Inaugural dissertation upon the cinchonas, their history, uses, and effects : submitted to the Faculty of Physicians and Surgeons of Glasgow, in conformity with the rules of that body / by William Dawson Hooker, M.D., candidate for admission as a member of the faculty of Physicians and surgeons, Glasgow, January 30, 1839.

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INAUGURAL DISSERTATION

UPON

THE CINCHONAS,

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THEIR

HISTORY, USES, AND EFFECTS:

SUBMITTED TO THE

FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW,

IN CONFORMITY WITH THE RULES OF THAT BODY.

BY WILLIAM DAWSON HOOKER, M.D.,

CANDIDATE

FOR ADMISSION AS A MEMBER OF THE FACULTY OF PHYSICIANS AND SURGEONS.

GLASGOW, *January* 30, 1839.

"Where Andes hides his cloud-wreathed crest in snow,
And roots his base on burning sands below;
Cinchona, fairest of Peruvian maids,
To Health's bright goddess, in the breezy glades
Of Quito's temperate plains, an altar reared,
Trilled the loud hymn, the solemn prayer preferred."

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TO

JOHN BURNS, M.D., F.R.S., &c., &c.

AND REGIUS PROFESSOR OF SURGERY IN THE UNIVERSITY OF GLASGOW,

NO LESS DISTINGUISHED

BY HIS LABOURS IN MEDICAL AND SURGICAL SCIENCE,

THAN IN

CHRISTIAN PHILOSOPHY,

THE FOLLOWING PAGES ARE DEDICATED

BY HIS GRATEFUL AND OBEDIENT FRIEND AND PUPIL,

THE AUTHOR.

ON CINCHONAS.

THE History of the early introduction of the *Cinchonas* or *Peruvian Barks* into Europe, is, to say the least of it, dubious, if not altogether fabulous. I allude to the Spanish tale, that an Indian of Peru, having been attacked by an intermittent fever, which, it may be stated, *en passant*, is a disease very common in the Cinchona districts, and being near death, was left alone to perish; when, urged by insatiable thirst, he crawled to a pool of water close at hand, and, bitter as the water proved to be, still he drank it, and, wonderful to relate, recovered! Justly attributing his unexpected cure to this *Meribah* of the New World, he made his case known, when multitudes flocked to quaff and be healed. In course of time, the water lost its bitterness and its virtues. But upon the reason of the curative properties of this notable puddle being ascertained, which was, a *Cinchona* tree having fallen into the water, and thereby forming an astonishingly strong infusion of Cinchona, the Indians used the bark of this species of tree, which was so providentially made known to them, and benefitted themselves by it, for many generations.

When the Jesuits settled among the Indians, they lost many of their number by fevers, till they learned from the natives the utility of the substance to which the latter owed

their immunity from those diseases; and upon this, they sent it to Europe, under the name of *Jesuits' Bark*, a *tour de ruse* well worthy the followers of Loyola.

The whole of this fanciful tale bears the aspect of improbability or fabrication; and the concoctors of it seem to have forgotten the fact, that *the Indians never will use the Cinchona as a remedy*, but consider it as a medicine producing gangrene and death: and though they *occasionally* allow the benefit which Europeans may derive from its administration, they prefer an almost certain natural death to what they consider as poisoning themselves; stating in their defence that though it may suit European constitutions and climate, to the Indians it acts as a poison. I said they may *occasionally* see its good effects upon foreigners, because European residents in the country do not approve of its use, on account of its really being a "heating remedy." Still, Dr Pöppig, while residing in the woods where the *Cinchona* grows abundantly, was attacked with tertian fever, while making scientific observations upon these very plants, and by peeling the green bark from the trees, which grew abundantly about a hundred yards from him, and eating it, taking at the same time doses of Epsom salts, he effected his cure during three several attacks. But whatever its efficacy really may be, the fact of the strong prejudice existing against it in the minds of the Indians and resident Spaniards, casts great doubt upon the above tale, if it does not altogether disprove it.

It would seem that the *Peruvian Bark* was first brought to Europe through the medium of the Spaniards in 1640; but all that we can state, as known with any certainty, is, that in 1638, the wife of the Count Chincon, then Viceroy of Peru, being attacked with intermittent fever, a Corregidor of Loxa brought the *Peruvian Bark* to his notice, by the use of which the Countess recovered. She lauded its vir-

tues, distributed the powder under the name of "the Countess' powder," and took it to Europe on her return in 1640. Still it was not generally employed, till the Jesuits of Rome, in 1649, having received a large quantity from America, brought it into vogue, calling it "Jesuits' powder;" and as it was always vended in the pulverized form, they kept the secret of its origin amongst themselves, until Louis XIV. bought the knowledge of it from an Englishman called Talbot. Since this period, our acquaintance with the properties and uses of this valuable drug has been gradually extending, though the source whence it is derived is still very imperfectly investigated, and but little known. Much has been published upon this subject, and nevertheless the pharmacologist is still kept in considerable darkness concerning the history of Cinchonas.

Mutis, a famous Spanish botanist, who was the first discoverer of the trees whence this bark was procured, and, I may add, of the *Psychotria emetica* also, by his publications only led succeeding writers upon Materia Medica into a labyrinth of blunders, from which we are not yet extricated.

I do not pretend, in the following pages, so to elucidate this point as to state decidedly from what species of *Cinchona* the different officinal kinds of bark are obtained; but by collecting and comparing all the information to which I can gain access, I may thus perhaps clear up a few of the apparent difficulties and contradictions which obstruct our knowledge of this valuable genus of plants.

The generic term of *Cinchona* is derived from the original introducer of the bark into Europe, the Countess Chincon, and the first common name by which the drug was known was "Countess' powder," long before it received any generic or scientific appellation. The botanical characters of the genus are, that it has the *calyx* five-toothed; *corolla* hypocrateriform, with a 5-parted limb, valvate in

æstivation; *anthers* linear, inserted within the tube of the corolla, and not projecting, unless in a very slight degree; *capsule* splitting through the dissepiment into two *cocci*, open at the commissure, and crowned by the calyx; *seeds* girted by a membranous lacerated wing. According to the Linnæan System, it ranks in Pentandria Monogynia; its *Natural Order* is Rubiaceæ, more recently called Cinchonaceæ.

The arrangement of Mutis has been long adopted in our British Pharmacopœias, and though decidedly erroneous, still it is sufficiently convenient to the druggist and drug-broker, though worse than useless to those who desire to become scientifically acquainted with this genus.

It seems that there are *nine officinal* species of *Cinchona*, though these are not certainly established. Mutis gives but *three;* viz.

1. Cinchona *lancifolia*,
2. Cinchona *cordifolia*,
3. Cinchona *oblongifolia*,

} which are said to yield the { *Pale bark.* / *Yellow bark.* / *Red bark.*

Now, these names appear to have been applied at hazard, for, in the first place, the *Cinchona lancifolia* certainly does not yield the *pale*, but a very inferior description of bark; it is the *C. Condaminea* that affords the finest *pale bark*, a species not to be found in Mutis' list.

The next species of Mutis is the *Cinchona cordifolia*, from whence, it is said, we obtain the *yellow bark:* here the species itself is a disputed one, and the tree in question is believed to be one from which a very inferior sort of bark is procured, called *Quina Baya*, or *Quina amarilla of Santa Fé.* The best *yellow bark* is taken from the *Cinchona lanceolata*, *C. hirsuta*, and *C. nitida*, but chiefly from the former of these.

Again, the *red bark* is said by Pharmacopœists to be prepared from the *Cinchona oblongifolia*. But, from what the

red bark is obtained we are ignorant, nor does Mutis' description of the *C. oblongifolia* agree with what is now so called; and it is thus uncertain what Mutis' plant really is, that which he describes not coinciding with any known species of *Cinchona.*

From this it may be readily seen that Mutis' names, as applied to the different kinds of officinal bark, are incorrect; for in no one instance does he refer the bark to that tree whence the best kind, so called, is procured. The more recent discoveries have certainly tended to throw some light upon the natural history of the *Cinchonas*; still I am far from thinking that all is nearly correct.

There are twenty-six different species of *Cinchonas* named, though all are not perfectly defined or known. It would thus be useless to describe or enumerate all these; I will, however, give the result of Professor Lindley's inquiries, as far as regards the officinal kinds, in the following table, which I find in his Medical Botany, though much of this is uncertain and incomplete.

(*a.*) *Pale barks.*

Crown or Loxa bark.....Cinchona Condaminea.
Silver grey, or Huanuco bark..Cinchona micrantha.
Ash grey.....(*not ascertained*).
White Loxa bark.....(*not ascertained*).

(*b.*) *Yellow barks.*

Yellow bark..... { Cinchona lanceolata (chiefly) and Cinchona hirsuta and C. nitida.
Calisaya .....Cinchona lanceolata?
Carthagena bark.....Cinchona cordifolia.
Cusco bark.....(*not ascertained*).

(*c.*) *Red barks.*

Red Cinchona bark of Lima...(*not ascertained*).
Cinchona nova.....Cinchona magnifolia.

(*d.*) *Brown barks.*

Huamalies bark .....Cinchona purpurea.

From this table it is seen, that only the sources whence we procure the best *Pale Bark*—viz. the *Crown* or *Loxa Bark*, the *Silver grey* or *Huanuco Bark*, and the best *Yellow Bark*, are distinctly ascertained. It is however, more than probable, that other trees may yield the same officinal drug as do those whence we obtain it; though, doubtless, those already mentioned give the best.

C. Condaminea, which undoubtedly affords the most valuable, as well as the most certainly known Bark, (viz. the *Pale Bark*,) grows chiefly near Loxa, between the elevations of 5700 and 7500 feet above the level of the sea. The *twigs* are smooth as high up as the inflorescence; *leaves* smooth, ovato-lanceolate, at the axils of the veins underneath, when fully grown, furnished with a little pit or scrobiculus; *petioles* smooth, about $\frac{1}{4}$ the length of the leaves; *stipules* oblong, obtuse, membranous, smooth; *peduncles* panicled, corymbose, in the axils of the upper leaves, forming a large loose *thyrse*, covered with a short thick down. *Tube of the calyx* downy, like the pedicels, its *limb* very shortly urceolate, 5-toothed, pubescent, not shining, with the teeth roundish, triangular, acute; *tube of the corolla* slender, about four times as long as the tube of the calyx, tomentose; *limb* very shaggy internally.

Professor Lindley says, that this species furnishes the *Pale Crown* or *Loxa Bark* of English commerce, or, at all events, a principal part of it. The tradition of the bark-collectors of Loxa affirms, that this is the identical species of bark sent by the Corregidor, Don Francisco Lopez de Cañizares, in 1638, to the Viceroy of Peru, the Conde de Chincon.

There are three species of *Cinchona* which furnish the *Yellow Barks*, *C. lanceolata*, *C. hirsuta*, and *C. nitida*. The first of these species is said to be that from which most of the *yellow bark* of commerce is obtained, though perhaps not the very finest quality. It grows chiefly in the province of

Huanuco. *Twigs* smooth; *leaves* elliptical and acute at each end, coriaceous in texture, and very glossy on the upper surface; *petioles* smooth, except sometimes downy when young, from $\frac{1}{10}$ to $\frac{1}{6}$ the length of the leaf; *peduncles* panicled, corymbose, hardly longer than the upper leaves, in which they are axillary, forming a close, compact thyrse, covered with a short, thick down; *tube of the calyx* downy, as are the pedicels, its *limb* campanulate, shining, and almost always smooth, with acute or even acuminate triangular teeth; *tube of the corolla* cylindrical, tomentose, about three times as long as the tube of the calyx; *limb* very shaggy internally.

Of the species of *Cinchona* which yield the *Red bark* of commerce, I can obtain no positive information. Upon consulting the French authors, I find they are inclined to think it is obtained from the *C. oblongifolia* of Mutis; but this, in fact, is saying nothing; for what Mutis calls the *C. oblongifolia*, is a species *non inventa* by his description of it; though that to which it most approximates is the *C. magnifolia* of Ruiz and Pavon; but Pöppig ("Reise in Chili und Peru,") states that this tree yields only a kind of bark of very ordinary quality, chiefly employed in the adulteration of the better kinds.

Amidst all this confusion and uncertainty, we can arrive at no conclusion, but must still remain in comparative ignorance, using the old pharmaceutical names, erroneous as they certainly are. It is evident that each bark of commerce is obtained from more than one tree, though perhaps one individual species affords the best of its kind, and the others, more or less indifferent sorts.

It is more than probable, that much of the excellence of the bark depends upon the part of the tree whence it is taken; indeed, it has been said, that *all* the difference is traceable to the age of the trees, the parts whence the bark is peeled, and the season of the year when it is cut. I

cannot imagine this to be really the case; indeed the season of the year cannot account for any difference in respect to the quality, as the barks are all gathered during a certain period, viz., from August to November. Of this fact, however, I have little doubt, that the barks of the warm vallies, and those of the colder hilly regions, differ so much in quality, that the former are almost worthless, while the latter are very excellent, although I am not prepared to say whether the same species does or does not grow both in the hills and in the vallies. Still a range of altitude of 1800 feet, in the case of *Cinchona Condaminea*, combined with humidity of atmosphere below, and dryness in the higher situations, no doubt makes an immense difference in the efficacy of the drug, and most probably causes much of the discrepancy existing between the statements of different authors regarding the same individual species of tree.

The *Cinchonas* are of different sizes; the same species varying very much; those trees found at considerable altitudes being the smallest, scarcest, and the best; while others of the same kind inhabiting the warm and humid vallies, though large and luxuriant in their growth, are too rapid in attaining their great size, and consequently comparatively valueless. It is said that the bark is fit for gathering, when, upon being peeled off the branch, it becomes red by the action of the air; this is in the dry season, from August to November. The *Cascarillero* then starts for the forests, and disregarding those trees which stand singly, ascends some high tree or elevated point, to look out for the clumps of *Cinchonas*, which are recognized by their dark glistening foliage,—he then proceeds straight to the desired spot, and felling the trees close to the roots,* makes longitudinal

* If this precaution be not attended to, and the barked tree be left standing, the insects and rapid decay soon combine to destroy it, trunk,

incisions in the bark, about two feet long and of considerable breadth. After allowing the trunk to remain three or four days, till the moisture which exists between the cuticle and wood be evaporated,† the bark is peeled off and dried as speedily as possible in the sun, for upon the celerity with which this operation is performed, depends much of the value of the bark, which if not quickly and well dried, loses colour, or becomes mouldy. Dew or a little moisture falling upon the article during this process, ruins the colour, and takes away much of its worth. When properly prepared, it rolls upon itself, except the largest and thickest pieces, which remain pretty nearly flat; it is then placed in dry stores for sale. We do not obtain the barks in such fine large and easily distinguishable pieces as are first procured in the bark districts, but so broken and mixed that it is not easy to pick out the good from the bad, and

branch, and root; while, if the tree be cut down first, and then barked, this evil is avoided, for the Cinchonas spring up from the roots, like the oak coppices of Britain which are cut every few years; six years' growth rendering the Cinchonas again fit for cutting; even burning the tree will not destroy the vitality of the root. The plan of barking the trees as they stand, is pursued only in Loxa, and even there, it is a practice which is fast giving way to the other method as employed in Huanuco, Cuchero, &c.

† If the bark be separated from the trunk too quickly, the epidermis loses its attachment to the bark and drops off. Thus as it is very much from the presence of *Cryptogamiæ* which cover this epidermis, and with it disappear, that the European drug merchants judge of the excellence of the article, so the price of such bark as wants the epidermis, is considerably depreciated. I may however, mention, that this plan of estimating the barks is very erroneous; nor is the colour either always a criterion; for Pöppig assures us that the hues may vary from slaty, ash, and even reddish grey, and still be equally of the best kind. The quilling, too, depends greatly upon the age and the part of the tree whence the bark is taken.

the spurious from the genuine. I have seen, in the collection of a distinguished Professor, specimens of bark derived from the same identical tree, some of which are quite flat, and others again very much quilled; for instance, the same tree may afford the *Red bark*, which is described as very flat, and also bark which is as much quilled as the best *Crown bark*, owing to the circumstance of the former being taken from the trunk or larger branches, and the latter from the smaller boughs and twigs. It would therefore appear not impossible but that even the officinal species may frequently be confounded with each other. In a work published A.D. 1826, in Hamburgh, edited by H. Bergen, an extensive *Droguerie Makler* in that city, I find a beautiful series of plates, illustrative of the different forms under which the barks come into the drug-merchant's hands. In it I observe the *Pale bark* almost flat, rather broad and thick, and decreasing to the size of a tobacco pipe stem. The *Red bark* again, is not quite so small certainly, but about the thickness of an ordinary pencil, and tightly rolled upon itself, as much so as the pale bark; from this state it is represented as becoming gradually larger, flatter, and thicker, till it reaches the extreme of massive coarseness, far exceeding in this respect the largest specimens of the pale bark. Still many of the intermediate representations of every one of these barks resemble each other so very closely, that it would be easy to pick out specimens of all, and so to mix them, that I doubt if any but a most experienced eye could rearrange each in its own appropriate species, and I should say that were it done, it would not be from the colour, the lichens, or the quilling.

Seeing that no dependence is to be placed upon the *scientific names* of the *Cinchonas*, while the *officinal names* are, though merely conventional, perhaps the most conve-

nient in the present state of our knowledge, or rather of our ignorance, on this subject, I shall make use of the latter throughout this essay.

There are then *three officinal barks* recognized by our Pharmacopœias, though the French, German, and other foreign pharmaceutical authors, make four.

The latter plan, however, tallies with Mutis' original intention, as I find by a MS. in Mutis' own handwriting, which is in the possession of my father, Sir William J. Hooker; this additional species is the *White bark—Cinchona ovalifolia.* This name is, like the rest, quite incorrect; for it so happens that the species *C. ovalifolia* is worthless, while the true *White bark* is a very good variety of the *Pale bark*, with which it is generally found mixed.

I shall now proceed to take a short notice of the commercial barks, as they are given in the works on Pharmacy.

I. *Cinchona lancifolia—Pale bark.* This species has several varieties, or sub-species, which I need not specify. It is generally very much quilled, somewhat fibrous, more astringent than bitter, when reduced to powder of a greyish-fawn colour more or less deep, containing a large proportion of Cinchonine and little or no Quinine.

The best Pale bark is brought from Loxa; but is not now much used in Europe, though its tonic and febrifuge powers are at least equal to those of the *Yellow bark.*

II. *Cinchona cordifolia—Yellow bark.* This occurs in larger masses than the pale bark, and is not so much quilled; its texture is very fibrous, extremely bitter, and with a proportionably small degree of astringency; powder brighter coloured than that of the former, approaching to orange; it

contains a considerable portion of Quinine and hardly any Cinchonine. This bark is now chiefly employed in Europe, and is considered to be the best variety; but with what justice, we shall presently see.

III. *Cinchona oblongifolia—Red Bark.* This is brought to the European market in large heavy and thick pieces, generally flat, or nearly so, very rough and much cracked, having altogether a remarkably coarse appearance, its texture varies between that of the pale and yellow barks; its colour is rusty-red, fracture fibrous and unequal; it has little smell, the taste is astringent, bitter and very nauseous; and it contains the salts of Cinchonine and Quinine in pretty nearly equal quantities. I believe this to be the most valuable bark of the three, with this drawback, that though the yellow bark be now more sophisticated, on account of the larger demand for that article, adulterations are not so easily detected in the red bark.

The utility of the barks was no sooner known, than, like most remedies, when they first come into vogue, they were used for every thing, and in every form. Some of these preparations, as given in the manuscript of Mutis already alluded to, would excite a smile, as well as the cures which they are vaunted to perform. The first is that which he speaks of as "*Fermented Quinia:* the liquid resulting from this concoction is that *Balsam of Life*, so much valued in former times." Next comes the "*Vinegar*," which is to be made by "leaving the fermentation to pass from the vinous to the acetous;" and "a strong vinegar cannot be obtained till after three or four months have elapsed." "*Ptisans*" are prescribed, prepared in every imaginable way; "*clysters*"

are concocted from the sediments of many other preparations of the barks; next comes "*the precious Elixir of Quinia;*" then the "*Prophylactic beer;*" "*Syrups;*" and lastly, the prince of preparations, denominated the "*Polychrest fermented preparation,*" which, when mixed with Sarsaparilla, forms the "*Polychrest beer.*" The last words of Mutis' paper conclude with—"But of all the modes of using the Quinia, none has been more injurious and prejudicial to the patient, than that of taking it in powder." All this is, no doubt, vastly amusing, and perhaps interesting, to the lover of medical antiquities, but of little practical utility in our own day, except as gendering a salutary mistrust in dogmatical statements.

It is to modern chemistry that we owe our knowledge of the virtues of the Peruvian barks; and, by recent investigations, the *Pale Bark*, with which we shall begin, is found to be composed of

1. Cinchonine, united to kinic acid.
2. A red colouring matter, little soluble.
4. A soluble red colouring matter (tannin).
5. A yellow colouring matter.
6. Kinate of lime.
7. Gum.
8. Starch.
9. Woody fibre.

The active principle of this bark is *cinchonine*. This substance was first discovered by M. Gomez, but he neither knew its alkaline nature, nor did he examine its combinations.

It is with difficulty dissolved in water, but is soluble in alcohol, or more readily in an acid. Cinchonine unites with all the acids, forming neutral salts. These salts have a very bitter taste; the sulphate, nitrate, and hydrochlorate, are crystallizable.

The component parts of Cinchonine are, by ultimate analysis, found to be

	Pell. and Dumas.	Liebig.	Hendry & Plisson.
Carbon,.....	76·97	76·36	78·88
Hydrogen, ...	6·22	7·37	8·876
Azote, ...	9·02	8·87	9·3522
Oxygen, ...	7·97	7·40	2·8918
	100·18	100	100·0000

Pelletier and Caventou obtain the Cinchonine, by treating an alcoholic extract of the pale bark with very dilute hydrochloric ether; a solution of hydrochlorate of Cinchonine is thus procured, a red sediment remaining, which consists of a fatty matter; the solution is then filtered, and decomposed by magnesia, the precipitate is washed and treated with boiling alcohol, which takes up the Cinchonine; it is filtered again, concentrated, and the Cinchonine allowed to settle. It is then purified by being redissolved and recrystallized, till the solution becomes colourless; and it may be still farther purified by washing it, when cold, with hydrochloric ether. Sulphate of Cinchonine is a salt, strictly neutral, formed by uniting sulphuric acid with the Cinchonine; it is very soluble, easily crystallizable in prisms having four sides, two of which are larger than the other two, terminating in an inclined face; they occur usually in fasciculi. This salt is bitter, soluble in alcohol, insoluble in ether; it melts like wax at a temperature a little above that of boiling water; a degree higher decomposes it. Its composition is

Cinchonine,.....100·
Sulph. Acid,..... 13·0212

Its atom, 38·488.

Yellow Bark, which comes next under our consideration, contains

1. An acidulous kinate of quinia.
2. A small portion of kinate of cinchonia.
3. A kinate of lime.
4. A fatty matter.
5. A red insoluble matter.
6. A red soluble colouring matter (tannin).
7. A yellow colouring matter.
8. Starch.
9. Lignin.

Of the substances contained in the *Yellow bark*, Quinine is that to which it owes its efficacy as a febrifuge; and, as a very considerable portion of the Cinchonine is to be found in it, it becomes the object of the chemist to extract the former substance, which is effected in the following manner:—

160 ounces of the *Yellow bark* should be coarsely powdered, and infused in water, acidulated with one-hundredth part of its quantity of muriatic acid; this is allowed to macerate twenty-four hours, then strongly pressed, and again treated with more acidulated water, till the bark yields no more bitterness to the water.* To the infusions

* The first part of this operation will be considerably facilitated by the following plan:—Place the coarsely pulverized Cinchona in a tube, with its lower extremity terminating in a funnel, into the neck of which let some cotton be stuffed, in such a manner, that any liquor may percolate, but no powder find its way through; the powder should be kept in its place, with a disk placed above it, and pierced with numerous small holes. The acidulated water, when poured on the top of this, drains through the whole mass of the powder, extracting the active principle much more rapidly, and with less waste of acid, than by any other means; and the necessity of pressure is also obviated.

By tasting the percolating liquor, we can easily tell if the quinine is all extracted from the bark; for when that is the case, the drops will be purely acid, without any bitterness, and pressure will not cause it to yield any additional portion of quinine.

put together and filtered, add a slight excess of magnesia, (or milk of lime,) boil it and let it cool, then filter and wash the precipitate with cold water, next dry and treat it with alcohol, distil and finally evaporate it very gradually.

Quinine, uncombined with an acid, is almost incrystallizable, and was at one time thought quite so; it crystallizes in fine silky needles, but when crystallized it is in the state of a hydrate. When dry, it assumes a light porous appearance. Its ultimate analysis gives us the following results:—

	Pell. and Cav.	Pell. and Dumas.	Liebig.	Hendry & Plisson.
Carbon, ...	75·	75·02	74·40	75·552
Hydrogen, ...	6·25	6·66	7·61	8·4322
Azote, ...	8·75	8·45	8·11	8·2946
Oxygen, ...	10·	10·43	9·88	8·7212
	110·	100·56	100·00	100·0000

Its atom, 45·9069.

The following table will show how Cinchonine and Quinine differ from each other:—

	Cinchonine.	*Quinine.*
Form,	in prismatic needles,	in an amorphous mass.
Taste,	peculiar, bitter,	bitter, very disagreeable.
Fusibility,	infusible,	fusible, (in the state of a hydrate.)
Atomic weight,	38·488	45·9069.
Alcoholic action,	soluble in alcohol, crystallizable,	soluble in alcohol, incrystallizable.
Action of ether,	sparingly soluble, crystallizable,	very soluble, uncrystallizable.
Sulph. Appearance,	crystallizable in prismatic needles,	crystallizable in silky needles, with a pearly lustre.
Sulph. Composition,	base 100, acid 13·0210,	base 100, acid 10·9147.
Mur. Appearance,	crystallizable in needles,	easily crystallized in silky needles.
Mur. Composition,	base 100, acid 9·035,	base 100, acid 7·0862.
Hydrochlorate Appearance,	crystallizable in needles,	crystallizable in silky tufts.
Hydrochlorate Comp. parts,	acid 9·035, base 100,	acid 7·086, base 100.
Phosphate,	uncrystallizable, appearance gummy,	crystallizable in pearly needles.
Arseniate,	uncrystallizable,	crystallizable in prismatic needles.
Acetate,	very soluble in little crystallized grs.	less soluble, crystallizable in tufts, bundles, &c., &c.

What is called *Sulphate of Quinine*, is the substance almost universally employed in medicine; but there is seldom a strictly neutral sulphate; it is obtained usually in the form of a persulphate or subsulphate, and the latter is the preparation used. To obtain this, after the alcohol has

been recovered, in the latter stage of the process, from the alcoholic solution, add to the residue sulphuric acid, till it reddens litmus paper; evaporate the liquid, and set it aside till the crystals of sulphate of Quinine are deposited. The neutral sulphate is formed by adding a little sulphuric acid to the solution of the subsulphate, and then crystallizing it. It reddens vegetable blues, but its taste is not perceptibly acid.

There is still another alkali found in the Cinchonas—the *Aricine*, which was discovered in 1829, by Pelletier, and published in 1832. I am not aware from what bark it is to be obtained; it was discovered accidentally in barks *resembling* the yellow barks. Nor do I know any thing of its therapeutic action, or if it has ever been tried medicinally.

By analysis, it is found to be composed of

Carbon,.....	10
Hydrogen,.....	24
Azote,.....	2
Oxygen,.....	3

It will thus be seen, that Aricine only differs from Cinchonine and Quinine in the proportion of oxygen which it contains. This is a very curious fact, and renders it extremely probable, that *Cinchonine*, *Quinine*, and *Aricine*, are the same substances in different degrees of oxygenation,—an hypothesis which explains why more acid is necessary for saturating Aricine, than either Cinchonine or Quinine; and we can also explain how it is possible, that, in the same vegetable, two salifiable bases are found.

The powerful febrifuge properties of the Sulphate of Quinine, have brought it into general use in every part of the world; and it has, on this account, become an important article of manufacture, especially in France, where the

cheapness of alcohol enables the maker to produce it at a much lower price than can be done in this country, notwithstanding the duties levied upon it, in the British ports, as an article of foreign manufacture.

The annual produce of Sulphate of Quinine, in Paris, where it is chiefly made, exceeds 120,000 ounces annually; and, when we consider that the largest proportion of Quinine obtainable from the bark by the most economical plan is only 1 ounce to 80 of the best yellow bark, it is not surprising if those who are not well acquainted with the natural history and mode of growth of the *Cinchonas*, fear the extirpation of the trees whence this valuable medicine is obtained. From these *panics*, as well as from other causes, which so often influence the value of merchandise, the price of the Sulphate of Quinine varies considerably, and very suddenly; sometimes in a few days, indeed in any state of the market, the price of sulphate of Quinine being sufficiently high to tempt the venders to adulterate it to a great extent. The following tests will enable any one to detect the more common sophistications to which the drug is subject.

1. *Sugar*. To ascertain the presence of this substance, dissolve the suspected salt in water, and throw down the acid by barytes water; the Quinine will fall at the same time, and a current of carbonic acid gas will precipitate any excess of barytes which may have been added, leaving nothing but the sugar, easily recognizable by its taste.

2. *Sulphate of lime*, and *Boracic acid*, are both detected by subjecting the Quinine to a red heat, when it flies off, and the foreign substances remain behind. The presence of the *Boracic acid* may be further distinguished, by dissolving the salt in alcohol, and then, if, upon setting fire to the spirit, it burns with a green flame, we may be satisfied that Boracic acid is present.

3. *Margaric acid* may be separated by weak muriatic

acid, which dissolves the sulphate of Quinine, but does not affect the Margaric acid.

4. *Stearine* is detected by acting upon the adulterated salt with sulphuric acid, which leaves the Stearine undissolved.

5. *Starch* is recognised by dissolving the suspected Quinine in cold water, and a part will remain insoluble; if the mixture be then heated to 170° Fahrenheit, and afterwards cooled, and the tincture of iodine added, the blue colour caused by the iodine and fecula, will satisfactorily prove the sophistication.

Sulphate of Quinine is incompatible with the salts of iron, sulphate of zinc, nitrate of silver, oxymuriate of mercury, tartarized antimony, solutions of arsenic, &c.

Red bark, according to the latest analysis, appears to contain—

1. Much kinate of Quinine.
2. Much kinate of Cinchonine.
3. Kinate of Lime.
4. Much cinchonic red.
5. A soluble red (Tannin).
6. A fatty matter.
7. A yellow colouring matter.
8. Woody fibre.
9. Starch.

The first of these two active principles exists in almost equal proportions in the red bark, constituting, of course, its active properties, which are strong, as both the Cinchonine and Quinine are found in considerable quantities.

The comparative efficacy of the different species of barks, has been much disputed; the diversity of opinion being perhaps mainly attributable to the uncertain state in which they are found in the shops. At its first introduction, the *Red bark* was represented as far superior to the pale and yel-

low barks, and was esteemed accordingly; but the great preference given to it, led to so general an adulteration, that it lost much of its reputation. It was a common practice, also, to offer the bark for sale after having extracted the active properties, by making tinctures, infusions, &c. from it. The *grey* or *pale Bark* next came into notice and use, and perhaps similar causes depreciated its value in like manner; so that now the *Yellow bark* has superseded all the others; and so long as *Quinine* alone is employed in the cure of intermittent fever, it must hold its place in popular favour. Why *Cinchonine* should be excluded from general use, I know not, as it seems, from the most recent experiments, that the efficacy of these two substances is equal, or at least very nearly, so that their doses do not differ. It has, indeed, been affirmed that *Cinchonine* is the most powerful febrifuge of the two.

When administered in substance, the *Red bark* has a more decided tonic effect than any other kind, and it is difficult to say why *Cinchonine* and *Quinine* may not both be extracted from this bark, as the same process will suffice for both. If employed as one substance, it would seem to be a plan more convenient and economical than that of using the Quinine exclusively as at present.

With regard to the action of *Cinchona* upon the animal economy, it decidedly exerts a *tonic* influence, which must not be confounded with that of a mere *stimulant.* Its power in changing diseased into healthy action, and restoring the vigour and vitality of the debilitated frame, every day's experience has proved, especially in fevers of an intermittent and remittent character.

In all diseases which assume an intermittent type, whether they appear as gout, rheumatism, exanthemata, eruptive fevers, catarrh, and even phthisis, the bark and its alkaloids prove serviceable, and rarely injure, even in local

affections. Their administration should always be prefaced with an aperient, and especially in warm climates; the bowels should always be kept open during their use. Care must also be taken not to exhibit these remedies while an irritable state of stomach and bowels exists; they are contra-indicated by hepatic symptoms; and all inflammations should be reduced by bleeding and other means, before Bark or Quinine is employed. It is by neglecting these cautions that this valuable febrifuge has, with some practitioners, been undervalued, or so injudiciously exhibited, that the remedy has proved really worse than the disease.

Its mode of administration in intermittent fevers is now, generally, to give small and repeated doses immediately after the paroxysm, gradually increasing them as the time for the next attack draws near; but it has been sometimes exhibited in one large dose, such as grs. x., immediately before the expected access.

The British Pharmacopœias order powder, infusion, decoction, tincture, extract, and sulphate of Cinchonine and Quinine.

The *powder* was given in doses of ʒij. to ℥ss. and even ʒj. As a *general tonic, cæteris paribus*, this is perhaps even better than the Sulphate of Quinine. Port wine is an excellent vehiculum. In agues, powdered bark used to be prescribed in doses of ʒj. to ʒvj. every second or third hour, during the intermissions; but the quantity requisite was so great, that the stomach could seldom bear it. The *decoction* and *infusion* are only employed as topical remedies.

The best preparations are the *Sulphates of the Alkaloids;* and their superiority is now so universally admitted, that hardly any other is employed. I might enter at great length upon the virtues of this important drug, which may perhaps be justly termed the greatest discovery in Pharmacy; but it must suffice here to state, that these

alkaloids, in the state of salts formed by an acid, especially the sulphates, may be administered beneficially wherever the Cinchona itself would prove useful, very few trifling instances excepted.

We know how advantageous it is in the treatment of diseases to be certain of the precise doses of the medicines we give. This remark applies with much force in the present case, because the proportion of alkalies contained in the different species of bark sold in the shops varies very considerably, according to the nature and quality of the bark, its place of growth, age, preparation, &c. It is often desirable, nay, absolutely requisite, to administer the remedy in a small volume and agreeable form. Patients frequently die of malignant fever, because their stomachs cannot retain the requisite quantity of bark in the form of powder; by some it is rejected as soon as swallowed, while, in other instances, superpurgation takes place, so that the powder passes through the intestinal canal, having undergone no change, and of course produced no effect. Even in the most favourable cases, it is necessary that the patient's stomach should, as it were, chemically analyze the bark with which it is treated, and extract its febrifuge principle; a process always difficult and fatiguing. How valuable, then, the discovery by which the weakened organs are spared this labour!

The best and most general mode of administering the Quinine, is with an acid, thus rendering it more soluble; a very common prescription being grs. ij—x, dissolved in a few drops of dilute sulphuric acid. An elegant form is now very commonly employed; instead of common sulphuric acid, the aromatic sulphuric acid being the solvent; but this is said to injure the action of the Quinine. Orange or lemon peel is the best substance with which to disguise the taste, for all aromatic bitters cover the intense bitterness of the

Sulphate of Quinine. The following prescription may then be given as a formula equally effective and agreeable :—

Sulph. Quiniæ .....gr. vj.
Infus. confect. Ros.....℥vj.
Acid sulph. .....gtt. jv.

From the idea (an erroneous one, however,) that the Cinchonas will soon become extinct, several substitutes have been recommended; there is but one of these which is worth notice, this is a resinoid called *Salicine*, obtained from the barks of the

Salix fragilis.....Crack Willow,
Salix capræa .....Round-leaved Willow, and
Salix alba .....White Willow.

But neither are these barks nor is their active principle much in use; and earnestly it is to be hoped that we may never be compelled to seek such comparatively poor substitutes for the invaluable remedies which have been the subject of this Essay.

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