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Key words: Biological chemistry, Bouchardat reagent, diabetes, diabetology, digestion, fertilizers, food chemistry, hygiene, iodoform and haloderivatives, metabolic diseases, rotatory power, quinquina, toxicology.

RESUMEN. Apollinaire Bouchardat (1809-1886), farmacéutico y médico francés, considerado el fundador de la diabetología, estudió en forma detallada los fenómenos fisiológicos relacionados con la diabetes, sugirió una dieta sin componentes farináceos acompañada de gimnasia y sudoríficos, etc. Realizó investigación en problemas relacionados con el medio ambiente, la higiene pública y laboral, desórdenes fisiológicos, fertilizantes, fisiología vegetal, química de los alimentos, química orgánica, etc.

ABSTRACT. Apollinaire Bouchardat (1809-1886), French pharmacist and physician considered as the founder of diabetology, studied in detail the physiological phenomena associated with diabetes, suggested a diet without farinaceous components and accompanied by exercise and sudorifics. Carried a large number of researches on environment protection, public and work hygiene, metabolic disorders, fertilizers, plant physiology, food chemistry, organic chemistry, etc.

Life and career¹⁻⁴

Apollinaire Bouchardat (Fig. 1) was born on July 23, 1809, in l'Isle-sur-Serein (Yonne department, France), the son of Jean-Baptiste Bouchardat, a tanner.



Fig. 1: Apollinaire Bouchardat (1809-1886).

His father had served as a soldier under Napoleon and did not have the economic resources to give a proper education to his children. For this reason, at the age of eight, he was sent to live with his uncle Alphonse Bouchardat, who had a pharmacy at Avallon. There he began his basic education at the Avallon college, an almost free liberal institution, while simultaneously working as an apprentice in his uncle pharmacy. After graduation at the age of 19, he moved to Paris to complete his education, while earning his living giving private lessons. The experience acquired during his apprenticeship led to a position in the Muséum d'Histoire Naturelle with the pharmacist Félix Cadet de Gassicourt (1789-1861), for (1825-1827) and then as a *préparateur* with the chemist Louis Nicolas Vauquelin (1763-1829).

In 1831 he won the first place in a competition for a position of pharmacy intern in the Hôpital de la Pitié; during this period he begun to study pharmacy at the École Supérieure de Pharmacie and medicine at the Faculté de Médecine de Paris. In 1832 he was granted his medical diploma after successfully defending a thesis about the nature, treatment and prophylaxis of cholera morbus.⁵ He spent the next six months at Dampierre, near Paris, working as a

young physician with the people affected by the cholera epidemic affecting Paris. In 1833 he graduated from the École de Pharmacie with a thesis about the modifications experimented by inorganic substances under the influence of natural agents⁶, and in the following year he was appointed hospital pharmacist taking a position at the Hôpital Saint-Antoine (1833-1834); two years later he became chief pharmacist at the Hôtel-Dieu, a position he kept for the next 22 years (1832-1855). While at the Hôtel-Dieu he began his research on diabetes and nutritional diseases, which afterwards would bring him fame and honor. In 1833 he was appointed professeur agrégé at the Faculty of Medicine, a position that allowed teaching and conducting research. In 1850 he won the competition for the chair of hygiene at the Faculté de médecine, after presenting a thesis about the health effects of insufficient food.⁷

Bouchardat received many honors for his academic and public work. Bouchardat was appointed administrator of the Bureau de Bienfaisance (1843); elected member of the Société Central d'Agriculture de France (1848), of the Conseil d'Hygiène Publique et de Salubrité (1851), and of the Administration Générale de l'Assistance Publique (1868), member of the l'Académie Impériale de Médecine (1850) and President of the same (1866), member of the Société de Pharmacie (1847). Awarded a medal for his devotion to the wounded in June 1848 and the cholera victims at the Hôtel Dieu, chevalier of the Légion de Honneur (1845) and promoted to officier in 1866, commander of the Order of Charles II, Spain (1861), of the Order of Danneburg of Denmark (1865), etc.

Bouchardat died on 7 April 1886 and was buried in the Père-Lachaise cemetery in Paris.

Scientific work

Bouchardat was a prolific writer, publishing over 140 papers, booklets and books in the areas of chemistry and plant physiology, human physiology, metabolic disorders, vegetable principles, analytical and organic chemistry, etc. He also wrote a short booklet describing his academic activities and his research and results.¹ In addition to the subjects discussed below Bouchardat wrote a series of textbooks on chemistry, physics, medicine and pharmacy,⁸⁻¹³ private and public hygiene and hygiene in public hospitals and hospices;¹⁴⁻¹⁵ vegetation and agriculture;¹⁶ studied the relations that existed between electrical and chemical effects;¹⁷ the transformations of sugars and molasses;¹⁸ blood and its alterations;¹⁹ the distillation of natural rubber;²⁰ alcoholic enzymes and fermentation;²¹⁻²³ fermentation of sugar;²⁴ the cultivation of vines and its diseases;^{25,26} the scientific and commercial aspects of quinquinas;²⁷ etc.

Diabetes

In a memoir read to the Académie des Sciences in 1838 Bouchardat applied the name *diabetes* only to the cases where the urine contained sapid or insipid sugar that made it susceptible of alcoholic fermentation.²⁸ The most common case of the illness was sapid sugar, which could be crystallized by slow evaporation. He reported his analysis of urines containing one or the other kind of sugar and summarized his findings as follows: (1) the amount of sugar contained in diabetic urine and the characteristic thirst were directly proportional to the amount of bread and sugary or starchy substances ingested by the affected person; (2) the sick had a marked taste for this kind of food; (3) for every part of bread eaten, the patient drank about 10 parts of water, the quantity necessary for the total conversion of the starch into sugar by means of diastase; (4) the transformations that took place in the patients were comparable to the ones that could be carried on in the laboratory by contacting starch with diastase; (5) diastase was not the only substance capable of transforming starch into sugar; it could also be effected by yeast, gluten, albumen, and modified fibrin, that is, by substances that probably accompanied starch in the stomach; (6) both types of sugars (sapid and insipid) had essentially the same composition, which was very similar to that of sugar obtained from starch; (7) insipid sugar boiled with dilute sulfuric acid transformed into sapid sugar; (8) the diabetic sick could be cured almost completely by preventing their intake of sugar or feculent food; after 12 hours the thirst and the appetite decreased to normalcy.²⁸

In a following paper Bouchardat described his efforts to find a staple that could be used to replace ordinary bread and the means to restore the chemical balance of the body. He also mentioned that at the recommendation of Jean-Baptiste Biot (1774-1862) he had begun using a polarimeter to determine more rapidly the progress of the treatment).^{29,30}

It so happened that not long before a chemist by the name Emile Martin had discovered and patented a very simple procedure for separating the starch of grain cereals without destroying the gluten: The flour was thoroughly kneaded with half its weight of water and the resulting dough washed, with constant kneading, under a stream of water, in an apparatus consisting chiefly of a semi-cylindrical trough having sides partly built of wire gauze. A fluted cylinder worked the dough continuously while the water, charged with starch granules, passed through the metallic mesh and the gluten remained behind in the form of a flexible mass. At the request of Bouchardat Martin prepared bread containing the maximum possible of gluten (which turned out to be 80% gluten and 20% flour). This bread was very light and had a pleasant flavor. Although this was not the ideal situation it seemed to be good enough because it reduced the daily amount of starch ingested to 35 g.^{29,30}

The answer to the second question (chemical balance) was based on the observation that during diabetes the acid secretion of the mouth was almost totally suppressed, and as a consequence, the mucosa and glands of the digestive apparatus provided now modified fluids; alkaline production was almost completely replaced by an acid one. Was it possible that the large excess of acid present in the apparatus reacted with starch and transformed it into sugar? This assumption proved to be wrong because acids and organic or mineral substances were unable to act on starch at body

temperature. Nevertheless, it was known that organic acids in contact with modified albumen were able to transform starch into sugar. Was it possible then to solve the problem by reestablishing the normal function of the mouth? Bouchardat tested two alternatives: (a) dressing the sick with heavy layers of wool to provoke constant sweating, and (b) internal administration of sudorifics such as ammonium salts and opiates. Bouchardat's memoir described the observations collected during the treatment of several patients: (a) the amount of urine and its sugar content decreased rapidly when ordinary bread was replaced by gluten bread; and (b) use of heavy wool clothes and internal sudorifics such as ammonium carbonate, rum, and opium extract resulted in the release of normal urine, absent of sugar. Bouchardat believed that these results paved the way for finding the proper medical procedure for reducing the ill effects of diabetes.^{29,30}

In another paper Bouchardat wrote that some scientists and physicians had only partially understood his results and now he wanted to answer the questions and doubts they had raised: (a) He first returned to his claim that in the persons affected by diabetes there was a direct relation between the amount of ingested starchy food and the sugar content of the urine, hence an important step in the treatment of the illness was to reduce the intake of feculent material and replace it by food such as gluten bread and wine; (b) he had also patronized the ingestion of a mixture of ammonium carbonate and opiates, as a secondary medicament; (c) he had analyzed the fresh vomit of diabetic persons and found that they always contained diastase, in a rather pure form, particularly the first portion of vomit ejected. This diastase was identical with the one obtained from germinated barley; (d) he had always found sugar in samples of fresh blood taken from diabetic patients and had confirmed this result by chemical analysis and polarimetry; not only that, he had also found that their blood had the same alkalinity as the blood of normal persons; (e) thirst was a typical symptom of someone afflicted by diabetes and the extra amount of water taken was exactly equal to the one that had to be added to diastase to allow it to completely convert starch into glucose; and (f) the patients should wear appropriate wool clothing and do physical exercise to increase sweating.³¹

Bouchardat summarized all his experiences of diabetes in a book, which saw many editions.³² A paper by Chast and Slama gives a very detailed description of the contribution of Bouchardat to diabetology.³

Digestion

Bouchardat and his colleague, the physician Claude Marie Sandras (1802-1856), carried a large number of experiments on the chemical modifications suffered by the main immediate principles, which constituted the base of animal food (fibrin, gluten, starch, soluble starch, and fats). For their purposes they fed dogs with a diet rich in the particular component, killed them at different time intervals, and carried on a pathological examination of the contents of the stomach, intestines, and chyle. As a reference frame they carried the same procedure with a group of dogs kept without food and killed at the corresponding time intervals.³³

For example, a dog was kept for 36 hours in total abstinence and afterwards fed during two days only with fibrin extracted from beef blood. The third day it was fed with 300 g of fibrin and four hours afterwards, killed by strangulation. The stomach was found to contain 200 g of swollen fibrin, transparent and soft, and mixed with 50 g of a turbid and very acid liquid, with density 1.017 (6°C). The duodenum contained a small quantity of a yellow green semi-transparent mucus substance, which did not react with litmus paper. The rest of the small intestine contained a brown green mucus substance, while the cecum and rectum contained brown excremental matter. The chyle extracted from the thoracic canal coagulated spontaneously forming white clots composed almost entirely of fibrin. The serum was very transparent, basic, and found to contain albumen, sodium carbonate, lactate, and phosphate, calcium carbonate and phosphate, and potassium and sodium chloride. The same matters were found in the intestines and chyle of the dogs killed when fasting, except that it contained a slightly smaller proportion of fibrin in a dissolved or fluid state. These results indicated that fibrin was dissolved in the stomach by means of HCl. Further proof of this latter claim was substantiated adding fibrin to an aqueous solution of HCl: after 12 hours the fibrin had converted into a gelatinous mass, which did not differ in any chemical character from the dissolved fibrin found in the dog stomach. Similar experiments were performed with dogs fed with gluten, starch, sugar, and fat. The results showed that digested fat went through a different pathway: it went through the stomach unchanged until in the duodenum it came into contact with the pancreatic fluid and bile. It was then emulsified without changing its chemical nature, absorbed by the orifices of the chyloferous vessels, and then carried into the thoracic duct to mix with the chyle.³³

Bouchardat and Sandras reached the following conclusions: (1) In digestion, the functions of the stomach consisted in dissolving with the aid of HCl all the albuminous matters, such as fibrin, albumen, casein, and gluten; (2) HCl diluted with 5000 parts of water, was capable of dissolving the above mentioned substances externally, as long as they are not cooked; otherwise it had no action on them. The fact that they were found dissolved in the stomach of the animal body suggested the presence of additional agent, although the presence of HCl seemed to be always indispensable; (3) the digestion and absorption of albuminous matter took place exclusively in the stomach; only traces of it were found in the intestines; (4) the solution of starch also took place in the stomach; starch did not appear to pass into the state of sugar, more likely it did it in the state of lactic acid; (5) sugar was only partially absorbed in the stomach, a circumstance which would proceed according with the particular disposition and length of the intestines in animals not carnivorous; (6) fatty matters were not attacked in the stomach: they passed into the duodenum in a state of emulsion, as a result of the alkalis furnished by the liver and pancreas. This emulsion was found abundantly throughout the whole course of the intestines; and (7) the chyle appeared to be somewhat less

abundant but quite similar in the animals which were killed after long fasting, and in those killed after being fed albuminous matters and starch, and not very different from those fed fatty materials.³³

As stated by Bouchardat and Sandras, their results offered a very simple and rational theory of the digestion phenomena, which differed with the one presently accepted. Accordingly to the latter, the food introduced in the stomach were converted into an homogenous soft gray substance, slightly acid substance, having a bitter sweet taste, named *chyme*, which kept some of the properties of the food. This chyme was converted in the small intestine, absorbed by the chyloferous vessels, and finally transformed into chyle. Bouchardat and Sandras believed that the chyme was actually a mixture of residual not dissolved food and that the dissolution was slowly continued in the intestinal tract, the glandular excretions, and the intestinal mucus, and eventually transformed into the excremental matter, and not into a concoction especially prepared for assimilation. In addition, the purpose of the chyloferous vessels was not limited to the absorption of fatty matter. The gastric juice produced by the excitation effect of food, contained a large amount of HCl and lactic acid, which most probably originated by decomposition of the sodium salts existing in the system. The abdominal glands prepared for the chyloferous vessels and thoracic canal a chyle much more alkaline than the acidity developed in the stomach. This chyle, which was not solely produced by the absorption of aliments, but by a process of true secretion, would mix with the blood and neutralize exactly the acid indispensable for the dissolution of the food in the stomach. This simple process allowed the blood to be continually repaired, without appreciably changing its nature.³³

This publication was followed by several others analyzing in more detail the digestion and assimilation of fatty matter and the role of bile and chyloferous apparatus,³⁴ the digestion of starchy and sugar matter and their role in nutrition,³⁵ the function of the pancreas in the digestion of starches,³⁶ the influence of alcohol on respiration³⁷ the digestion of alcoholic drinks and their role in nutrition,³⁸ and the functions of the pneumogastric nerves.³⁹

Influence of ammonium salts on vegetation

Bouchardat carried on several projects on the influence exerted on vegetation by substances absorbed by the roots. Although it was accepted knowledge that the presence of ammonia salts in manures improved their efficiency, Bouchardat believed that the results of his experiments using ammonia carbonate, bicarbonate, sulfate, chloride, and nitrate, which were available to the root of plants in the natural course of things, indicated that this fact was not as general as reported.⁴⁰

Bouchardat placed branches of *Mimosa pudica* in separate flasks provided with perforated corks and filtered Seine water or distilled water solutions containing 1/1000 of the ammonium salts being tested. He only used branches provided with adventitious roots, which were vigorous and had very green and very sensitive foliage. After twenty-four hours he observed that the plants still vegetated well, but the leaves had lost much of their sensitiveness. After forty-eight hours the plants vegetating in the flasks containing solutions of ammonium had lost their motility and the inferior leaves had drooped; next day, the plant was dead. The mimosa, vegetating in the solution of ammonium nitrate held out one day longer and that which was in a solution of chloride, two days longer. At the end of six days all the plants had perished. Analogous results when the concentration of the solution was reduced to 1/1500.⁴⁰

Bouchardat understood that a possible objection to his experiments was the fact that the branches of mimosa provided with adventitious developed roots absorbed the solutions very slowly and, in general vegetated in water with very little energy and that, sooner or later, they would perish. To eliminate this possibility he carried similar experiments with branches, which had remained in water and held out very well. In addition he selected for his experiments plants, which do not perish in pure water, even when they are kept in it for a whole year, and which may fulfill in it all the phases of their vegetation and develop fecund seeds [e.g. water mint (*Mentha aquatica*), horse mint (*Mentha sylvestris*), and princess feather (*Polygonum orientale*)]. The last variety was particularly appropriate because it developed numerous roots, carried out in water all the phases of vegetation, and quickly absorbed a large quantity of liquid. In these experiments very healthy branches of these plants were placed in flasks filled with filtered water. As soon as they showed abundant adventitious roots and the absorption of the liquids was very active, the filtered was with a solution 1/1000 of the ammonium salt. The results were similar as those of the previous runs, except that the plants perished much more quickly because the absorption was likewise more rapid. Identical results were obtained when the concentration of the salt was reduced to 1/1500 and down to 1/3000. Bouchardat remarked the actual results could be different because in practice the roots of plants exercised their function in the soil and not in water.⁴⁰

Another series of experiments was conducted with cultivated cabbage (*Brassica oleracea*), a plant that did not vegetate in water, but which grew quickly and well in the earth, and which was supposed to require much nitrogenous food. After 30 days no effects, good or bad, were detected, even with cabbages irrigated with Seine water. According to Bouchardat, the ammonium salts did not produce any injurious effects because they were not absorbed but were only retained by the earth. He believed that his results indicated clearly that vegetables did not assimilate the nitrogen present in solutions of ammonium carbonate, bicarbonate, chloride, nitrate, and sulfate. In addition, these solutions in concentration 1/1000 acted on the roots as energetic poisons.⁴⁰

In a second memoir on the subject Bouchardat reported the effect of alkaline salts on the development of corn, wheat, barley, and beans.⁴¹ Seeds of these plants were planted the same day in crates containing one kilo of mixture of good earth and loam and watered alternatively one month with pure water and another with water containing one 1/100 of the salts being tested (ammonium carbonate, chloride, and nitrate, sodium chloride, potassium nitrate, potassium

bicarbonate, and iron sulfate). The reason for using more concentrated solutions than in the previous work was the fact that now the plants were grown in soil, and not in water. The relative effect of growing the plant in soil or in water was expressed by comparing the weight of grains collected at the end of the experiment. In general, it was found that all the above salts seemed to have no effect on the growth of the cereals wheat and barley. This was not the case for corn and beans. The results of the experiments indicated: (a) ammonium carbonate slightly improved the yield of corn and beans; (b) ammonium chloride slightly increased the yield of corn and caused an early death of the beans; (c) ammonium nitrate slightly improved the yield of corn and beans; (d) sodium chlorides substantially increased the yield of corn. The experiment with beans failed because of technical difficulties; (e) potassium bicarbonate seriously affected the growth of corn and beans and led to a substantial smaller crop; (f) potassium nitrate had not effect on corn and beans; and (g) iron sulfate did not allow corn to fructify and did not affect the yield of beans.⁴¹

Vegetable principles

Bark of tulip tree

In 1840 Bouchardat published a short booklet describing the analysis of the bark and roots of tulip tree, *Liriodendron tulipifera*, growing in North America and reaching a height of thirty meters. The bark of the tree was known to contain a large proportion of an aromatic essential oil; the local inhabitants had long used the bark as a substitute of quinquina for the treatment of periodic fevers and headache affections, consumption, rheumatism, gout, stomach disorders, and as anthelmintic. The origins of good quality quinquina were unknown and its continuous importation doubtful. Bouchardat believed that it was convenient to investigate the possibility of finding valuable trees, which perhaps could be acclimatized in France as a substitute of quinquina.⁴²

As described by Bouchardat, the roots of tulip had a thick and spongy bark, gray on the outside and red brown inside; its smell and taste pointed to the presence of an essence and a bitter principle. The bark of the trunk and branches was smooth, flexible and easy to separate and colored gray to brown. Bouchardat extracted the branch bark with ether mixed with a little of water and distilled the extract. After the ether had evaporated, the water was seen covered by a colorless essence having a pleasant taste and hot flavor. Previous work by other scientists had shown that steam distillation of the bark released a few particles having a taste similar to camphor. All these results suggested that the bark of the roots contained an acrid stearoptene (the solid and crystalline component of an essential oil); solid at room temperature, and the trunk bark a liquid essence having a balsamic odor. This essence was present in the alcoholic extract of the bark used for preparing a table liqueur. The buttery extract had a deep green color and a penetrating smell. Bouchardat separated the different components of the extract by treating it with a concentrated alcoholic solution of KOH, evaporation, extraction with boiling refined alcohol, neutralization with HCl, etc. His results indicated the presence of a white crystalline insipid solid, melting above 100°C, insoluble in cold water, and soluble in ether and acetic acid. This substance turned red intense in contact with cold concentrated sulfuric acid and yellow green with nitric acid. The mode of preparation of this solid and its characteristics suggested it was identical with the piperin that Hans Christian Oersted (1777-1851) had extracted from *piper nigrum*.⁴³ Another component was a green soft resin, of acid character, liquid at 35°C and solid at 5°C, having a strong acrid taste, insoluble in water and in nitric and acetic acid, but soluble in sulfuric acid and fixed alkalis (NaOH and KOH). Bouchardat named it *tulip acrid acid resin*. Bouchardat also macerated the root bark with water, heated the ensuing juice to 100°C, separated the resulting green coagulum, and identified it as pectin.⁴²

All the analytical exams indicated that tulip bark was composed of essential oil, piperin, a soft acrid resin, a vegetable alkali, tannin, pectin, gum, inorganic salts, and ligneous matter.⁴²

Alkaloids

Bouchardat's reagent

Bouchardat wrote that the hydroiodides of vegetable alkalis reacted with iodine to form the corresponding ammonia analog; thus, ammonium hydroiodide added a new portion of iodine to form the iodide of ammonium hydroiodide, which Jöns Jacob Berzelius (1779-1848) had named ammonium bi-iodide. Vegetable alkalis exhibited the same behavior except that their combinations were more defined because they crystallized easily and most of them presented only one iodide of the hydroiodide. A solution of iodized KI was the best reagent for isolating vegetable alkalis because it caused their complete precipitation from an acid solution. The vegetable alkali was easily separated from this precipitate. Careful execution of this procedure allowed obtaining the iodide of the alkali hydroiodide in crystalline state.⁴⁴

A detailed examination of the characters of the iodides of the alkali hydroiodides allowed a precise method for distinguishing one from the other because they differed in their coloration and mode of crystallization. The effect of KOH on these compounds was quite remarkable: the oxygen of the base added to part of the vegetable alkali transforming it into another vegetable alkali or into a new substance, soluble in water and still retaining alkaline properties. Nevertheless, this was a partial oxidation; it did not take place uniformly on the whole compound.⁴⁴

When heating the iodide of alkali hydroiodide with water and zinc, one-half of the iodine combined with the metal forming zinc iodide, which then reacted with the vegetable alkali hydroiodide to yield salts soluble in water and easily crystallizable. Iron reacted in the same manner.⁴⁴

A commercial quinquina of poor quality

Bouchardat wrote that the discovery of quinine had diminished the importance attached to recognizing quinquina of good quality. Nevertheless, since there were still physicians that prescribed quinquina or some of its preparations, it was necessary to avoid the commercialization of quinquinas of poor quality. Upon Bouchardat's recommendation the French Codex had adopted gray quinquina as the medicinal variety, yet, a very popular gray quinquina was sold commercially although it did not contain cinchonine or quinine. It was not a new variety of the material because it was well known in Germany under the name of *china Jaen*, in England as *ash-bark*, and in Spain as *cascarillo pálido*. In France, Nicolas Gaston Guibourt (1790-1867) had named it *loxa cendré*.⁴⁵

This particular quinquina was remarkable by the usually whitish color of its epidermis, which had originated the name *ashy quinquina*. The internal color of the bark, usually sold as rolled tubing, was yellow orange or yellow red, depending on its size. It had the peculiar odor of gray quinquinas, a taste somewhat astringent and bitter, particularly on the tongue. In other words, it had the two most important properties of good quinquina. It was not surprising then that the experts of the hospitals administration had accepted its use by the Central Pharmacy.⁴⁵

It so happened that a particular time Bouchardat needed to prepare cinchonine for his research and for this purpose he got a batch of this particular gray quinquina; to his surprise instead of getting the base he was looking for he obtained an alkali which was not quinine or cinchonine. The same as quinine, it crystallized very easily as flat needles from an alcoholic solution but was very soluble in ether and sparingly soluble in water acidulated with sulfuric or nitric acids. In addition, its nitrate crystallized as fine needles, which did not separate from a boiling aqueous solution. The best procedure to differentiate it from quinine was to treat a highly diluted solution of the three vegetable alkalis (quinine, cinchonine, and the new one) with an aqueous solution of KI or an iodized solution of KI. Only quinine produced a precipitate with KI and only cinchonine did it with the second reagent. Bouchardat believed that his new base was *aricine* (cinchovatine), which was not colored green nitric acid.⁴⁵

As stated by Bouchardat, his findings demonstrated the inconvenience of classifying quinquinas in groups separated by their color; colors were more conventional than real and exposed to damaging errors. Thus the yellow quinquina of La Condamine was the same as the French gray Loxa quinquina. Nothing was farther from the truth that claiming that the quinquinas of Arica or Cusco, the white quinquina of Loxa and pale quinquina were produced by the same tree, *cinchona ovata*.⁴⁵

Optical properties of vegetable alkalis

In 1843 Bouchardat published an extensive memoir describing the action of vegetable alkalis (morphine, noscapine, piperin, strychnine, brucine, cinchonine, and quinine), pure and impure, and their compounds on polarized light. The results were summarized in individual tables reporting the temperature, composition of the medium, concentration weight percent of the solute dissolved in a solvent with no optical activity, the density of the solution relative to distilled water, the length (mm) of the observation tube, the deviation of the primitive polarization plane observed through a tube of length *l* and measured with a tube 100 mm long, the deviation of the blue tint observed with the naked eye, the deviation observed through a red glass, and molecular rotatory power. The results indicated that all vegetable alkalis, dissolved in a basic or acid medium, exhibited a clear influence on polarized light. Five of the examined alkalis, dissolved in alcohol or ether, were levorotatory; cinchonine was strongly dextrorotatory. Addition of an acid altered temporarily the molecular constitution of the alkalis. The tabulated values allowed differentiating one vegetable alkali from another, and also judging if they were in a pure or impure state.⁴⁶

Bouchardat used the same technique to determine the molecular rotatory power of a large number of other organic substances, for example, salicin, phlorizin, and cnisin,⁴⁷ amygdalin, mandelic acid, and amygdalates,⁴⁸ turpentine and its essences,⁴⁹ salicin derivatives,⁵⁰ inulin,⁵¹ camphoric acid,⁵² quinidine, codeine, narceine, papaverine and picrotoxin,⁵³ etc.

Iodoform and halo derivatives

In 1823 and 1824 Georges Simon Sérullas (1774-1832) reported an improved process for obtaining iodine derivatives of methane by reacting potassium with an alcoholic solution of alcohol. He found that there were two iodized derivatives, one solid and one liquid, which he named *carbon periodide* (iodoform) and *carbon protoiodide* (methyl iodide), respectively. The names were based in the assumption that these compounds contained hydrogen. Iodoform was prepared by adding an alcoholic solution of KOH over a supersaturated alcoholic solution of iodine until discoloration. The resulting solution was filtered, mixed with water, and evaporated until all the alcohol had disappeared. The resulting iodoform was washed with cold water and dried. The protoiodide was prepared by adding iodine to iodoform, followed by addition of an equal amount of phosphorus pentaiodide, and heating the resulting mixture in a flask having its elongated neck submerged in very cold water.^{54,55}

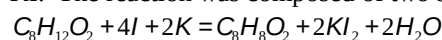
Iodoform was a yellow citrine, sweet tasting solid, crystallizing as bright flakes having an aromatic odor and density about twice that of water, sparingly soluble in water, soluble in fatty and volatile oils, not reacting with sulfuric acid, sulfur dioxide, nitric acid, chlorine, and HCl. On heating it volatilized at about 100°C without decomposition; it melted between 115⁰ and 120⁰C, and afterwards it decomposed into iodine vapors and hydrogen iodide, leaving a bright carbon residue.⁵⁵

In a following paper Sérullas wrote that Eilbert Mitscherlich (1794-1863) had analyzed carbon protoiodide and carbon periodide and found that they did not contain hydrogen.⁵⁶ Sérullas now accepted Mitscherlich's claims and indicated that he had previously determined hydrogen by induction (by difference); his error was due to the incomplete desiccation of his products. He also reported the synthesis of the similar carbon bromides, protobromide and perbromide, and their being composed of carbon and bromine alone.⁵⁷

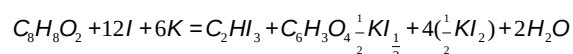
It was left to Jean-Baptiste Dumas (1800-1884) to determine the correct composition and formula of iodoform: 3.20% of carbon, 0.33% of hydrogen, and 96.47% of iodine (the correct values are 3.05% of carbon, 0.26% of hydrogen, and 96.69% of iodine), corresponding to the formula C_2HI_3 (using the values of the atomic masses prevalent at the time).⁵⁸

In his first paper on the subject Bouchardat reviewed the work done by Sérullas and indicated that the original method of preparation of iodoform had gone through a series of modifications; from the reaction of potassium or its antimony alloy with an alcoholic tincture of iodine, to the action of iodine chloride upon an alcoholic solution of KOH, and to the reaction between an alcoholic solution of KOH with another of iodine. In very case it was necessary to use concentrated ethanol.⁵⁹

Bouchardat added that carbon periodide (iodoform) had been thoroughly studied, but this was not the case for carbon protoiodide. His first results indicated that it was not necessary to employ concentrated alcohol; a small amount of ethanol was enough to prevent the formation of potassium iodate; this made the synthesis much cheaper: eight ounces of alcohol were enough for each kilo of iodine. Since the reaction was highly exothermic it was recommended to add the iodine little by little. Bouchardat indicated that with his procedure it was possible to obtain 192.53 g of iodoform per kilo of iodine. The residue could be used to recover the remaining iodine or transform it into KI. The reaction was composed of two steps; the first stage produced acetic ether, KI, and water, according to



while the second yielded iodoform, potassium formiate, water, and KI, according to



(These equations are stoichiometrically wrong, as printed in the paper) The reaction could also be carried with acetic ether or diethyl ether; the first solvent produced a higher yield of iodoform; the second produced potassium iodate as a secondary product. No reaction occurred in the presence of acetone.⁵⁹

Bouchardat reported that a mixture of equal parts of iodoform and HgO, heated slightly, reacted with violence, producing water, formic acid, CO₂, and a mixture of HgI and HgI₂. He believed that the high iodine content of iodoform, combined with carbon and hydrogen, suggested it should be easily assimilable by the body and possibly used for treating scrofula and lymphatic obstructions.⁵⁹

The next section discussed the compound chloro-iodoform, which Sérullas had discovered and named initially *carbon protohydroiodide*, thinking that it contained hydrogen, and afterwards, *carbon protoiodide*, when he changed his mind and assumed it did not contain hydrogen. The protoiodide was prepared by heating iodoform with phosphorus pentachloride or mercuric chloride. Bouchardat prepared chloro-iodoform by the same procedure, that is, heating in a small retort equal weights of either chloride with iodoform. The passing liquid had a deep red color, which disappeared when mixed with aqueous KOH. Distillation in the presence of sulfuric acid produced a liquid slightly colored amber, which in contact with air turned rose. Its smelled like chloroform, had a sweet taste, and density 1.96. Elemental analysis indicated it contained about 5.82% carbon, 0.47% hydrogen, 33.67% chlorine, and 60.04% iodine, corresponding to the formula C_2HCl_2I .⁵⁹

Bouchardat also described the preparation and properties of bromo-iodoform, C_2HBrI_2 , and sulfoform. The latter was synthesized by slightly heating in a retort 60 g of red mercury sulfide with 20 g of iodoform. This compound was yellow oil, heavier than sulfuric acid, tasting sweet, soluble in alcohol and ether, and slightly soluble in water. Alkalis decomposed it into sulfide and formiate. Bouchardat was unable to determine its elemental composition but because of its properties he believed the name *sulfo-iodoform* was more appropriate.⁵⁹

Bouchardat summarized his findings as follows: (1) it was possible to synthesize iodoform with diluted or concentrated ethanol; (2) the reaction of iodine with potassium ethoxide produced first acetic (diethyl) ether and 0.5 atoms (molecules) of iodoform and 1.5 atoms (molecules) of potassium formiate; (3) in the preparation of iodoform it was possible to substitute the alcohol by either dimethyl ether or diethyl ether. No reaction occurred with acetone; (4) the substance named carbon protoiodide by Sérullas contained hydrogen and chlorine, it was a chloro-iodoform containing two atoms of carbon, one of hydrogen, 2 of chlorine, and one of iodine ($CHCl_2I$); (5) in these compounds chlorine could be replaced in a undefined proportion, in the same manner that isomorphous substituted each other in inorganic compounds; (6) the substance named carbon bromide by Sérullas was a bromo-iodoform composed of two atoms of carbon, one of hydrogen, two of iodine, and one of bromine ($CHBrI_2$); and (7) sulfoform could be prepared reacting three parts of mercury sulfide with one of iodoform; sulfoform was a yellow oily substance denser than sulfuric acid.⁵⁹

In a short note Bouchardat reported that at room temperature alcohol containing an excess of iodine did not react to form iodoform, and in the presence of KOH it did not form acetic ether. Heating to 60°C for a few hours a mixture of an aqueous solution of potassium carbonate with alcohol, KI, and an excess of iodine, produced an abundant amount of iodoform, and mixed with iodine.⁶⁰

This paper ended with a note regarding the crystallization of potassium iodine. Bouchardat reported that evaporation of a saline solution containing iodine, KI, and acetic ether deposited light yellow-colored semi-transparent octahedral crystals, which upon heating in a tube produced traces of iodine and a residue composed entirely of KI. Similar crystals were produced by spontaneous evaporation of a solution of potassium biniodide containing a large excess of iodine. Bouchardat remarked the curious fact that KI was able to lose its usual form in the presence of a small amount of iodine; the resulting crystals did not have a defined composition because the proportion of free iodine was extremely small (less than 1/1000). It seemed possible the many bodies when in the presence of small amounts of impurities assumed different shapes, or ones derived from the preponderant one.⁶⁰

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