MEDICINE-PHARMACOLOGY

Quinine from Peruvian Bark

"A Classic of Science"

Isolation of the Bitter, Astringent Principle Which Is So Valuable in Treating Malaria and Other Fevers

RECHERCHES CHIMIQUES SUR LES QUINQUINAS (Chemical Researches on the Cinchonas). By MM. Pelletier and Caventou. Read before the Academie des Sciences September 11, 1820. *Published in Annales de Chimie et de Physique (Gay-Lussac and Arago), Vol. XV. Paris,* 1820. *Translated for the* SCIENCE NEWS LETTER *by Helen M. Davis.*

AT EVERY EPOCH of those great discoveries which have extended the sphere of science, chemists have thought that they ought to take up again some of the work of their predecessors; guided by new light, they have often arrived at results which had escaped distinguished scientists who lived under less advantageous circumstances.

The cinchonas take their place at the head of those substances which are thus periodically subjected to new investigation: it would, in fact, be difficult to enumerate the researches undertaken upon these barks, from Bucquet to those with which M. Lauber has enriched science. But we must be allowed to recall the great dissertation of Fourcroy, which was long a model of organic analysis. We must cite also the analysis of eighteen species of cinchona, undertaken by M. Vauquelin, a project remarkable for its scope and for its results, since, in that Memoir, M. Vauquelin enriched organic chemistry with a new acid, gave the sure characteristics by which the true febrifuge cinchonas can be recognized, and gave chemists a new method of analysis. We should also recall a memoir by M. Reuss of Moscow, if the work of M. Gomès of Lisbon did not claim all our attention: it is to this last chemist that we owe the discovery of a special principle in cinchona, a principle which we have recognized as a salifiable organic base, the study of which will be one of the chief objects of our memoir.

Now, if we should be asked to give the reasons which have induced us to work with the cinchonas after such worthy chemists, we should avow the following considerations which have presented themselves to us. The discovery of organic bases marked an epoch in science; they explain a set of anomalies which are met with in organic analysis. The salifiable organic bases have such special properties, they are so constantly the active material of the organic compounds which contain them, that it was natural to search for them in the cinchonas: besides, if cinchonine, discovered by M. Gomès in gray cinchona, is, as that physician asserts, the substance by virtue of which the bark acts upon the animal organism, although that scientist assures us that it is neither acid nor alkaline, was it not necessary to find out whether there were not some error in the last part of its preparation? These are the reflections which suggested to us the idea of undertaking new researches upon the cinchonas: once entered upon this project, we have pushed the work beyond the goal which we at first set for ourselves. The properties which we found in cinchonine are so related to those of the other substances which accompany it that we have not been able to avoid studying these substances in their entirety.

Having examined several species of cinchona, we shall find in the statement of the species the titles of the sections which should divide this memoir; the particular account of the different principles which they contain will be set forth in the several chapters. We shall first take up the chemical analysis of gray cinchona (*Kina laxa, Cinchona condaminea*), generally regarded as the type of the various barks. . . .

Gray Cinchona

This is the method which we first thought should be employed to give us cinchonine in the state of purity.

We heated 2 kilograms of crushed gray cinchona with 6 kilograms of strong alcohol; we repeated this operation four times; the alcoholic tinctures were combined and distilled to remove all the alcohol. We took care to add 2 kilograms of distilled water, in order that the material dissolved in the alcohol would be protected from the direct action of the heat after the separation of the alcohol. This material, received upon a filler which allowed the aqueous liquor to pass through, was of a reddish color and a resinous appearance; in this state it was washed upon the same filter, with water slightly alkalinized with potassium hydroxide. The liquor which had passed through the filter served for the first wash water, after having been first alkalinized; after washing for several days, the alkaline liquors passing through the filter limpid and colorless, the material remaining upon the filter was washed with a considerable amount of distilled water; it was then a greenish white, very fusible, soluble in alcohol, and forming crystals: it was the cinchonin of Dr. Gomès; it had, in this state, some characteristics of resinous substances; but, upon dissolving it in acid much diluted with water, it lost a considerable quantity of fatty material of a green color which had all the properties of the fatty green material obtained for the first time by M. Lauber, in treating cinchona immediately with sulphuric ether. We note here that if too concentrated an acid is employed, a large quantity of fatty material remains in solution in the liquor, and the cinchonin which is afterward obtained is contaminated with it.

East of the Stoney Mountains

the geology of North America was studied by William Maclure in 1823. His work foreshadows many later discoveries of the work of water and ice in forming this continent. It will appear in the next issue as

THE NEXT CLASSIC OF SCIENCE

The acid liquor (we used hydrochloric acid) was a golden yellow. Evaporated, it gave crystals soluble in alcohol and in water. Its taste was very bitter; it was abundantly precipitated by alkaline solutions, the gallates, the alkaline oxalates giving precipitates soluble in alcohol, etc. Without stopping longer over its properties, which we cannot explain at the moment, we treated the solution with very pure magnesia and with the aid of slight heat: the mixture was then thrown on a filter after it was quite cold, and the magnesia precipitate was washed with water. The first wash waters were yellow; they end by being colorless. The magnesium precipitate, sufficiently washed and dried on the water-bath, was treated three times with alcohol at 40°. The alcoholic liquors, very bitter, slightly yellow, gave, upon evaporation, crystals in needles of a dirty white. These crystals, redissolved in alcohol, and allowed to crystallize again, gave a crystalline material very white and brilliant. We may also obtain very white crystals by washing them in the cold with a little sulphuric ether. These crystals are pure cinchonine.

To preserve harmony in the nomenclature, it will be necessary to change the name *cinchonin* to *cinchonine,* since the salifiable organic bases already known have names of this sort: out of respect for the rights of M. Gomès, we did not make this change at the time of the reading of our memoir before the Academy; but MM. Vauquelin, Thenard and Déyeux, commissioners of that society, have passed upon this consideration.

Cinchonine

The cinchonine obtained by gentle evaporation of the alcoholic solution, appears as slender prismatic needles, of which the crystalline form cannot be determined. Upon very rapid evaporation, it appears in translucent crystalline white plates, refracting light.

Cinchonine is very slightly soluble in water; it requires two thousand five hundred parts of boiling water to dissolve it: upon cooling, the liquor becomes slightly opaline, thus proving that cinchonine is even less soluble in the cold.

Cinchonine has a particularly bitter taste; but this taste is long in developing, and has little intensity by reason of the insolubility of this substance; it appears in cinchonine rendered soluble by union which acids; it is then very bitter, styptic and persistent, on the whole similar to that of a strong decoction of cinchona, except that it is less astringent, the astringence of cinchona being due especially to another principle. Cinchonine, exposed to the air, is not changed: except that after a time, it absorbs carbon dioxide, and when it is dissolved in an acid solution, it produces a gentle effervescence.

Exposed to the action of heat in closed vessels, it does not melt before beginning to decompose. The products which it gives by distillation over the naked flame are those usually produced by organic matter not containing nitrogen: distilled with oxide of copper in a convenient apparatus, it forms only water and carbon dioxide. It is therefore composed of oxygen, hydrogen and carbon in certain proportions, and nitrogen does not enter into its composition: burned with ammonium nitrate, it leaves only a trace of mineral material, akaline or earthy.

Cinchonine is very soluble in alcohol, especially with the aid of heat; an alcoholic solution, saturated at the boiling temperature, crystallizes upon cooling; alcoholic solutions of cinchonine are very bitter, which proves again that the slight bitterness of pure cinchonine is due to its insolubility.

Cinchonine dissolves in ether: but it is much less soluble in it than in alcohol, especially in the cold; it dissolves also, although in very small quantities, in fixed or volatile oils, especially in oil of terpentine. These solutions are bitter. Oil of terpentine, saturated with cinchonine at an elevated temperature, gives up a great part in crystalline form, upon cooling: it is not thrown out of solution in fixed oils.

We shall now consider cinchonine from the point of view of its alkalinity which we have recognized. Cinchonine restores to blue litmus turned red by acid; it combines with all the acids, and is able to form neutral combinations which do not affect litmus, with the stronger mineral acids. These combinations show different properties, and have constant proportions.