to an annual requirement of 182,500 kilograms. In the year 1881, however, the import of Germany (after deducting 119,200 kilograms, which again went out of the country) amounted to 2,048,600 kilograms; 1,876,100 kilograms of bark had thus probably become worked up for alkaloid in the 6 quinine manufactories of Germany, and may have furnished more than 50,000 kilograms of sulphate of quinine.

[1] In December, 1881, a ring of speculators placed themselves in possession of the largest part of Cinchona bark stored there, which was estimated at about 40,000 *colli*, or over 2 million kilograms, and among which Cinchona cuprea was present to the largest extent.

[2] The present price of sulphate of quinine is nearly 300 *marks* per kilogram. One may thus be permitted to assume that the amount of cinchona alkaloids and their salts which are annually manufactured represent in the world's market a sum of from 30 to 40 million marks (about 7½ to 10 million dollars). An indication of the great fluctuations in this department may moreover be given by the following extremes in the selling price of sulphate of quinine from Zimmer's manufactory at Frankfort-on-the-Main, in the interval from 1875 to 1881. A kilogram of this salt was quoted:

at 195	marks	in January, 1876;	at 545	marks	in May, 1877;
at 260	"	February, 1878;	at 440	"	May, 1879;
at 240	"	November, 1881;	at 430	"	August, 1880.

[3] According to the last statements contained in the Imperial Statistical Office (March, 1882), there existed in the year 1875, in the German Empire, 4531 pharmacies.

SECTION XIII.

CHEMICAL CONSTITUENTS OF THE CINCHONA BARKS.

An odor is not entirely foreign to the Cinchona barks; Weddell[1] found it, *e. g.*, in the case of fresh Calisaya and amygdalifolia, to resemble that of elder bark, although more feeble. Also in some varieties of commercial barks, *e. g.*, that of flava fibrosa (p. 44) and of Loxa (p. 47), a slight aroma cannot be entirely ignored. A slight aromatic odor is already perceived when the powdered fresh bark of the Indian C. succirubra is dried with milk of lime. Hesse[2] also makes mention of an odorous principle in the Cinchona barks.

The barks of some of the Rubiaceæ which are most closely related to the Cinchonas, have a decidedly agreeable odor, thus, *e. g.*, that of Ferdinandusa chlorantha Pohl (Gomphosia chlorantha Weddell).

In regard to the taste, there occur, in part, significant distinctions. Younger barks have a predominating, but not disagreeably astringent taste (*saveur styptique* of Delondre and Bouchardat), more rarely, as, *e. g.*, those of Huánuco and Loxa, at the same time astringent acidulous, although to a less extent. In trunk barks the astringent tang becomes more and more lost, and the pure bitter taste appears strong and prominent.

In the case of the Calisaya, the pure bitterness appears even with young barks, while the more diminutive C. scrobiculata always possesses the astringent tang, which occasionally predominates.

In the C. pubescens, which is likewise poor in alkaloid, Weddell[3] perceived, even in fresh trunk barks, only a somewhat bitter and at the same time nauseating taste.

A disagreeable and at the same time a somewhat sharp tang is observed in the so-called *Cinchona* (*China*) *Jaén vel Pará fusca*, in which the Cinchona bases are wanting; its botanical origin is not known.[4]

Among the universally distributed principles of the vegetable kingdom, which also occur in Cinchona barks, prominence has already been given to the directly observable starch and calcium oxalate. Since the latter is in crystalline granules and only

[1] *Hist. Nat. des Quinquinas*, pp. 33, 45.

[2] *Berichte der Deutschen Chemischen Gesellschaft*, 1877, p. 2162.

[3] *Hist. nat.* p. 56, Note 2.

[4] Compare Flückiger's *Pharmakognosie*, first edition, 1867, pp. 396, 403, where, however, the structure of true Cinchona barks has erroneously been ascribed to this bark.

deposited in isolated cells, it comes but little into consideration. The total ash of bark dried at 100° C. (212° F.) attains, according to Reichardt,[1] to a maximum of about 3 per cent. (in Cinchona rubra); the amount of lime to about 1 per cent. Howard[2] obtained from the inner portion of the bast of C. succirubra 0.91 per cent. of calcium carbonate, corresponding to 0.5 per cent. of lime. On the other hand Reichel estimated the amount of oxalic acid (in Huánuco bark, p. 46) to be in maximum 0.29 per cent., and Reichardt (in Cinchona rubra) as 0.33 per cent., wherefrom may be deduced that the amount of never-failing oxalate cannot readily exceed 1 per cent., in that, presumably, a portion of the calcium is contained in the form of other compounds.

The ash remaining by the combustion of the Cinchona barks, fluctuating from ¾ to 3 per cent., consists for the most part of the carbonates of calcium and potassium, which, together, *e. g.*, in the flava fibrosa, according to Reichardt, represent $\frac{4}{5}$ of the entire amount of ash. Very much smaller is the quantity of magnesium carbonate, which, *e. g.*, in flat Calisaya, amounts to but $\frac{1}{15}$ of the ash. Cinchona cuprea afforded me 1.65 per cent. of ash. Conclusions as to the distribution of the constituents of the ash in the different forms of tissue of the bark appear premature. I found carefully isolated bast fibres to be poor therein.

The presence of ammonium salt may readily be demonstrated in the extracts of Cinchona barks, although its amount, on an average, is probably but very small. Carles, in 1873, obtained only fractions of a per mille. of ammonia.

Substances which may be designated as *resin* are also contained in the barks in but very insignificant amounts. Delondre and Henry found such in the red juice exuding from the trunks of Cinchonas as the result of incisions.

If Cinchona barks be extracted with boiling alcohol, a principle is separated in the cold which has been regarded as *wax*, and which, occasionally colored with chlorophyll, may also be obtained when specimens of bark are analyzed simply for the purpose of estimating the alkaloids. Kerner (1859, 1862) has designated this principle as cinchocerotin.[3] When prepared from flat Calisaya it forms, after purification, handsome, purely white, neutral, crystalline laminæ, which first melt at about 150° C. (302° F.)

[1] Title under section XVIII.

[2] *Nueva Quinologia, Microsc. observat.*, fol. 6.

[3] Cinchocerotin is not a wax; for a thorough investigation of it see Helms' paper in the *Archiv der Pharmacie*, April, 1883, and abstracted in the *Amer. Journ. Pharm.*, July, 1883.

The presence of gum, as also of sugar, has not been more accurately proved in the Cinchona barks.

The *phlobaphen* which, in 1844, was precipitated by Stähelin and Hofstetter from an alcoholic tincture of the yellow Cinchona by means of sulphuric acid, as also the *lignoin*, prepared in 1856 by Reichel, are quite as insufficiently investigated as the corresponding substances occurring in oak bark.[1] Reichel's lignoin may be obtained when Cinchona, which has been exhausted by ether, alcohol and water, is extracted with caustic lye, and is then precipitated, on the addition of an acid, as a dark brown substance, which, in its dry state, may amount to from 2 to 19 per cent. of the bark.

The Cinchona barks contain tannin, which affords with ferric salts a bright green, or, when other coloring principles of the barks co-operate, a darker brownish-green precipitate. This *cincho-tannic acid* also produces a precipitate in a solution of gelatin. Reichardt found in Cinchona (China) flava fibrosa 1 per cent., in flat Calisaya 3⅓, and in quill Calisaya, 2 per cent. of tannic acid; Reichel, in flava fibrosa (the Tunita bark mentioned on page 18), 3.8 per cent. When separated from the lead salt, the cincho-tannic acid represents, according to Schwarz (1851), a bright yellowish, very hygroscopic mass, of an acidulous, and at the same time astringent, but not bitter, taste. Upon heating the cincho-tannic acid at but 100° C. (212° F.), or by the evaporation of its aqueous solution, especially after the addition of acids or alkalies, red products are formed—in the latter case with absorption of oxygen. By precipitating the red-brown ammoniacal extract of Cinchona with an acid, the *cinchona-red* is obtained, which, when dried, is a dark red or brownish-red, odorless and tasteless mass, insoluble in ether, water, and dilute acids, but soluble in alcohol. The ammoniacal solution of cinchona-red affords, with alum, a red lake. With a fraudulent purpose, the attempt has already been made to impart to yellow Cinchona barks the appearance of the more expensive red varieties by moistening them with ammonia. The aqueous extract of a bark which has been treated in this way is remarkably colored, and affords, with Nessler's reagent,[2] a reddish-brown, not a white precipitate; chloride of platinum also produces an abundant precipitate, while the Cinchona barks, as previously intimated, p. 59, can furnish but very little ammonio-platinic chloride.[3]

[1] Flückiger, *Pharmakognosie*, 1882, p. 475.

[2] Flückiger, *Pharm. Chemie.*, 1878, p. 38; Kubel and Tiemann, *Anleitung zur Untersuchung von Wasser*, 1874, p. 142; Hoffman and Power's *Examination of Medicinal Chemicals*, p. 40.

[3] Thomas et Guignard, *Répertoire de Pharmacie*, 1882, p. 337.

The amount of water contained in air-dried Cinchona barks amounts usually to from 9 to 11 per cent. (Compare also page 34.)

The oldest observation which relates to the peculiar constituents of Cinchona barks, or at least to those which are characteristic of them, reverts to the year 1745, when Claude Toussaint Marot de Lagaraye, of Paris, perceived the deposit of a salt from an extract of Cinchona.[1] S. F. Hermbstädt, of Berlin, in 1785, recognized therein the calcium compound of an acid, the peculiarity of which was established in 1790 by Friedr. Christian Hofmann, an apothecary of Leer, in Hanover, who named it *chinasäure* (kinic acid).

Vauquelin, in 1806, determined more precisely the properties, and Liebig the composition, of kinic acid. It occurs in all true Cinchona barks, in amounts of as much as 9 per cent., and upon it depends the acid reaction of their aqueous extracts; it is, however, without any considerable physiological action. Hlasiwetz, in 1851, found kinic acid also in the Cinchona nova, mentioned on page 49. Since, according to Hesse, it is absent in the Cinchona cuprea, it would be desirable to know its distribution in the group of the Cinchoneæ, the more so as it belongs to those plant acids which are of quite common occurrence. Kinic acid forms large, hard, monoclinic crystals, which are soluble in somewhat more than twice their weight of water. The solution is odorless, of a purely acid taste, not bitter, and deviates the plane of polarization to the left. According to its constitution, $C_6H_7(OH)_4$ CO-OH, and that of its derivatives, the acid belongs to the class of aromatic compounds; by the action of hydriodic acid it may be reduced to benzoic acid and protocatechuic acid, and by energetic oxidation may be converted into quinone (or kinone). In closest relation to kinic acid stands the so-called acorn-sugar, or quercite, $C_6H_7(OH)_5$.

In the barks of the Cinchonas and the most closely related Rubiaceæ, there is found an uncrystallizable bitter principle, *chinovin*[2]

[1] Chymie hydraulique, pour extraire les sels essentiels des végétaux, animaux et minéraux avec l'eau pure, par M. L. C. D. L. G. (Monsieur le comte de la Garaye), Paris, 1749, 114. The Count occupied himself with chemistry for philanthropic purposes.

[2] According to recent researches of Liebermann and Giesel, *Berichte der Deutsch. Chem. Gesellschaft*, 1883, pp. 926–941, the chinovin obtained from cinchona cuprea is not identical with that obtained from the true cinchonas, but only isomeric therewith; the former they designate as β chinovin, and the latter as *a* chinovin. Both substances, in a pure state, form a white, very loose, crystalline powder, but differ in their behavior to solvents and in some chemical reactions. Thus the β, in distinction from the *a* chinovin, is insoluble in absolute ether and in acetic ether, while the β compound is much more freely soluble in cold absolute alcohol. Both varieties of chinovin have the same elementary composition, which is provisionally regarded by the authors as corresponding to the formula $C_{38}H_{62}O_{11}$, while that of chinovic acid is regarded as $C_{32}H_{48}O_6$. The

(quinovin or kinovin). It was discovered in 1821 by Pelletier and Caventou, in Cinchona nova surinamensis, and named by them "acide quinovique"; it was afterward designated by others as *chinova-bitter* or *cinchona-bitter*, and in 1859 was recognized by Hlasiwetz as a glucoside. Chinovin is best extracted from fresh Indian barks by means of a dilute alkali, and is precipitated therefrom, according to De Vrij, by hydrochloric acid. In order to purify it, the chinovin is dissolved in milk of lime and again precipitated. After having been subjected to this treatment several times, it is finally dissolved in chloroform. Chinovin is scarcely soluble in water, but is soluble in acetone, ether and alcohol; although neutral, it forms compounds with the alkalies, which are mostly soluble in water, and possess a very bitter taste. It is probable that a portion of the alkaloids in Cinchona barks is in combination with chinovin. According to Hlasiwetz, chinovin, $C_{30}H_{48}O_8$, in alcoholic solution, is split, by the action of hydrochloric acid, into *chinovic* (quinovic or kinovic) *acid* $C_{24}H_{38}O_4$, and a smeary variety of sugar (afterward recognized as *mannitan*),[1] $C_6H_{12}O_5$, whereby a molecule of water is absorbed.

$$\underbrace{C_{30}H_{48}O_8}_{\text{Chinovin}} + H_2O = \underbrace{C_{24}H_{38}O_4}_{\text{Chinovic Acid.}} + \underbrace{C_6H_{12}O_5}_{\text{Mannitan.}}$$

If an alcoholic solution of chinovin, diluted with a little water, is brought in contact with sodium amalgam, there is obtained, upon concentration, chinovate of sodium, as Rochleder (1867) has shown.

Chinovin participates in the medicinal activity of Cinchona barks.[2] The plane of polarization is deviated by its solutions, as well as by those of chinovic acid, to the right. The latter forms rhombic laminæ, and is of a feebly acid nature; it dissolves only in boiling alcohol somewhat abundantly, but neither in chloroform nor in water. Chinovin, associated with chinovic acid, is not confined in the Cinchonas to the bark, but is distributed through all their parts. De Vrij, in 1860, found in dried leaves of Cinchonas cultivated in India as much as 2 per cent.; in the trunk bark as much as 1.4 per cent., and in the root bark 1 per cent. of chinovin;

decomposition of chinovin is thus considered to take place according to the following equation :—

$$\underbrace{C_{38}H_{62}O_{11}}_{\text{Chinovin}} = \underbrace{C_{32}H_{48}O_6}_{\text{Chinovic acid}} + \underbrace{C_6H_{12}O_4}_{\text{Chinovin sugar.}} + H_2O.$$

[1] Liebermann and Giesel, *loc. cit.*, p. 935, place the identity of this sugar with mannitan in question, but find the sugar obtained by the decomposition of both varieties of chinovin to be identical. (F. B. P.)

[2] Kerner, in the Göschen *Deutsche Klinik*, 1868, No. 9.

the maximum, however, of 2½ per cent. in the wood of the root. Reichardt has obtained from Huánuco bark 1¾ per cent., Reichel quite as much from Cinchona flava fibrosa (p. 44), and Howard[1] 4.28 per cent.

Whether Cinchona barks exist in which this bitter principle is wanting, still requires proof.

For the detection of the active principles of the Cinchona barks, experiments were already instituted in the preceding century, although Gomes was the first who, in 1810, and more completely in October, 1811, succeeded to any extent in the preparation of the alkaloids from the Cinchona barks.[2] He dissolved an alcoholic extract of Cinchona in water, and precipitated by potassa a body which he re-crystallized from alcohol, and named cinchonine. That this preparation was of a basic nature, was first observed by Houtou-Labillardière in the laboratory of Thénard, at Paris, and communicated to Pelletier and Caventou.[3] To these chemists, who were guided by Sertürner's brilliant discovery of morphine,[4] we are indebted for a more precise acquaintance with Gomes' cinchonine, and the proof (1820) that two basic principles, quinine and cinchonine, are contained therein, to which the therapeutic effects of Cinchona belong. It is the former upon which almost exclusively the value of Cinchona bark depends.

The following bases occur in noteworthy amounts in Cinchona barks:—

Quinine,	$C_{20}H_{24}N_2O_2$
Quinidine,[5] discovered by Henry and Delondre, in 1833,	of the same composition.
Cinchonine,	$C_{19}H_{22}N_2O$
Cinchonidine, discovered by Winckler, in 1847,	of the same composition.

[1] Examination of Pavon's Collection of Peruvian Barks contained in the British Museum, London, 1853, 8vo, pp. 47 (From the *Pharm. Journ.*, June, 1852).

[2] Ensaio sobre o chinchonino, Lisboa, 1810. A translation in the *Medical and Surgical Journal*, Edinburgh, 1811, p. 420. More extended in *Memor. da acad. real das Sciencias de Lisboa*, III (1812), pp. 202 to 217: Ensaio sobre o cinchonino, e sobre sua influencia na virtude da quina e d'outras cascas. Antonio Bernardino Gomez was a Portuguese physician, who spent the last years of the eighteenth century in Brazil, then lived in Lisbon, and died there in 1823. In 1801 there appeared there his "Memoria sobre a Ipecacuanha fusca do Brazil ou Cipó das nossas boticas;" in 1801 and 1809, in Rio Janeiro, two essays on the cultivation of cinnamon, and finally the above notice relating to cinchonine. Compare Colmeiro, La botánica y los botánicos de la peninsula hispano-lusitana. Madrid, 1858, pp. 58, 199.

[3] *Annales de Chimie et de Phys.*, XV (1820), p. 292. Houtou-Labillardière died, in 1867, at Alençon. For the discovery of the cinchona bases, Pelletier and Caventou received, in 1827, from the Institut de France, the Montyon prize of 10,000 francs. In the year 1826 there had already been prepared at Paris 90,000 ounces (more than 2700 kilograms) of sulphate of quinine. Berzelius, *Jahresbericht der Chemie.*, VIII (1829), page 246.

[4] Flückiger, *Pharmakognosie*, second edition, 1881, p. 176.

[5] *Betachinin*, Van Heijningen, 1849, and Koch, 1861; *cinchotin*, Hlasiwetz, 1850; *betachinidin*, Kerner, 1862; *conchinin*, Hesse, 1865. See Liebig's *Annalen*, 192 (1878), p. 192. *Archiv. der Pharm.*, 216 (1880), p. 259, etc.

The Cinchona barks contain, furthermore, in smaller amounts:

Homocinchonidine, discovered by Hesse, in 1877	$C_{19}H_{22}N_2O$
Cinchonamine, obtained in 1881 by Arnaud, from Remijia Purdicana (p. 54)	$C_{19}H_{24}N_2O$
Homoquinine, found in 1882 by D. Howard and other English investigators, in Cinchona cuprea	$C_{19}H_{22}N_2O_2$
Quinamine, discovered by Hesse, in 1872	$C_{19}H_{24}N_2O$
Conquinamine, " " " 1877	of the same composition.
Cinchamidine, " " " 1881	$C_{20}H_{26}N_2O$

Quinine and cinchonine stand at the head of two groups of alkaloids, which, indeed, individually, show quite broad distinctions, but present, however, with regard to their physiological action,[1] some agreement. From these distinctive cinchona alkaloids the following bases are very considerably separated in every respect:

Aricine, discovered by Pelletier and Coriol, in 1829,[2] and analyzed by Hesse, in 1876	$C_{23}H_{26}N_2O_4$
Cusconine, discovered by Hesse,[3] in 1877	of the same composition.
Cusconidine, " " " " 1877	not yet analyzed.
Cuscamine, " " " " 1880	not yet analyzed.
Cuscamidine, " " " " 1880	not yet analyzed.
Paytine[4], " " " " 1870	$C_{21}H_{24}N_2O$
Paricine, in the bark from Para, mentioned on pages 58 and 68, discovered by Winckler, in 1845	not yet analyzed.

With the exception of paricine, cusconidine, and cuscamidine, the above named alkaloids are crystallizable. Besides the former, there occur however, other *amorphous bases*[5] in Cinchona barks, the knowledge of which is still but slightly satisfactory. They are perhaps first formed, in part, from the crystallizable alkaloids, in the process of manufacture. The *chinoidin* of the manufactories consists, for the most part, of amorphous bases.

Hesse[6] isolated from the mother liquids of Cinchona barks, obtained from the manufactories, the slightly odorous *cincholine*, a base volatilizable with aqueous vapor, but which, however, may

[1] It is only in the case of quinine that this has been satisfactorily determined from a medical standpoint.

[2] In a bark of unknown botanical origin, which was exported a few times from Arica (see p. 32), and which may possibly belong to a Cinchona.

[3] From barks which have not been botanically determined; the name relates to Cusco, in southern Peru.

Hesse, *Berichte der Deutsch. Chem. Ges.*, 1883, pp. 58-63, announces the presence of two new alkaloids in a variety of "cuprea" bark, viz: concusconine and concusconidine, both having the composition $C_{23}H_{26}N_2O_4$; and the list appears not yet completed. (F. B. P.)

[4] In a so-called *white Cinchona bark*, which was once exported from Payta, the most northerly port of Peru, but is not to be met with in commerce. Compare, regarding the same, Flückiger, *Jahresbericht der Pharm.*, 1872, p. 132; also section 18, No. 35, of this work.

[5] Every Cinchona bark contains amorphous alkaloids. Bernelot Moens, in 1881, states that their quantity varied from 0.13 to 1.45 per cent., as ascertained from 85 analyses performed by him.

[6] *Berichte der Deutschen Chemischen Gesellschaft*, 1882, p. 858.

possibly only originate from the hydrocarbons employed in the process of manufacture. (See section 15.)

From the first named alkaloids, on page 63, there are formed, by the action of potassium permanganate:[1] *cinchotine*, *hydroquinidine*, (hydroconchinine), *hydrocinchonine* and *hydrocinchonidine*, which, according to Forst and Böhringer (1882), are said to originally exist in Cinchona barks.

Only the two first mentioned pair of alkaloids (p. 63) are employed medicinally; they have a very bitter taste.

Quinine may be obtained in a crystalline form with $3H_2O$; it is soluble in about 20 parts of ether, more abundantly in alcohol and chloroform. These solutions deviate the plane of polarization to the left. Quinine is soluble at 15° C (59° F.), in 1600 parts of water. This solution, as also the aqueous solutions of quinine salts, when treated with chlorine-water or bromine vapor and ammonia, in the manner described in my *Pharmaceutische Chemie*,[2] 1878, p. 410, affords a green precipitate of so-called *thalleioquin*, or a beautifully green, clear solution. Quinine salts of the oxygen acids show, under the circumstances described in the previously mentioned work, page 409, a blue fluorescence. Quinine itself is but little used; in medicine the sulphate $(C_{20}H_{24}N_2O_2)\ H_2SO_4+7\ H_2O$[3] is particularly employed, as also the hydrochlorate of quinine.

Quinidine (conquinine or conchinin) readily yields crystals having the composition $(C_{20}H_{24}N_2O_2)_2 + 5H_2O$, but which readily effloresce. It is less abundantly soluble in ether than quinine, and its solutions deviate the plane of polarization to the right. In regard to fluorescence and the thalleioquin reaction, quinidine shows the same behavior as quinine.

Cinchonine is not capable of combining with water of crystallization ; it dissolves first in 400 parts of ether, and, even by alcohol, is not abundantly taken up.

Cinchonidine crystallizes likewise only in an anhydrous condition, is more abundantly soluble than cinchonine, and its optical behavior is the reverse of the latter.

Some noteworthy properties of this group of cinchona alkaloids, in a restricted sense, to which may still be added homoquinine and

[1] Compare Kerner, *Jahresbericht der Pharm.* 1869, p. 313; also Strecker's *Jahresbericht der Chemie.*, 1869, p. 718.

[2] See also *Pharmacographia*, second edition (1879), p. 360.

[3] It is not definitely established whether this salt contains 7 or 8 molecules of water of crystallization, or perhaps an intermediate amount.

the, indeed, very different quinamine, may be summarized as follows :—

a. Hydrated crystals are formed by	Quinine, Quinidine.
Not containing water of crystallization	Cinchonine, Cinchonidine. Quinamine, Homoquinine.
b. Abundantly soluble in ether	Quinine, Quinidine. Quinamine.
Slightly " " "	Cinchonidine, Cinchonamine.
Very sparingly " " "	Cinchonine.
c. Levogyrate solutions afforded by	Quinine, Cinchonidine.
Dextrogyrate " " "	Quinidine, Cinchonine, Quinamine.
d. Thalleioquin is afforded by	Quinine, Quinidine, Homoquinine.
" is not " "	Cinchonine, Cinchonidine, Quinamine.
e. Fluorescence is displayed in the acid solutions of salts of	Quinine, Quinidine, Homoquinine.
No fluorescence is displayed by	Cinchonine, Cinchonidine, Quinamine.

The amount of alkaloids[1] which the Cinchona barks contain is subject to considerable variation. Karsten pursued this investigation, *e. g.*, in the Cinchona corymbosa discovered by him, the trunks of which, at elevations of 3500 meters (11,375 feet), on the South-Colombian volcanoes, Cumbal and Chiles, furnished no quinine. Barks grown at other parts of this district afforded ¾ per cent. of quinine, and those from the central elevated regions, which this handsome species[2] inhabits, 1¼ to 3½ per cent. of sulphate of quinine. Cinchona lancifolia, taken in the neighborhood of Bogota from one and the same mountain ridge, contained in the bark of the branches no quinine, or only insignificant traces of the same, while trunk bark from another place gave 2, and even 4½, per cent. of sulphate of quinine.

Variations not less in extent have been proved by De Vrij[3] to occur with Cinchonas grown in Java. Calisaya trunk barks, 7 years old, gave 0.64 per cent., and those of 6½ years, from another plantation, 5 per cent. of total alkaloids. In 1873, he found in the bark of Cinchona officinalis, from Ootacamund, 1¼ to 9.1 per cent. of quinine.

In the bark of Cinchona pubescens Vahl, which, indeed, is unsalable, Hesse, in 1871, found no alkaloid at all.

[1] The analytical statements frequently refer to sulphate, and not to the amount of the bases themselves, directly separated from the bark. 100 parts of sulphate of quinine = 64 of quinine; 100 of quinine = 135 of sulphate. The Dutch analyses state the percentage of alkaloid of barks dried at 100° C. (212° F.); these values, therefore, on account of the average amount of water, 13.5 per cent. (see p. 34), must be multiplied by 0.865, in order to correspond to an air-dried product.

[2] Figure: plate X of the Flora mentioned in section 18, No. 12; also copied therefrom (uncolored) in Markham's publication (section 18, No. 21 of this work).

[3] *Pharm. Journ.*, VI (1864), p. 16.

From the few, but striking, analytical results which are here summarized, it is evident that external characteristics, including histological relations, scarcely afford a criterion for the chemical valuation of Cinchona barks. If we must abandon the attempt of determining for one and the same Cinchona a constant average percentage, this applies in a very much higher degree to the commercial varieties.

Between the complete absence of bases, and the maximum of more than 13 per cent. of quinine,[1] which has been observed up to the present time, numerous gradations occur regarding quality and quantity.

The barks of the roots appear regularly to be richer in alkaloids than those of the trunks. De Vrij, in 1869, obtained from the root bark of C. succirubra, grown in Ootacamund, 12 per cent. of alkaloid.

Of the bark of *Calisaya Ledgeriana*, grown in Java, Bernelot Moens, in 1879, examined 80 specimens. They afforded a minimum of 1.09 per cent., and a maximum of 12.50 per cent. of alkaloids, although only in 13 cases less than 5 per cent. The quinine varied between 0.8 and 11.6 per cent. The same bark furnished in following years, according to the estimations of the above-named chemist, in 100 parts of artificially (page 34) dried bark:—

	1880	1881
Total alkaloids, in minimum,	4.3	2.
" " " maximum,	9.	9.
Quinine, in minimum,	2.3	1.2
" " maximum,	8.	8.1

In the Indian C. succirubra, whose total alkaloid readily amounts to from 6 to 11 per cent., as was, moreover, already known to be the case with the original Red Cinchona of South America, the amount of quinine is small. The Indian bark often affords but 1 per cent., more rarely about 4 per cent. of quinine, and very commonly from 3 to 4 per cent. of cinchonidine. In the year 1881 the amount of total alkaloid from the bark of C. succirubra harvested in Java varied between 3.2 and 9.8 per cent., that of quinine from 0.4 to 2.5 per cent., and of cinchonidine between 1.3 and 5.2 per cent.

The above analyses of Bernelot Moens refer to average specimens from separate packages, the weight of which was from 200 kilograms, and even less, to some thousands of kilograms.

The *wood* of the roots and of the trunks of Cinchona, the latter

[1] *Blue Book*, 1870, p. 282. Bernelot Moens, in 1882, obtained as much as 13.61 per cent. of alkaloids from C. Ledgeriana.

of which, according to Van Gorkom, is adapted for cabinet-makers' work, contains, besides chinovin (see p. 61), occasionally about ½ per cent. of alkaloids, as stated by Bernelot Moens, in the annual report of the Javanese cultivation for 1880.

The *leaves* of the Cinchonas have an acidulous, bitter taste, and, after drying, an odor resembling tea. It is placed beyond doubt that they contain an insignificant amount of alkaloids, the preparation of which, in a pure state, however, is attended with greater difficulty than from the bark. Broughton, in 1870, obtained from the leaves of the Indian C. succirubra, only fractions of a per mille of alkaloid.[1] According to the experience of English physicians in India, which, indeed, is, as yet, not very extended, the leaves of *C.* succirubra deserve consideration as a febrifuge.[2] Their taste is due chiefly to chinovin, of which, *e. g.*, in the last named species, they contain as much as 2 per cent., and in general appear to contain, on an average, more than the bark. The amount of chinovin stands presumably in inverse proportion to the percentage of alkaloids.

Still more bitter than the leaves are the *flowers*, the bitterness of which, however, is not taken up by the aqueous infusion. Broughton, in 1869, found them to contain chinovin, but no alkaloid.

The *Cinchona fruits*, which likewise have a bitter taste, contain either no bases, or but an extremely small amount. O. Henry, in 1835, found none therein, as likewise DeVrij, in 1870; Broughton, in 1867, met with doubtful traces of alkaloids in fresh capsules.

If quinine or cinchonine be heated with volatile organic or inorganic acids, or with such substances as are capable of yielding them, a beautiful red decomposition product is formed. Grahe, assistant at the laboratory of the University of Kasan, has shown (1858) that the same product may be very nicely obtained from Cinchona barks. No other bases show this behavior, and barks also which contain no cinchona bases do not afford this red product. A red tar, indeed, appears also upon heating cinchona red (in so far as the latter is not most carefully freed from the alkaloids?).

Grahe's test, in combination with the simplest microscopical examination, therefore, affords an admirable means of furnishing the proof whether a bark provided with Cinchona alkaloids is at hand or not. By the entire absence, or extremely small percentage, of Cinchona bases, this reaction is not obtained, even when using a true Cinchona bark. Thus, *e. g.*, with the Cinchona from Para, and the bark designated by Winckler[3] as Calebeja, which possess

[1] *Blue Book*, 1870, p. 238.

[2] *Blue Book*, 1863, p. 264.

[3] Compare also Wigger's *Pharmakognosie*, 1857, p. 355: "clove-brown Calebeja."

the structure of true Cinchona barks, but contain, however, no cinchona bases, but paricine. Cinchona nova surinamensis does not give the red tar, which, however, is afforded by Cinchona cuprea.

Hesse renders Grahe's test more delicate by extracting with alcohol the bark to be tested, drying the tincture with an appropriate amount of powder of the same bark, and first heating the latter product.

SECTION XIV.

QUANTITATIVE ESTIMATION OF THE ALKALOIDS.

The estimation of the alkaloids may be quite satisfactorily accomplished by the following method:—

I. Twenty grams of a well selected, average specimen of the bark is very finely powdered, moistened with ammonia water,[1] and, after standing for an hour, mixed with 80 grams of hot water; it is then allowed to cool, subsequently intimately mixed with milk of lime (prepared by triturating 5 grams of dry caustic lime with 50 grams of water,) and the mixture evaporated upon a water-bath until it is uniformly converted into small, somewhat moist, crumb-like particles. This is then transferred to a cylindrical glass tube (see figure), which at *A* is 2.5 centimeters (1 inch) wide, and from *A* to *B* 16 centimeters (6.4 inches) long. At *B* a small brass sieve is inserted, upon which a disc of filtering paper is secured by means of a bunch of loose cotton. The powder having been quite compactly adjusted upon the cotton, it is again covered at *A*, as in *B*, with a little cotton; the latter having been previously employed for removing the last traces of the powdered bark from the capsule. At *E*, a tightly-fitting cork is inserted, which is penetrated by the tube *R*, and connected with an inverted, small, glass condenser. The lower end of the apparatus, *C*, is tightly connected, by means of a cork, with the flask *K*, containing about 100 cubic centimeters of ether. The flask is then heated by means of a constantly supplied water-bath; and in the same degree as the vapors of ether are expelled through *D*, they become again condensed in the condenser—the liquid dropping through the tube *R* upon the powder at *A*, penetrating the entire column of powder *A B*, and flowing at *C*, saturated with alkaloid, into the flask *K*. To effect the complete exhaustion of the bark by the ether, the operation

[1] This effects a remarkable swelling and disintegration of the tissue.

of displacement should be continued uninterruptedly for nearly a day, but when once in progress it requires but little attention. In order to determine whether the bark is completely exhausted, a few drops of the ether, falling at *C*, are collected in a test-tube, and mixed with about an equal volume of a solution of potassio-mercuric iodide (0.332 gram potassium iodide, and 0.454 gram red mercuric iodide, in 100 cubic centimeters of water); no turbidity should occur if the process of extraction has been sufficiently long continued. When this is accomplished, 36 cubic centimeters of one-tenth normal hydrochloric acid (3.65 grams HCl in 1 liter) are added to the ether in the flask *K*, the ether distilled off, and subsequently so much hydrochloric acid added as may be required to impart to the liquid an acid reaction. After having cooled, the liquid is filtered from the separated mixture of wax, chinovin and chlorophyll, 40 cubic centimeters of one-tenth normal sodium hydrate solution (4 grams NaOH in 1 liter), are added, and the whole allowed to repose until the precipitate has subsided, and the supernatant liquid has become perfectly clear. Sodium hydrate is then gradually added to the liquid as long as a precipitate continues to be produced, for which purpose a solution of the spec. grav. 1.3, is the most serviceable. The precipitated alkaloids are afterwards collected on a filter, and gradually washed with a little cold water, until a few drops of the washings, when allowed to flow on the surface of a cold, saturated, neutral, aqueous solution of quinine sulphate, cease to produce a turbidity. The drained precipitate contained on the filter is then gently pressed between bibulous paper, and dried by exposure to the air. It may afterwards readily be removed from the paper without loss, and, after thoroughly drying upon a watch-glass over sulphuric acid,[1] is finally dried at 100° C (212° F.), and weighed. The weight of the precipitate, multiplied by 5, will give the total percentage of mixed alkaloids in the bark.

If it is desired to accomplish the estimation of the alkaloids with more simple apparatus, the ether may be substituted to advantage, either wholly or in part, by higher boiling liquids; *e. g.*, by Toluol (boiling point, 111° C.), Xylol (137°), or Amylic Alcohol (129°). A method of this description has been furnished by Squibb,[2] and is very worthy of recommendation.

II. SQUIBB'S METHOD:—

"To 1.25 grams (19.29 grains) of well-burnt lime, contained in

[1] By operating in this way, the agglutination of the precipitate is avoided, and the elimination of the water facilitated.

[2] *Ephemeris of Materia Medica, Pharmacy, etc.*, Brooklyn, N. Y., 1882, pp. 78, 105.

a 10-centimeter (4-inch) capsule, 30 cubic centimeters (1 fluidounce) of hot water are added, and when the lime is slaked, the mixture is stirred, and 5 grams (77.16 grains) of the powdered cinchona[1] are added, the mixture very thoroughly stirred, and digested in a warm place for a few hours, or over night. The mixture is then dried, at a low temperature, on a water-bath, rubbed to powder in the capsule, and transferred to a flask of 100 cubic centimeters (3.3 fluidounces) capacity, and 25 cubic centimeters (0.8 fluidounce) of amylic alcohol added. The flask is afterward corked, and digested in a water-bath at a boiling temperature, with frequent, vigorous shaking, for four hours. It is then allowed to cool, and 60 cubic centimeters (2 fluidounces) of stronger ether, spec. grav. 0.728, added, and again shaken vigorously and frequently during an hour or more. The liquid is now filtered through a double filter of 10 centimeters (4 inches) diameter into a flask of 150 cubic centimeters (5 fluidounces) capacity, and the residue transferred to the filter. The flask is rinsed, and the rinsings brought on to the filter with a mixture of 10 volumes of amylic alcohol and 40 volumes of stronger ether, and the residue on the filter percolated with 15 cubic centimeters (0.5 fluidounce) of the same mixture, added drop by drop from a pipette to the edges of the filter and surface of the residue. The residue is afterward returned to the flask from whence it came, 30 cubic centimeters (1 fluidounce) of the amylic alcohol and ether mixture added, shaken vigorously for 5 minutes or more, and the whole returned to the filter, and the residue again percolated with 15 cubic centimeters of the menstruum, applied drop by drop from a pipette, as before. The filter and residue are now put aside, in order that the latter may afterward be tested in regard to the degree of exhaustion.

"The ether is now boiled off from the filtrate in the flask by means of a water-bath, taking great care to avoid the ignition of the ether vapor, and also to avoid explosive boiling, by having a long wire in the flask. When boiled down as far as practicable in the flask, the remainder is transferred to a tared capsule of 10 centimeters (4 inches) diameter, and the evaporation continued on a water-bath until the contents are reduced to about 6 grams (92 grains). This is transferred to a flask of 100 cubic centimeters (3.3 fluidounces) capacity, rinsing the capsule with not more than 4 cubic centimeters (64 minims) of amylic alcohol, and adding the same to the contents of the flask. 6 cubic centimeters (96 mimins) of water and 4 cubic centimeters (64 minims) of normal solution of

[1] A previous moistening of the bark with ammonia is also recommended.

oxalic acid are then added, and the mixture shaken vigorously and frequently during half an hour. The mixture, while intimately well mixed, is poured on to a well-wetted double filter of 12 centimeters (4.75 inches) diameter, and the aqueous solution filtered from the amylic alcohol into a tared capsule of 10 centimeters (4 inches) diameter. The filter and contents are washed with 5 cubic centimeters (80 minims) of water, applied drop by drop from a pipette to the edges of the filter and surface of the amylic alcohol. The amylic alcohol is then poured back into the flask, over the edge of the filter and funnel, rinsing the last portion in with a few drops of water. 10 cubic centimeters (160 minims) of water and 1 cubic centimeter (16 minims) of normal solution of oxalic acid are now added, again shaken vigorously for a minute or two, and the whole returned to the wetted filter, and the aqueous portion filtered off into the capsule with the first portion. The amylic alcohol is again returned to the flask, and the washings repeated with the same quantities of water and normal oxalic acid solution. When this has drained through, the filter and contents are washed with 5 cubic centimeters (80 minims) of water, applied drop by drop by drop from a pipette. The total filtrate in the capsule is evaporated on a water-bath, at a low temperature, until it is reduced to about 15 grams (241 grains) and this transferred to a flask of 100 cubic centimeters (3.3 fluidounces) capacity, rinsing the capsule with 5 cubic centimeters (80 minims) of water, and adding this to the contents of the flask. 20 cubic centimeters (0.66 fluidounce) of purified chloroform are now first added, and then 6.1 cubic centimeters (98 minims) of normal solution of sodium hydrate, and shaken vigorously for five minutes or more. While still intimately mixed by the shaking, the mixture is poured upon a filter of 12 centimeters (4.75 inches) diameter, well wetted with water. When the aqueous solution has passed through, leaving the chloroform on the filter, the filter and chloroform are washed with 5 cubic centimeters (80 minims) of water, applied drop by drop. The chloroform solution is then, by making a pin-hole in the point of the filter, transferred to another filter of 10 centimeters (4 inches) diameter, well wetted with chloroform, and placed over a tared flask of 100 cubic centimeters (3.3 fluidounces) capacity. The watery filtrate is washed through into the chloroform-wet filter with 5 cubic centimeters (80 minims) of purified chloroform, and when this has passed through into the flask, the chloroform-wet filter is also washed with 5 cubic centimeters (80 minims) of chloroform, applied drop by drop to the edges of the filter. When the whole chloroform solution of alkaloids is collected in a flask,

the chloroform is boiled off to dryness in a water-bath, when the alkaloids will be left in warty groups of radiating crystals, adhering over the bottom and sides of the flask. The flask is then placed on its side in a drying-oven, and dried at 100° C. (212° F.) to a constant weight. The weight of the contents multiplied by 20 gives the percentage of the total alkaloids of the cinchona in an anhydrous condition, to within 0.1 to 0.2 per cent., if the process has been well managed."

If it is desired to avoid the use of ether, the alkaloids liberated by lime may be taken up by xylol, toluol, or amylic alcohol at the boiling temperature, and subsequently abstracted from these solutions by means of dilute acids.

Estimation of Quinine.

"Into the flask containing the total alkaloids, after these have been weighed, are placed 5 grams (78 grains) of glass, which has been ground up in a mortar to a mixture of coarse and fine powder, and 5 cubic centimeters (80 minims) of stronger ether added. The flask is then corked, and shaken vigorously until, by means of the glass, all the alkaloids have been detached from the flask and ground up, in the presence of the ether, into fine particles. In this way the definite quantity of ether which is large enough to dissolve all the quinine that could possibly be present becomes entirely saturated with alkaloids, in the proportion of their solubility, and the solution will necessarily embrace all the very soluble ones as the quinine.

"Two test-tubes are now marked at the capacity of 10 cubic centimeters (160 minims) each, and a funnel and filter of 7 centimeters (2.8 inches) diameter placed over one of them. The filter is well wetted with ether, and the mixture of alkaloids, ether and glass poured on to it from the flask. The flask is rinsed out two or three times on to the filter with fresh ether, the filter then washed, and the glass percolated with fresh ether, applied drop by drop from a pipette, until the liquid in the test-tube reaches the 10 cubic centimeter (160 minim) mark. The funnel is then changed to the other test-tube, and the washing and percolation with ether continued until the mark on the second test-tube is reached by the filtrate. The contents of the two test-tubes are poured into two small tared capsules, evaporated to a constant weight and weighed. The first capsule will contain what may be called the ether-soluble alkaloids, and if from the weight of these the weight of the residue in the second capsule be subtracted, the remainder will be the approximate weight of the quinine extracted from the 5 grams of

bark. These weights multiplied by 20 will give the percentage of ether-soluble alkaloids, and of quinine."

Another process, which is essentially that adopted by the PHARMACOPŒIA GERMANICA (editio altera), but since improved by a slight modification, is as follows:—

III. Twenty grams of the finely-powdered bark are repeatedly and actively agitated with a mixture of 10 grams of ammonia water (spec. grav. 0.960), 20 grams of alcohol (spec. grav. 0.830 to 0.834), and 170 grams of ether (spec. grav. 0.724 to 0.728), and, after standing for a day, 120 grams of the clear liquid are poured off. After the addition of 30 cubic centimeters of one-tenth normal hydrochloric acid (containing 3.65 grams HCl in 1 liter) to the decanted liquid, the ether and alcohol are completely removed by distillation or evaporation, and, if necessary, so much hydrochloric acid added as is required to acidulate the solution. This is then filtered, and the cooled liquid mixed with 3.5 cubic centimeters of normal solution of potassium or sodium hydrate. After the alkaloids have been separated, the solution of alkali is added to the clear supernatant liquid until no further precipitate is produced. The entire precipitate is finally collected upon a filter, and gradually washed with a little water until the drops of liquid escaping from the filter, when allowed to fall upon the surface of a saturated neutral solution of quinine sulphate in cold water, no longer produce a turbidity. After being allowed to drain, the alkaloids are gently pressed between bibulous paper, then dried by exposure to the air sufficiently to admit of bringing them into a glass capsule, in which they are placed over sulphuric acid, and finally completely dried in a water-bath. The weight of the dry alkaloids, which, according to the requirement of the Pharmacopœia Germanica, should amount to not less than 0.42 gram, or 3.5 per cent., does not relate to 20 grams of the powdered bark, but only to 12 grams of the same, since only 120 cubic centimeters of liquid were decanted.

The alkaloids, which by this method are obtained somewhat less pure than by the preceding, may again be dissolved in hydrochloric acid, precipitated by alkali, then taken up by chloroform or ether, and, after the evaporation of the latter, weighed.[1]

The method of De Vrij, as adopted by the UNITED STATES PHARMACOPŒIA (Sixth Decennial Revision, 1880), for the assay of Cinchona barks, is as follows:—

[1] Compare Prollius, *Archiv. der Pharm.*, 219 (1881), p. 86; Biel, *Ibid*, 220 (1882), p. 355; and H. Meyer, *Ibid*, 220, (1882), pp. 721, 812. The weight of the residue remaining upon the evaporation of the ether corresponds approximately to the amount of quinine.

1.' For Total Alkaloids.

IV. "Twenty grams of the cinchona, in very fine powder, and fully dried at 100° C. (212 F.), are thoroughly mixed with 5 grams of lime which has previously been made into a milk with 50 cubic centimeters of distilled water, and the mixture completely dried at a temperature not above 80° C. (176° F.). The dried mixture is digested with 200 cubic centimeters of alcohol, in a flask, near the temperature of boiling, for one hour, and, when cool, the mixture poured upon a filter of about 15 centimeters (6 inches) diameter. The flask is rinsed and the filter washed with 200 cubic centimeters of alcohol, used in several portions, and allowing the filter to drain after the use of each portion. To the filtered liquid enough diluted sulphuric acid is added to render the liquid acid to test-paper, any resulting precipitate (calcium sulphate) allowed to subside, the liquid decanted, in portions, upon a very small filter, and the residue and filter washed with small portions of alcohol. The filtrate is then distilled or evaporated, to expel all the alcohol, allowed to cool, passed through a small filter, and the latter washed with distilled water, slightly acidulated with diluted sulphuric acid, until the washings are no longer made turbid by solution of sodium hydrate. To the filtered liquid, concentrated to the volume of about 50 cubic centimeters, when nearly cool, enough solution of sodium hydrate is added to render it strongly alkaline. The precipitate is collected on a wetted filter, allowed to drain, and washed with small portions of distilled water (using as little as possible), until the washings give but a slight turbidity with test-solution of barium chloride, and the filter drained by laying it upon blotting or filter papers until it is nearly dry.

The precipitate is then carefully detached from the filter, and transferred to a weighed capsule; the filter is washed with distilled water, acidulated with diluted sulphuric acid, the filtrate made alkaline with solution of sodium hydrate, and, if a precipitate results, this is washed on a very small filter, allowed to drain well, and also transferred to the capsule. The contents of the latter are now dried, at 100° C. (212° F.), to a constant weight, cooled in a dessicator, and weighed. The number of grams multiplied by 5 equals the percentage of total alkaloids in the cinchona."

The U. S. Pharmacopœia recognizes under "Cinchona" the bark of any species of cinchona containing at least 3 per cent. of its peculiar alkaloids, while the "Cinchona Flava" (Calisaya Bark) and "Cinchona Rubra" (Red Bark) are required to contain at least 2 per cent. of quinine.

2. For Quinine.

"To the total alkaloids from 20 grams of Cinchona, previously weighed, distilled water, acidulated with diluted sulphuric acid, is added, until the mixture remains for 10 or 15 minutes after digestion just distinctly acid to test-paper. It is then transferred to a weighed beaker, rinsing with distilled water, and adding of this enough to make the whole weigh 70 times the weight of the alkaloids. Solution of sodium hydrate, previously well diluted with distilled water, is now added, in drops, until the mixture is exactly neutral to test paper, digested at 60° C. (140° F.), for 5 minutes, then cooled to 15° C. (59° F.), and maintained at this temperature for half an hour. If crystals do not appear in the glass vessel, the total alkaloids do not contain over 8 per cent. of their weight of quinine (corresponding to 9 per cent. of crystallized sulphate of quinine). If crystals appear in the mixture, the latter is passed through a filter not larger than necessary, prepared by drying two filter papers of 5 to 9 centimeters (2 to 3.5 inches) diameter, trimming them to an equal weight, folding them separately, and placing one within the other so as to make a plain filter fourfold on each side. When the liquid has drained away, the filter and contents are washed with distilled water of a temperature of 15° C. (59° F.), added in small portions, until the entire filtered liquid weighs 90 times the weight of the alkaloids taken. The filter is then dried, without separating its folds, at 60° C. (140° F.), to a constant weight, allowed to cool, and the inner filter and contents weighed, taking the outer filter for a counter weight. To the weight of effloresced quinine sulphate so obtained, 11.5 per cent. of its amount is added (for water of crystallization), and 0.12 per cent. of the weight of the entire filtered liquid added (for solubility of the crystals at 15° C. or 59° F). The sum in grams multiplied by 5 equals the percentage of crystallized quinine sulphate equivalent to the quinine in the cinchona."

For the preparation of the extracts and tinctures, as also for the direct application of the bark in dispensing, it suffices to know the total amount of alkaloids. One must furthermore convince himself that quinine is present, by dissolving 1 part of the crude alkaloid in the smallest possible quantity of hydrochloric acid, precipitating the bases with caustic soda, decanting the liquid, and agitating the deposit with 20 parts of ether. The etherial solution is allowed to evaporate, and 1 part of the residue boiled with 300 parts of water and filtered, when, upon cooling, some quinine separates out. If

to 5 parts of the clear liquid there be added 1 part of chlorine water, it must assume a beautiful green color upon the direct addition of a few drops of ammonia water.

If it is desired to ascertain how much quinine is contained in a mixture of alkaloids, the latter must be accurately neutralized with either dilute sulphuric acid or with tartaric acid, as above described; the corresponding salts of quinine, on account of their sparing solubility, may readily be separated from those of the associate alkaloids.[1]

The solutions of quinine and of cinchonidine, and their salts, deviate the plane of polarization to the left, in proportion to the amount of these bases contained therein. The solutions of cinchonine and quinidine (conquinine) show an opposite behavior. With consideration of these facts, De Vrij has founded an optical method for the quantitative estimation of these alkaloids,[2] which, as further developed by A. C. Oudemans,[3] affords in very experienced hands good results.

A more recent method adopted by De Vrij[4] for the quantitative estimation of quinine consists in precipitating the latter in the form of *herapathite*, $4C_{20}H_{24}N_2O_2 + 3H_2SO_4 + 2HI + 4I + 3H_2O$, by means of a solution of iodosulphate of chinoidine.

1. Preparation of the Iodosulphate of Chinoidine.—One part of commercial chinoidine and two parts of benzol are heated together on a water-bath, whereby a solution of chinoidine in benzol is obtained. The clear solution, after cooling, is poured off from the insoluble part and agitated with an excess of diluted sulphuric acid, which, combining with the chinoidine dissolved in the benzol, yields a reddish-yellow solution of acid sulphate of chinoidine. To this clear solution, contained in a capsule, a solution of one part of iodine and two parts of potassium iodide in fifty parts of water is *slowly* added, *with continuous stirring*, so that no part of the solution of chinoidine comes in contact with an excess of iodine. One part of iodine is required for two parts of chinoidine contained in the acid solution. By this addition an orange-colored flocculent precipitate of iodosulphate of chinoidine is formed, which, either spontaneously or by a slight elevation of temperature, collects into a dark brown-red, resinous substance, while the supernatant liquid

[1] Compare Flückiger, *Pharmaceutische Chemie*, 1878, p. 414.

[2] *Pharm. Journ.*, II (1871), 521, 642.

[3] Pouvoir rotatoire spécifique des principaux alkaloïdes des Quinquina. *Archives néerlandaises* X (1875) and XII (1877).

[4] *Pharm. Journ.*, XII (1882), p. 601. A method for the rapid quantitative estimation of quinine is still wanting.

becomes clear and slightly yellow. This liquid is poured off,[1] and the resinous substance is washed by heating it on a water-bath with distilled water; after washing it is heated on a water-bath until all the water has evaporated. It is then soft and tenacious at the temperature of the water-bath, but becomes hard and brittle after cooling. One part of this substance is now heated on a water-bath with six parts of alcohol of ninety-two or ninety-four per cent., and is thus dissolved, and the solution allowed to cool. On cooling, a part of the dissolved substance becomes separated. The clear, dark-colored solution is evaporated on a water bath and the residue dissolved in five parts of cold alcohol. This second solution leaves a small portion of insoluble substance. The clear solution obtained by the separation of this insoluble matter, either by decantation or filtration, constitutes the reagent employed for the qualitative and quantitative estimation of *crystallizable* quinine.

2. Estimation of Quinine.—To determine the quantity of quinine contained in the mixed alkaloids obtained from a cinchona bark, one part (one gram) of these alkaloids is dissolved in twenty parts of alcohol, of ninety-two or ninety-five per cent., containing 1.5 per cent. of H_2SO_4, and this solution is diluted with fifty parts of pure alcohol. From this solution the quinine is separated *at the ordinary temperature*, by adding carefully, by means of a pipette, the above-mentioned solution of iodosulphate of chinoidine as long as a dark brown-red precipitate of iodosulphate of quinine (*herapathite*) is formed. As soon as all the quinine has been precipitated, and a slight excess of the reagent has been added, the liquid acquires an intense yellow color. The beaker containing the liquid with the precipitate is now covered by a watch-glass, and heated until the liquid begins to boil and all the precipitate is dissolved. The beaker is then left to itself, and, in cooling, the herapathite is separated in the well-known beautiful crystals. After twelve hours' rest, the beaker is weighed, to ascertain the amount of liquid, which is necessary in order to be able to apply later the necessary correction, the herapathite being very slightly soluble in cold alcohol. The clear liquid is poured off, as far as possible, on a filter, leaving most of the crystals in the beaker, which is now weighed again, to ascertain the amount of liquid, and the weight noted. The few crystals on the filter are now washed down into the beaker, and as much alcohol added as is necessary to redissolve all the crystals at the boiling point. The object of this redissolving is to be absolutely

[1] To prevent the use of an excess of iodine, the amount of the latter is intentionally made insufficient to precipitate all the chinoidine in the form of iodosulphate. Therefore the liquid still contains chinoidine, which can be obtained in a very pure state if a little sulphurous acid is added before precipitating the alkaloid by sodium hydrate.

certain that by surface attraction no trace of iodosulphate of cinchonidine has adhered to the crystals of herapathite. After perfect cooling, the weight of the beaker is ascertained again, the crystals of herapathite carefully collected on a small filter, and the empty beaker again weighed. The difference in weight will indicate the amount of liquid, which is added to that of the first liquid, and from the sum of this addition the necessary correction is calculated. If the operation is effected at a temperature of 16° C. (60.8° F.), the weighed quantity of the two liquids will indicate the correction if multiplied by 0.125 and divided by 100. If the temperature be lower or higher, the solubility of herapathite at that temperature must be ascertained by experiment, which can easily be performed by a standard solution of hyposulphite (thiosulphate) of sodium, as 21.58 parts of iodine found by this reagent indicate 100 parts of herapathite. The herapathite collected on the filter is thoroughly washed with a saturated alcoholic solution of pure herapathite, and after this washing is completed the liquid retained by the crystals is expelled as much as possible by slightly knocking the side of the funnel. The filter is then taken from the funnel and laid upon blotting paper, often renewed, to take away as quickly as possible the still adhering liquid. As soon as the filter is air-dry, the crystals of herapathite can be completely removed from the filter and dried on a water-bath in one of a couple of large watch-glasses closing tightly upon each other, so that the weight of the substance contained in the glass may be taken without the access of the air. If, after repeatedly weighing, the weight remains constant, it is noted, and to it is added the product of the calculated correction. The sum of this addition is the total amount of iodosulphate of quinine obtained from the mixed alkaloids subjected to the operation, and from this weight the amount of quinine can be calculated from Jörgensen's formula: $4C_{20}H_{24}N_2O_2 + 3H_2SO_4 + 2HI + I_4$. According to this formula one part of herapathite, dried at 100° C. (212° F.), represents 0.55055 parts of pure anhydrous quinine.

SECTION XV.

MANUFACTURE OF QUININE.

The preparation of quinine and the other alkaloids on a manufacturing scale consists likewise in separating them from the compounds in which they are contained in the bark, by means of lime. From the moist mixture, containing lime, the bases are extracted by means of warm shale oil, brown coal-tar oil, or petroleum of a low

boiling point, or also by means of alcohol. In the latter case the alcohol is distilled off,[1] the residue taken up by a dilute acid, and the alkaloids precipitated from the solution by means of caustic soda. From the solutions of the alkaloids in the hydrocarbons the bases may be still more conveniently taken up by dilute acids, and precipitated therefrom by caustic soda. If the washed precipitates are dissolved, by the aid of heat, in dilute sulphuric acid, avoiding an excess of the latter, there separates, upon cooling, neutral and quite pure sulphate of quinine, while the sulphates of the other alkaloids, in consequence of their much greater solubility, remain for the most part in the mother liquid. The purification of the sulphate of quinine is effected by recrystallization.

In India, Broughton (1870), in consequence of an impulse given by Markham, has taken into consideration the separation of the alkaloids in the cheapest manner. According to the suggestion of De Vrij (1872), which has been carried out since 1873 by Wood, the bark is extracted with water, to which some hydrochloric acid has been added, and the bases precipitated by means of caustic soda. The precipitate, after being washed, is dissolved in dilute sulphuric acid, again precipitated by caustic soda, and subsequently washed and dried. In 1876 the average percentage composition of such a "Febrifuge,"[2] which had been prepared by Wood, in Sikkim, from the bark of Cinchona succirubra, was found to be as follows: Cinchonine, 33.5; cinchonidine, 29.0; amorphous alkaloids, 17.0; quinine, 15.5; and coloring matter, 5.0. It is now purified to such an extent as to form a white crystalline powder. In 1877 it was calculated by the English Government that the "Febrifuge," with consideration of all expenses, could be placed at but little more than 60 *marks* (about fifteen dollars) per kilogram. It should accordingly be presumed that great significance would be attributed to this cheap remedy for India; it appears, however, at least in Madras, to enjoy no favor.

[1] Hereby cinchonine crystallizes out, when it is present in abundant amount.

[2] Also designated by De Vrij as "Quinetum." Compare *Jahresbericht der Pharm.*, 1876, p. 142, and 1878, p. 111, as also the *Blue Books*, 1870–1875, fol. 126. "Febrifuge" is now being made at Mungpoo, British Sikkim; 6196 pounds of it were used in 1881, in the Government hospitals and dispensaries in India.

SECTION XVI.

HISTORY OF THE CINCHONA BARKS TO THE YEAR 1737.

The agreeably odorous legumes of the Peru balsam tree, Toluifera Pereiræ *Baillon* (Myroxylon Pereiræ *Klotzsch*), and to a greater degree the very similar legumes of the much more widely distributed Myroxylon peruiferum *L. fil.*, have presumably been for a long time in medicinal use in Central America and in the northern portion of South America.[1] The latter in the northwestern part of South America are still called *Pépitas* (kernels) de *Quina-quina*, *Quinoquino* or *Kina-kina*.[2] According to Chifflet[3] and Joseph de Jussieu, as also according to Ch. M. de la Condamine,[4] the febrifuge bark had been referred to the same tree, and it is for this reason that the same designation has been transferred to it, which has finally become simplified into *Quina*, *Kina*, or *China*. In the South American languages, by a duplication of the sound, a superior quality of the respective substance is emphasized. Although the designation "Quina-quina" was adopted by the Europeans, the Spanish expression, "Cascarilla," obtained by the natives, even in Condamine's time, the supremacy.

From the time of the first Spanish invasion of Peru, in 1513, no proofs of an early acquaintance of the natives with Cinchona bark have been transmitted, although Arrot[5] and Condamine, as also Jussieu, heard it stated in Loxa that such was the case, and, in concurrence with Ruiz and Pavon, found the reports worthy of credence. According to these statements, the Peruvians had kept the Spaniards uninformed regarding the medicinal virtues of the Cinchona, and in Loxa, *e. g.*, they had been known from a much earlier period than in Lima. The acceptance of this statement appears to have been generally prevalent, at least toward the end of the seventeenth century, as the reminiscences of the past ages were still more active. That precise statements are wanting is explained by the entire deficiency of written documents from the old kingdom of the Incas.

[1] Compare Flückiger's *Pharmakognosie*, 2d edition, pp. 124, 131, 132, 136.

[2] Weddell, *Hist. nat. des Quinquinas*, pp. 15, 22.—Cross, *Blue Book*, 1866, p. 276.

[3] *Pulvis febrifugus Orbis Americani ventilatus*. Brussels, 1653.

[4] Weddell, loc. cit. The noble Parisian druggist, Pierre Pomet, made honest endeavors to obtain for his "*Histoire générale des Drogues*," which appeared in 1694, more accurate information regarding the trees which furnish the cinchona barks. The vague reports which he procured evidently relate also to Myroxylon.

[5] *Phil. Transactions*, vol. XL, for the years 1737 and 1738. London, 1741, No. 446. "An account of the Peruvian or Jesuit's bark."

Wellcome[1] shares the opinion, which he heard from the natives, that their ancestors were acquainted with the Cinchona bark before the Spanish conquest, although it has not been met with as yet in the ancient tombs of the Incas, as, *e. g.*, is the case with coca leaves. The reverse conviction, which is universally prevalent, is explained by Wellcome from the fact that it was the endeavor of the Spanish conquerors to appropriate to themselves all such honors. Digressive views have, however, also become current. Since the Peruvians adhere with the greatest tenacity to transmitted customs, and even at the present time do not employ Cinchona, but, on the contrary, regard it with fear, Humboldt[2] concludes that the case must have been similar with their ancestors. Markham,[3] who traveled through Peru in 1859, confirms the statement that the wallets of the native itinerant doctors,[4] who, according to a very ancient custom prevailing throughout the entire country, travel from the mouth of the Rio de la Plata to Ecuador, do not contain cinchona bark, although these still highly celebrated "Botánicos del Imperio de los Incas," also called *Chiritmanos* or *Collahuayas*, live in the West Bolivian province of Munecas, in the region of the best Cinchona trees. There prevails in general, as Pöppig (1830) and Spruce (1859) found,[5] precisely in the Cinchona districts, a strong repugnance to this remedy, even in Guayaquil.

The most probable view, however, is afforded that the earliest knowledge of Cinchona remained confined to the neighborhood of Loxa. Although the Spaniards were firmly located there as early as the middle of the sixteenth century, their earliest authors from that district are silent in regard to the Cinchona, even to the commencement of the seventeenth century. Here, in the village of Malacatos, a traveling Jesuit is said to have been cured by a *cacique*[6] of a fever by means of cinchona, and to have extended a knowledge of the remedy. To the same place and the same remedy the Spanish corregidor of Loxa, Don Juan Lopez de Canizares, is said to owe his recovery from intermittent fever, in 1630.

[1] *Proc. Amer. Pharm. Assoc.*, 1879, p. 830.

[2] Page 60 of the essay mentioned on p. 24, Note 2. Also a manuscript seen by Ch. P. von Martius, entitled "Memoria sobre el estado de las Quinas en particular sobre la de Loxa," which was written between the years 1803 and 1809, notices the intense prejudice of the Indians against the use of the "Cascarilla."—*Bulletin der Münchener Akademie*, 1846, No. 55; *Gelehrte Anzeigen*, p. 342.

[3] Clements R. Markham. "Two Journeys in Peru," 1862, 2. The German Translation, Leipsic, 1865, 186.

[4] Compare Beck, in Petermann's *Geogr. Mittheilungen*, 1866, p. 377; also Markham, "Peruvian Bark," 162.

[5] Compare also the *Blue Book*, 1863, p. 75.

[6] Priest of the worshipers of the sun.

On the 11th of August, 1621, Ana de Osorio, widow of Don Luis de Velasco, married Don Luis Geronimo Fernandez de Cabrera y Bobadilla, of Madrid, the fourth Count of Chinchon. The year 1628 brought to the Count the highest distinction that was attainable in Spain—he was appointed Viceroy of Peru, *i. e.*, regent of the entire Spanish territory in South America. On the 14th of January, 1629, the vice-regal pair entered Lima.[1] As the Countess, in 1638, was prostrated by a fever in the palace at Lima, the same corregidor of Loxa sent Cinchona bark to the vice-regal physician, Dr. Juan de Vega. In the treatment of the Countess Chinchon the virtues of the remedy were also confirmed, so that she caused it to be distributed in Lima.[2] Even here the powdered bark acquired the name of *Polvo de la Condesa* (Countess Powder). A knowledge of this febrifuge must have very soon penetrated into Spain, even if it may be doubted that this took place as early as the year 1632, before the cure of the Countess, as has been stated by Villerobel.[3] In 1639 Cinchona bark certainly appears to have been used in Alcala de Henares, near Madrid.[4]

Perhaps, also, with relation to the first Jesuit treated therewith at Malacatos, the bark soon received the name of *Polvo de les Jesuitos*, as this Order, especially through the Cardinal connected therewith, Juan de Lugo, residing at Rome, began to zealously adopt the new remedy.[5] As Nicolas Lémery declared, the Jesuits derived great profit therefrom. In the meantime, however, the same physician, Juan de Vega, on the occasion of the return of the viceroy to Spain, had, as early as 1640, likewise taken Cinchona with him, and, *e. g.* sold the same in Seville at 100 *reals* (about 100 dollars) per pound.

The Cardinal de Lugo, Attorney-General of the Order of Jesuits, had, as it appears, the superintendence of a pharmacy belonging to them, but permitted, however, also in his palace the distribution of cinchona bark to the indigent sick, which, therefore, became known as "Pulvis eminentissimi Cardinalis de Lugo," or "Pulvis

[1] With regard to the Count Chinchon, who conducted the Government of Peru until the 17th of December, 1639, compare also Flückiger's *Pharmakognosie*, p. 85.

[2] With relation to the earliest history of the cinchona barks, compare further the publications of H. von Bergen, Weddell and Markham, which are mentioned by name in Section 18 of this work.

[3] H. von Bergen, 84, 90.

[4] Sebastiano Bado. *Anastasis, Corticis Peruviæ, seu Chinæ Chinæ defensio.* Genoa, 1663, 202.

[5] Chiffletius, l. c. According to the *Biogr. Universelle*, Paris, 1821, Juan de Lugo was born in 1583, at Madrid, entered the Order of the Jesuits in 1603, was made a cardinal in 1643, and died at Rome in 1660. Also the same, according to Lorenzo Cardella, *Mem. storiche de' Cardinali della Santa Romana Chiesa* VII. (Roma, 1797) 47.

patrum."[1] In 1649, de Lugo, in passing through Paris, recommended the remedy to the Cardinal Mazarin for the young Louis XIV, who was sick with a fever. The Jesuits in Rome received at this time a quantity of Cinchona from their Provincial from America, who, in 1643, went to the Chapter of the Order at Rome.[2] Michael Belga at this time likewise brought Cinchona from Lima to Antwerp and Brussels.

Belgian physicians likewise contributed materially to the knowledge and distribution of Cinchona. Through Chifflet, physician to the Archduke Leopold, of Austria, Governor of the Netherlands, this was effected in a publication which appeared at Brussels, in 1653 (or 1651?), entitled "Pulvis febrifugus Orbis Americani ventilatus." Although Chifflet prized the Cinchona bark as a marvel of his time, he recommended it, however, so mildly that a heated controversy[3] arose, in which, *e. g.* Glantz (1653), an imperial physician at Ratisbon, as also Godoy, a physician of the Spanish King, and Moreau and Plempius (1655) stood and wrote in Chifflet's defence. As active opponents of these physicians there appears decidedly in favor of the bark the Jesuit, Honoratius Faber, Fonseca, physician to Pope Innocent II, Sebastian Bado,[4] of Genoa, and especially, in 1653, Doctor Roland Sturm,[5] of Louvain. The latter communicates also the detailed directions for its use in 1651, which the apothecaries of Rome were accustomed to give with the bark when dispensing it.[6]

The Cinchona began to be known in England about the year 1655, and in 1658 was repeatedly advertised for sale in the "Mercurius Politicus," one of the earliest newspapers of England, by the Antwerp merchant, James Thompson, as "*the excellent powder known by the name of the Jesuits' Powder.*" Brady and Willis, two distinguished English physicians, prescribed Cinchona bark in the year 1660.[7]

It is very remarkable that Cinchona bark is not contained in the Pharmacopœia of the Hague, of the year 1659; in 1664 it was designated a dutiable product at Lyons.[8]

[1] Roland Sturm. *Febrifugi Peruviani vindiciarum pars prior: Pulveris historiam complectens ejusque vires et proprietates . . . . . exhibens.* Delphis, 1659, 12°.

[2] Chiffletius, l. c.; Sprengel, *Geschichte der Arznayhunde*, IV (Halle, 1827), 513.

[3] The more complete title of these older publications is given by H. von Bergen, pp. 1–72; also in Mérat et De Len's *Dictionnaire de Mat. Med.* V (1833), p. 632.

[4] Page 83, note 4. [5] Note 1.

[6] "Modo di adoprare la corteccia chiamata della febre," reprinted in Flückiger and Hanbury's *Pharmacographia*, second edition, p. 343.

[7] See *Pharmacographia*, second edition, p. 344.

[8] Martiny, *Rohwaarenkunde*, I (1843), p. 3.

In Germany, "*China Chinæ*" is met with in the pharmaceutical tariffs of Leipsic and Frankfort for the year 1669. According to the latter, one "quint" (one-eighth of an ounce) cost 50 kreuzers (about 38 cents), whereas the same amount of opium was quoted at 4 kreuzers, camphor at 2 kreuzers, and balsam of Peru at 8 kreuzers.

It is conceivable that at that time other barks possessing a bitter taste might be mistaken for Cinchona bark. An indeed very remarkable example of this kind is afforded by the *Cascarilla bark*[1] from Croton Eluteria, a small tree belonging to the family of Euphorbiaceæ. This drug from the West Indies, which possesses a bitter, but at the same time, however, a strongly aromatic taste, made its appearance in Germany toward the close of the seventeenth century, under the name of *China nova;* but, as it appears, soon passed into oblivion, and at the beginning of this century the same name was again bestowed upon an entirely different bark, namely, that of Cascarilla magnifolia (mentioned on p. 48). It may, indeed, be accepted that in the meantime still other barks were frequently confused with or used to adulterate the Cinchona barks.[2]

The further distribution of Cinchona was advanced in a high degree by Robert Talbor, a physician who emanated from a pharmacy in Cambridge, and who, in 1672, made himself known through the publication of "*Pyretologia, a rational account of the cause and cure of agues,*" in which also "Jesuits' Powder" is spoken of. In 1678 Talbor was appointed physician to King Charles II, and also made a knight; in 1679 he treated the King at Windsor with Cinchona, and received then also not less favor at the French Court.[3] It is remarkable that Talbor knew how to envelop his cures with such secrecy that he was able to make his chief remedy, cinchona bark, contribute in the most successful manner to his personal profit. As, in 1681, after Talbor's death, King Louis XIV caused the composition of the remedy to be made known, cinchona bark was revealed as its chief constituent, and now attracted the renewed attention of physicians.[4]

A worthy successor of Talbor, Nicolas Blegny,[5] likewise physi-

[1] Flückiger, *Pharmakognosie*, second edition, p. 573.

[2] Compare Flückiger, *Pharmakognosie*, 2d edition, under Quassia, p. 461; *Pharmacographia*, 2d edition, p. 106—*Quina de Caroni.*

[3] Mérat et De Lens, *Dictionnaire de Matière médicale*, V (1833), 627.

[4] More complete information regarding Talbor is contained in *Pharmacographia*, 2d edition, pp. 344 and 766.

[5] Compare further regarding the character of this swindler, who followed the occupation of physician and apothecary in Paris, until, in 1686, he was placed in the Bastile. Grave, *État de la Pharmacie en France.* Mantes, 1879, p. 179.

cian to Ludwig XIV, dedicated in 1682 to the "Remède Anglais," an oft-quoted pamphlet. The first physician of the King, Antoine d'Aquin, and Fagon, physician to the Queen, were commissioned to receive from Talbor the secret recipe.[1] Fagon, in 1704, assigned to the Franciscan botanist, Charles Plumier, who was to undertake his fourth journey to South America, the commission to determine the origin of the Cinchona barks. Plumier died, however, at Cadiz.[2]

In the meantime, living Cinchonas had already found their way to London, or were cultivated there from seed,[3] and for a not uninteresting short report on the "Peruvian Bark" or "Jesuits' Bark," we are indebted to the Scotch surgeon, William Arrot, who, about the year 1730, had made observations in Loxa.[4] He described accurately the work of the Cascarilleros, and, even at this time, expressed solicitude regarding the extermination of the trees.

SECTION XVII.

MORE RECENT HISTORY OF THE CINCHONA BARKS.

The knowledge of the Cinchonas was introduced in a scientific spirit by the otherwise celebrated expedition of the Paris Academy. In their commission, the astronomers, Charles Marie de la Condamine, Bouguer and Godin, were occupied, from the year 1736 to 1744, in measuring the arc of a degree in Peru. At the same time improving every opportunity for the advancement of other branches of natural science, Condamine, in accordance with the directions of Joseph de Jussieu, on the 4th of February, 1737, on the journey from Quito, by way of Cuenca, to Lima, observed one of the Cinchona trees on the mountain of Cajanuma, 2½ leagues southward from Loxa, which Arrot (page 81) had also already named. In the following year Condamine's[5] description and figure of his "arbre de quinquina" was laid before the Paris Academy, and was published by the latter in 1740. According to Howard, this first

[1] *Les admirables qualitez du Kinakina, confirmées par plusieurs expériences.* Paris, Jouvenel libraire, 1689. 164 pages, in 8°. (Without the name of the author).

[2] Cap, *Études* (mentioned on p. 47).

[3] According to the short notice in Semple, *Memoirs of the Botanic Garden at Chelsea*, belonging to the Society of Apothecaries in London, 1878, p. 16: "In 1685, August 7th, I went to see M. Watts, Keeper of the Apothecaries' Garden of Simples at Chelsea, where there is a collection of innumerable variety of that sort; particularly . . . . the *tree bearing Jesuits' bark*, which had done such wonders in quartan agues."

[4] See p. 81, Note 5.

[5] *Hist. de l'acad. roy. des sciences, ann*, 1738, *avec les mém. de math. et de phys. pour la même année.* Paris, 1740, pp. 226–243.

described Cinchona tree is the Cinchona officinalis, Var. *α* or *β* Uritusinga of the present day. Jussieu, the botanist of the above-mentioned French expedition, who was moreover also an engineer and physician, collected likewise, in 1739, near Loxa, a Cinchona—the subsequent C. pubescens *Vahl.* Mutis also soon received what was presumably the same, from the same district, and sent it to Linnæus. The latter, in honor of the Countess *Chinchon*, as shown on page 18, did not name the genus *Chinchona*, but *Cinchona.* This orthography has also found universal acceptance, and, in 1866, was even sanctioned by a resolution of the International Botanical Congress at London.[1] Markham, to whom we are indebted for a handsome publication,[2] dedicated to the memory of the Countess Chinchon, had effectuated that the English authorities at first made use of the orthography Chinchona.

In the beginning of the eighteenth century the commerce in barks at Loxa was already much developed; and it was necessary for good barks to be recommended by a certificate of their origin from this locality. In Payta (5° S. lat.), the nearest port, an examination of the bark for adulterations was already established.[3]

In 1752 the "Superintendente general de la moneda," superintendent of the mint at Santa Fé, Don Miguel Santisteban, was delegated to go to Loxa, in order to organize the commerce in Cinchona bark. He reported thereon, in 1755, to the respective administration, "Estanco de Cascarilla," and added that he had met on the way with Cinchona trees. Among these, according to Triana,[4] was also the present Cinchona cordifolia, which Santisteban had found between Pasta and Barruecos, in the southwestern part of New Granada. He brought specimens of the plant with him for Mutis, who visited Santa Fé in 1761.

José Celestino Mutis, who was born at Cadiz in 1732, arrived in 1760 at Carthagena, in New Granada, with the newly-appointed viceroy, the Marquis de Vega, as his physician,[5] and soon found an opportunity to make application of his botanical knowledge in the exploration of the flora of that country. He first started from

[1] Howard, Observations on the present state of our knowledge of the genus *Cinchona. Proceedings of the Internat. Horticult. Exhibition and Botanical Congress, held in London*, 1866, p. 195–223. Abstracted in the *Archiv der Pharm.*, 130 (1867), p. 91, and more completely in Buchner's *Repertor für Pharm.*, 17 (1868), p. 65.

[2] Title under section 18, No. 22.

[3] *Pharmacographia*, second edition, p. 345.

[4] *Études*, title under section 18. Also Humboldt, p. 113, of the essay mentioned on p. 24, note 2.

[5] In 1772 Mutis entered a religious order, and afterward became a teacher of mathematics and astronomy at Santa Fé de Bogotá, where he died, on the 2d of September, 1809.

Cácota and La Montuosa, near Pamplona, then, since 1782, from Real del Sapo and Mariquita, at the foot of the Quindia, and, finally, since 1784, at the head of an "Expedicion botanica del Nuevo Reino de Granada," in Santa Fé.

In the meantime (1776) Don Sebastian José Lopez Ruiz[1] presented to the viceroy in Santa Fé a Cinchona, which, according to Triana, was *Cinchona lancifolia*, or *Tunita*, in the language of that country. This species (p. 18) grows only in the eastern district of the Cordilleras of Bogota. Mutis himself, before his removal to the capital, explored only the western chain of mountains at the upper part of the Magdalena River, near Mariquita, Tena, and Honda, where, according to the experience of Triana, no true Cinchona grows. The pretended Cinchona found by Mutis in this district, in the year 1771, is rather simply one of the species of Cascarilla comprehended by him under the name of C. oblongifolia, probably Cascarilla magnifolia (compare p. 48). The Cinchona collected by Mutis, in 1766, in the province of Pamplona, northward from Santa Fé, is also, according to Triana, only *Cosmibuena obtusifolia* Ruiz et Pavon, and by no means a true febrifuge tree.

All of the true Cinchonas which are contained in the "Quinologia de Bogota," of Mutis, under the names of C. lancifolia and C. cordifolia, were discovered by Santisteban, Lopez Ruiz, or his nephew, Sinforoso Mutis, and the pupils of the former; not a single one by Celestino Mutis himself.

Triana produces valid reasons for this statement, so that the contention for priority, which at that time was carried on with much animosity between Mutis on the one hand and Ruiz and Pavon on the other, together with the adherents of both parties, is herewith brought to a close. In consequence of Mutis having transferred the name of *Red Cinchona*, *Quina*, or *Cascarilla colorada*, or *roja* to the worthless bark of the trees which he named Cinchona oblongifolia, containing no quinine, whereas it properly belongs only to the bark of C. succirubra, rich in alkaloid, a complication ensued, which was first removed by the discovery of quinine, in the year 1820.

After the Cinchona barks, since about the year 1640, had only been exported from Peru and Ecuador of the present day, through the activity which Mutis and his pupils developed in the northwestern part of the South American Continent, the attention of botanists and merchants was directed to the Cinchona trees of this

[1] This otherwise insignificant man appeared as an opponent of Mutis in the publication: *Defensa y demonstracion del verdadero descubridor de las Quinas del reino de Santa Fé.* Madrid, 1802 (Colmeiro p. 69). Compare further, Triana, *Études*, p. 45.

district. From a practical point of view, it was, indeed, important enough to no longer be compelled to transport the barks around Cape Horn or over the Isthmus of Panama. This result remains in its significance uncontended to the favor of Mutis even though Triana has proved that it was not Mutis himself who first recognized a Cinchona outside of the above-mentioned original Cinchona region.

The particular circumstances of the personal meeting of Humboldt with Mutis at Santa Fé de Bogotá, in the year 1801, were, indeed, as Triana has shown, of so happy a nature that it may readily be conceived how Humboldt was led to esteem the Spanish dilettante higher than posterity, which is more inclined to estimate the achievements alone, independent of the background of the station in life of the respective individual.

Humboldt and Bonpland took consideration of the collection of Mutis, and rendered prominent therefrom the particularly handsomely executed colored drawings of the plants of his district. Humboldt, in a biography,[1] written with warm recognition, dedicates to this man a memorial replete with honor, which even Linnæus has over-estimated, and termed "phytologorum americanorum princips."

In 1777 the Spanish Government appointed Hipolito Ruiz director of a natural science expedition for the exploration of Peru and Chili. Ruiz, accompanied by José Pavon and the French botanist, Joseph Dombey (p. 47), arrived in 1778, at Lima, and, after the return of the latter, continued his labors with Pavon. In 1788 they likewise went again to Madrid, where Ruiz, in 1792, as the first fruit of the expedition, published the *Quinologia ;* this was followed, in the years 1798 to 1802, by the *Flora peruviana et chilensis.* In Peru and Chili the task of Ruiz and Pavon was continued by their pupil, Juan Tafalla, who, in turn, was assisted by Mancilla,[2] and likewise contributed to the knowledge of the Cinchonas.

While Mutis did not bring his labors to any conclusion, and the botanical collection left by him, perhaps not even complete, first

[1] *Biographie Universelle*, Tome XXX, Paris, 1821. The celebrated *Plantes équinoctiales* Humboldt and Bonpland have adorned with a handsome likeness of Mutis. Regarding Mutis, compare further Triana's *Études*, and Schumacher's interesting disquisition, "Linné's Beziehungen zu New Granada." *Verhandlungen der Gesellschaft für Erdkunde zu Berlin*, 1880, pp. 98–110.

[2] Compare regarding the above-named Spanish botanists, Colmeiro, *La botánica y los botánicos de la peninsula hispano-lusitana*, Madrid, 1858; as also Chiarlone y Mallaina, *Historia critico-literaria de la Farmacia.* Tercera edicion. Madrid, 1875. The latter name Ruiz more completely, Don Hipolito Ruiz Lopez. He was born in 1754, at Belerado, in the old Castilian province of Burgos, and died in 1816, at Madrid.

arrived at Madrid about the year 1820, and has remained deposited there,[1] Ruiz published in the *Quinologia*, and in 1801, conjointly with Pavon, in a supplement thereto, the most important results relating to the Cinchonas. The material left by the latter has served in our day for the foundation of the magnificent work of Howard. (See section 18, No. 9).

The investigations of these botanists, to which we are indebted for the first knowledge of most of the Cinchonas, led to a revolution in the commercial relations of the barks, in that, gradually, about the year 1785, central and southern Peru, as also New Granada, entered into competition with the district of Loxa, and began to export barks by way of Callao and the ports located on the Caribbean Sea.

The selection of the barks which were at that time preferred was confined to the barks of the branches and twigs, although Condamine had himself ascertained in Loxa that originally the strongest, and thus, presumably, the trunk barks, had been more highly valued. The greater difficulty of drying experienced with the thick trunk barks presumably contributed thereto that the collectors directed their attention more to the bark of the twigs. The Paris druggist, Pomet,[2] expressly recommended only the "petites écorces fines, noiratres et chagrinées au dessus, parsemées de quelques mousses blanches . . . . . " and likewise, in 1724, in the London market, according to the druggist, Berlu,[3] the thick, flat trunk barks were valued much less than the barks of the twigs. After the discovery of the cinchona alkaloids it was shown that the trunk barks, particularly the flat Calisaya, were usually richer in quinine, so that these were again more highly prized until, namely, Calisaya Ledgeriana furnished the proof that also in young barks much quinine can be formed.

After the discovery of quinine and cinchonine the botanical and pharmacognostical investigation of the Cinchonas also received a new impulse, which was due, *e. g.*, to the labors of Laubert, Lambert, and particularly in 1826 to Heinrich von Bergen's 'Versuch einer Monographie der Chinarinden." As a drug-broker in Hamburg, this industrious man, in his work, not only made application of a practical experience extending through many years, but also in other considerations placed everything

[1] Planchon, *Quinquinas*, p. 14.

[2] *Histoire générale des Drogues.* 1694, p. 133.

[3] *The treasury of drugs unlock'd.* London, 1724 (first edition, 1690), "Cortex peruanus, Jesuits' bark, China China, Cascarello, Cortex Patrum, from smaller twigs ; that which is very thick and flat is nothing near so good."

together which science could offer regarding this subject; and especially with regard to the history of the remedy, reference must also be made to Bergen's monograph. A valuable supplement consists in 7 colored plates with admirable figures of Cinchona rubra, Huánuco, Calisaya flava, Huamalies, Loxa and Jaen; the descriptions of these barks accomplished all that is possible without the aid of the microscope.

For the application of this latter and most important aid in the study of the Cinchona barks, and for the first figurative representations of the anatomical views thereby obtained, we are indebted to Weddell (died July 22, 1877). The extraordinary significance of his *Histoire Naturelle des Quinquinas*, the fruits of extended travels (1845 and 1848) in Bolivia and Peru, has been everywhere in the preceding pages sufficiently valued.

How much we are furthermore indebted to the two above frequently mentioned works of Howard and Karsten is manifest from this entire representation. In the "Floræ Columbiæ terrarumque adjacentium specimina selecta" the latter gives, as the fruits of observations extending through many years at the place itself, descriptions and magnificent figures of Cinchona cordifolia, C. corymbosa, C. lancifolia, and C. tucujensis, as also a number of species still comprehended by him as Cinchonas, which, at the present time, are no longer enumerated among the latter, as has been explained on pages 10, 20 and 51.

The knowledge of the Cinchonas received further enrichment through the likewise above-mentioned "Quinologie," for the publication of which, in 1854, the quinine manufacturer Delondre, and the chemist and apothecary Bouchardat had associated, after the former (accidentally), in Weddell's company, had made a visit to the forests of Santa Ana, near Cusco. Among the 23 plates of this *Quinologie* are found not only the officinal Cinchona barks, but in general all those which occurred in the wholesale trade of that time, together with some false Cinchona barks, very accurately reproduced; with each bark the yield of alkaloid on a manufacturing scale is designated. Phœbus[1] has dedicated to the barks of the "Quinologie" an elaborate microscopical investigation.

The conclusion of so many still open questions regarding the Cinchonas remains to be hoped for through their forest cultivation, concerning the development of which the interesting official reports of the English and Dutch continually afford information.

It would be very desirable to have a complete systematic knowledge of the entire division of the Cinchoneæ, and the comparative

[1] *Die Delondre Bouchardat'schen Chinarinden.* Giessen 1864, 8°, pp. 74.

examination of the barks of every individual species from a chemical and anatomical point of view.

SECTION VIII.

LIST OF THE MORE RECENT PUBLICATIONS RELATING TO THE CINCHONAS AND THE CINCHONA BARKS.

1. Berg (Otto). *Die Chinarinden der pharmakognostischen Sammlung zu Berlin.* Berlin, 1865. 48 pages and 10 plates. Quarto. Price 8 marks (about $2). The plates give transverse sections of the barks of the following Cinchonas: C. amygdalifolia, Calisaya, Chahuarguera, Condaminea, cordifolia, heterophylla, lancifolia, lucumæfolia, macrocalyx, micrantha, microphylla, nitida, ovata, Palton, Pelletiereana, scrobiculata, succirubra, umbellulifera, Uritusinga. Furthermore, transverse sections of Cinchona (China) nova surinamensis (from Cascarilla magnifolia, see page 48), and of the bark of Nauclea Cinchona D. C.
2. Bergen (Heinrich von). *Monographie der China.* Hamburg, 1826. 4°. 348 pages and 7 colored plates, with figures of Cinchona Calisaya, C. flava, C. Huamalies, C. Huanuco, C. Jaén, C. Loxa and C. rubra.
3. Bidie. *Cinchona culture in British India, being a brief sketch of its origin, with practical hints on the chief points connected with the industry.* Madras, 1879. 24 pages, with (not handsome) figures of Calisaya Ledgeriana and the so-called Cinchona "pubescens" (mentioned on page 15).
4. *Blue Books.* Under the titles of *Return, East India, Cinchona Plant* or *Cinchona cultivation*, are published the official proceedings which relate to the introduction of the Cinchonas into India and the British colonies.[1]

The following Blue Books, which are dedicated to this subject and its further development, have at present appeared (small folio with maps and wood-cuts):—

a. *Copy of Correspondence relating to the Introduction of the Cinchona plant into India*, etc., from March 1852 to March 1863. 272 pages and 11 maps (Cinchona region in South America, environs of Lake Titicaca, Province of Caravaya, the Chimborazo).

Contains correspondence of Royle, Markham, Spruce, Pritchett, Cross, McIvor, Anderson and others.

b. *Copy of further Correspondence*, etc. April 1863 to April 1866. 379 pages, with two maps of New Granada and Southern India.

[1] The Blue Books can be purchased at No. 13 Great Queen street, Lincoln's Inn Fields, London.

Contains monthly reports of the plantations on the Neilgherry Hills; annual reports for 1863–64, 1864–65, with details of method of propagation and cultivation, barking, mossing, attacks of insects, illustrated by wood-cuts and 4 plates; report of Cross's journey to Pitayo, with map; Cinchona cultivation in Wynaad, Coorg, the Pulney Hills and Travancore, with map; in British Sikkim, the Kangra Valley (Punjab,) the Bombay Presidency and Ceylon.

c. *Copy of all Correspondence*, etc. April 1866 to April 1870. 285 pages and one map of Southern India.

Contains reports on the Neilgherry and other plantations; appointment of Mr. Broughton as analytical chemist, his reports and analyses; reports on the relative efficacy of the several cinchona alkaloids; on cinchona cultivation at Darjiling and in British Burmah.

d. *Copy of the Cinchona Correspondence.* August 1870 to July 1875. 190 pages.

Contains also reports on the manufacture of the alkaloids in India, collection, shipment and analyses of barks.

The numerous facts derived from the Blue Books in the present representation of this subject may give an idea of the richness of their contents.

5. Delondre (Augustin). See Soubeiran et Delondre.
6. Delondre (Augustin Pierre) et Bouchardat (Apollinaire). *Quinologie*, Paris, 1854, 48 pages and 23 plates. Quarto. Colored figures of more than 30 different true and false Cinchona barks, representing their natural appearance very accurately.
7. Gorkom (K. W. van). *Die Chinacultur auf Java.* Leipsic, 1869, 61 pages. An account of the management of the Dutch plantations. *Handbook of the Cinchona Culture*, translated by P. D. Jackson, London, 1883; royal 8vo, 292 pages and one plate.
8. Hesse (Oswald). The researches of this chemist are summarized in the articles *Chinarinden*, *Chinin*, *Cinchonin*, Conchinin, etc., in Fehling's *Neues Handwörterbuch der Chemie*, Band II, 1876 to 1877.
9. Howard (John Eliot). *Illustrations of the Nueva Quinologia of Pavon.* London, 1862, 163 pages and 30 plates; large folio; 28 beautifully colored figures of Cinchonas, and two plates representing the microscopical structure of the barks. Price 126 *marks* (about 30 dollars). A *German* edition of the "Nueva Quinologia" has been published by the Austrian Pharmaceutical Association. Vienna, 1862, 178 pages, 8vo, *without* the figures

(to be had in London at Lovell, Reeves & Co., Henrietta street, Covent Garden).

10. Howard (J. E.) *Quinology of the East Indian Plantations.* London, one part, 1869; folio; X and 43 pages, with three plates, representing the microscopical structure of cultivated Cinchona barks.

Parts II and III, 1876; folio; XIV and 74 pages, with two (not very successful) views of Indian Cinchona plantations, and beautiful figures of Calisaya Ledgeriana, Cinchona officinalis, C. pitayensis Wedd. (C. Trianæ Karst.), and others. Price of the three parts 84 *marks* (about 21 dollars). Compare furthermore page 63, note 1, and page 87, note 1.

11. Karsten (Hermann). *Die medicinischen Chinarinden New Granadas.* Berlin, 1858, 62 pages, 8vo, and two plates, representing the microscopic structure of transverse sections of Cinchona Calisaya, C. lancifolia, C. Uritusinga, Cascarilla (Ladenbergia) oblongifolia, Cascarilla macrocarpa and others. An English translation, prepared under the supervision of Mr. Markham, has been published by the India Office, under the title of *Notes on the Medicinal Cinchona Barks of New Granada,* by H. Karsten, 1861. The plates have not been reproduced.

12. Karsten (Hermann). *Floræ Columbiæ terrarumque adjacentium specimina selecta.* Berlin, 1858; large folio. The first four parts of this magnificent work give colored figures of the following Cinchonas and allied species, which are likewise designated by the author as Cinchonas: Cinchona barbacoënsis, C. bogotensis, C. cordifolia, C. corymbosa, C. Henleana, C. lancifolia, C. macrocarpa, C. macrophylla, C. Moritziana, C. pedunculata, C. prismatostylis, C. Trianæ, C. tucujensis, C. undata.

13. King (George). *A Manual of Cinchona cultivation in India.* Calcutta, 1876, 80 pages; small folio. Second edition, 1880, 105 pages (out of print).

14. Kuntze (Otto). *Cinchona. Arten, Hybriden und Cultur der Chininbäume.* A monographic study based upon personal observations in the plantations of Java and the Himalaya. Leipsic, 1878, 124 pages, with 3 plates. Compare the review in the *Archiv. der Pharm.* 213 (1878) pp. 473–480.

15. Lambert (Aylmer Bourke). *A description of the genus Cinchona, comprehending the various species of vegetables from which Peruvian and other barks of a similar quality are taken.* London, 1797, 4to, 54 pages and 13 plates, in which are figured a specimen of Cinchona officinalis sent by Condamine, in 1740, to London, C. pubescens, derived from a plant of Jussieu (see pages

18 and 19), as also nine other Rubiaceæ designated as Cinchona. This publication, pages 30–36, gives also the history of the so-called *China* (*Cinchona*) *bicolor*, *China* (*Cinchona*) *Pitoya or Tecamez*, found by the naval physician, D. Brown, in Tecamez, or Atacamez, on the coast of Ecuador. The origin of this bark, which is free from alkaloid, and is occasionally mixed with the American varieties, still remains unknown; it has not the remotest resemblance to any Cinchona bark.[1]

16. Lambert. *An illustration of the genus Cinchona, comprising descriptions of all the officinal Peruvian barks, including several new species, Baron de Humboldt's Account of the Cinchona Forests of South America and Laubert's Memoir on the different species of Quinquina, etc.* London, 1821, 4°.

17. Laubert. *Recherches botaniques, chimiques et pharmaceutiques sur le Quinquina. Journal de Médecine, chirurgie et de pharm. milit.* Juillet 1816. An English translation is given in Lambert's "Illustration," etc.

18. MacIvor (William Graham). *Notes on the propagation and cultivation of the medicinal Cinchonas or Peruvian bark trees.* Madras, 1867. 33 pages and 9 plates. The second edition, Madras, 1880, 90 pages, includes the following publication, both as unchanged reprints.

19. MacIvor (W. G.). *A letter on the cultivation of Cinchona in the Nilgiris.* Printed for private circulation only. Ootacamund, 1876. 27 pages. 8°. The principal information contained in both of these publications may also be found in the Blue Books, further in Gorkom's publication, see page 93 No. 7.

20. Markham. *Zwei Reisen in Peru.* A German translation. Leipsic, 1865.

21. *Markham. The Chinchona species of New Granada, containing the botanical descriptions of the species examined by Drs. Mutis and Karsten; with some account of those botanists, and of the results of their labors.* London, 1867. 139 pages. The five plates are reduced, uncolored lithographic copies of the (colored) figures of the true Cinchonas in Karsten's work, mentioned on page 94, No. 12; they represent the following: Cinchona corymbosa, C. Trianæ, C. lancifolia, C. Cordifolia, C. tucujensis.

22. *Markham. A Memoir of the Lady Ana de Osorio, Countess of Chinchon and vice-queen of Peru (A. D. 1629–1639), with a plea*

[1] An, indeed, somewhat imperfect figure of the "Tecamez bark" is contained in Göbel and Kunze, *Pharm. Waarenkunde* I (1827–1829) Plate XII. Compare further regarding this bark, Martiny, *Rohwaarenkunde* I (1843), 387. Vogl, *Falsche Chinarinden* 10. Oberlin et Schlagdenhauffen, *Journ. de Pharm.* 28 (1878), 252.

for the correct spelling of the Chinchona genus, by Clements R. Markham, C. B., F. R. S., commendador da Real Ordem de Christo, Socius Academiæ Cæsareæ Naturæ Curiosorum, cognomen Chinchon. London, Trübner & Co., 1874. 99 pages, 4°, with wood-cuts, a map, and 2 heraldic figures in gold print. Price 28 *marks* (about $7).

The title of this elegantly executed polemic represents its purpose, the displacement of the word Cinchona by the diplomatically more correct *Chinchon* (see page 87). The author gives, furthermore, all the information regarding the Countess Chinchon, which, through his sagacity, was still capable of being obtained from her home. Compare, regarding this publication, the review in Buchner's *Repertorium für Pharmacie*, XXIV (1875), 178; also Hanbury, *Science Papers*, 1876, page 475.

23. Markham. *Peruvian Bark. A popular account of the introduction of Chinchona cultivation into British India.* With maps and illustrations. London, 1880, 550 pages, three maps, and three tolerably good illustrations. This book is based upon those mentioned under Nos. 4, 20 and 21, without presenting any new results. Price 14 *marks* [about 3½ dollars]. The principal chapters contained therein are the following: The knowledge of the bark possessed by the natives of Peru; the Countess Chinchon; discovery of the Cinchona trees; description of the same and of their barks; their removal to India; cultivation of coca (Erythroxylon Coca); Ledger's merit; services of the English travelers, Spruce, Pritchett, Cross, Weir, Markham; plantations in India, Ceylon, Java, Jamaica and Mexico; preparation of the crude alkaloids ("Febrifuge," see p. 80) in India; financial results in India; trees in India; cultivation of cotton and of caoutchouc in India.

24. Martius (C. F. Ph. von). *Die Fieber-Rinde, der Chinabaum, sein Vorkommen und seine Cultur.* 54 pages. (*From Buchner's Neues Repertorium für Pharmacie*, XII, 1863, pages 335 to 390).

25. Oudemans (Anthony Cornelis). See page 77.

26. Owen (C. T.). *Cinchona Planter's Manual.* Ceylon, 1881. 203 pages. A guide for the cultivation of the Cinchonas in India.

27. Planchon (Gustave). *Des Quinquinas.* Paris et Montpellier, 1864. 150 pages. A good critical review of the Cinchonas and their barks. An English translation has been issued, under the superintendence of Mr. Markham, by the India Office, under

the title of *Peruvian Barks*, by Gustave Planchon, London, printed by Eyre and Spottiswoode, 1866.

28. Reichardt. *Chemische Bestandtheile der Chinarinden.* Braunschweig, 1855. 164 pages. 8°. 3 plates.

29. Reichel. *Chinarinden und deren Bestandtheile.* Leipzig, 1856. 56 pages. 8°.

30. Ruiz (Hipolito Ruiz Lopez). *Quinologia, a tratado del árbol a Quina o Cascarilla, can su descripcion, y la de otras especias de Quinas unevamente descubiertas en el Perú ; del modo de beneficiarla, de su eleccion, commercio, virtudes su,* Madrid, 1794. 4°. 103 pages.

31. Ruiz. *Suplemento á la Quinologia.* Madrid, 1801. 4°. 154 pages and 1 plate.

32. Soubeiran (J. Léon) et Delondre (Augustin). *De l'introduction et de l'acclimatation des Cinchonas dans les Indes néerlandaises et anglaises.* Paris, 1868. 165 pages.

33. Triana (Josè). *Nouvelles Études sur les Quinquinas d'après les matériaux présentés en 1867 à l'exposition universelle de Paris et accompagnées de fac-simile des dessins de la Quinologie de Mutis, suivies de remarques sur la culture des quinquinas.—Ouvrage honoré des encouragements du governement de S. M. Britanique.* Paris, 1870. F. Savy, Folio. 80 pages and 33 plates. Price 70 francs (about $14).

A review of this publication will be found in Just's *Botanischer Jahresbericht,* 1873, page 484.

34. Vogl (August). *Chinarinden des Wiener Grosshandels und der Wiener Sammlungen.* Wien, 1867. 8°. 134 pages.

A very exhaustive description (without figures) of the microscopic structure of the barks occurring in the Vienna market, or preserved in the museums of that city.

35. Vogl (A.). *Beiträge zur Kenntniss der sogenannten falschen Chinarinden.* Wien, 1876. 4°. 24 pages, and figures of 7 microscopic sections. (From a commemorative essay in celebration of the 25th anniversary of the zoölogical botanical society of Vienna).

The barks, which are here considered and figured, belong on the one hand to *Buena* (*Cascarilla*), *Exostemma, Gomphosia, Nauclea, and Remijia,* and on the other to undetermined mother-plants. Among the latter, *e. g., Cinchona* (*China alba*) *Payta,* which contains the alkaloid paytine, (see page 64), *Cinchona* (*China*) *bicolorata* (page 95), and *Cinchona* (*China*) *of Trujillo.*

36. Vrij (John Eliza de). *Kinologische Studien.* 33 essays, re-

lating chiefly to the chemical constituents of the barks from Java and British India. These studies have appeared, since 1866, in Haaxman's *Tijdschrift voor Pharmacie in Nederland;* other publications of De Vrij upon this subject are contained in the London *Pharmaceutical Journal* and in the Paris *Journal de Pharmacie.*

37. Weddell (Hugh Algernon). *Histoire naturelle des Quinquinas, ou monographie du genre Cinchona, suivie d'une description du genre Cascarilla et de quelques autres plantes de la même tribu.* Paris, 1849. 108 pages, 30 plates and 1 map. Folio. Price 60 francs (about $12).

38. Weddell (H. A.). *Notes sur les Quinquinas. Extrait des Annales des Sciences Naturelles,* 5^e^ série, tomes XI et XII. Paris, Masson et fils, 1870. 8°, 75 pages. A systematic arrangement of the genus Cinchona, and description of its (33) species, accompanied by useful remarks on their barks. An English translation has been printed by the India Office, with the title—*Notes on the Quinquinas,* by H. A. Weddell, London, 1871, 8°, 64 pages. A German edition by Dr. F. A. Flückiger has also been published under the title *Uebersicht der Cinchonen,* von H. A. Weddell, Schaffhausen and Berlin, 1871, 8°, 43 pages, with additions and index.

Compare Just's *Botanischer Jahresbericht,* 1873, page 489.

INDEX.

CORRIGENDA.

Page 48, 2d and 4th line from top, *read* Crown *for* Brown.
Page 50, foot-note 1; *read* Aribine *for* Arabine.

EXPLANATION OF THE PLATES.

I. *Cinchona succirubra.* After specimens grown by Mac Ivor, in 1875, in Ootacamund.

II. *Cinchona Calisaya, Var. Ledgeriana.* After specimens from Java. *a*, longitudinal section of a flower. *b*, longitudinal section of a flower with a short style (the so-called male form, *macho* of the Spanish). *c*, longitudinal section of a flower with a long style (the so-called female form, *hembra*).

III. *Cinchona Calisaya, Var. Ledgeriana.* After specimens from Java. Representing the magnified capsule of a form provided with hairy fruits, and seed magnified ten-fold.

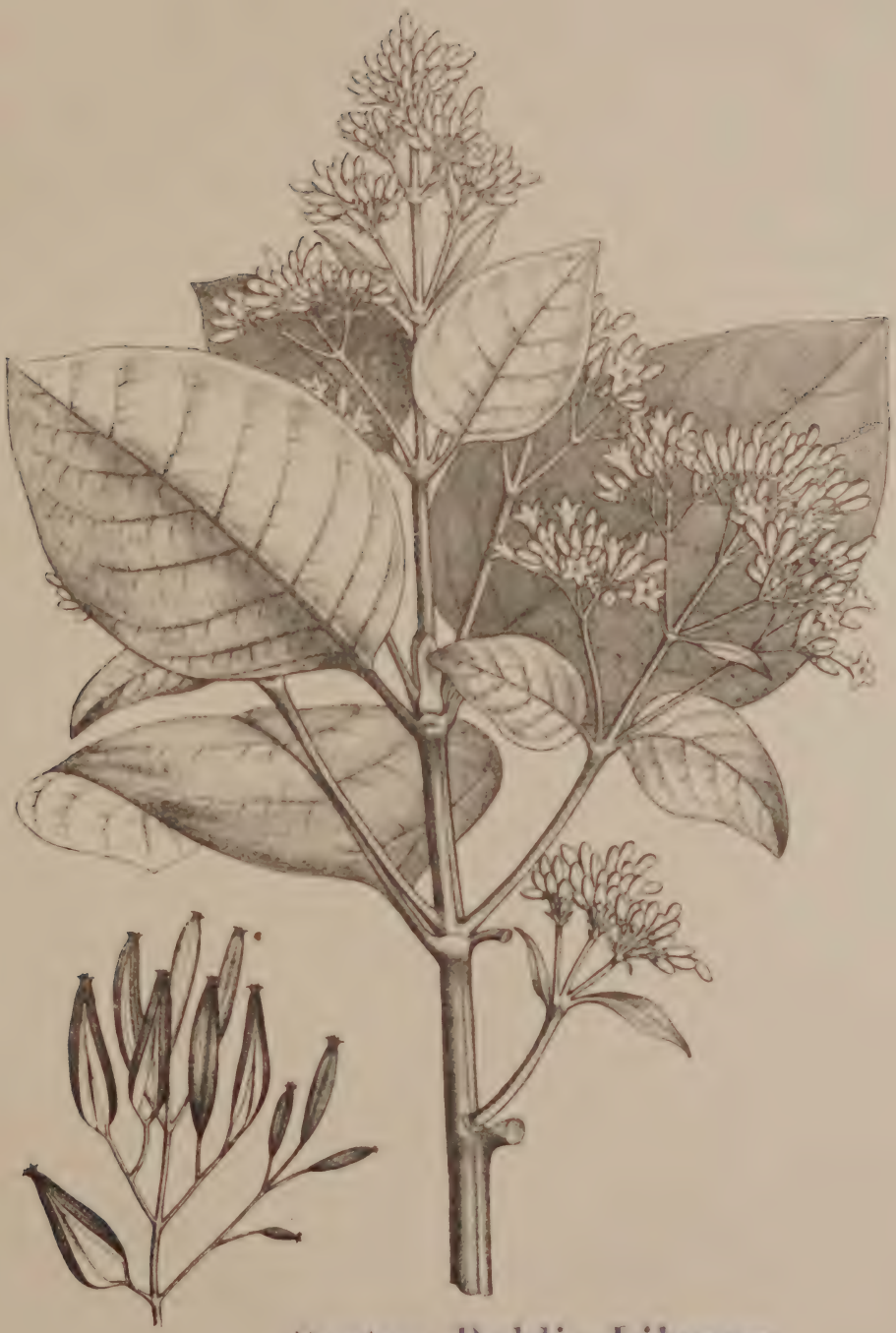
IV. *Cinchona lancifolia.* After specimens from Java, with the use of plates XI and XII in Karsten's *Flor. Columb. specim. select.*

V. *Cinchona officinalis.* A flowering branch from Darjeeling. *Cascarilla heterocarpa* (*magnifolia*). After Karsten's *Flor. Columb. specim. sel.*, plate VI. Representing the capsules, dehiscing from the apex.

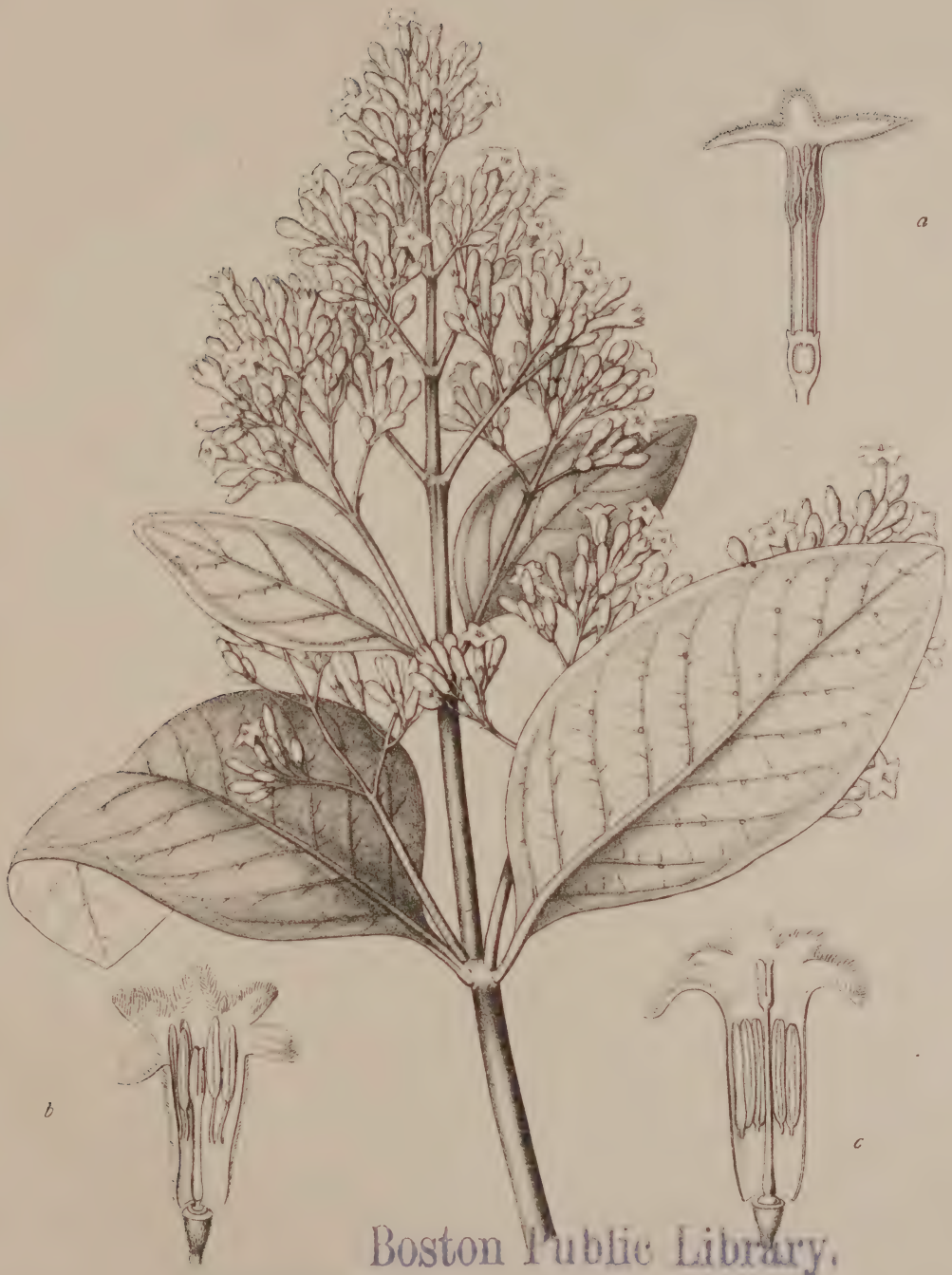
VI. *Remijia pedunculata.* (Cinchona pedunculata) from Karsten's *Flor. Columb. spec. sel.* Tab. XXVI.

VII. *A. Cinchona Calisaya*, transverse section of a young bark. *B. Cinchona Calisaya*, transverse section of an older bark. *C. Cinchona lancifolia*, transverse section of the bark. *e*, cork; *k*, sclerenchyma (stone-cells); *o*, outer bark; *p*, lacticiferous ducts; *q*, bast rays (bast wedges); *r*, medullary rays; *s*, bast fibres (bast tubes); *u*, staff-shaped sclerotic cells (staff fibres); *v*, bast. In the lower figures, *sr* represents bast fibres of *Cinchona cuprea*; *sc*, bast fibres of *Calisaya* and other "true" Cinchona barks.

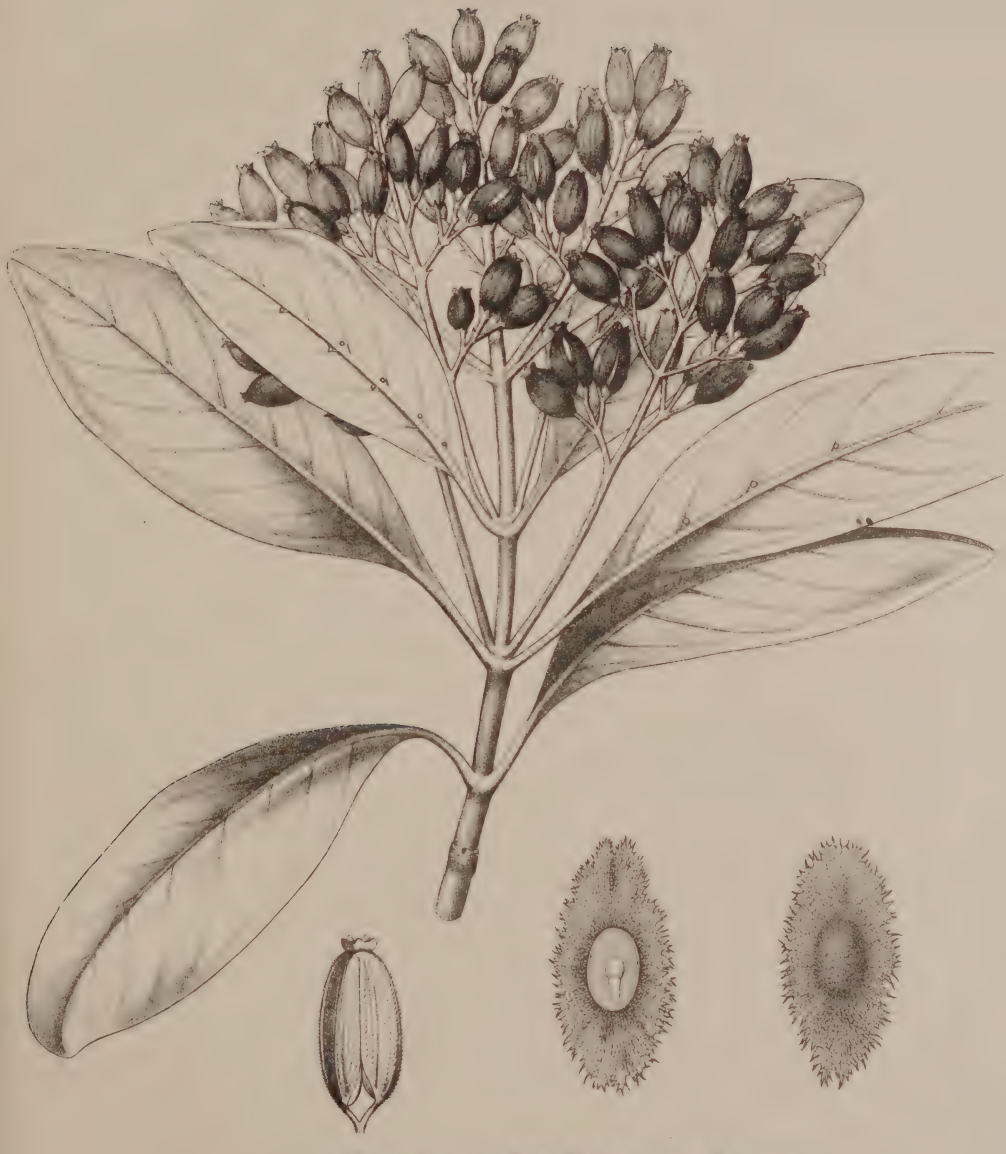
VIII. *Cinchona cuprea.* A highly magnified transverse section. *e*, older; *f*, younger cork; *k*, sclerenchyma (stone cells); *o*, outer bark; *p*, lacticiferous ducts; *r*, medullary rays; *s*, bast fibres (bast tubes); *v*, bast; *x*, crystal ducts.



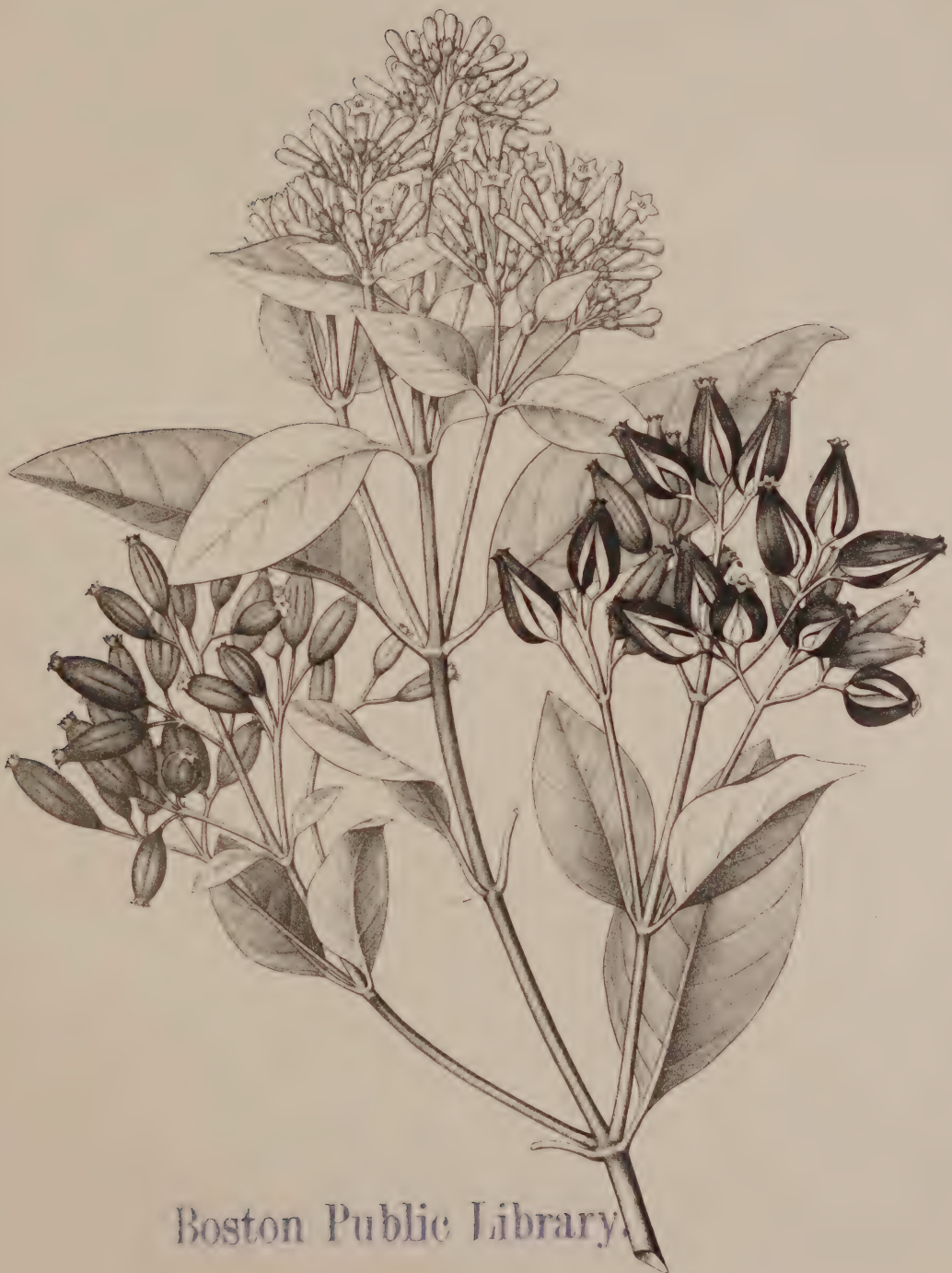
Cinchona succirubra.



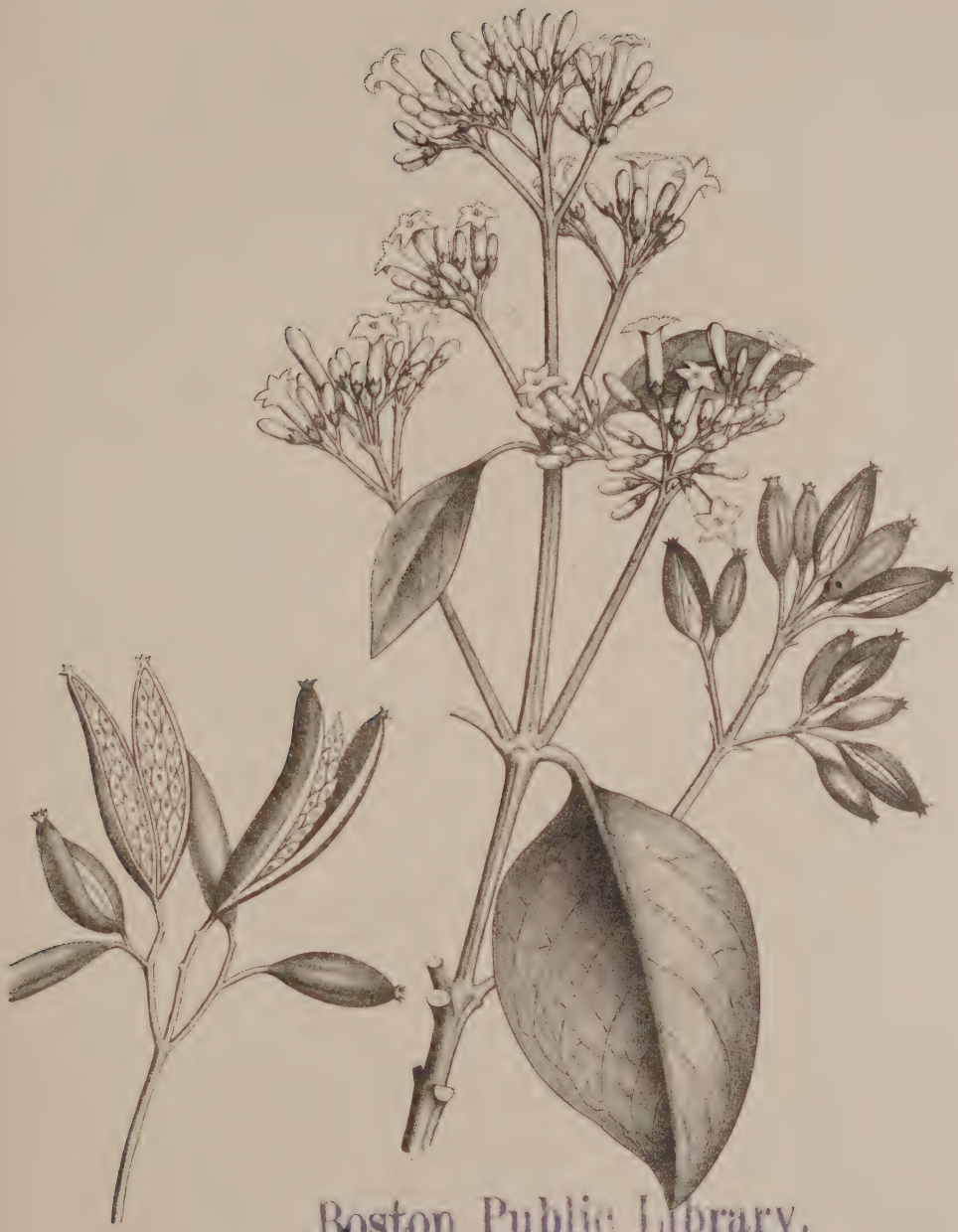
Cinchona Calisaya, Var. Ledgeriana.



Cinchona Calisaya, Var. Ledgeriana.

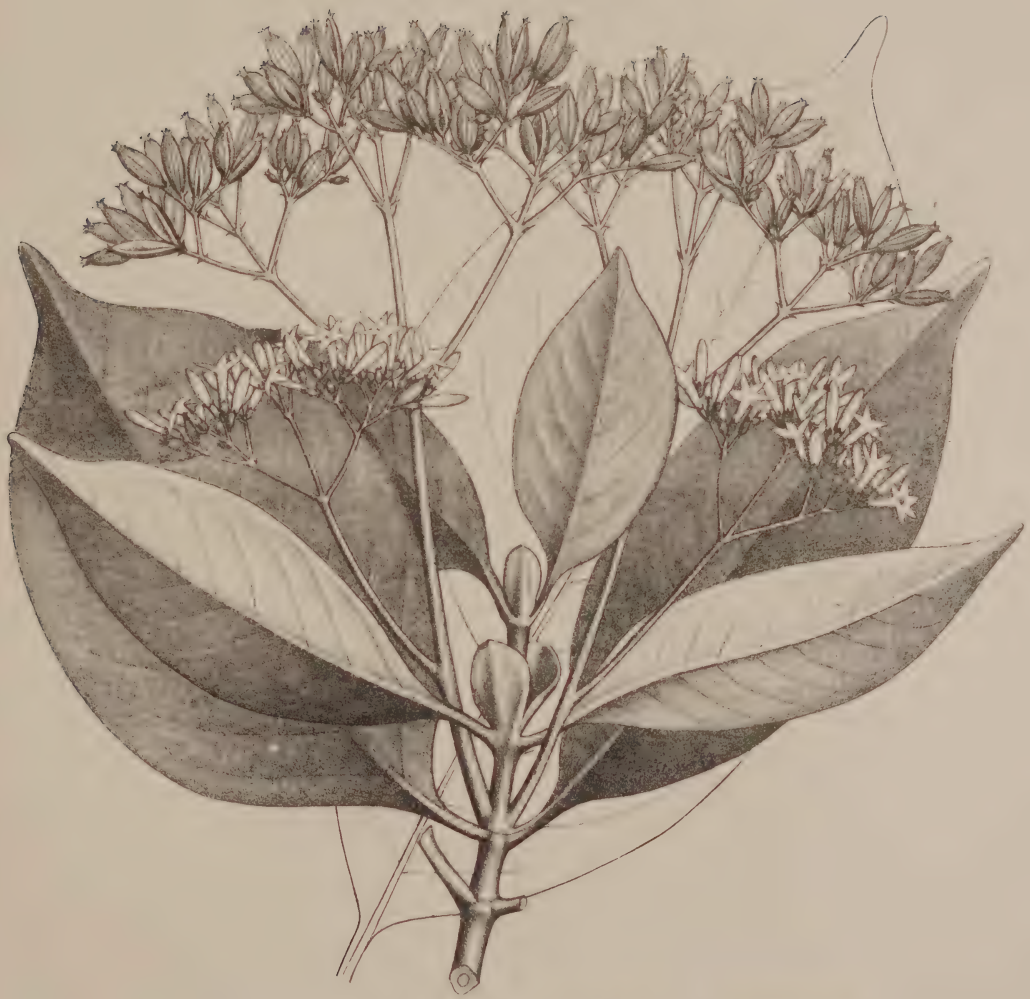


Cinchona lancifolia.



Cinchona officinalis

Cascarilla heterocarpa (magnifolia.)



Remijia pedunculata.