1-1-1852

Dissertation on cinchona

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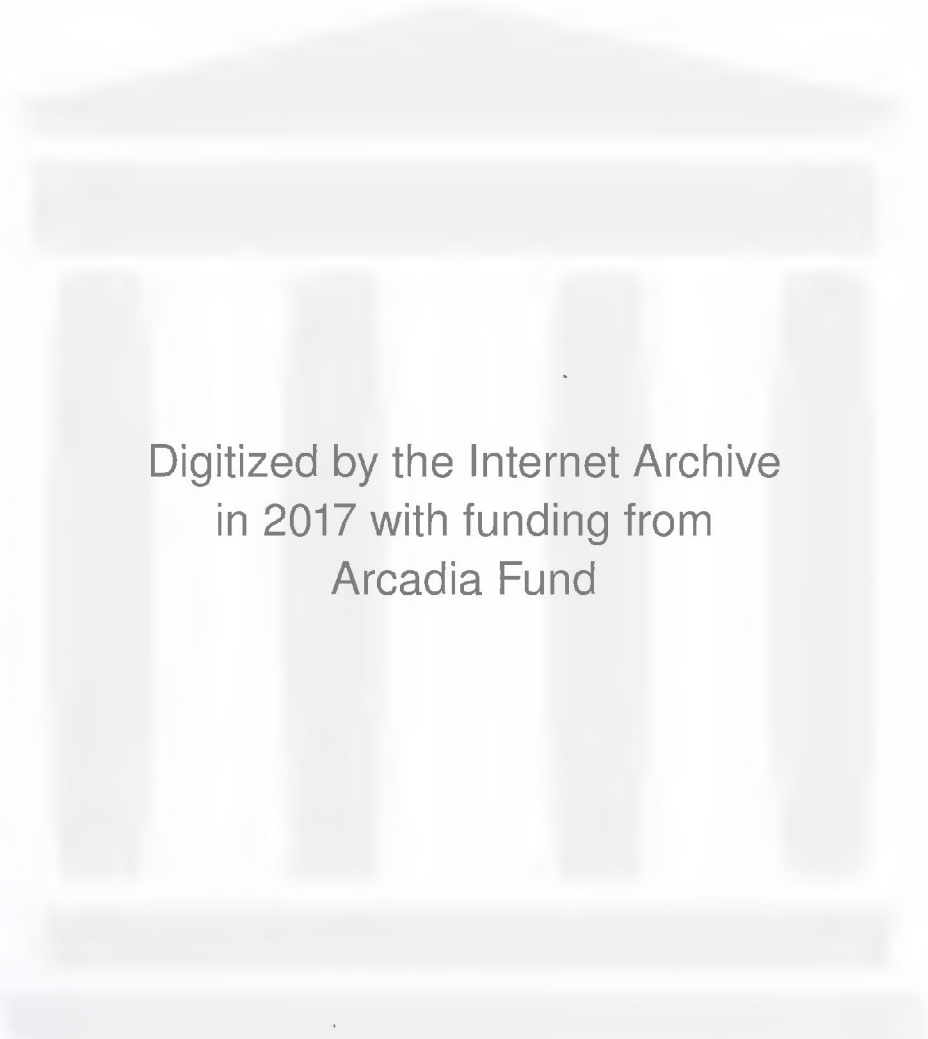

Dissertations

read by the

Candidates for the Degree

of

Doctor in Medicine

at the

Annual Examination

in the

Medical Institution of Yale College

January 14–15, —— 1852.

Cinchona.

The Botany of Cinchona. Cinchona; a genus of the Vegetable Kingdom; of the monopetalous exogens, natural family Cinchonacea and genus Cinchona. It is classified, according to the Linnaan system, in the class Pentandria, order Monogynia. The plants belonging to this genus, are large and majestic trees, 30 or 40 feet high, or shrubs 8 or 9 feet, growing between 22° S. lat. and 10° N. lat., thriving best in mountaineous regions. The general characters are: Calyx, five toothed. Corolla, hypocrateriform, with a five parted limb, valvate in aestivation. Anthers, linear, inserted within the tube and not projecting unless in a very slight degree. Seeds, girted by a membranous lacerated wing. (Lindley). The number of species is doubtful; Humboldt has 9, Ruiz & Pavon, 19, La Condamine 3. etc. It is to that distinguished South american botanist, José Celestino Mútis, whom Linnaus calls Phytologorum americanorum princeps, and of whose name he says: Nomen immortale quod nullas atas unquam delebit, and whose powerful mind not only mastered Botany and Astronomy but also other sciences, that we owe the knowledge of many species, discovered by himself, and the true geographical distribution of this interesting genus. His name will be handed

down to posterity, with all the glory that, by his works, he deserves. He was born the 6th of April 1732, and after a long, laborious and useful life, was called to enjoy the blessings of his Creator the 18th of September 1808. —— This genus is easily recognized by the botanist, especially, when to description, drawings are added. The organaleptic properties are better learned by practice, and even old apothecaries find it difficult to discriminate between different kinds of bark, so I will say nothing about them.

The Chemistry of Cinchona. After its introduction in Europe and after its astonishing curative properties were widely known, the investigation of its mode of action, on scientific principles, began. The inquiry was, at first, directed only to the action of water and alcohol upon it, and to estimate the ammount of gummy or extractive matter. It appears that the first chemist that made an analysis of it, was Fourcroy, who ascertained the existence of certain principles, besides those that came under the vague appellation of extractive. Dr. Westring attempted to discover the active principle, but was not successful. M. Deschamps, first obtained a distinct crystallizable salt of Lime, the acid of which, Vauquelin first isolated, and called it Quinic acid. It crystallizes in

rhombic prisms. Its formula is $C_{7}H_{10}O_{5}$, 240. Some salts of this acid have been obtained, the quinate of lime, from which it is isolated, is one. I will speak only of the quinates of Cinchonine and quinine. Their formation is easy; by merely putting together a solution of quinic acid with either of the alkaloids, the salts will be formed. The quinate of cinchonine has a bitter astringent taste, that of quinine, a very bitter one. Both of them more or less soluble in water and alcohol. Their medicinal uses are the same as the other salts, of the same alkaloids, however, they may be preferred when others do not produce the desired effect. — The first step towards the discovery of Cinchonine seems to have been taken by Dr. Gómez, a portuguese physician, and not, as it is erroneously stated in the U. S. Dispensatory, by Dr. Duncan. The results of MM. Pelletier et Caventou, form a new era in the chemistry of Cinchona. They discovered the true nature of the cinchonine of Dr. Gómez and a new and most extensively used alkaloid, Diimine. The process given by Dr. Gómez for its preparation, did not give a pure article, but it was cinchonine and some oleaginous matter, and accordingly, he did not discover the true nature of the substance. Pelletier & Caventou, were enabled to procure the pure article by other process, and readily ascertained its alkaline nature. The Cinchona

Condaminea was employed. They prepared an alcoholic extract which was of a brown colour; this by being repeatedly washed, left a white-greenish matter. This was the cinchonine of Dr Gomez, but by mixing it with a dilute acid (HCl) a greasy matter separated, and the solution was of a golden yellow. From this solution it was precipitated by Magnesia and the precipitate, a dirty white, by repeated recrystallizations from alcoholic solutions, gave a brilliant, white, crystalline substance; pure cinchonine. It was very little soluble in water, soluble in alcohol or ether, decomposed by heat before fusing. When a hot solution of cinchonine in water, was mixed with iodine, this last was converted into iodic and hydriodic acids, which form white salts with the cinchonine, and precipitate on cooling. Treating the precipitate with sulphuric acid, the iodine was set free, which reaction, after its behaviour with test papers, left no doubt of the alkaline nature of cinchonine. These chemists formed various salts, the analysis of one of which only, I will give. Sulphate of cinchonine is composed of cinchonine 100, Sulphuric acid 13.0210. At a later period the action of iodine on cinchonine, was studied by M. Pelletier and his results are: When cinchonine, with its weight of iodine, is treated with alcohol, all is dissolved and by spontaneous

evaporation one obtains iodide of cinchonine in plates of a saffron-like colour, and also hydriodate of cinchonine. On heating them with warm water, this last salt is dissolved and the iodide is left fused. In this way, the two salts are separated. His analysis gives { Iodine 29.87 / cinchon. 71.13 } or according to Serullas { Iodine 33.85 / cinchonine 65.15 }. There is also an iodate and the hydriodate. The composition of cinchonine is according to the analyses made by Pelletier et Caventou, Liebig and Henry & Plisson.

	P.C.	L.	H.P.	Formula.	
Carbon	76.97	76.36	78.88	Liebig	$C^{20} Az H^{11} O$
Hydrogen	6.22	7.37	8.876	Regnault	$C^{40} Az^2 H^{24} O^2$
Nitrogen	9.02	8.87	9.3522	Laurent	$C^{38} Az^2 H^{22} O^2$
Oxygen	9.92	7.40	2.8918	Hlasiwetz	$C^{20} Az H^{12} O$.

As regards the formula, it will be seen, there has been and is yet a good deal of difference. M. Hlasiwetz confirms all the first three formula and adds one more. He has found that under different circumstances, all these formula result. That of Liebig he obtained by analyzing the cinchonine prepared in Darmstadt by M. Merck. He found another substance and called it cinchotine, agreeing with the Hquinine of Heinisen who found it in the Quinoidine of commerce, and by analysis found isomeric with quinine. In this state, as far as I know, the formula rests. — Cinchonine combined with

most of the acids and many salts with the most common, have been obtained. Sulphate of cinchonine, neutral sulphate of Barup. Sulphuric acid and cinchonine unite and form a neutral salt, very soluble in water and alcohol, insoluble in ether. Crystallizes in four sided prisms of very bitter taste. It fuses a little above the boiling point of water, and a slight increase of temperature decomposes it. Its analysis gives, Cinchonine 100, Sulphuric acid 13.021. Calculating from this we get the atomic weight of cinchonine equal to 38.488. M.E. Barup, some time after, described two sulphates, a neutral and a supersulphate. By adding sulphuric acid to the neutral sulphate and evaporating till a pellicle begins to show itself, we obtain, after some time, the supersulphate. It crystallizes in rhomboidal octahedrons, soluble in water and alcohol, but not in ether. The other salt has already been described. Their composition, according to M. Barup, is as follows:

Neutral Sulphate. Cinchonine 100. Sulphuric acid 12.820

Supersulphate. Cinchonine 100 Sulphuric acid 23.461.

Gallate of Cinchonine. Mixing a hot solution of gallic acid with cinchonine, the liquid remains clear, on cooling it becomes milky and then again clear, leaving the salt precipitated in the form of translucent little crystals. I mention the iodides, the

galates and associates more particularly, as they are sometimes used by the practitioner. The arseniate I pass over and shall say something more on the arseniate of quinine. There are many other salts, which I must leave unnoticed. The preparations of cinchonine, are on the whole much less used than those of quinine. Quinine was first discovered by Pelletier et Caventou, who treated the yellow bark, C. cordifolia (Mutis) by the same process as the C. condaminea (Humb. & Bonp.). Quinine is an alkaloid, crystallizes with difficulty, in pearly silky crystalline needles, though at first it was thought amorphous. Little soluble in water, very soluble in alcohol and in ether. Decomposed by heat, and as cinchonine, gives non azotized vegetable products. It has a very disagreeable bitter taste, like that of yellow bark and much stronger than that of cinchonine. The analysis of quinine have been made by Pelletier et Caventou, Pelletier et Dumas, Liebig and Henry & Pelletier. Their results are:

	P. C	P. D.	L.	H. P.
Carbon	75.	75.02	74.40	74.552
Hydrogen	6.25	6.06	7.61	8.4322
Nitrogen	8.75	8.45	8.11	8.2946
Oxygen	10.	10.43	9.88	8.7212

Its formula is $C^{20}H^{12}AzO^2$ or (Regnault) $C^{38}H^{24}Az^2O^4$. The combinations of quinine are numerous and the one known to

every body almost, is the sulphate. MM. Pelletier & Caventou gave the analysis of it in their memoir. They say, and I translate word for word "Sulphuric acid dissolves the quinine and forms with this base a neutral salt that crystallizes very easily". Forms either needles or plates, very straight, elongated, slightly flexible and resembling those of amianthus. When fused it presents a waxy aspect. It is very soluble in water and in alcohol, very little so in ether. The mean of some analyses is: Quinine 100, Sulphuric acid 10.914. Therefore the atomic weight of quinine is 15.906, much higher than that of cinchonine. Of the sulphates, there are two, corresponding with those of cinchonine. Baup says "The neutral sulphate" the one already described "effloresces in the air and the water lost is three fourths of the total quantity of crystallization". The formula of these I put because of the great confusion generally experienced by the mixture of the old and new names. Then, $(C^{20}H^{12}Az\,O^2)^2 SO_3 + 8HO$ is the old neutral sulphate and the present disulphate; the salt used in medicine. Of its manufacture etc. I say nothing, these being known to all medical men. The other salt, the old superdisulphate, the present sulphate and the formula of which is $C^{20}H^{12}Az\,O^2, SO_3 + 8HO$, can be obtained by adding a slight excess of sulphuric acid to the

disulphate and evaporating to dryness. Its crystalline form is either a rectangular prism or needles very much like the fibres of amianthus. It is distinguished from the official sulphate by its acid reaction and greater solubility. The analysis by Bauf is: Quinine 100, Sulphuric acid 22.222. There are many other analysis, but I need not give them.

Gallate of quinine. On the addition of gallic acid to all the soluble salts of quinine, there is always a precipitate formed, provided the solutions are not too dilute. This acid unites to quinine and forms a salt very sparingly soluble in cold water. It is dissolved by heat and on cooling, the liquid becomes lactescent and deposites the opaque gallate. Combinations with iodine there are three, the iodide, the iodate and hydriodate. For the preparation of the first salt, one employs the same process as for the iodide of cinchonine, from which it is very difficult to distinguish, as it presents almost the same properties. Its composition, as given by Pelletier is: Iodine 30.31, Quinine 69.69, or Iodine 71.58 Quinine 28.42. Iodic acid unites with quinine and this salt is much less soluble than that of cinchonine. Theoretic analysis gives: Iodine 33.59, Quinine 66.41. There is nothing particular about the hydriodate. Dr. Donné undertook the inquiry; whether by

combining with iodine, the organic bases lost their power upon the animal economy. I have not seen this report, nor do I know his result, but I suppose that some do not. The next combination and the last of which I shall speak, is with arsenic. Arseniate of Quinine. Arsenic acid combined with quinine to form an arseniate, which, in form, resembles very much the phosphate. Comparing the arseniate of quinine, which crystallizes easily, in needles, with that of cinchonine, which does not crystallize, we find a method of distinguishing the two alkaloids. Arsenite of quinine. Dr. Ringdom found the arsenite very serviceable, especially in chronic cutaneous deceases. He prepared an arsenite of potash; 64 grains of arsenious acid with 32 grains of carbonate of potash and decomposed the salt with two scruples of sulphate of quinine. A white precipitate, diarsenite of quinine, is formed, which being washed and dried, can be given in the dose of one third of a grain, at first twice and afterwards three or four times a day. The dose of the other salts of quinine is the same as that of the sulphate. Many other substances have been subsequently found in or made from the cinchona, such as: Cinchovatine (Aricine), $C^{44}H^{27}Az^{2}O^{3}$,

Quinoleine, $C^{18}H^{7}Az$,

Quinon $C^{24}H^{8}O^{8}$, Hydroquinon $C^{24}H^{12}O^{8}$, Quinonique acid $C^{24}H^{12}O^{10}$
Quinonamide $C^{24}H^{12}Az^{2}O^{6}$, Chlorsulphoquinon $C^{24}H^{10}O^{8}Cl\,S^{4}$, etc. etc.
which, it is obvious, I must necessarily omit. To collect all new discoveries about the great remedy, would require much time and a lengthened writing, two things incompatible with my present purpose. The adulterations of quinine or its salts, are to be ascertained by the chemist, and this is not the place to point out a course of analysis. A few facts are given in the books. — Some reactions of quinine. When to a solution of sulphate of quinine, ammonia and chlorine are added, there is a beautiful green coloration. If instead of ammonia, one employ potash, the solution is colored sulphur yellow. Puting in the solution, chloride of calcium with hydrochloric acid, a green powder is also precipitated. Cinchonine does not produce any of these reactions. A method to determine the value of cinchona barks, is given by Dr. Buchner. It is by making an infusion of the bark in water acidulated with dilute sulphuric acid, at 122° to 140° F. After having exhausted completely the bark, which is known by not giving to acidulated water a bitter taste, the infusion is evaporated to a proper bulk, the quinine precipitated by ammonia. The precipitate is collected in a filter,

washed, dried and weighed. From the weight, the ammount of quinine is ascertained. The quinine is precipitated as a brown mass, if purified, it will not give good results; while the impure quinine gives the ammount very nearly. Another method, by Chloroform, is given in the Annuaire de Chimie p. 437. And with this, I must close what I have to say about the chemistry of Cinchona, though I reluctantly leave this part of the subject.

The History of Cinchona. Quinquina is the term more commonly used in Europe. This comes from Quina Quina, which in its turn is made from the Peruvian (Quichoa) longue, and La Condamine made its derivation from the word Quina qui, signifying a sort of shawl or mantilla. If not strictly correct, it is, at least, the most probable derivation. The bark seems to have been known to the inhabitants of Peru for a long period before the Spaniards, and made acquainted of its virtues by accident. Some say that a native having been taken sick with fever, accidentally took the bark and was cured; others, that it was discovered by observing that the lions when seized by an intermittent generally chewed the bark of the tree and tried found beneficial. Others again, say that the jesuits following the

custom of the country; to recognize trees by chewing the bark, and finding it so much more bitter than any other, those among them who were physicians, were led to apply it to cure deceases and found its properties. Geoffroy attributes its discovery to a man being obliged to drink, when thirsty and sick with intermittent, from a pool saturated with the bark, from fallen trees in it, and being cured. It seems to be certain, that the natives knew of its virtues and concealed them from the Europeans, whom they hated, with reason. The story is related, and seems, according to La Condamine, to be a true one, that in 1638, the vice queen of Perú, the countess of Cinchona, being attacked with a fever that yielded to no treatment, was cured, at the suggestion of the Corregidor, by taking the bark. — When she left for Europe, the 17th of December 1639, She carried some of the bark, as also her physician, Juan de Vega. The latter distributed the bark at Sevilla and the jesuits followed the same practice at Perú, hence the two names, Countess's powders and Jesuits' powders. Its reputation spread and finally it was sold in parts of the Continent, remote from Spain. In its turn, it lost much of its credit, by being mixed with other inert barks, but it soon revived. — The source of this great remedy was unknown in Europe until Louis XIV in 1679, made it public, having bought the secret from an Englishman,

Talbot, an empiric who sold an infusion of bark in Portwine, and contemporaneous with Sydenham. The tree which produced the bark, was not known till 1738, when La Condamine described it and Jussieu named it Cinchona officinalis. The knowledge of this remedy, its sources, properties, etc. have rapidly increased since then, and I omit this part of its history, as it is to be found in most books, suffice it to say that the demand for the bark is very extensive, the exportation carried on very largely and no physician willing to deny that if there is any specific in our Materia Medica, it is the bark or its alkaloids.

The Medicinal uses of Cinchona. Cinchona, I include under this term some of its alkaloids, is ranked among the powerful tonics and anti-intermittents. Its applications are very numerous, and I intend to give only a few. — When the bark is first taken into the stomach, it produces a sense of warmth in the epigastrium which diffuses itself over the abdomen; a sense of fullness or slight pain in the head. Singing in the ears and perfect deafness is experienced by some who are brought completely under its influence. Nausea, vomiting and even more distressing effects may be produced by the injudicious administration of this remedy, especially when given in an irritable state of the stomach. It may be employed in all the morbid conditions of the system,

when the tonic power is desired, provided there are no symptoms of gastric irritability. In low, typhoid forms of decease. In scarlatina, measles, small pox, carbuncle and when the system is exhausted by a large, purulent ulcer. Its great use, however, is in intermittent fever. M. Tshudy observes in his travels, that the fresh bark is more efficacious than the dried, and not only the cure is more speedy, but that it insures the patient against the return of the decease. Its use, mode of administration and effects, in this decease, are well known, so I pass them over. In remittent fever also, it is useful; but not in that class of remittents that take an inflamatory, bilious, congestive type. However, even in these, with some precautions, it is recomended by Dr. Chapman. This author, in some cases, obtained better results by a mixture of the bark with serpentaria. In certain kinds of diarrhea, I think that the gallates will be found useful. Used also in gleet leucorrhea, gonorrhea dormientium, in combination with steel, with some of the happiest effects. In gangrene, cancer, and the other malignant affections, the remedy is doubtful. It is indicated in remittent nervous affections. M. Pearson, praised it very highly, in certain forms of venereal decease, in incipient bubo, ulceration of the throat, etc. In these cases it is necessary to administer mercury also, to eradicate the de-

cease from the system. — To finish this part of the subject, it is necessary to do it abruptly: for Cinchona has been employed in so many deceases; different circumstances and different results, that to enumerate all, would, probably, be impossible. As an example of the extravagant ideas, I will give the belief of some, which cannot but make us laugh. It is: "Que la quinquina ne guérit ni les fièvres intermittents ni les maladies périodiques, mais l'intermittence et la periodicité". The mode of administration is various; in powder, infusion, tincture, pills, &c. I will give only two recipes.

Pulvis chocolatæ chinatæ.

Coffea cum cortice Peruviano.		Cocoa almonds	℥vi
Coffee, ground	℥ji	Cinchona, powd.	℥iii
Cinchona, powd.	℥j.	Sugar	℥viii
		Balsam of Peru	℥j.

An ounce of either, boiled in three or four spoonsful of milk or water, make a dose. There is a beer, unknown in Europe, and used by Mutis in New Granada, made by letting 32 lb of sugar and 3/4 lb of white cinchona, C. ovatifolia, with 15 bottles of water, ferment. This makes an alcoholic liquor, rather intoxicating and very useful to the convalescent. This can be made into vinegar by allowing the fermentation to go on longer. — In prescribing, care should be taken, not to give any of the incompatibles.

The deceases of Cinchona. I mean by this, those caused by it. M. Reimer of Frankfort has named one, the "Quinic fever," the description of which I have not been able to see, owing to a deficiency of a number of the "Comptes Rendues" &c. What I here say is from the same source. Dr. Gierad reports a case of a man being attacked with a tertian in a manufactory of quinine, against which the sulphate of quinine was unsuccessful. Salicine cured him. Another man in the same circumstances was cured by small doses of sulphate of quinine. M. Riviere proposes inoculation with the matter of the pustules of the quinic fever patients as a prophylactic against fevers of a marshy origin. Roseola also appear in rheumatic patients treated with sulphate of quinine. — I will conclude with a remark by Liebig. "We are able to produce urea, allantoine, the oils of valerian root, of the Spiraea ulmaria, of the Gaultheria procumbens, etc., all natural products, by chemical forces. The chemist makes allantois from the excrements of snakes and birds, he makes urea from charred blood, the oil of valerian from potatoes, etc. These results are enough to justify us, in entertaining the hope that we shall, ere long, succeed in producing Quinine, morphine and those combinations of which albumen and fibrine, or muscular fibre consist, with all their characteristic properties." This, if not exactly his own words, is the substance of them. But, even if once Quinine be artificially obtained, as not only that, but many

of the most important articles of our Materia Medica, are found only in the Cinchona's home (besides the articles found in the U. S. Dispensatory) I state only two of the many more that I could enumerate. These are: the Mikania Guaco, discovered by Mutis and the Simaba Cedron (Planchon) an analysis of which is in progress by Mr. Lewy, late Professor of Chemistry at Bogotá), and as not only through its quinine but by many other articles South America has bettered and alleviated our condition and thrown happiness around us when we least expected it or could hope for it; South America, will, in this respect, ever be the first country in the world. Oh the subject of Cinchona, perhaps all that is interesting has been passed over in the preceding pages, but however imperfect my writing may have been, I must here bring it to a close.

Ezequiel Uricoechea