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Edme-Jean-Baptiste Bouillon-Lagrange

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Life and career[1,2]

Edme-Jean-Baptiste Bouillon-Lagrange was born in Paris on July 12, 1764. His father, who was an archivist of the House of Orleans, used to take him to the Royal Palace where he often participated in the activities of the young duke of Chartes, Louis Philippe I (1773-1850), who was to become King of France during 1830 to 1840. At the age of 12 years, Bouillon-Lagrange entered the college Mazarin where he studied humanities; not much is known about this particular part of his life. After graduation he took the medicine and chemistry courses dictated by Pierre-Joseph Desault (1744-1795), Jacques-François Demachy (1728-1803), Guillaume François Rouelle (1703-1770), and Antoine-François Fourcroy (1750-1809). Hesitating between his interests in medicine and chemistry, he chose the latter as his career and went on to study chemistry and pharmacy. After graduation (1787) he bought the pharmacy owned by his brother in law, Jean Baptiste Jacques Felix Sureau, which he sold two years later to devote himself totally to chemistry.[1,2]

Bouillon-Lagrange was involved in the French Revolution and became a suspect, subject to possible arrest. A member of the Duke family warned him of the impending danger; he ran away but returned to Paris after the detention order had been nullified. He was afterwards appointed *pharmacien major* of the Armies, playing an important role in the organization of the Army hospitals; in this position he participated in the royalist rebellion of Vendée (1793-1796). After returning to Paris, he was appointed essayeur chimique (assayer) at the agency of gunpowder and saltpeter, and well as chef des travaux chimiques (head of the chemistry laboratories) at the École Polytechnique. There, Claude-Louis Berthollet (1748-1822), who was in charge of the teaching of chemistry, appointed Bouillon-Lagrange as his assistant. This position led him to meet Napoleon, who in 1777 appointed him military pharmacist, sometime later, professor of chemistry at the *École de Pharmacie* and then director of the institution, as well as attaching him to the empress Josephine (1763-1814).[1,2]

In 1804, Bouillon-Lagrange was appointed professor of mathematics at the *Lycée* Napoleon. In his first years, Fourcroy entrusted him with part of the course he was teaching at the *Athénée* de Paris. Afterwards, Bouillon-Lagrange taught physics and chemistry at the École Centrale du Panthéon where he became one of its administrators. Pressed by Josephine, he took his medical examinations at Strasburg, was awarded the degree of physician in 1806 (the subject of his thesis was *Réflexions sur les affections nerveuses et sur quelques médicaments usités dans ces sortes de maladies*), and became the personal physician of la empress. In 1816, he was appointed to the chair of chemistry, physics, and natural history at the Collège Henri V and in 1817 he was awarded the degree docteur ès sciences by the Faculty of Paris. As a result of the experience accumulated, Bouillon-Lagrange published his *Manuel d'un Cours de Chimie*[3] where, for the first time, were collected and described all the apparatus adopted by the school of Lavoisier for studying chemical phenomena. All these activities took him away from laboratory work and put an end to his publications (around 1814).

In 1806, after Napoleon repudiated Josephine to marry Marie Louise (1791-1847), the daughter of Francis I, the Emperor of Austria, Bouillon-Lagrange accompanied Josephine to her private retreat at *La Malmaison*, to continue to be her private physician. Bouillon-Legendre was a member of many scientific societies, among them, the *Lycée des Arts*, the scientific societies of Caen, Toulouse, Montpellier, Brussels, Liege, and Bologne, the *Académie Impériale Pharmaceutique de Saint-Petersburg*, etc. He was member de la *Société de Pharmacie de Paris* (which in 1979 became the *Académie Nationale de Pharmacie*), its first general secretary at the time of its foundation in 1803, and its Vice-President (1808) and President in three opportunities (1809, 1813 and 1819). At the creation of the *Académie de Médicine* (1820) he was appointed honorary member. He was also a member of the *Conseil de Salubrité* (1836) and secretary of the *Journal de la Société des Pharmaciens.*[1,2] Bouillon-Lagrange passed away on August 23, 1844, in Paris.

Bouillon-Lagrange dedicated most of his research efforts to the study of the physical and chemical properties, as well as the analysis, of vegetable and animal materials used as medicines. As stated by him: "*A medicine is an engine that can be known well only after you have examined all the parts that compose it.*" Among the many substances he studied the author can mention: styrax, senna, ambergris, scammonees, truffles, willow bark, agarics, birdlime, garlic, starch, milk, lactic acid, tannin, gallic acid, and saffron. He reacted cork with nitric acid, and noticed the presence of an acid of unknown nature, which many chemists believed to be oxalic acid. Bouillon-Lagrange showed it was a new acid, which he named suberic. He studied camphor and confirmed experimentally Kosegarten´s results about camphoric acid. He also showed that tannin was composed of carbon, hydrogen and oxygen. In 1811, he reported that a light roasting of starch changed it into a new substance (dextrin), which dissolved easily in water.

Scientific contribution

Bouillon-Lagrange published over 50 papers mainly on the subject of physical and chemical properties, and analysis of many vegetable and animal substances used in the preparation of medicines, as well as several books about pharmacy and chemistry.[3-5] Her the author describe some of his results.

Suberic acid

Luigi Valentino Brugnatelli (1761-1818) was the first to experiment on the nature of cork.[6] By means of nitric acid he converted it into an acid, which he named suberic acid (from *suber*, Latin name of the cork-tree). Several chemists believed it was oxalic, because it possessed several properties in common with it, among them, forming an insoluble salt with calcium. These assertions induced Bouillon-Lagrange to undertake a set of experiments on suberic acid, where he distilled in a retort at gentle heat a mixture of one part of small pieces of cork and 6 parts of nitric acid of specific gravity 1.261.[7] Initially red vapors escaped while the cork swelled and turned yellow and ultimately turned into a floating foaming material. The resulting mixture was then poured into a glass vessel, placed upon a sand-bath over a gentle fire, and constantly stirred with a glass rod. The material thickened gradually and begun releasing white vapors, exciting a tickling in the throat. In due course an orange-colored mass was obtained having the consistence of honey and a strong and sharp odor while hot, and aromatic when cold. This mass was diluted with boiling water and the insoluble part separated by filtration. The filtrate was evaporated to dryness. This solid was suberic acid, which could be purified, either by saturating it with potash, and precipitating it by an acid, or by boiling it with charcoal powder.

According to Bouillon-Lagrange, suberic acid was a non-crystallizable substance having a slightly bitter acid taste; when dissolved in a small quantity of boiling water, it acted upon the throat and excited coughing. It reddened vegetable blues and turned green a solution of indigo in sulfuric acid; when exposed to the air it attracted moisture, especially if it was impure; exposed to the daylight, it slowly became brown. It was slightly soluble in water and not attacked by oxygen or acids. When exposed to the heat of the blowpipe on a spoon of platinum, it first melted and then became pulverulent and finally sublimed completely with a smell resembling that of sebacic acid. Its action on metallic salts was particularly interesting; it converted lead acetate and nitrate into their suberates; it changed the blue color of copper nitrate and sulfate into green; green iron sulfate turned deep yellow; and zinc sulfate golden yellow. Suberic acid did not react with platinum, gold, or nickel; but it oxidized silver, mercury, lead, tin, iron, bismuth, arsenic, cobalt, zinc, antimony, manganese, and molybdenum. With alkalis, earths, and metallic oxides, it formed suberates.[7]

Bouillon-Lagrange concluded that cork was different from other vegetable matter in that nitric acid converted it into an acid different from all other acids known, and also into a resin, equally different from those known.[7]

Camphor and camphoric acid

Bouillon-Lagrange wrote two papers on this subject.[8.9] In the first one he pointed out that he was interested in verifying the claim of David August Joshua Friedrich Kosegarten[10] that nitric acid converted camphor into a crystalline acid with peculiar properties. Kosegarten had distilled to dryness one part of camphor with 12 parts of strong nitric acid and observed that during this process a large quantity of CO_2 and nitrous gas was disengaged, while the acid in the receiver was covered with a thin layer of acid oil of camphor. A small portion of the camphor sublimed into the upper part of the retort and the mass at the bottom of the vessel was camphor approaching to the state of a vegetable oxide, which did not have the peculiar odor of the original substance. When laid on a hot coal it evaporated with a somewhat resinous odor, but without undergoing combustion; it was soluble in alcohol but not in water. Distilling it twice to dryness, each time with ten parts of nitric acid, converted it into a white pulverulent salt, soluble in hot water, which was given the name *camphoric acid*.[8]

Bouillon-Lagrange remarked that acids dissolved camphor, and nitric acid was commonly used for this purpose, to form a medical preparation known by the improper name of oil of camphor. It was known that it was impossible to use this oil in any vehicle without regenerating the camphor.

Bouillon-Lagrange tried to decompose camphor by three different methods: (1) distillation of a dry paste of camphor and clay; (2) distillation of a mixture of finely divided camphor and finely divided clay, and (3) distillation of paste of camphor and alumina or a pulverulent mixture of both components. His results indicated that the first two methods led to sublimation of the camphor, with formation of a very small amount of a volatile oil. The third method produced a distillate of a yellow gold volatile oil, which floated on water and left in the retort a very deep black residue composed of carbon and alumina.[8]

The volatile oil had an acrid burning taste and smelled like thyme or rosemary. When exposed to air it partly evaporated leaving a brown thick residue having a very sharp taste. The oil, treated with alkali, afforded a homogenous mixture, soluble in water, and having all the characters of soaps made with volatile oils. It differed from the material obtained with nitric acid in that when mixed with water, with alkali, or HCl, it regenerated camphor.[8]

The next set of experiments was devoted to study the reaction of camphor with nitric acid. The first experiment was a repeat of the one reported by Kosegarten, except that camphor was mixed with concentrated nitric acid (density 1.33) in the ratio 1 : 4. The results indicated that 1729 g of nitric acid were enough to acidify 100 g of camphor. The acidified camphor crystallized in the resulting liquid; the crystals were separated by filtration, dissolved in hot distilled water, and the solution left to evaporate until its volume was halved. The crystals of camphoric acid separated on cooling. A total of 53.5 g camphoric acid was thus produced.

Bouillon-Lagrange concluded that camphoric acid was a peculiar acid that differed from other vegetable oils by (a) its crystallization, (b) being slightly soluble in water, (c) burning without leaving a residue, (d) not precipitating limewater, (e) not changing a sulfuric solution of indigo (suberic acid turned this solution green), and (f) forming peculiar salts which burned with a blue flame with the blowpipe.[8]

The second memoir described in detail the preparation and properties of camphorates of calcium, potassium, sodium, ammonia, barium, aluminum, and magnesium. Bouillon-Lagrange reported that all these salts were characterized by the following properties: (1) they were inodorous if the camphoric acid was pure, otherwise, they had a slight smell of camphor; (2) the camphorates of aluminum and barium had an acid taste; the others were slightly bitter; (3) all were decomposed by heat, the acid separated and sublimed while the base remained pure (except in the case of ammonia); (4) the calcium and magnesium camphorates were slightly soluble in water, the other dissolved easily; (5) all were decomposed by mineral acids, and (6) all the camphorates were soluble in alcohol; those of calcium, magnesium, and barium decomposed leaving only the acid in solution.[9]

Senna

According to Bouillon-Lagrange, senna was widely employed in medicine as an infusion, a tisane, or in powder form. Since the mode of preparation affected its effects, Bouillon-Lagrange decided to study in detail these methods, using *senna alexandrina* (Cassia alexandrina) as starting material.[11] The leaves of this plant are yellow green, having a nauseous odor, and a bitter taste. Bouillon prepared an infusion and a tisane of senna and treated it with a number of reagents, such as mineral acids, oxalic acid, sodium carbonate, mineral salts, nut galls, alcohol, etc., and reported the properties of the different fractions obtained. He also distilled the leaves as such. The cold infusion yielded a soapy material, partially soluble in alcohol and completely soluble in water. The fraction soluble in alcohol was not a resin but the active principles; and the fraction soluble in water contained the different salts. Left in contact with air, the infusion became turbid and deposited a yellow brown powdery sediment insoluble in water and alcohol, while the liquor became covered by a dark brown pellicle, which attached to wall of the glass container. Different chemical analyses indicated the presence of potassium salts, calcium carbonate, magnesia, silica, and a resinous matter.[11]

Bouillon-Lagrange observed that the medicinal action of the solution was non-existent or active, depending if it was prepared in the absence or presence of oxygen. Only in the presence of oxygen it operated as a purgative. The cold infusion should be used alone and not combined with acid tinctures and alcoholic liquids, which changed the nature of this medicine by oxygenating the saponaceous principle, which, by that means, acquired the nature of resins. For the same reason, the tisane obtained by boiling the leaves in water, resulted in the precipitation of the active principles, and left a useless liquid.[11]

Liquid Styrax

Styrax is a genus of about 130 species of large shrubs or small trees in the family Styracaceae, mostly native in eastern and southeastern Asia. Its bark exudes benzoin resin, which has long been used in perfumes, incenses, and medicines (particularly as disinfectant and local anesthetic).

According to Bouillon-Lagrange, the preparation of a compound medicine could never be made with success, unless the nature of the substance of which the mixture was composed was well understood. There were many pharmaceutical preparations, such as liquid styrax, about which different conjectures have been stated, although its nature had not hitherto been completely determined. Liquid styrax had been employed since times in a medicament named styrax ointment and its preparation and composition varied according to different authors.

In the first part of his paper on the subject, Bouillon-Lagrange gave an historical review of the information available about the styrax resin: It was a sticky transparent gray brown liquid, having the strong, but disagreeable smell of solid storax, and of a somewhat pungent aromatic taste. It was very seldom if ever, found in a pure unadulterated state.[12]

A great diversity of opinions prevailed relative to the origin of this species of resinous balm; some believed it was turpentine, compounded or boiled up with oil, wine, etc.; others claimed that it was an extract obtained by the decoction of several parts of the amber-tree. Bouillon-Lagrange mentioned that James Petiver (1663-1718), a London apothecary, Fellow of the Royal Society, had published a short note saying that liquid styrax was the exudation of the tree named *Rosa Mallos*, which grew in the island Cobras, at the upper end of the Red Sea near Cadess, three days journey from Suez.[13] The bark of this tree was removed every year and boiled in seawater until it became consistent as birdlime. The floating resinous substance was then separated, purified by additional washes of seawater, and then put into small casks and brought to Mocha at the time of famous Arab fair. Bouillon-Lagrange added that there was another substance named styrax, which was imported from America, but was in fact liquid amber.[12]

The second part of the paper was a description of the physical or sensible properties of the liquid styrax used as an article of commerce: it was of a greenish-grey, the taste rather aromatic, and leaving a slight acidity on the tongue. The product exuded from the tree, and not having undergone the boiling process described above (true styrax), was of a deep red color, having an agreeable smell and a pungent taste, leaving on the tongue a sharp impression of acidity.[12]

Bouillon-Lagrange submitted liquid styrax to the action of numerous agents in order to determine its chemical properties; among them, heat, atmospheric air, quicklime, alkalis, mineral acids, and alcohol. The main conclusions were that: (1) styrax was a resinous balm, analogous to styrax or benzoin; (2) it was composed of benzoic acid and of a resin, and that the other matters found in it were foreign impurities; (3) the simple and most advantageous method of purifying styrax was to make a tincture of it in highly rectified spirits of wine; (4) in order to prepare the ointment of styrax, and in general, all unguents composed in part of resinous substances, the mixing of the ingredients should be done, at most, under a mild heat, particularly with styrax, which was easily decomposed by heat; it readily absorbed oxygen, while the benzoic acid was volatilized at a low temperature; (5) there was a remarkable difference between the ointment prepared with the styrax purified by alcohol and that purified by the action of heat (melting at low temperature followed by filtration); the former had an agreeable flavor of storax, and produced no feculent impurities by its union with other substances; while the latter had a strong, rather disagreeable smell, and always left behind a considerable sediment.[12]

Ambergris

In his paper about this material, Bouillon-Lagrange made a short survey of was known about ambergris and the geographical zones were it was found.[14] It was generally accepted that ambergris formed in the stomach of the cachalot or spermaceti whale (*Physeter macrocephalus*), and appeared to be a product of its digestive processes. The physician Franz-Xaver Svediaur (1748-1824) had found that ambergris was also present in the beaks of the cuttlefish as well as the bellies of whales belonging to the species called by Linneus *sepia octopodia*, which fed largely on the large species of cuttlefish. The presence of ambergris in these beaks of ambergris and other foreign bodies was a clear proof that the material was originally in a soft state and gradually acquired the solidity it was known to possess. According to Svediaur, these whales belonged to the same class as those from which spermaceti was extracted. There was not doubt that ambergris was not of animal origin; many substances resembled it greatly in smell, particularly the excrements of ox and pig; some chemists had classified it within the bitumens. Ambergris was a solid opaque grey substance with brownish-yellow and white streaks, lighter than water and slightly odoriferous. The odor became stronger as the material grew old, or when it was mixed with musk or other aromatic substances.

Bouillon-Lagrange made a detailed study of the properties of ambergris and reported that it was a compound substance, which burned and could be entirely volatilized; on distillation it yielded a slightly acid liquor, and an oil partially soluble in alcohol and having an empyreumatic smell; by sublimation it yielded benzoic acid. It was insoluble in water, partially soluble in alcohol, soluble in ether, fixed oils (e.g. rape, olive, etc.) and volatile oils (e.g. turpentine, hyssop, and savine), and had a density between 0.844 and 0.849. Diluted mineral acids did not react with ambergris but concentrated sulfuric acid, HCl, and chlorine, easily converted it into a coal; alkalis reacted with it forming soluble soaps. Alcohol allowed separating ambergris into the following fractions: 52.7 % adipocerous substance, 30.8 % resin, 11.1 % benzoic acid, and 5.4 % carbon matter.[14]

Agaric

Another paper of Bouillon-Lagrange was related to the study of two varieties of mushrooms, white agaric (*Boletus larix*) and the agaric of the oak (*Boletus iguairius*).[15] According to his description, white agaric was white, light, tender and friable; it was covered by a gray calloused crust, easy to remove. Its initial taste was sweet and then turned bitter and acrid. It reddened rapidly litmus paper. The agaric of the oak grew on the trunk of old oaks, elms, and beech trees; its substance was solid and woody and was covered by a white calloused crust. Under this crust was a soft fungus matter, which in the past had been used as an astringent during surgery (replacing sutures), and to manufacture tinder.[15] In order to study the properties of these mushrooms, Bouillon-Lagrange treated them with cold and hot water, distillation, combustion, acids (sulfuric, nitric, HCl), alcohol, alkalis, etc. and concluded that the results of his experiences left no doubt that both agarics were completely different. On the one hand, white agaric contained a free acid; water dissolved a small amount of extractive matter, as well as the sulfates of calcium and potassium, potassium chloride, and an animal matter. Distilled in a closed vessel it generated ammonia acetate and carbonate; its cinders contained potassium and calcium carbonates, potassium chloride, calcium sulfate, and calcium and iron phosphates; treated with nitric acid it formed malic and oxalic acids, as well as a mixture of resin and adipowax substance; alcohol extracted a large amount of an acid resin (the acid was benzoic); and caustic alkalis released a large amount of ammonia.[15] On the other hand, water dissolved the extractive matter present in agaric of the oak as well as calcium sulfate and potassium chloride. Its cinder contained calcium, iron, and magnesium sulfates. Treatment of this agaric with nitric acid formed malic and oxalic acid and treatment with caustic alkalis showed that it contained a much larger amount of animal matter than the one present in white agaric. Alcohol extracted from it a very small amount of resin.[15]

Birdlime

Birdlime is a glutinous substance that may be made from the berries of mistletoe, the tender bark of holly (*Ilex*) and other kinds of tree, macerated in water. According to Bouillon-Lagrange, Fourcroy was the first to consider this material glutinous.[16] Although several authors had given indications about the preparation of birdlime, no detailed study about its nature had been published. Bouillon-Lagrange indicated that commercial birdlime was never in a pure state; it was frequently a composition of vegetable and animal matter, and was even adulterated with turpentine or vinegar. For these reasons he had selected the second bark of holly as raw material for preparation of birdlime. The barks were boiled in water for some hours, the solution filtrated, and the barks left to rotten or until they became viscous, while moistening them from time to time. After an adequate degree of fermentation had been achieved, the residue was cleaned by washing to eliminate all heterogeneous matter. The resulting substance had a greenish color, sour flavor, and smelled like linseed oil; it was gluey, stringy and tenacious, and reddened litmus paper. In contact with air it dried and became brown and could be reduced to a powder which had no adhesive qualities. Put in a platinum crucible it burned with a lively smoking flame and left a whitish residue, which was shown to contain potassium phosphate and chloride. Water dissolved the mucilaginous substance and very little of the extractive matter, while ether dissolved it completely.[17] Bouillon-Lagrange studied the reactions of birdlime with a variety of reagents, among them, sulfuric, nitric, and acetic acids, HCl, KOH, chlorine, hot and cold alcohol, etc, etc. From their results he concluded as follows: birdlime was a viscous elastic substance, which became brown in contact with air, and was dissolved by concentrated alkalis forming soaps, while dilute acids softened and partially dissolved it. Nitric acid changed its color to yellow while converting it partially into malic and oxalic acids and partly into resin and wax. Chlorine converted into a white solid formed by oxygenated birdlime. These characteristics indicated that birdlime differed from gluten because it contained acetic acid and could yield mucilaginous and extractive mater; in the large amount of resin it produced when treated with nitric acid, and in being totally soluble in ether.[17]

Tannin and gallic acid

A study of the information available about tannin led Bouillon-Lagrange to understand that the following questions remained unanswered; (a) Is the substance known as tannin a pure material?, (b) is it the same in all the vegetables that contain it?, (c) is it present in all the substances known as astringents or bitter?, (d) can its combinations be considered as salts?, (e) can tannin be considered a kind of radical from gallic acid?, and (f) is gallic acid produced in Scheele's process for obtaining tannin. The first part of the memoir he published on the subject was divided into five sections: (1) examination of the infusion and decoction of nutgalls, (2) description of the processes for extracting tannin, (3) chemical and physical properties of tannin, (4) combinations of tannin with earths, alkalis, and metals, and (5) examination of substances presumed to contain tannin. The second part of the memoir discussed the extraction and analysis of gallic acid and a comparison of the acids obtained by the methods of Scheele and Deyeux.[18]

Bouillon-Lagrange experiments indicated that a cold extraction and a decoction produced very different results, when using both solutions to separate tannin. After cooling the decoction precipitated a large amount of a thick and elastic grey substance, which became darker in contact with air. When ground with chalk or KOH, this material released ammonia and an aqueous solution turned red litmus paper. The cold infusion was a clear liquid colored dark brown, which reddened litmus paper and did not produce a precipitate (all the tannin remained in solution).

In a following memoir Bouillon-Lagrange wrote that experiments gallic acid had been the object of the inquiries of many famous chemists, among them, Claude Louis Berthollet (1748-1822), Nicolas Deyeux (1745-1837), Pierre Joseph Macquer (1718-1784), William Lewis (1708-1781), Anthony Grimoald Monnet (1734-1817), Joseph Louis Proust (1754-1826), Jeremias Benjamin Richter (1762-1807), and Carl Wilhelm Scheele (1742-1786).[19] Monnet and his associates had been the first to report the presence of an acid in substances called astringent, and shown that the products distilled from gallnuts blackened a solution of ferric sulfate and that its infusion reddened litmus paper. Scheele had been the first to separate the acid.[20] In 1792, G. Charles Bertholdi (?-1849) had described another process for separating the acid and reported that all bodies that gave up oxygen (e.g. mercuric oxide and manganese dioxide) to the gallic acid made its color brown, and that in these operations the acid carbonized and formed, after a slight combustion, coloring particles. All these efforts had led gallic acid to be one of the best known vegetable acids.

In the first part of his memoir, Bouillon-Berthollet described and repeated the methods used by Scheele, Bertholdi, Deyeux, and Richter, for preparing gallic acid. The methods of Scheele, Deyeux and Richter were found to be the most advantageous, but they differed in the purity of the acid obtained. Additional experiments proved Bouillon-Lagrange that sublimation was the best method for purifying the gallic acid produced by Scheele's process, although this additional step seemed to change the properties of the acid. For this reason Bouillon-Lagrange decided to carry on a detailed comparison of the properties of gallic acid, crystallized or sublimed, For this purpose he prepared aqueous solutions of both acids and treated them with a series of reagents, among them, limewater, barite water, ammonium carbonate, KOH, the sulfates of iron and other metals, chlorine, glue, etc. The results indicated that the sublimed acid was less acid than the crystallized one, it decomposed in the presence of air, and did not react with barite water, ammonium carbonate and tin chloride; it did not give a constant color with ferric sulfate, and was not precipitated by glue. In addition, he studied the influence of heat and water on gallnuts, and prepared the gallates of calcium, barium, sodium, and potassium. Bouillon-Lagrange observed that solutions of the gallates were neutral, became red violet colored when treated with a solution of ferric sulfate, and hardly precipitated glue. The dried salts, treated with diluted sulfuric acid and distilled, always produced acetic acid. An additional significant result was that analysis of the gases released when heating gradually gallic acid proved that it contained oxygen, hydrogen, and carbon.[19]

Bouillon-Lagrange summarized his results as follows: (a) the gallic acids of Scheele and Richter differed essentially from that obtained by sublimation, and that the crystallized one was preferable as a reagent, on account of the uniformity of the color it gave with iron; (b) that gallic acid seemed to be composed of acetic acid, tannin, and extractive matter, and that it could be freed from tannin by crystallization; (c) that the acid obtained by sublimation did not contain tannin, at least that can be ascertained by acting on glue, and that it could, not on any occasion replace the crystallized acid; (d) that the sublimed acid also appeared to be composed of acetic acid, united with a peculiar aromatic volatile oil; (e) that an oily matter separated when pouring water into the ethereal tincture of galls, or ether containing the sublimed acid; (f) that there was no process known for purifying Scheele's acid completely, that is to say, all the tannin could be removed totally from it, without reducing it to the state of acetic acid, which proved that the portion of tannin it retained was necessary to constitute gallic acid, and that to this result we owed its excellent properties in the art of dyeing; (g) that this acid was decomposed by mercuric oxide, tin oxide, and carbon; (h) that acetic acid was produced when distilling galls with water, and that heat by acting more immediately on galls, produced a more intimate combination between the acid and tannin; (i) that in the same manner, the decomposition of the earthen and alkaline gallates generated acetic acid, and finally (j) that gallic acid, like the other vegetable acids, was composed of oxygen, hydrogen, and carbon.[19]

Scammonies from Aleppo and Smyrna

Scammony (*Convolvulus scammonia*) is a bindweed native to the countries of the eastern part of the Mediterranean basin; it has having large roots that yield a resin formerly used as a cathartic. In 1809, Bouillon-Lagrange and Vogel reported the results of their analysis of the properties and nature of the scammonies brought from Aleppo (Syria) and Smyrna (Turkey).[21] The juice of root was normally extracted by an incision made in the root or by expression of the same. The juice was then dried in the sun and then sold. Many times the juice was adulterated with that of other milky and acrid plants. The scammony from Aleppo was light and colored ash gray; that of Smyrna was compact, heavier, and of deeper color.

According to Bouillon-Lagrange and Vogel pure Aleppo scammony put on a heated iron plate melted completely and gave out nauseous vapors. When mixed with water and pounded it yielded a milky liquor. With alcohol this liquor formed a slight precipitate and with lead acetate it produced a precipitate of yellow flakes, soluble in nitric acid. The alcoholic tincture of scammony was of a brownish yellow color, which reddened litmus paper; after evaporation it left a yellowish white and transparent resinous residue, soluble in nitric acid and in KOH. The part of scammony insoluble in alcohol had a gray color; treated with boiling water it produced a yellow solution, which alcohol precipitated as white flakes. Distillation of the Aleppo scammony yielded a very acid brown liquid and a light blackish oil. The residue was black and brilliant and found to contain the carbonates of potassium and calcium, alumina, silica, and a little iron.[21]

The scammony from Smyrna melted less completely than that from Aleppo; treated with water it became lumpy and the water was dyed yellow. The solution was neutral;

treated with lead acetate it gave a yellow flaky precipitate. This scammony, treated with alcohol, produced a deeper-colored tincture; evaporation to dryness of the alcoholic solution left a brownish transparent resin.

Bouillon-Lagrange and Vogel concluded from their experiences that the Aleppo scammony contained 60 % resin, 3 % gum, 2 % extractive principle, and 35 % debris; while the corresponding figures for that of Smyrna were 29, 8, 5, and 58 %, respectively.[21] As the composition of both scammonies was much the same, Bouillon-Lagrange and Vogel decided to find if there was any difference in their medicinal properties. Several physicians made the corresponding experiments and reported that there was no difference in the emetic properties of both resins. Bouillon-Lagrange concluded that scammony was a true gum resin mixed with a little extractive matter. It contained indeed much less gum than other gum resins, but enough to form a milky liquid with water. Although they could not prove it definitely, they believed that the resin was a compound of a vegetable acid.

Saffron

As stated by Bouillon-Lagrange and Vogel, no exact analysis was available of saffron, a spice derived from the flower of *Crocus sativus*, which was used mainly as a seasoning and coloring agent. Some chemists had reported that the color of saffron could be extracted with water, alcohol, or oils, leaving the fibers white and without flavor and aroma. Five pounds of saffron distilled with water yielded one ounce of golden-yellow heavy oil smelling strongly as saffron. The alcoholic extract was precipitated by ether, indicating that saffron was mainly composed of a soapy principle and did not contain gum, resin, or mucilage.[22]

Bouillon-Lagrange and Vogel decided to carry on a more detailed analysis of this material. They first observed that saffron placed inside a glass bell deprived of air, lost its color completely when exposed to sunlight. Cold water became instantly yellow by the addition of saffron, and of a deep red on standing twenty-four hours. The solution was slightly bitter and turned yellow litmus paper; the color was not eliminated by water washes. A concentrated water infusion treated with sulfuric acid, effervesced, turned brown black, and part of the surface became covered with saffron oil. The aqueous infusion was bleached immediately by chlorine; treated with limewater deposited yellow flakes and treated with a solution of baryte produced an abundant reddish precipitate, soluble in nitric cid and HCl. Crystallized acetate of lead did not alter the infusion, but lead sub-acetate gave place to a copious yellow precipitate. Digestion of the water extract with boiling alcohol of density 0.798 dissolved all the coloring matter forming a deep yellow tincture and leaving a colorless and tenacious mucilage having all the properties of gum. When saffron was distilled with water the first fraction was milky, bitter, aromatic water, slightly acid. Two oils appeared at the same time, one swimming in the distilled liquor and the other sinking at the bottom. The latter had the same smell and taste as that of the first fraction, and was readily soluble in water. Evaporation of a mixture of 10 g of saffron mixed with distilled water, to a syrupy consistency, followed by repeated extraction with alcohol, and evaporation to dryness of the alcoholic extract, left a gray powdery gum residue weighing 0.6 g.[22]

To obtain the coloring matter of saffron separately, some saffron was repeatedly macerated in alcohol and the resulting tinctures evaporated to dryness. The resulting yellow red solid residue absorbed humidity from the air and became viscous. The coloring matter was obtained in a purer state, by first evaporating the aqueous infusion to the consistence of honey, followed by extraction with alcohol and evaporation to dryness; 100 parts of saffron yielded 65 parts of this substance, which had smelled sweet like honey and had a bitter taste with the peculiar flavor of saffron.[22]

According to Bouillon-Lagrange and Vogel, the alcoholic solution of the coloring extract was not made turbid by water, proving that it was not resin. A few drops of sulfuric acid added to a dilute solution of the coloring matter turned a lilac blue, affording a useful test to determine the presence of saffron in any compound tincture of pharmacy. The coloring extract was insoluble in fixed and essential oils; it possessed a very intense degree of coloring power compared to its quantity, a very small portion communicating a deep yellow to a large bulk of any liquid in which it was soluble. For this reason Bouillon-Lagrange and Vogel decided to name it *polychroite* (also called crocin and safranin). They summarized their results indicating that 100 g of saffron contained 10 g of water, 6.50 of gum, 0.50 of albumin, 65.0 of polychroite, 0.50 of waxy matter, 10 of vegetable debris, and an unknown amount of volatile oil.[22]

Sugars

In 1801, Cavezzali wrote that he believed that honey was a mixture of sugar and mucilage; in order to separate the components he treated the honey with carbon and noticed that after some time the honey became very fluid, and whitened and polished metals. For this reasons he assumed that honey contained an acid, which prevented its crystallization. In order to separate the acid, he warmed the bleached honey and treated it with powdered egg shells and noticed a strong effervescence. He then added enough of the powder until the effervescence had ceased and then left the liquid to rest. After separating the very dense foamy material that formed on the surface, he noticed that the remaining material behaved like true sugar syrup.[23] Sometime later, Joseph Louis Proust (1754-1826) observed that white honey from Spain did not change the color of litmus paper, that it was totally soluble in alcohol, it preserved its taste and flavor for a long time, etc., etc. properties which pointed out that it did not contained an acid.[24]

According to Brouillon-Lagrange and Vogel, the information available was insufficient to show that Cavezzali´s conclusions were correct or incorrect; hence it was important to determine if there were several varieties of sugar, or it the obstacle to crystallization was the presence of a foreign substance.[25] Hence they conducted a series of experiences on cane sugar, and not on honey, because the nature of the latter was too complicated to separate it into its components. In the first step, they converted white dry sugar to syrup, containing 67 % sugar, and then they treated the syrup with several acids (HCl, oxalic, acetic, and tartaric). The results of these experiments indicated that acids inhibited the ability of cane sugar to crystallize. In the next set of experiments they studied the behavior of a large number of juices of different origin, among them, lemon, barberry, currants, cherries, raisins, etc., and found that their crystallization led to crystals different from those of cane sugar; they were soft, lumpy, deliquescent, and shaped like cauliflower. Addition of an alkaline or earthen base to a syrup slightly acidified, or syrup prepared with an acid juice, did not allow its crystallization. Addition of an acid to cane sugar seemed to transform it into a sugar very similar to the one obtained from raisin. Honey changed to a thick syrup was susceptible of yielding soft lumpy crystals, while honey mixed with a little acid (for example, acetic acid), refused to crystallize. Raisins grown in Rouen crystallized more difficultly that those grown in southern France.[25]

An interesting set of experiments was related to the crystallization of a solution prepared by adding white sugar to a decoction loaded with mucilage and the extractive obtained from the roots of marsh mellow, dandelion, chicory, rhubarb, etc. The resulting crystals were very hard and strong. Similar results were obtained with violet syrup; its crystallization yielded beautiful crystals, similar to those of cane sugar. In other words, addition of any of these materials did not prevent the crystallization of cane sugar.[25]

Brouillon-Lagrange and Vogel concluded that the results of their experiences seemed to suggest that the non-crystallization of several sugars was due to the presence of a pure acid or of acid sugars. Certain experiments done with ammonia or with calcium carbonate suggested the presence of a small amount of acid chemically combined with the sugar, or that during the process the sugar changed its nature.[25]

Dextrin

In a short notice published in 1811 by Laurent-Charles de la Planche it was reported that by a mild roasting of starch Bouillon-Lagrange had transformed it into a substance soluble in cold water and appropriate to prepare a thick mucilage, which could be employed successfully as gum for preparing ink.[26]

In a following publication Bouillon-Lagrange gave a detailed description of his procedure.[27] He indicated that gum had long be used in preparing the sizing used in the manufacture of clothes, for coating paper, for printing on fabrics, and for fabricating of inks and different leather polishes. In addition, he had also reported that he had developed procedures for using indigenous substances for replacing the gum and gallnuts in the manufacture of inks and black dyes. The high price of Arabic gum and the low quality of local gums had led him to search of ways of employing starch for these purposes.[27]

Bouillon-Lagrange´s basic procedure consisting in grinding commercial starch and mildly roasting it in an iron stove, under continuous agitation, until it achieved a gray cinder color. The resulting substance had a sweet mucilagous taste, and was completely soluble in cold and hot water, yielding a totally transparent solution, similar to that of solution of gum. Evaporated to dryness, it left a solid brittle mass, soluble in water. This substance burned on glowing coal as gum did, was not soluble in alcohol, was decomposed by sulfuric acid, releasing an acetic acid odor, was transformed by nitric acid into oxalic acid, and was not affected by HCl or acetic acid. In summary, it had all the properties of a mucous substance, except for its color. Bouillon-Lagrange concluded his paper giving indications on how to use the substance he had prepared in the manufacture of common inks and of hats.[27]

***Lactose* (milk sugar)**

According to Bouillon-Lagrange and Vogel, the numerous investigations that had been carried on lactose had still not given an exact knowledge of the substance. Étienne Louis Geoffroy (1725-1810) seemed to have been the first to have subjected lactose to distillation and noticed the passing over of an acid liquid and a thick oil, together with a carbonaceous residue, which humidified in contact with air. Antoine Baumé (1728-1804) believed that lactose was the common salt present in the cream, which mixed with sugar crystals during the distillations. In 1780, Scheele had reported that the distillation of lactose gave the same products as any other sugar. The only difference was that the empyreumatic oil that passed over smelled like benzoic acid. According to Scheele, treating this sugar with nitric acid produced oxalic acid and ordinary sugar, so that lactose contained an acid which he called sach-lactic. In 1782, Sigismumd Friedrich Hermstaedt (1760-1833) had claimed that purified lactose did not contain free acids, alkalis, or neutral mineral salts, and that it was composed of a true sugar, similar o cane sugar and another terreous substance that modified the properties of ordinary sugar (a calcareous saccharate with an excess of acid). Antoine Augustin Parmentier (1737-1813) and Deyeux believed that the slight sweet flavor of lactose and its low solubility in water was due by the presence of this sach-lactic acid. When treating lactose with nitric acid, the acid acted only on the sugary material converting it into oxalic acid, and liberating the sach-lactic acid as a precipitate. An interesting result was that boiling a highly diluted solution of sach-lactic acid with sugar seemed to regenerate the lactose.[28,29]

Bouillon-Lagrange and Vogel repeated Parmentier and Deyeux´s experiment and were unable to produce a substance having the properties of lactose; they always obtained a mixture having the properties of sugar cane and sach-lactic acid. Alcohol dissolved completely the sugar cane and left a residue having all the properties of sach-lactic acid. For this reason they decide to carry on new experiences to try to determine the true nature of lactose. The experiments they carried included the action of heat, water, acids (nitric, HCl, acetic), chlorine, KOH, salts, alcohol, ether, and yeast. From their results they concluded as follows: (a) lactose was a peculiar substance which had at the same time a certain analogy with sugar cane and gum, and such differences that it was impossible to confuse it with neither of these substances; (b) it dissolved in five parts of cold water without producing a syrupy and mucilagous solution; hot water dissolved a much larger amount, part of which precipitated on cooling; (c) a small amount of nitric acid made lactose soluble in water, and gave it all the physical properties of sugar cane in tablets; (d) gaseous HCl combined with lactose yielding a gray dry powder; treating this powder with sulfuric acid released the HCl combined; (e) chlorine decomposed lactose into CO_2 and water; (f) acetic acid dissolved lactose and prevented its crystallization; (g) concentrated KOH decomposed lactose, producing water, CO_2, acetic acid, and a particular coloring material; (h) lactose was insoluble in alcohol and ether; (i) lactose was not fermented by yeast, in spite of being sweet, a result which distinguished it from cane sugar; and (j) lactose should be considered a particular substance, which was not to be confused with cane sugar or gum.[28]

Manna

The little information was available about manna was confusing and contradictory. Pure manna was a very light material, which seemed to be composed of a conglomerate of very fine capillary crystals; although it had a sweet flavor, it left a nauseous impression in the tongue. It was also known to act as a mild laxative. Dried carefully it was slightly acid and an aqueous or alcoholic concentrated solution tinted litmus paper red.[30]

Bouillon-Lagrange prepared an aqueous solution of manna and noticed that after two weeks the solution became turbid by precipitation of small lumps. The liquid became clearly acid and smelled like acetic acid. These phenomena took place more rapidly with a more concentrated solution. Addition of a small amount of yeast led to the formation of small bubbles and generation of an alcoholic smell. The fermentation process became faster at a higher temperature (20 ^{0}C). Distillation of the solution passed over an alcoholic liquid and left in the flask a very acid flocculent residue, which produced a yellow-orange precipitate with mercuric nitrate and clear yellow with the lead nitrate and tin chloride. Manna dissolved in warm alcohol and the solution abandoned to itself it deposited a very white and light spongy crystalline substance, which had a very sweet and pleasant taste. This material was substantially different from cane sugar and was probably pure manna. Extracted repeatedly with alcohol showed that it was constituted of two different substances; one soluble in cold alcohol, producing an amber-colored fluid, and having properties very similar to those of cane sugar the other was insoluble in cold alcohol. The latter, treated with nitric acid formed the malic and oxalic acids, and a quantity of the mucous acid, which was precipitated.[30]

Malic Acid

In 1817 Bouillon-Lagrange and Vogel reported their results on their experiments on the malic acid extracted from several organic substances (sugar, apple juice, houseleek juice, and beer yeast.[31]

Their results indicated that nitric acid, however weak, formed with sugar an extractive matter, which united intimately to the acetic acid, which also resulted from the action of nitric acid on sugar. This extractive matter combined with lime, barytes, alumina, and many of the metallic oxides, and formed with them compounds, which were nearly or totally insoluble in water. It did not decompose the earthy salts, but it decomposed many of the metallic salts, and especially those with bases of lead and tin. Sometimes it was found perfectly white, at other times more or less colored, as in the sap of the sycamore, and the birch, and the juice of the houseleek.

The juice of apples and of buckthorn contained free acetic acid; and a great amount of this extractive matter, and the malic acid, which was obtain from these substances, was a compound of acetic acid and this extract. The fluids, which did not form a precipitate with lead acetate, did not contain any of the extract; of this kind were the solutions of sugar and gum, and linseed mucilage. Finally, the extract could be separated by barytes; malic acid could be recovered from the barite product by reacting it with acetic acid.[31]

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