bark. The roots break with a short fracture, have a thick bark, and contain a ligneous cord branching into three or four rays." Cimicifuga, it is said, should be collected in the autumn; it should be used moderately fresh, as it grows much less active with the lapse of time.

Composition.—Not satisfactorily determined: *starch, sugar, gum, resin*, which were early recognized, are common vegetable derivatives, and found in most plants. Couard obtained a neutral, crystalline, very acrid substance (allied perhaps to *anemonin*). Trimble, working more recently, was unable to get Couard's crystals, but obtained an acrid, amorphous substance. No alkaloid appears to be present, unless Couard's crystalline substance proves to be such, as surmised by Mr. Falck, who, in 1884, obtained it from the fresh rhizome.

Action and Use.—There is no question that recently dried, or, still better, fresh, cimicifuga is an active substance. Vomiting, diarrhœa, and cardiac depression are caused by large doses; faintness, restlessness, and dizziness, foul breath, and dryness of the pharynx are common results. Smaller doses are said to be tonic, to improve the appetite and digestion, and to strengthen the heart's action. It is reputed to be aphrodisiac and ecbolic, but is not at all reliable in these directions. The most important and acknowledged uses of cimicifuga are, however, established empirically. It has for many years had a reputation in chorea, and is generally believed to be useful in that obstinate disease. It is also given in chronic rheumatism, and occasionally in pulmonary troubles.

The official extract is given in doses of .06 to .5 gm. (gr. i. to viij.); the fluid extract, 2 to 4 c.c. (fl. ʒ ss. to i.); the twenty-per-cent. tincture, 2 to 8 c.c. (fl. ʒ ss. to ij.).

W. P. Bolles.

CINCHONA.—In use, this word has three distinct significations, differing in their comprehensiveness.

Cinchona L. is a genus of some forty species of trees or shrubs of the family *Rubiaceæ*, natives of the eastern slope of the Andes, from Southern Bolivia northward, many of them destitute of medicinal properties, others so inferior as not to be in use.

Cinchona, Quina, Quinquina, and *Peruvian Bark*, in materia medica, are names applied to the barks of many of the above-mentioned species, and to at least one of another genus, which contain active alkaloids. The most of these barks are so weak and inferior that their use is to be discouraged, and mention of them is deferred until the close of this article.

Cinchona and *Cinchona Succiruba*, U. S. P., are the official names of a few of these barks which reach a certain standard of alkaloidal excellence, and these will now be separately considered.

Cinchona Calisaya, Yellow Bark.

"The bark of *Cinchona Calisaya* Weddell, *Cinchona officinalis* Linné, and of hybrids of these and of other species of *Cinchona* (nat. ord. *Rubiaceæ*), yielding not less than five per cent. of total alkaloids, and at least 2.5 per cent. of quinine" (U. S. P.).

A thorough knowledge of cinchona, even of its therapeutics, calls for a perfect understanding of this definition. The name C. *Ledgeriana* Moens should precede "C. Calisaya." It was omitted by the Pharmacopœia revisers in the belief that it was but a variety of the latter, but there is little doubt that the two are distinct species, and the Ledger bark is by far the richest known. The bark of C. *officinalis*, which will be considered in our supplementary notes, never attains to the official standard, but is included because some rich hybrid barks are of its parentage. *C. Ledgeriana* and *C. Calisaya* originated in Northern Bolivia and Southern Peru, at an elevation of 2,500 to 6,000 feet. The former was always rare and was known to the natives as "Zamba," and recognized as very superior. The hybrids were not at that time differentiated, though they were recognized as being numerous. The present alkaloidal standard was rarely reached. Indeed, the barks were for a long time not examined in this way, but were selected solely upon their appearance. The threatened extermination of the species led to their cultivation, in which the Dutch and British governments were concerned. The French made early attempts, but were not concerned in the practical operations. The history of this industry is of the greatest interest, and has an extensive literature. Only the most important facts relating to it can be here considered. The attempt was made to select the best varieties and forms for cultivation. This attempt but partially succeeded, and large quantities of inferior material came into the plantations. Mistakes of nomenclature also occurred, and some of them persist to this day. At the same time, very superior varieties also came into cultivation. These were propagated as soon as recognized, at the expense of the poorer ones. The mere processes of cultivation and soil enrichment increased the richness of the barks. Hybridization occurred freely, and was resorted to artificially, and astonishingly rich products were thus originated and multiplied. Special methods of treatment were devised, such as allowing the bark to grow with the light excluded by some covering ("mossing") and removing strips of bark to allow the spaces to be again covered under the above-mentioned condition ("renewing"), which also resulted in astonishing gains in the percentage of active constituents. At the same time that this increase of quality was taking place, there was an even greater cheapening in the cost of producing and marketing. The result was that the wild barks were practically driven out of the market, and now occupy a very unimportant place in commerce.

The young bark is deficient in alkaloids. It reaches its full strength at from six to nine years of age, when the trunks are five to eight inches in diameter, and this "ripeness" is indicated by a characteristic appearance. The root bark is much richer than the stem bark.

The regions of cultivation are chiefly the Dutch East Indies, especially Java, and British India and Ceylon. Rather large areas of cultivation exist in Bolivia, but they are relatively unimportant, chiefly because of the great cost of getting the product to the coast. Mexico, Brazil, Jamaica, Australia, and Africa have had experimental plantations, but these have failed to become of importance. The bark, from selling in 1880 to 1885 at from three to four dollars per pound, is now (1889), in doubly rich quality, to be had at much less than twenty cents. The trees ultimately reach a great height and a trunk diameter of several feet. They are very beautiful, with opposite, large, luxuriant dark glossy-green leaves, often bright purple underneath, and large terminal lilac-like panicles of very fragrant flowers, white or of varying shades of pink or purple.

Description.—Detailed descriptions of the bark are for the most part no longer of importance, as manufacturers' bark, and to a great extent "druggists' bark" also, are now purchased upon the testimony of chemical assay. Nevertheless, it is perfectly easy to determine the good quality, as well as the identity of bark for pharmacists' use, by the external appearance alone. Such bark arrives mostly in the form of entire or but little broken quills. Formerly, it all arrived in this form, but economy in transportation now leads to its being broken up ("chip-bark"), and this is known as manufacturers' bark. Of this, the root bark is distinguished by a brown, instead of a gray, outer surface, and by the warped curvature of the pieces, with crookedness of grain, or striation. Inferior branch bark may be known by its thinness and the lesser roughness and lesser grayness of the outer surface. Druggists' bark, in which we are more interested, is in quills of one and a half to two feet long and one or two inches in diameter. They are frequently rolled in at both edges, the so-called "double quill." The bark is 2 to 5 mm. ($\frac{1}{10}$ to $\frac{1}{5}$ in.) thick. The inner surface is of a light cinnamon brown and finely striate, the outer bright gray (a bluish or steel gray from Bolivia, a tawny or yellowish gray from Java). Deep, for the most part completely circular, transverse fissures mark the nodes of

the stem, smaller and incomplete ones being numerous in the intervening space, and much interconnected by irregularly vertical ones. The surface thus becomes cut up into angular scales resembling those upon the tarsus of a fowl. The abundance and closeness of this "chicken-leg" marking is indicative of high quality. *C. officinalis* parentage is indicated by a broad and gaping condition to these fissures, at least the principal ones, and the bark is thicker relatively to the size of the quills. A distinct longitudinal ridging is characteristic of *C. succirubra*

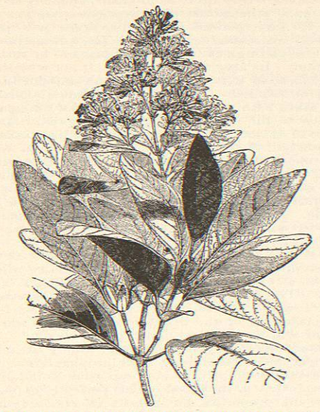

Fig. 1324.—Cinchona Calisaya. One-third natural size. (Baillon.)

parentage. The bast layer has a finely splintery, the outer a short, fracture. The odor is slight but characteristic, the taste bitter and slightly astringent. The powder is light yellow, whence the common name of the bark. Flat, *tabla*, or table bark is the inner bark only, flattened out, the outer surface of a cinnamon brown and smoothish.

Composition.—The distribution of the principal constituents of the cinchona barks will be exhibited in a table toward the close of this article. The nature and properties of the important individual alkaloids will be fully discussed after our discussion of the barks. Their percentage, absolutely and relatively to one another, varies with the age of the bark, as well as with the conditions described above. Exposure to rain during curing or in transit, or to sea water, also injuriously modifies the composition. As will be seen from the table of substances presented below, the variety now being considered contains about three per cent. of tannin, wax, gum, sugar, a trace of volatile oil, red coloring matter, and resin-like acids. These, however, do not require attention, except from pharmaceutical considerations, as calisaya is used for the antiperiodic effect of its alkaloids, more especially of the quinine. It contains from five to ten, rarely twelve to fifteen per cent., of total alkaloids, about three-fourths of which is quinine. Owing to this preponderance of quinine, calisaya is used for the effect of that alkaloid (which see), and may be considered therapeutically as its equivalent. It is like the others an excellent simple bitter and tonic, but when these effects are desired the red bark is more commonly employed. The powdered bark is sometimes given, in doses of 0.6 to 4 gm. (gr. x.–lx.), the equivalent of ♏ x. to lx. of the official fluid extract, or of gr. ss. to iij. of quinine. The official extract is given in doses of 0.3 to 1 gm. (gr. v.–xv.), the 20-per-cent. tincture, 2 to 8 c.c. (fl. ʒ ss.–ij.), and the 6-per-cent. infusion, 30 to 60 c.c. (fl. ʒ i.–ij.).

Cinchona Rubra, Red Cinchona.

"The bark of *Cinchona succirubra* Pavon, containing not less than five per cent. of its peculiar alkaloids" (U. S. P.). This tree is native upon the slopes of Mount Chimborazo and, like the last, becomes a large tree. It also has been largely introduced to cultivation in the East Indies, but has not, in consequence, undergone such great changes. Its characters can be best discussed by comparing it with the last.

It more frequently occurs in quills, and the bark is commonly thicker and more splintery in fractures. The inner surface is usually, though not always, of a deeper color, varying to deep red. The outer surface, in typical samples, is almost wanting in the checkered, scaly appearance, and indeed fissures are commonly almost wanting. It has instead longitudinal ridges, originating in rows of warts which afterward become confluent. In old barks, these ridges become fissured longitudinally. The powder is of a deep red, which gives the common name to the bark. In general, its composition is the same as that of calisaya. It, however, contains far more red coloring matter and more astringent principles, and only about one-fifth of its alkaloid is quinine, the rest being mostly cinchonidine and cinchonine. Its properties differ accordingly. It is accounted decidedly inferior as an antiperiodic, and its use is commonly as a vegetable bitter. However, following the differences in the alkaloids described below, this is no mean antiperiodic, and is frequently of great service in cases not favorably influenced by quinine. The only official preparation is the compound tincture, or Huxham's Tincture, consisting of ten per cent. of this bark, eight of bitter orange peel, two of serpentaria, and seven and one-half of glycerin. The dose is 4 to 16 c.c. (fl. ʒ i.–iv.).

The Cinchona Alkaloids.

The alkaloids reported in cinchona barks are numerous. Many of them are known or believed to have originated in the chemical manipulation of the bark. Others exist in very small amount, or in barks which possess but little value. Most of them are therefore of chemical interest merely, and only those of practical importance will be here discussed.

Quinine ($C_{20}H_{24}N_2O_2 + 3H_2O$) is the most common, abundant, active, and important, and is thus described in the Pharmacopœia:

A white, flaky, amorphous, or crystalline powder, odorless, and having a very bitter taste; permanent in the air.

Soluble, at 15° C. (59° F.), in 1,670 parts of water, and in 6 parts of alcohol; in 760 parts of boiling water, and in 2 parts of boiling alcohol; in 23 parts of ether, 5 parts of chloroform, and 200 parts of glycerin; also soluble in carbon disulphide, benzin, benzol, ammonia water, and diluted acids.

When heated to about 57° C. (134.6° F.), it melts; at 100° C. (212° F.), it loses about 9 per cent. (or about two molecules) of its water of crystallization, the remainder being expelled at 125° C. (257° F.). The anhydrous alkaloid, when pure, melts at 173° C. (343.4° F.). Upon ignition it is consumed, leaving no residue.

Quinine has an alkaline reaction upon litmus paper.

A solution of quinine in diluted sulphuric acid has a vivid, blue fluorescence.

On treating 10 c.c. of an aqueous, acidulated solution (about 1 in 1,500) of quinine with two drops of bromine water, and then with an excess of ammonia water, the liquid will acquire an emerald-green color. With proper adjustment of the reagents, more dilute solutions will give a paler tint, while more concentrated ones will acquire a deeper color, or deposit a green precipitate.

Quinine should not impart more than a faintly yellow-

ish tint to concentrated sulphuric acid (limit of *readily carbonizable, organic impurities*), nor produce a red color with nitric acid (difference from *morphine*).

If 2 gm. of quinine be mixed, in a small mortar, with 1 gm. of ammonium sulphate and 10 c.c. of distilled water, the mixture thoroughly dried on a water-bath, the residue (which should be strictly neutral to test paper) agitated with 20 c.c. of water, then allowed to macerate for half an hour at 15° C. (59° F.), with occasional agitation, and filtered through a pellet of glass-wool, 5 c.c. of the filtrate, transferred to a test tube and gently mixed, without shaking, with 7 c.c. of ammonia water (specific gravity, 0.960), should produce a clear liquid. If the temperature during the maceration has been 16° C. (60.8° F.), 7.5 c.c. of ammonia water may be added; if 17° C. (62.8° F.), 8 c.c. (In each case, a clear liquid indicates the absence of more than small proportions of *other cinchona alkaloids*.)

Quinine yields two official preparations. *Ferri et Quininæ Citras*, or Citrate of Iron and Quinine, contains 85 per cent. of ferric citrate, 3 of citric acid, and 12 of quinine. It is slowly soluble in water and not completely soluble in alcohol. The soluble form (*Ferri et Quininæ Citras Solubilis*) is made with the addition of a little ammonia water, and is rapidly soluble in water. It is in greenish, golden-yellow scales; the former in reddish-brown scales. The dose of each is 0.3 to 0.6 gm. (gr. v.–x.). The soluble form is used to make the bitter wine of iron (*Vinum Ferri Amarum*).

A very great number of salts, as well as a number of double salts, have been formed with quinine, nearly a hundred in all being listed by manufacturers. The following are official.

Quinine Sulphate, soluble in 740 parts of water, 30 of boiling water, or 65 of alcohol. It is neutral to litmus paper. About three-fourths of it is quinine. It enters into the formation of the official *Syrupus Ferri Quininæ et Strychninæ Phosphatum*, the dose of which is 4 to 8 c.c. (fl. ʒ i. to ij.).

Quinine Bisulphate, soluble in 10 parts of water and 32 of alcohol, and acid to litmus paper. About five-eighths of it is quinine.

Quinine Hydrobromide, soluble in 54 parts of water and 0.6 of alcohol, neutral or faintly alkaline to litmus paper.

Quinine Hydrochloride, soluble in 34 parts of water and 3 of alcohol, reaction like the last.

Quinine Valerianate, soluble in 100 parts of water and 5 of alcohol, reaction like the last.

The acetate, citrate, bitartrate, benzoate, salicylate, and phosphate are also considerably used, as is the carbamide (hydrochlorate of quinine and urea). Being very soluble, they are specially useful for hypodermic injection.

The quinate is supplied on the guess that, being the natural salt of the living plant, it might be more efficient. It is very soluble in both water and alcohol, and is used hypodermically.

The tannate has been very much used, but most testimony is against its efficacy. It has little taste, but this is because of its great insolubility.

The arsenite, arsenate, antimonate, etc., may be regarded rather as medicinal forms of the associated substances.

Action and Uses of Quinine.—In using quinine it is always to be borne in mind that under alkaline conditions it is precipitated. The antiseptic properties of quinine are very similar to those of salicylic acid. It is especially antizymotic, and one-half per cent. may be added as a preservative to solutions. Advantage is taken of this property to prevent urinary decomposition by injecting it into the bladder. It may also be applied in powder or solution to unhealthy sores as a disinfectant. It is at the same time stimulating to the healing tissues, but care must be taken to avoid undue irritation. As a parasiticide it works very irregularly and, upon the whole, uncertainly; yet its domestic repute as a hair tonic is probably due to some destructive or inhibitory effect upon the micro-organisms of the scalp. A solution painted upon the nares has in some cases aborted an attack of hay fever, but the mode of action is uncertain.

Quinine, so applied as to be maintained in solution, is stimulant or irritant to mucous membranes. It possesses precisely the same appetizing, stomachic, and tonic properties as other vegetable bitters, tends like them to inhibit digestion of the food mass in which it is contained, and, like them, should be administered for these purposes in small doses, well diluted and taken slowly just before meals. After long administration, gastric irritation and indigestion are very apt to be produced and may be reflected by an erythematous or urticarious eruption of the skin. In some persons even small doses will produce these very distressing symptoms. The reflex stimulation of quinine through the stomach appears to be rather unimportant. Its absorption is almost, if not wholly, from the stomach, so that the conditions for rapid absorption should be secured. There should be an abundance of water taken with it, and if drink is avoided for some time previous to the dose absorption is favored. A slight amount of alcohol favors absorption. If these conditions are observed, the very large doses required in treating the pernicious malarias of the tropics can be readily absorbed. In most cases, quinine is a remedy the effect of which is particularly strengthened by prompt absorption. Authorities are agreed that it exists in the blood as the chloride. It favors alkalinity of the blood. Elimination is almost wholly by the kidneys, except for the unabsorbed portion which passes out with the fæces. Elimination begins very quickly but proceeds rather slowly.

Concerning the systemic effects of quinine after absorption, a very great amount of research has been recorded. The results are here very briefly summarized for the reason that their bearing upon the two leading therapeutic uses of the drug is very simple, and other relations will be discussed under Toxicology.

Its most important power is that of killing the malarial plasmodia and of inhibiting their propagation. This it does directly, promptly, and in proportion to the percentage in solution in the blood. This perfectly explains its antiperiodic properties, but not its effects in removing neuralgia and other sequelæ of malaria after the disappearance of the plasmodia from the system. It is natural to ascribe these results to the tonic action, through nutritive restoration; but sometimes the result is immediate, from large doses, and it must be due to some unexplained nerve action.

Its next most important effect is to reduce the temperature of fever, which it will not do to the normal temperature. This is done in two ways: 1. The drug has a marked power to lessen the oxidation of hæmoglobin, as well as the transfer of oxygen to the tissues, thus decreasing heat production. 2. It inhibits the heat-producing centres. All metabolism and tissue waste are strongly checked, one of the factors favorable to its tonic action; consequently there is markedly decreased elimination of urea, uric acid, etc.

The above facts will partly explain the power of quinine to check inflammatory processes. This is further explained by the fact that the drug is a general depressant of vital power. It depresses both the irritability and power of muscular tissue, being thus a cardiac and arterial depressant. In this way, and by acting upon the cardiac ganglia and the vaso-motor centres, it markedly reduces blood pressure. It must be understood, however, that this is a secondary effect and an effect of large doses, and that it is possible to so administer small doses as to get a slight vaso-motor and cardiac stimulation, not followed by any appreciable reaction.

These facts in turn have a bearing upon the power of quinine to inhibit pus formation. The further claim is made that it checks the migration of leucocytes, as it certainly lessens their activity. Although the counter claim is made that this migration is checked only by impracticably strong solutions, the former view appears sustained. The reflex inhibitory centres are also stimulated, resulting in a pseudo-reflex depression.

Quinine causes contraction of the spleen, especially if

enlarged. The cerebral effect appears in contrast to the generally depressing effects, being that of a direct and prolonged increase of circulation, with correspondingly increased functional activity. This contrast is in reality misleading, as the principal cause appears to be depression or paralysis of the arterial walls, leading to local congestion. The symptoms induced constitute the state known as cinchonism, in which there is fulness in the head and often a slight dull headache, ringing in the ears, usually with some deafness, and some disorders of vision. These symptoms are taken to indicate the full physiological effect of the drug, and preliminary to acute poisoning, in which there are dizziness, blindness, and unsteady gait, going on to great muscular depression, convulsions, and generally the condition of collapse, with failure of respiration.

Most of the uses of quinine are directly in line with its activities as above defined. As a tonic and restorative, one to three grains may be given before meals for some time.

In malaria, its great field of usefulness, the methods of administration differ widely. There are two principal rules, one to administer a few large doses, the other many small doses, and each has many adherents. The latter method is most likely to disturb the stomach. Proximity of the paroxysms to one another frequently renders the former method unavoidable, as the effects of administration during the paroxysm are not so favorable. It has been suggested that just after a paroxysm of fever the plasmodia are at their weakest and hence most easily affected by the quinine. All considered, the most rational method appears to be the administration of a large dose of five to ten grains just after the paroxysm and then say two grains every two hours to keep the system under its influence until the danger of recurring attacks is past. At intervals of seven days there is special danger of recurrence, and the prophylactic dose should be doubled at that time. After each seven days the dose may be progressively reduced, ceasing after the twenty-eighth day. If the patient continue exposed to infection, the cure need not be regarded as permanent except upon the best of evidence, and many such persons have to take quinine habitually. There can be no question of the frequent injuriousness of the drug under such circumstances, in spite of all statements to the contrary. Gastric and cutaneous disorders, as well as disturbances of sight and hearing, are not uncommon. Quinine should be used with caution when there is aural inflammation, and generally when cerebral congestion exists, and it should be lessened when gastric irritation comes on.

In the pernicious malaria of the tropics, very large doses, up to fifty or sixty grains, preferably of the bisulphate, with abundance of water, often prevents immediate death, and permits of cure. A little alcohol greatly aids its action. The disagreeable cerebral symptoms which would ensue from such large doses may be avoided by an accompanying dose of bromide. The use of mercurials favors the effects of quinine. The certainty of the antiperiodic action of quinine was established by an Indian Government commission, which determined the proportion of failures to be not more than seven per thousand cases.

The antipyretic action of this alkaloid can be secured by the administration of twenty grains or more. If the temperature is ascending at the time, more is required. It is then also slower in its action, requiring only about an hour under the most favorable circumstances.

Acute tonsillitis is apt to be most favorably affected by a prompt dose of ten grains, and an impending cold may often be averted in the same way. Here, again, a small or moderate dose of alcohol will emphasize the effect of the quinine.

Various methods have been resorted to to disguise the bitter taste of this drug, exceedingly objectionable to many persons. The use of tannin and substances containing it weakens its medicinal effect. Yerba santa probably acts chiefly in this way. Probably there is nothing, in the liquid form, better than licorice for this purpose. The best general method, however, is the use of the soft gelatin capsule, or, almost as good, the ordinary hard gelatin capsule.

Other Alkaloids.—The only other alkaloids which require mention are quinidine, cinchonidine, and cinchonine, the last of comparatively little value. As to dosage, it is taught that for antiperiodic purposes, the dose of quinidine and cinchonidine is about one-third more than that of quinine, that of cinchonine double that of quinine. The failures per thousand stand 6 for quinidine, 7 for quinine, 10 for cinchonidine, 23 for cinchonine. The relative antipyretic effects are, quinine 10, quinidine 9, cinchonidine 7, cinchonine 4. As stomachics and tonics, there is little difference among them, with the injurious effects more pronounced from quinine. Cinchonidine, and still more cinchonine, is less apt to cause the disagreeable effects of cinchonism, and they may frequently be given to those who cannot tolerate quinine. Cinchonine and its sulphate, and the sulphates of cinchonidine and quinidine, are official and their descriptions follow, as well as brief accounts of some rather important alkaloidal substances.

Cinchonina or Cinchonine ($C_{19}H_{22}N_2O$).—White, lustrous prisms or needles, without odor, at first almost tasteless, but soon developing a bitter after-taste, and permanent in the air.

Soluble, at 15° C. (59° F.), in 3,760 parts of water, and in 116 parts of alcohol; in 3,500 parts of boiling water, and in 26.5 parts of boiling alcohol. Also soluble in 526 parts of ether, and in 163 parts of chloroform.

At 240° C. (464° F.) the crystals fuse together, and at 258° C. (496.4° F.) they melt, forming a brown liquid. When ignited, they are consumed without leaving a residue.

When placed on moistened red litmus paper, cinchonine shows an alkaline reaction.

On adding to a neutral or not more than faintly acid solution of cinchonine, or of one of its salts, enough potassium ferrocyanide T. S. to redissolve the precipitate first formed, and afterward an acid, a golden-yellow precipitate will be formed, which, when redissolved by gently warming the liquid, will separate, on cooling, in minute scales or needles.

On adding an excess of ammonia water to a solution of cinchonine in a dilute acid, the alkaloid will be precipitated.

The precipitate is but feebly soluble in ammonia, and should require not less than 300 parts of ether for solution.

Its sulphate is neutral, and is soluble in 66 parts of water and in 10 of alcohol.

Cinchonidine Sulphate ($(C_{19}H_{22}N_2O)_2H_2SO_4 + 3H_2O$).—White, silky, acicular crystals, without odor, having a very bitter taste and slightly efflorescent on exposure to air.

Soluble, at 15° C. (59° F.), in 70 parts of water, and in 66 parts of alcohol in 1.42 parts of boiling water, and in 8 parts of boiling alcohol. Also soluble in 1,316 parts of chloroform, and almost insoluble in ether. The presence of sulphates of other cinchona alkaloids increases its solubility in ether and chloroform.

At 100° C. (212° F.) the salt gives off its water of crystallization. At 215° C. (419° F.) it melts, and, when ignited, it is consumed without leaving a residue.

The salt is neutral, or has a faintly alkaline reaction on litmus paper.

On adding ammonia water to the aqueous solution of the salt, a white precipitate (cinchonidine) is produced, which is but slightly soluble in ammonia, but dissolves in about 75 parts of ether.

If concentrated sulphuric acid be added to a small quantity of the salt, not more than a faintly yellowish color should be developed (limit of *readily carbonizable, organic impurities*). Upon adding to this liquid a crystal of potassium dichromate, a yellowish-green color is produced, which gradually changes to grass-green.

Addition of barium chloride T. S. to an aqueous solution of the salt produces a white precipitate insoluble in hydrochloric acid.

A solution of the salt (about 1 in 1,000) in diluted sulphuric acid should not exhibit more than a faint blue fluorescence (absence of more than traces of the *sulphates of quinine* or *quinidine*).

If 1 gm. of the salt be dried at 100° C. (212° F.) until it ceases to lose weight, the residue, cooled in a desiccator, should weigh not less than 0.920 gm. (absence of an *undue amount of water*).

If 0.5 gm. of the salt be macerated, with frequent agitation, at the ordinary temperature, with 20 c.c. of distilled water, 0.5 gm. of potassium sodium tartrate then added, the maceration continued, under repeated agitation, for one hour at 15° C. (59° F.), and the mixture then filtered, the addition of one drop of ammonia water to the filtrate should not produce more than a slight turbidity (absence of more than small proportions of the *sulphates of cinchonine* or *quinidine*).

Quinidine Sulphate ($(C_{20}H_{24}N_2O_2)_2H_2SO_4 + 2H_2O$) is soluble in 100 parts of water or in 8 of alcohol, and is neutral or faintly alkaline.

Quinoidine, *Chinoidine*, or *Black Stick*, is a blackish, resinous, alkaloidal mass precipitated from the mother liquor and without definite composition. It is nearly equal in efficacy to quinine, and may often be used in the same dose as quinine in chronic malaria, when other alkaloids have failed, or when quinine cannot be used.

Febrifuge is a name applied to an alkaloidal mass manufactured in India as a cheap substitute for quinine for home consumption. One form is made of the total alkaloids of red bark, another as a by-product after the extraction of quinine, with the addition of the alkaloids of some hybrid bark. It is used on an immense scale. Its composition is reported by Hooper (*Pharmacographia Indica*) as quinine 15.1 per cent., cinchonidine 29 per cent., cinchonine 33.5 per cent., amorphous alkaloids 17 per cent. It is a pale yellowish-white powder, of peculiar odor. The dose is slightly larger than that of quinine.

Unofficial Cinchona Barks.

Only two of these are important, namely, Pale Bark and Maracaibo Bark.

Pale Bark.—This is the product of *Cinchona officinalis* L. and its several varieties. These vary so greatly in appearance that there are various forms of this bark recognized, as Crown, Huanuco, Cuenca, Loxa or Loja. The native bark came from Ecuador, and still does so in rather large amounts. It comes from large shrubs and occurs in rather crooked, thin quills, from the thickness of a lead pencil to that of the finger, and is rather thick for the size of the quill. It is generally of a dark brown, the Huanuco a rather light brown, and is very apt to be excessively shaggy with lichens, when it is highly prized and really contains more alkaloid, as a result of the exclusion of light during growth. It is less bitter than the other barks. It and various hybrids have come largely into cultivation, but this cultivation is not now continued on the same scale. These hybrid forms grow much larger, the quills becoming as large as an ordinary calisaya. They retain their proportionally greater thickness. They are usually of a dingy gray and the fissures are wide and gaping. The color of the powder is very light, giving the name "pale." This bark (if typical) usually contains about three per cent. of alkaloids, one-half to nearly two-thirds being quinine. It is chiefly consumed in Southern Europe. It was formerly official, and its fluid extract is still a favorite with many American physicians. This preference is however erroneous, unless a double dose is given to secure the same effect.

Maracaibo Bark.—This is from one of the most northerly growing species. What that species is, is not certain. The bark occurs in warped, chip-like, thick pieces commonly as large as the hand, and is of coarsely striated structure, and hard and heavy. It is of a bright but pale yellow, with silvery soft patches of periderm easily scraped off with the thumb-nail. Its only interest is because many ignorant pharmacists purchase it, under the name of "yellow bark," for calisaya. It is quite worthless except as a vegetable bitter, containing a great amount of resin, but practically no quinine or other valuable alkaloid.

The other unofficial barks, Cuprea, Pitaya, Gray, Hard, and Soft Colombian, Hard and Fibrous Carthagena, Hamalies, Cuzco, Cocola, Pajinal, are in the market, if at all, only as relics. They are no longer collected. When cinchona was valuable, great quantities of these were accumulated in London, and when the price fell they were stored to await a favorable market. This never came, and many tons are still there, for which their owners would be glad to take five per cent. of the cost price. From time to time small quantities of these are worked off upon ignorant or careless buyers, but their use can be regarded only as objectionable.

Remijia.—One of these, Cuprea Bark, is the product of the related genus Remijea and contains a small amount of quinine.

The following composition table by Dr. Bolles, taken from the last edition of this work, is of interest:

1. Alkaloids.

Name.	Discovery.	Composition.	Source.
Quinine	Pelletier and Caventou, 1820.	$C_{20}H_{24}N_2O_2$.	In all the best cinchonas, especially *C. Calisaya*, *Ledgeriana*, *officinalis*, *lancifolia*, *pitayensis*, etc., associated with cinchonine, etc.
Quinidine	Henry and Delondre, 1833.	Same formula	*C. pitayensis* and other good species.
Cinchonine	Pelletier and Caventou, 1820.	$C_{19}H_{22}N_2O_2$.	Red bark, *C. succirubra*, also in most of the others, common and abundant.
Cinchonidine.	Winckler, 1847..	Same formula	*C. tucujensis*, also in other species.
Homocinchonidine.	Hesse, 1877.....	$C_{19}H_{22}N_2O_2$.	South American red bark.
Quinamine	Hesse, 1872.....	$C_{19}H_{24}N_2O$.	*C. Ledgeriana*, *officinalis*, etc., also in *Remijia*.
Cinchamidine	Hesse, 1881.....	$C_{20}H_{26}N_2O$.	From the mother liquor of homocinchonidine. Frequently present in commercial cinchonidine.
Aricine	Pelletier and Coriol, 1829 ...	$C_{23}H_{26}N_2O_4$.	*C. pubescens*, etc., Arica or cusco bark.
Cusconine	Hesse, 1877.....	$C_{23}H_{26}N_2O_4$.	Accompanying the above.
Cusconidine	Hesse, 1877.....	Not analyzed.	
Cuscamine	Hesse, 1880 (...	Not analyzed.	*C pelletieriana* ("cusco bark").
Cuscamidine	Hesse, 1880 (...		
Paricine	Winckler, 1844..	.....	*C. succirubra* (Hesse, 1877).

2. Acids.

Cinchonic acid, kinic acid.	Hoffman, 1790..	$C_7H_{12}O_6$.	In all cinchonas and many other plants. A widely distributed vegetable acid.
Chinovic acid.	Hlasiwetz.....	$C_{24}H_{38}O_4$.	In cultivated cinchonas; probably more general. Also in Tormentilla.
Cinchotannic acid.	Berzelius	.....	All cinchonas.

3. Neutral and Miscellaneous.

Chinovin. A glucoside.	Pelletier and Caventou, 1821.	$C_{30}H_{38}O_8$.	Cinchonas, Remijias, and other *Cinchoneæ*.
Cinchona red.	Reuss, 1812.....	$C_{28}H_{32}O_{14}$.	All cinchonas, especially the red.
Lignoin	Reichel, 1856 ...	$C_{20}H_{22}NO_8$.	Cinchonas—doubtful substance.
Cinchocerotin.	Kerner, 1859 ...	$C_{27}H_{48}O_2$.	Calisaya.
Water			

Henry H. Rusby.

CINCINNATI, the chief city of Ohio, is situated on the north bank of the Ohio River. "It is surrounded by hills from 400 to 465 feet in height, forming one of the most beautiful amphitheatres on the continent, from whose hilltops may be seen the splendid panorama of the cities below, and the winding Ohio" (Appleton's "Guide to the United States and Canada"). It is a city of three hundred thousand or more inhabitants, more than a third of whom are Germans or of German parentage. The chief public park is Eden Park, situated on a hill affording a striking view of the city, the valley of the Ohio, and the surrounding country. The climate is indicated by the accompanying chart.

Climate of Cincinnati, Ohio.—Latitude, 39° 6′; Longitude, 84° 30′. Period of Observations, December 1st, 1870, to December 31st, 1883.

Data.	January.	July.	Year.
Temperature (Fahr.)			
Average or normal	34.4°	78.3°	55.90°
Average daily range	14.0	16.3	
Mean of warmest	41.4	86.8	
Mean of coldest	27.4	70.5	
Highest or maximum	69.0	103.5	
Lowest or minimum	−10.0	38.2	
Humidity—			
Average relative	72.3%	64.4%	66%
Precipitation—			
Average in inches	3.54	4.29	44.36
Wind—			
Prevailing direction	S.W.	S.W.	N.W.
Average hourly velocity in miles	6.4	4.8	9.8
Weather—			
Average number of clear days	4.8	9.2	94.9
Average number of fair days	10.2	12.2	140.4
Average number of clear and fair days	15.0	21.4	235.3

E. O. Otis.

CINCINNATI ARTESIAN WELL.—Hamilton County, Ohio. This well is located at the Cincinnati gas-works, and is 1,245 feet in depth. There is a continuous flow of water. The following analysis is by E. S. Wayne:

One United States Gallon Contains:

Solids.	Grains.
Magnesium carbonate	8.14
Calcium carbonate	17.33
Potassium sulphate	27.27
Sodium chloride	519.90
Magnesium chloride	18.14
Calcium chloride	22.26
Potassium chloride	3.27
Magnesium bromide	.26
Magnesium iodide	.19
Iron oxide	.37
Silica	.49
Total	617.32
Gases.	**Cu. in.**
Sulphureted hydrogen	7.76
Carbonic acid	10.32

This is a very rich saline sulphureted water, and ought to be of value in the treatment of diseases for which such waters are used. *James K. Crook.*

CINNAMIC ACID AND CINNAMATES.—Cinnamic or *phenyl-acrylic* acid ($C_9H_8O_2$) results from oxidation of oil of cinnamon, the oil being chemically cinnamic aldehyde, and it also exists ready formed in conjunction with benzoic acid, to which it is closely related, in many balsams, such as the balsams of tolu, of Peru, and of benzoin. It can be formed synthetically also. Cinnamic acid is a colorless crystalline body, volatilizable without taste or smell, freely soluble in alcohol, but only feebly so in water (one-tenth per cent.). The commercial article is obtained chiefly from styrax.

Cinnamic acid is non-poisonous, and is said to resemble salicylic and benzoic acids in antiseptic power. It has been suggested as a practical antiseptic for use in surgical dressings. Lint, jute, etc., may be charged with the acid by soakage in an alcoholic solution. It has also been employed for the constitutional treatment of phthisis, by the intravenous injection, twice a week, of a few minims of a five-per-cent. emulsion of the acid. Such injection is practised upon a vein of the forearm, with proper antiseptic precautions, and the treatment continued for at least three months.

Cinnamic acid is oxidized readily into benzoic acid, and it is supposed that this action takes place in the human system, since the two acids have the same effect upon the urine and its constituents.

Sodium cinnamate is a salt freely soluble in water, and has been proposed as a substitute for cinnamic acid because of such free solubility. *Edward Curtis.*

CINNAMON.—The cinnamon products include cinnamon and cassia barks, cassia chips, cassia leaves and cassia flowers, and the oils distilled therefrom. They are all yielded by species of the genus *Cinnamomum* Blume, in the family *Lauraceæ*. The genus contains some fifty-four species, all natives of tropical Asia and Australasia. The section containing the camphor tree is markedly distinct, and would probably be better regarded as forming a separate genus. Many of the species yield useful products of minor importance, and these will be enumerated at the close of this article. Three species, two of them known, the third doubtful, yield the highly esteemed and official cinnamon barks, and will now be considered separately.

1. Ceylon Cinnamon, Cinnamomum Zeylanicum.—"The inner bark of the shoots of *Cinnamomum Zeylanicum* Breyne" (U. S. P.). This well-known species is a native of the hills and woods of the island of Ceylon. It has also been long cultivated in the same island, and it is from these cultivated plants that all the true cinnamon now comes. It has also been introduced into other islands of the Indian Ocean, and into the mainland of Asia, as well as into the West Indies, but it produces in these places inferior barks. On the cinnamon plantations the trees are trimmed down to make them send up sprouts from the base; these are allowed to grow until they are about two years old and 3 or 4 cm. in diameter, when they are cut, and the bark is peeled off in pieces about 30 cm. (1 ft.) in length. These strips are then put together in rolls and allowed to wilt for a day or so, when they are separated and each piece is laid upon a suitable stick around which it will fit, and the outer cellular layers of the bark are scraped off and rejected. The quills of inner bark so prepared constitute cinnamon, and are rolled together in successive layers until a solid cylinder about a metre long and 1.5 or 2 cm. thick is formed (1 yd. by 0.5 or 0.75 in.), of sometimes a dozen layers of brittle, splintery bark. The Pharmacopœia thus describes the bark:

"*Ceylon cinnamon* is in long, closely rolled quills, composed of eight or more layers of bark of the thickness of paper; pale yellowish brown; outer surface smooth, marked with wavy lines; inner surface scarcely striate; fracture splintery; odor fragrant; taste sweet and warmly aromatic."

This is altogether the finest, and in general the best cinnamon of the market, though it is not nearly so strong, sweet, or expensive as the third variety. If taken young and of good quality, it has scarcely a trace of bitterness and but little astringency. It contains only a moderate amount of sugar and mucilage. It yields a large percentage (up to five per cent.) of ash. It is rich in oil, yielding up to one and a half per cent., and this oil is very fragrant. The features of this cinnamon, as a perfuming and flavoring agent, are its delicacy and permanence. It is the only species official in the British Pharmacopœia.

2. Cassia Cinnamon, Cinnamomum Cassia, Cassia Lignea, Cassia Vera.—"The bark of the shoots of one or more undetermined species of Cinnamomum grown in China" (U. S. P.). In spite of this statement, the article is known to be the product of *C. Cassia* (Nees) Blume. Like Ceylon cinnamon, it is collected both from wild and from cultivated trees, mostly the latter. It comes from Southern China, and is therefore often called Chinese cinnamon. The name is a bad one, however, as it does not distinguish it from No. 3. The trees are cut down when about six years old, and the long straight