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TO GET RID OF ITS DUST

Nicolas-Jean-Baptiste-Gaston Guibourt

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Abstract Nicolas-Jean-Baptiste-Gaston Guibourt (1790–1867), a French pharmacist, who studied the oxides, sulfides, and other compounds of mercury, arsenic and its compounds, a large number of natural products, among them turpentine, starch, astringent juices, and musk; also established the norm to express the power of pepsin.

PALABRAS CLAVE
Alcaloides;
Compuestos de arsénico;
Mercurio;
Óxidos de mercurio;
Sulfuros de mercurio;
Almizcle;
Productos naturales;
Pepsina;
Almidón;
Trementina

Nicolas-Jean-Baptiste-Gaston Guibourt

Resumen Nicolas-Jean-Baptiste-Gaston Guibourt (1790-1867), un farmacéutico Francés; que investigó los óxidos, sulfuros, y otros compuestos del mercurio; el arsénico y sus compuestos, un gran número de productos naturales, entre ellos, trementina, almidón, jugos astringentes y almizcle, y estableció la norma para expresar la potencia de la pepsina.

Life and career (Mialhe, 1867; Buignet, 1872)

Nicolas-Jean-Baptiste-Gaston Guibourt was born in Paris, July 2, 1790. At the age of 16, after finishing his basic education, he entered as an apprentice in the pharmacy of Jean-Pierre Boudet (1748–1828), the best-known Parisian

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establishment. Boudet promptly recognized the innate abilities of the intern and initiated him in the art of laboratory operations, the manipulating and compounding mixtures, and preparing medicaments. Afterwards, Guibourt served as intern of the hospitals (1808) where he took the first prizes of chemistry and pharmacy at the École de Pharmacie de Paris (1810). In 1816 he was awarded the pharmacist degree (*maître en Pharmacie*) after successfully defending a thesis about mercury and its combinations with oxygen and sulfur (Guibourt, 1816a, 1816b). He now began a meteoric professional, research, and academic career. He was appointed as an intern at the Hôtel Dieu (the oldest hospital of Paris), director of the annex of the Hôtel de la Pitié, assistant director of the central pharmacy of the civil hospitals, and director of the magazine of the same (1816). The experience accumulated in these positions led him to publish his first major books, *Histoire des Drogues Simples* (describing the origin, nature and properties of common drugs) (Guibourt, 1820b) and *Pharmacopée Raisonnée; ou, Traité de Pharmacie Pratique et Théorique* (Henry & Guibourt, 1828). The first edition of the latter was published in collaboration with his mentor Étienne Ossian Henry (1798–1873), later editions appeared under his name only. Guibourt was intent in publishing an updated edition of his first book, but unfortunately he died before. His colleague Gustave Planchon (1833–1900) carried on the desires of his mentor (Guibourt & Planchon, 1869). All the professional achievements were accompanied by a large number of scientific publications and promptly led to parallel success in the academic field. In 1824 Guibourt became a member of the Académie de Médicine and in 1832 he was appointed Professor of Materia Medica at the École Supérieure de Pharmacie de Paris, succeeding Pierre-Joseph Pelletier (1788–1842) (Buignet, 1872; Mialhe, 1867).

In 1845 the heavy load of his many professional and academic pursuits led Guibourt to give up the pharmaceutical business he had followed for 27 years and devote all his efforts to his activities at the École de Pharmacie. To this institution he donated his large collection of samples, properly labeled and ordered by scientific groups, and described with scrupulous detail.

Guibourt received many honors and awards for his professional scientific activities. He was a member of many French and foreign scientific societies, among them: the Société de Pharmacie de Paris (1818) and twice its President; resident member of the Société de Médicine de Paris (1823) and its treasurer for 26 years (1828–1854), resident member of the Académie Royale de Medicine de Paris (1824); honorary member of the Société des Pharmaciens de l'Allemagne septentrionale (1830), associate member of the Société Physico Médicale d'Erlangen (Bavaria, 1841), member of the Académie des Sciences, belles-lettres et arts de Rouen (1851), honorary member of the Pharmaceutical Society of Great-Britain (1861), foreign member of the Société de Medicine of Norway (1856), member of the Colegio Farmacéutico de Madrid (1864–1865), honorary member of the Association General de Pharmaciens of Austria and of the Société Pharmaciens du Nord et du Sud (united) of Germany, member of the Pharmaceutical Society of St. Petersburg (1867), member of the Chemical Society of Naples, etc. He was elected chevalier of the Legion d'Honneur (1846) and then promoted to officer (1863). Guibourt was a member of the French Redaction Committee of the Codex Medicamentaria; together with Stephan Robinet (1796–1861) he represented the Société de Pharmacie at the first International Pharmaceutical Congress held at Brunswick in 1865; he was Provisional President of the French Pharmaceutical Congress, which met in August 17, four days before his death (August 22, 1867). He was buried at the Montmartre cemetery. Planchon replaced him at the chair in the École de pharmacie (Buignet, 1872; Mialhe, 1867).

Guibourt researches covered a very wide range of subjects. In addition to the ones described below in detail we can mention the preparation of ethyl acetate (Guibourt, 1817), the properties of copahu and its balm (Guibourt, 1830b, 1852c); analysis of a false jalap having a rose odor (Guibourt, 1843); a description of the resins of copal, dammar, and animé (Guibourt, 1844); description of the rye fungus, *Clavicaps purpurea* (Guibourt, 1848); the properties of bamboo tabashir (Guibourt, 1855), etc.

Scientific contribution

Guibourt wrote over 190 papers and books (e.g. Guibourt, 1820b, 1849–1851, 1852a, 1855) in the areas of physics, toxicology, materia medica, pharmacy, mineral and organic chemistry, and animal chemistry. In 1832 he published a partial list of them (Guibourt, 1832). A detailed list appears in the book by Guibourt and Planchon (1869). Here we described a few of the most important ones.

Combinations of mercury

As mentioned above, Guibourt's thesis for receiving the title of *Maître en Pharmacie* was devoted to the combinations of mercury with sulfur and oxygen. An abstract of this work was afterwards published in the *Journal de Pharmacie* and *Annales de Chimie* (Guibourt, 1816b).

When reading the following material it must be considered that he was following the chemical nomenclature used at the time, where the names of compounds of mercury were provided with the suffixes *proto* and *deuto*, to indicate what today we call mercury (I) and mercury (II), respectively.

Although the original plan was to investigate the oxides, sulfides, sulfates, nitrates, and chlorides of mercury, Guibourt limited the subject to the oxides and chlorides because of their wide used in pharmacology. The first chapter was devoted to an historical description of the discovery of mercury, its natural state, extraction, purification, physical properties, and oxidation in contact with air. Mercury was known not to oxidize in the presence of dry air or dry oxygen, at room temperature. In the presence of humid air, it became covered with a very small amount of gray powder containing mercury oxide. According to Guibourt, this oxide dissolved in HCl forming mercury protochloride (HgCl), which then changed to mercury deutochloride ($HgCl_2$). Since this oxidation procedure always produced extremely small amounts of the oxide, Guibourt tried to prepare it by decomposing salts containing a minimum of mercury (mercury in the state II), for example, mercuric nitrate. Decomposing the protonitrate or the protochloride of mercury with KOH, in the total absence of atmospheric air, yielded a yellowish-black precipitate, which treated with HCl,

produced a mixture of the protochloride and deutochloride of mercury. This precipitate, washed and dried, was found to contain small globules of mercury, which could be observed with a magnifying glass, or the naked eye when it had been pressed between two hard bodies. This result indicated that the protoxide of mercury could not be obtained by triturating together the metallic mercury with its peroxide, against the belief of many chemists. The procedure produced only a brown colored mixture – a color due to the minute division of the metal and even of that of the oxide. A more detailed analysis of this phenomenon showed that the brown color was simply due ''to a particular disposition of the surface of the particules caused by an accumulation of caloric''. This outcome also explained why it was impossible to produce immediately the protoxide by heating mercury in the open air. All the experimental results indicated the existence of the protoxide of mercury, as long as it was in combination with acids, but it could not exist in an isolated state (Guibourt, 1816a, 1816b).

According to Guibourt, although it was impossible to isolate the protoxide of mercury, it was possible to determine its oxygen content by ascertaining that which existed in the mixture of mercury and peroxide, prepared as described above. Guibourt did so by heating the mixture to a temperature high enough to decompose the peroxide. The results indicated that the protoxide was composed of 100 parts of mercury and of 4.5 of oxygen, and the peroxide of 100 parts of mercury and of 8 of oxygen. These proportions were very similar to the ones reported by Antoine-François Fourcroy (1750–1809) and Louis-Jacques Thenard (1777–1857) (Fourcroy & Thenard, 1806; Guibourt, 1816a, 1816b).

Guitourd found that after a long exposure to light, part of the peroxide was completely decomposed. The red oxide was soluble in water and the resulting solution had a strong metallic taste, it turned the violet syrup from violet to green, assumed a brown color when treated with hydrogen sulfide, oxidized the metals, and turned turbid immediately in the presence of ammonia, forming an ammoniuret less soluble than the oxide itself. In contact with air it became covered with a shining pellicle, which was constantly precipitated and renewed. Inspection of the dry pellicles under a magnifying glass, showed globules of metallic mercury. The deutoammoniure of mercury did not explode when thrown over a glass capsule heated red; heated to a higher temperature led to the release of ammonia. Its analysis indicated that it contained 108 parts of mercury oxide and 5.74 parts of ammonia. The protoxide of mercury also formed an ammoniuret (Guibourt, 1816a, 1816b).

Guitourd mentioned that two sulfides of mercury were known, a black one, named *mineral ethiops*, and a red one, named *cinnabar*. Guibourt named them proto and deutosulfide of mercury since they corresponded perfectly with the two oxides. He prepared the protosulfide by treating the protochloride of mercury with an excess of H_2S. The protosulfide was a black powder, which on heating decomposed into a mixture of metallic mercury and cinnabar. The deutosulfide was prepared by treating a solution of mercuric chloride (corrosive sublimate) with an excess of H_2S; this sulfide was also black and impossible to distinguish from the preceding by its external appearance, but which when heated it transformed completely into cinnabar. Guibourt remarked that most chemists believed that mercury was able to form many sulfides; additional experiments proved him that this contention was wrong and that the only stable sulfide was the one corresponding to the deutoxide of mercury (Guibourt, 1816a, 1816b).

Guibourt summarized his findings as follows: (a) Mercury, in contact with atmospheric air, particularly when humid, yielded a black mass composed of a mixture of its proto (Hg_2O) and deutoxides (HgO). When trying to separate the protoxide in a free state, it decomposed immediately into mercury and mercury deutoxide; (b) the red deutoxide turned brown black when heated, this change in color was due only to an accumulation of caloric (!); mercury with the largest amount of mercury contained 100 parts of mercury and 4 parts of oxygen, that is, of one dose (atom) of oxygen = 10 and 2 doses of mercury = 250 (Hg_2O); (c) the red oxide was composed of 100 parts of mercury and 8 parts of oxygen, that is, of one dose of oxygen = 10 and 1 dose of mercury = 125 (HgO); (d) the red oxide did not sublime; it was soluble in water and this solution turned green the violet tincture (the same as alkalis did); (d) the red oxide combined directly with ammonia in such proportions that the hydrogen of one saturated the oxygen of the other. The resulting compound was not a simple nitrure, as Gay-Lussac had proposed (Guibourt named this compound *ammoniure*); (e) cinnabar was the only existing mercury sulfide; it contained 100 parts of metal and 16 parts of sulfur, that is, 1 dose of sulfur = 20 and 1 dose of mercury = 125 (HgS); it corresponded to the protochloride and the deutoxide; (f) the protosulfide of mercury did not exist because the same as the protoxide, it decomposed immediately into mercury and cinnabar. If it existed, it would be composed of 100 parts of mercury and 8 parts of sulfur, that is, of one dose of sulfur = 20 and 2 doses of mercury = 250 (Guibourt, 1816a).

Guibourt's results overturned the prevailing theory of the existence of two oxides and two sulfides of mercury.

In the following two memoirs Guibourt discussed the preparation and properties of different ammonia–mercury compounds, such as Hahnemann's soluble mercury (mercurious solubilis Hahnemanni, an homeopathic preparation), the white precipitate resulting of the reaction between mercuric chloride and ammonia, *alembroth salt* (the salt of wisdom of the alchemists), and of the protochloride of mercury prepared by precipitation (Guibourt, 1820a, 1829a). For example, Hahnemann's soluble mercury was prepared by precipitating an aqueous solution of mercury protonitrate, $HgNO_3$, with ammonia, in such proportion that the remaining liquid retained a slight excess of the nitrate. According to Guibourt, the precipitate should be considered a sub-ammonia protonitrate of ammonia. Addition of an excess of ammonia produced a mixture of metallic mercury and the ammoniure of mercuric oxide. Guibourt remarked that an essential requirement for the preparation of this soluble mercury was the use of protonitrate exempt of deutronitrate, and for this reason he a described a detailed procedure to achieve this goal. According to Guibourt, the white precipitate of the reaction between mercuric chloride and ammonia was an ammonia oxychloride of mercury. Alembroth was the product resulting of the simultaneous sublimation of a mixture of equal parts of mercuric chloride and ammonium chloride (Guibourt, 1820a).

In 1835 Guibourt demonstrated that an aqueous solution of mercury cyanide was decomposed in the presence of iron.

The oxygen of water oxidized the iron while the hydrogen combined with the CN group separating metallic mercury. This reaction was very slow but could be accelerated by adding a small amount of sulfuric acid (Guibourt, 1835).

Arsenic and its compounds

Guibourt was led to study the physical and chemical properties of arsenic and some of its compound by the fact that they were being used in increasingly amounts for criminal purposes. In the first series of experiments he purified arsenic and white arsenic oxide (As_2O_3) available from commerce and determined their density as 5.959, as well as the solubility of the latter in water at 15 °C. There was a serious discrepancy between the reported properties of white arsenic; Guibourt found that these were due to the fact that the oxide was transparent when freshly prepared, and opaque after being stored for a long time. The transparent form was denser (3.7885) than the opaque one (3.695), and was less soluble in water (1/100 parts) than the opaque one (1.25/100 parts) (Guibourt, 1826).

It was commonly accepted that the native arsenic sulfides did not have the same poisonous effects as those produced artificially (red arsenic and yellow arsenic). This was the reason why the manufacturers of colors avoided the use of yellow arsenic from Germany and preferred the orpiment variety (a deep orange-yellow colored arsenic sulfide mineral with formula As_2S_3). The natural red arsenic sulfide (realgar, α-As_4S_4) was known to contain 70% of arsenic and 30% of sulfur. According to Berzelius, the yellow arsenic sulfide contained 60.92% arsenic and 39.08% sulfur. The yellow arsenic was manufactured in Germany by sublimating a mixture of white arsenic oxide with sulfur in a cast iron vase; this variety was used as a deoxygenating substance in the composition of the indigo vats. The artificial red arsenic sulfur was produced in Germany by heating metallic arsenic or its oxide, with an excess of sulfur; André Laugier (1770–1832) had determined that it contained 56.18% of arsenic and 43.82% of sulfur. According to Guibourt, the poisonous nature of this sulfide was substantially lower than that of the same yellow arsenic; nevertheless, it was not innocuous as the natural red sulfide, indicating the probable presence of a small amount of arsenic oxide (as he demonstrated experimentally) (Guibourt, 1826).

In 1829 Guibourt, Prosper Sylvain Denis (1799–1863), and Étienne Ossian Henry (1798–1873) were requested by the judge Pinondel, to issue a second expert report on a case of presumed arsenic poisoning (Guibourt, Denis, & Henry, 1829). The dossier of the case contained a report of the first expert as well as a set of samples taken from the stomach and intestines of the deceased, and from the different solutions prepared during the examination, as well as from bottles found in his house. This report indicated that there was clear evidence of the presence of arsenic and barium sulfate in the stomach and intestines of the victim. Since barium sulfate was non-poisonous, its presence indicated that it was an impurity in the commercial arsenic that has been ingested by the deceased. The bottles contained copper sulfate and sulfate of aluminum and potassium. Although copper sulfate was a poison, the chemical analysis of the tissues had not shown that it was present in them (Guibourt et al., 1829).

Guibourt, Denis, and Henry made a detailed chemical analysis of all the samples and concluded that the amount of arsenic present in the internal organs was more than enough to have caused the prompt dead of the victim. An important result was detecting the presence of iron carbide because this substance was a known component of the arsenic sold in commerce under the name of *cobolt* or *mort aux mouches* (dead flies). Contrary to the results of the first expert, their findings indicated that the remains contained copper sulfate but did not contain barium sulfate (Guibourt et al., 1829).

According to Guibourt, the hydrate of ferric oxide had been proposed as an antidote for poisoning with white arsenic (As_2O_3) because it seemed to react easily with the poison. Guibourt thought that if this was the case, then it could probably be better to use ferrous oxide because of its stronger basic character. The many experiments he carried on proved this assumption to be wrong; ferrous oxide was unable to render white arsenic insoluble, while the reaction between ferric oxide and arsenious oxide yielded a salt insoluble in water (Guibourt, 1839b).

Guibourt presented to the Académie de Médicine de Paris a set of six different iron compounds to be tested as possible antidotes for arsenic poisoning (ferrous oxide moist, black iron oxide moist, ferric oxide moist, hydrate of ferric oxide, ferric sub-arsenite, and neutral ferric arsenite). The ferric sub-arsenite was assumed to form in the stomach by the reaction between the hydrate of ferric oxide and white arsenic. The committee appointed by the Académie to test these compounds, conducted several toxicological tests of arsenic poisoning of dogs to determine the time in which the poison become fatal (in the absence of an antidote), and to obtain a standard by which the beneficial effects of the antidote could be estimated. A moist ferrous oxide, containing 19% of anhydrous ferric oxide, and a black oxide containing 7% were entirely inefficacious; it did not decrease the time required to cause death. Similarly, ferric arsenite acted as a virulent poison because the HCl and lactic acids of the gastric secretion promptly decomposed it. More significant results were obtained with the moist hydrated ferric oxide and the common dry hydrated ferric oxide. All the animals lived many hours more that when the action of the arsenic was left uncontrolled. One important criticism to the report was the large quantities of the ferric oxide that had to be administered (even in the case when a very small quantity of arsenic had been ingested); the antidote would probably act slower than the usual procedure of eliminating the poison by forced vomiting (Guibourt, 1839b).

Natural products

Starch

According to Guibourt, François Vincent Raspail (1794–1878) had shown that starch was not a homogeneous body but that each grain was a true vegetable organ composed of (i) a smooth tegument or envelope, unaltered by water or acids at ordinary temperatures, and susceptible of long coloration by iodine; (ii) an internal substance, soluble in cold water, liquid even in its natural state; which by evaporation lost the power of being colored by iodine, and possessing all the properties of gum. Raspail believed that the coloration by

iodine was due to a volatile substance and not to the starch itself (Raspail, 1825). The fact that Raspail results had not been accepted by other researches led Guibourt to conduct his own experiments. For this purpose he used potato starch, which he prepared by himself (Guibourt, 1829b).

A microscopic observation of the grains revealed that they were present in all forms, changing from spherical for the small ones, to triangular for the largest. The starch was smooth, transparent, and grayish at the edges; all the grains were free, insoluble in cold water, even after many hours maceration. When rubbed in a mortar, they lost their whiteness and brilliancy, and sometimes adhered in humid air; addition of a little water transformed them into a paste, which became very hard when dry. The entire grain was slowly colored by iodine, without losing its transparency. The broken grains contacted with water caused rapid currents from the emission of soluble matter; part of the latter disappeared completely, the rest remained attached to the grains as a jelly, which disappeared promptly on application of heat. Addition of an aqueous iodine solution tinted everything sky-blue color to the whole, while the jelly material became deep blue (Guibourt, 1829b).

These experiments showed that the soluble and the insoluble part were equally colored by iodine, and differed only in density and structure. The soluble part, after long boiling, was still colorable by iodine, proving that the coloration was not a volatile compound, as claimed by Raspail. Rapid evaporation of the solution turned it into a jelly crust and gummy liquor; which were not completely soluble in cold water. Nevertheless, both parts were colored blue by iodine Guibourt remarked that his results showed that a long boiling and evaporation to dryness did not remove the property of coloring iodine, that the soluble starch was not a gum, as claimed by Raspail, and that both the soluble and insoluble parts consisted of one immediate vegetable principle. The only question remaining was the possibility that this principle was not the same in all vegetables, and probably offered a variety of forms. For this reason, Guibourt proceeded to analyze the starch present in a variety of vegetables: wheat, arrowroot (*Maranta indica*), cassava and tapioca (extracted from *Jatropha manihot*), and sago (extracted from *Sago farinaria*) (Guibourt, 1829b).

Wheat starch under the microscope appeared composed of spherical globules of various sizes; it was white and dull and gave to water a very stronger gelatinous consistency. Starch paste consisted of an aqueous solution of the soluble part, holding in suspension the teguments, and partially soluble in cold water. Boiling the paste for a long time in a large amount of water caused the teguments to divide more and more until they dissolved; in this state the liquor did not again acquire the gelatinous consistency on cooling. In the starch of commerce, a few of the globules had been broken by the mill or by the heating resulting from fermentation. Potato starch, not having suffered these processes, was always pulverulent.

Arrowroot starch was composed of grains larger than those of wheat starch, more brilliant, and quite transparent. They were mainly spherical, sometimes triangular, like those of potato starch, but were much smaller. Arrowroot gave less consistency to boiling water than wheat starch, probably because it contained more of the soluble principle (Guibourt, 1829b).

Cassava and tapioca starch were obtained from the root of the *J. manihot* and differed only in the first being dried in the free air, the latter on hot plates of iron, hence its agglomerated form. All the grains of cassava were spherical, remarkably equal in size, and smaller than those either of arrowroot or wheat starch. This latter property allowed distinguishing it from all other starches. Tapioca was in lumps, formed of broken and aggregated grains, partly soluble in cold water. The unbroken grains resembled those of cassava.

Sago starch appeared as small round, hard, white masses, which under the microscope were seen to be composed of adhering entire grains, resembling those of potato starch, and bursting when heated. The color of sago was due to the roasting process (Guibourt, 1829b).

An additional note described barley starch and its mixture of teguments, known as *hordein* (Guibourt, 1829c).

Tonquin musk

According to Charles Blondeau and Guibourt, musk was a material produced by the ruminant *Moschus moschiferus*, living in Tonquin and Tiber (The pouch that releases the musk is located between the navel and the sexual organs; the musk released by the female is weaker and of poorer quality than that of the male). Two kinds of musk were commercially available, named Tonquin and Kabardin, the first one being the most valuable and strong. The musk of Tonquin had been reported to contain ammonium carbonate, wax, resin, gelatin, albumin, salt, potassium, calcium carbonate, and no volatile oil (Blondeau & Guibourt, 1820).

Blondeau and Guibourt decided to make a more detailed analysis of musk and for this purpose they dried a sample over a water bath, extracted the dry residue with ether, alcohol, water, and ammonia, and treated the different fractions with a variety of chemical reagents (e.g. KOH, acetic acid, and nitric acid). The drying process was accompanied by the release of ammonia. Their report of the composition of the different fractions and their behavior with the reagents indicated that musk contained a large number of different principles: stearin, olein, gelatin, albumin, fibrin, an acid oil combined with ammonia, a volatile oil, cholesterol, traces of an acid soluble in water, a highly carbonated substance soluble in water and insoluble in alcohol; ammonium chloride, potassium chloride, calcium chloride; an unidentified acid partly saturated by the preceding bases, a combustible acid, carbonates, calcium phosphates, another soluble calcium salt; and a small amount of water (Blondeau & Guibourt, 1820).

Gooseberry juice

Many scientists attributed the coagulation of gooseberry juice (*Ribes grossularia*) to the fact that the gelatinous principle it contained in solution became insoluble when fermentation set on. According to Guibourt, there was another explanation for the phenomenon (Guibourt, 1825). Examination of freshly extracted currant juice showed that it was sprinkled with a variety of fibrous particles originating from the debris of the structure. These fibers were present in a small quantity and did not provide consistency to the juice, but when macerated they swelled and converted almost completely into a thick transparent mucilage; at the same time all the liquid became a gelatinous mass.

This last state preceded fermentation and was independent of it. The structure was destroyed by fermentation, which produced alcohol. Guibourt separated the gelatinous principle by diluting the gel with alcohol followed by filtration of the mixture. He reported that the principle presented itself as pinkish transparent flakes, which when heated in a glass tube carbonized without swelling. Guibourt studied the reaction of the principle with a wide variety of reagents, among them, litmus, alcohol, mineral acids, KOH, ammonia, silver nitrate, lead acetate, ferric sulfate, etc. The results indicated that the gelatinous matter of currants was different from the basorin and gum of plum and cherry fruits; Guibourt suggested naming it *grossulin* (Guibourt, 1825).

In a following work, Guibourt showed the presence of pectic acid in the different fractions produced during the refining of cane sugar (Guibourt, 1828).

Alkaloids

In 1830 Guibourt had the opportunity of examining a variety of quinquina originating from Cuzco, Peru (Guibourt, 1830a). Treatment of the bark with nitric acid resulted only in a darkening of its original orange color. Extracted with ether it produced a slightly yellow solution, which turned orange upon addition of nitric acid. The bark seemed to contain only one alkaloid (cinchonine) and a coloring substance (cinchonic red). Alcohol extracted a large amount of the coloring substance and a very small amount of cinchonine. Guibourt extracted the bark with boiling water slightly acidulated and then neutralized the filtered extract with an excess of calcium carbonate; the resulting calcareous precipitate was colored lie red; concentration by evaporation produced an additional amount of this precipitate. Further filtration and treatment with calcium carbonate produced an additional precipitate, which was filtered, washed, dried, and then extracted several times with distilled alcohol. The alcoholic extracts, left to dry by natural evaporation, yielded a precipitate of cinchonine. Extensive experimentation with the mother liquor led Guibourt to obtain an additional amount of white crystals of cinchonine. The overall results indicated that the bark contained about 8.4 g of cinchonine per kilo (Guibourt, 1830a).

In the second part of this paper, Guibourt reported his study of the mother liquor obtained during the preparation of quinine sulfate, a compound described by Pierre-Joseph Pelletier (1788–1842) and Joseph Bienaimé Caventou (1795–1877) in 1820 (Pelletier & Caventou, 1820) and Étienne Ossian Henry (1798–1873) (Henry, 1821; Henry & Delondre, 1830). The latter had shown that this mother liquor contained only cinchonine, quinine, and a particular yellow substance, which was identified as quinidine (a stereoisomer of quinine). In this publication Guibourt described a procedure for separating the cinchonine left in the mother liquor of quinine sulfate, based on its treatment with NaCl and ammonia, extraction with alcohol, and crystallization. Guitourd believed that the resulting liquid could be used as such for medical purposes, and could be prepared in large amounts from the process for making quinine sulfate; it also afforded cinchonine as by-product (Guibourt, 1830a).

In 1852 Antoine Alexandre Brutus Bussy (1794–1882) and Guibourt were asked to examine a sample of quinine sulfate, suspected of being adulterated (Bussy & Guibourt, 1852). Their results indicated that the sample contained a considerable amount of quinidine sulfate and an alkaloid, which presented the same external properties and many of the chemical properties of quinine sulfate. In 1844 Ferdinand Ludwig Winckler (1801–1868) had separated this alkaloid from commercial quinine sulfate and named it *quinidine*, and in 1849 J. van Heijningen, had separated it from quinoidine imported from Germany, and named β-*quinine*. Both chemists had also given a detailed description of the physical properties of their alkaloid.

Bussy and Guibourt conducted a series of experiments on both compounds and found that they were completely different, both in their chemical and physical properties: (1) Quinine separated from its aqueous alcoholic solution in the form of syrup, which on drying in the air remained transparent. Spread out in thin layers upon glass it became opaque, while the mass assumed a crystalline structure. In the first condition, the quinine appeared to contain 3 equivalents, or 14.29% of water; in the second condition only one equivalent, or 5.26%, on the supposition that its formula was $C_{20}H_{12}NO_8$. Quinidine, on the other hand, separated from its aqueous-alcoholic and alcoholic solutions in crystals belonging to the right rectangular or rhombic prism. The main crystal forms were the rectangular octahedron, the rhombic octahedron (very similar to that of sulfur), the right rhombic, and rectangular prisms. These crystals seemed to be anhydrous because they did not change weight when heated to 100 °C; (2) Quinine dissolved easily in cold ether and absolute alcohol, while quinidine required 140–150 parts of ether, 45 parts of absolute alcohol, 105 parts of alcohol of 90% and 3.7 parts of boiling absolute alcohol; (3) The crystalized quinine sulfate dissolved in 57 parts of absolute alcohol and in 63 parts of alcohol of 90%. The quinidine sulfate dissolved in 30–32 parts of cold absolute alcohol, and in 7 of alcohol of 90%; (4) Quinine sulfate dissolved in 256 parts of cold water and 24 of boiling water, while quinidine sulfate did it in 73 of cold and 4.20 of boiling water according to Howard, although other chemists had reported different values; (5) Quinine oxalate was completely insoluble in water, while quinidine oxalate was very soluble and crystallizable on evaporation of the solution (Bussy & Guibourt, 1852).

Another report described the analytical procedures to follow in order to determine the purity of quinine sulfate (water, salicin, phlorizin, gums, starch, calcium sulfate, lactose, fatty acids, sugars, and cinchonine sulfate) (Guibourt, 1852a,b).

Turpentine and its essence

In 1839 Guibourt published a detailed description of the characteristics and properties of the different varieties of turpentine available (Guibourt, 1839a). This was followed by another paper describing the optical properties of turpentines and their essences. According to Guibourt, turpentines were the secretions provided by many trees of the species of the *Pistacia* and *Phinophyta*; these materials deviated polarized light with quite different intensity, according to their origin. The essences derived from them also deviated polarized light notably by the direction and intensity. One particular example was the English and French commercial essences of turpentine; Éugene Souberain (1797–1859) and

H. Captaine had found that the distillation of turpentine in the absence or presence of water produced two essences of different rotating power. The essence obtained by steam distillation had a rotating power of −7°, while that of the one obtained in the absence of water was −19° (Soubeiran & Capitaine, 1839). These anomalies led Guibourt and Apollinaire Bouchardat (1806–1886) to determine the rotating power of a large number of turpentines and their essences, originating from France, England, and the colonies (Guibourt & Bouchardat, 1845).

The results of numerous experiments led them to conclude as follows: (a) the turpentines from Bordeaux, Strasburg, and Carolina, were levorotatory; the Canadian turpentine was dextrorotatory; (b) the French commercial essence of turpentine obtained by distillation of pine turpentine presented substantial modification in its molecular constitution, which depended on the manufacturing process. The material was always levorotatory over a wide range of values: (c) the essence obtained by steam distillation of the turpentine of larch, fir, and, white spruce was also levorotatory, but with intensity substantially lower than that of the original resin. The English essence obtained by steam distillation of the Carolina turpentine exuded by *Pinus tæda*, was dextrorotatory, while the turpentine itself was levorotatory (Guibourt and Bouchardart, 1845).

Astringent juices of cachou, gambir, or kino

In 1847 Guibourt published a long memoir (over 90 pages) describing the astringent juices derived from the fruits, wood, or leaves of *Areca catechu*, *Acacia catechu*, *Nauclea gambir*, *Kino* of Senegal, etc. (Guibourt, 1847). The first part of this work was devoted to an historical review of these substances. Guibourt wrote that catechu was an astringent substance used since long ago by people in Asia, in the same way as tobacco was used in other parts of the globe. This chewing substance, mixed with betel nut and a bit of calcium carbonate, and wrapped in a betel leaf, reddened saliva strongly and colored the teeth in an ugly manner. It was used to help prevent loosening of the gum and a weak digestive system. In India it was also used as a dye. Around 1820 catechu had begun to be imported into France as a dye for cloth and its commerce had grown to over 250 ton/year (this figure included also gambir and kino). The British physician Kerr had reported a detailed description of the tree *A. catechu* and the procedure for extracting cachou (Kerr, 1776). Two varieties of cachou were available in the bazaars of India, the *Cutta gamboo* and *casheuttie*, which corresponded to the British gambir and Pegu cachou. The first one was extracted from the leaves of *Uncaria gambir*.

The following section was a description of the astringent juice of the 46 varieties of cachou, gambir, and kino, commercially available, among them: red balls of cachou, brown cachou from polymorphous cachoum cachou of Siam, rectangular gambir, gambir in needles and cubes, aromatic gambir, juice of *Pterocarpus crinaceous*, *Butea frondosa*, kino from India, Mauritius, Jamaica, Colombia, and Brazil, juice from *Eucalyptus resinifera*, etc. This section included the physical properties and analysis of some of these materials. For example, the brown amylaceous cachou was found to contain 11.70% of cachutic acid and fatty material, 31% of an alcoholic red astringent extract, 12.80% of gum, extracted by water, 31.70% of an amylaceous substance, and 12.80% of lost material (Guibourt, 1847).

Pepsin

In 1859 the Société de Pharmacie de Paris recognized the need to update the French Pharmaceutical Codex and for this purpose appointed a large number of committees to deal with the numerous subjects. One of these committees, composed of Guibourt, Félix Henri Boudet (1806–1878), Jules Antoine Regnauld (1820–1895), and P.C. Boudault, was assigned the task of defining the composition of pepsin pills. The pills available commercially had a wide variety of compositions and most of them did not have the properties that had made pepsin important. It was necessary then, to define a product that had to have a constant set of properties and efficacy.

Pepsin was a principle secreted by the mucosa of the stomach of vertebrates, which helped convert raw food of these animals in a seemingly homogeneous pulp denominated chime. According to the physiologists the chime transformed the nitrogenous foods into a soluble body. When the stomach was injured, the secretion of pepsin was diminished or suppressed, with the consequent decreasing effect on the digestion of food. In this situation, it was customary to provide the sick person with an outside source of pepsin. Many procedures had been proposed for preparing pepsin, mostly based on using extracting it from the stomach of pork. The preferred procedure was the one developed by Boudault (1856). In the slaughterhouse of Paris, the main stomach of a just slaughtered ruminant was first opened and emptied of all the food it contained, washed, and the internal mucosa removed with a fiber brush. The resulting pulp was sent to Boudault to be processed for its pepsin. The basic process consisted of diluting the pulp with filtrated water and leaving it to macerate for about 2 h. The mixture was then filtered and the filtrate treated with an aqueous solution of lead acetate. The excess lead was removed with a stream of H_2S. The purified liquid was evaporated to dryness at a temperature not exceeding 45 °C. The resulting product was a firm amber colored paste, which Guibourt named *pepsin officinalis* (Guibourt, Boudet, Boudault, & Regnauld, 1865).

The committee determined the physical properties of this pepsin, its reaction with a large number of reagents, its neutralization with NaOH, decomposition by heating, and the acids and bases present in it. The next step was to study the possibility of using fibrin to determine the quality of pepsin. The fibrin used in these experiments was obtained from the blood of animals such as beef, veal, or sheep, and subject to a series of chemical tests with HCl, lactic acid, phosphoric acid, calcium acid phosphate, acetic, citric, and tartaric acids, gastric fluid (of a dog), and finally, with pepsin officinalis. Further exams were carried on with amylaceous pepsin (neutral and acid).

The committee reached the following conclusions: (1) The stomach of sheep submitted to the treatments indicated above for the preparation of pepsin officinalis, produced an amber color pasty acid substance, having a disagreeable but not repulsive smell. This substance dissolved slowly in distilled water, leaving a very small residue. It acted on fibrin on a very different manner than the diluted

acids, and very similarly to the action of gastric juice; (2) Most acids diluted, particularly hydrochloric, lactic and tartaric acids, swelled fibrin and dissolved it partially or totally. The resulting solution treated with nitric acid, produced a white precipitate; (3) The gastric juice of a dog contacted with wet fibrin, in the ratio 25:6, swelled it and then decomposed it into two different substances, one insoluble the other soluble. The filtrated liquid was not precipitated by cold nitric acid; (4) A solution of pepsin officinalis exerted on fibrin an action similar to that of the gastric juice of a dog, and transformed it mainly into a soluble substance, which was not precipitated by cold nitric acid; (5) pepsin officinalis had a variable composition, which varied according to its origin and method of preparation. Its degree of activity also varied considerably, that is, in the proportion of fibrin, which could transform it completely. Hence it had to be titrated to determine the proportion in which it was to be used in order to decompose completely a given quantity of fibrin (6 g); (6) Pepsin officinalis should the basis of a pharmaceutical preparation, in which it was present as a powder mixed with starch. One gram of this preparation should be able to decompose 6 g of fibrin; and (7) the normal medical dose of amylaceous pepsin should contain enough tartaric acid to give it an acidity corresponding to 0.19 g of dry sodium carbonate (Guibourt et al., 1865).

Conflict of interest

The authors declare no conflict of interest.

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