

AUGUSTE-NICOLAS-EUGÈNE MILLON

Millon reagent, chlorine derivatives, and blood

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ABSTRACT

Auguste-Nicolas-Eugène-Millon (1812-1867) was a pharmacist of the French Army who studied the compounds of chlorine with oxygen and sulfur; his results indicated that the bleaching compounds should not be considered as salts but rather the compounds corresponding to the peroxides where one equivalent of chlorine had replaced the corresponding amount of oxygen. He also assumed that bromine, iodine, sulfur, and metalloids formed analogous compounds. He synthesized and determined the properties of chlorous, hypochloric, chloric, chloroperchloric, perchloric, and hypochlorosulfuric acids, as well as numerous new similar compounds of iodine. He developed a method for preparing highly pure nitric acid and used it to prepare, for the first time, ethyl nitrate. Millon studied the presence of different metals and salts in human blood and demonstrated the presence of silica, manganese, lead, and copper. His results indicated that these were present in enough quantity to determine them by standard analytical procedures. To him we owe the Millon reagent, an extremely sensitive coloring agent for determining proteins and related substances. He prepared it by dissolving mercury in water containing nitric acid in a concentration equal to 4.5 times the weight of the element and showed that the active component was not mercurous or mercuric nitrate.

Keywords: blood; chlorine and derivatives; ethyl nitrate; iodine and derivatives; Million's reagent

RESUMEN

Auguste-Nicolas-Eugène-Millon (1812-1867) fue un farmacéutico militar francés que estudió en detalle los compuestos del cloro con oxígeno y azufre; sus resultados indicaron que los agentes de blanqueo no debieran ser considerados sales sino compuestos correspondientes a los peróxidos en que un equivalente de cloro había reemplazado la cantidad equivalente de oxígeno. Supuso igualmente que el bromo, yodo, azufre, y los metaloides generaban compuestos de la misma naturaleza. Millon sintetizó y determinó las propiedades de los ácidos cloroso, hipoclorico, cloro-perclórico, perclórico, e hipoclorosulfúrico, así como numerosos nuevos compuestos similares del yodo. Desarrolló un método para preparar ácido nítrico de alta pureza y lo utilizó para sintetizar, por primera vez, el nitrato de etilo. Millon estudió la presencia de varios metales y sales en la sangre humana y demostró la presencia de sílice, manganeso, plomo y cobre. Sus resultados

indicaron que estas sustancias estaban presentes en suficiente cantidad para poder determinarlas por métodos analíticos estándar. A él le debemos el reactivo de Millon, un agente colorante altamente sensitivo para determinar la presencia de sustancias proteínicas y similares; Preparó el reactivo disolviendo mercurio en agua conteniendo ácido nítrico en razón 4.5 veces el peso del elemento, y demostró que el componente activo no era el nitrato mercurioso ni el nitrato mercúrico.

Palabras clave: ácido nítrico; cloro y derivados; nitrato de etilo; reactivo de Millon; sangre; yodo y derivados.

INTRODUCTION

Scientific contribution

Eugène Millon was born on April 23, 1812, at Châlons-sur-Marne, the son of Henri-Auguste Millon, manager of a transportation company, and Marie-Elisabeth-Joseph-Louise Thibault. Eugène's father died in 1822 when he was 10 years old, a tragedy that led his mother to put him under the tuition of her brother, the abbé Thibault, a priest working as principal at the Collège Royale de Saint-Louis in Paris. Two years later the uncle was appointed teaching inspector at the University of Paris and the heavy load of the new position forced him to return the child to his mother at Chalons, where she enrolled him as an external student in the local school (1825-1830). After receiving *his baccalauréat ès science*, he prepared himself for a competition at the military health services, while working as teacher at the Collège Rollin in Paris. In 1832 he was admitted as student surgeon at the Val-de-Grâce military teaching hospital in Paris and two years later he won first place in a competition to enter active service as *chirurgien sous-aide major*. The progress of his medical studies was affected by his obligations as active soldier. He was assigned successively to positions in Bitche, Lyons, Algiers, and Metz. In 1836 he received he obtained his doctorate in medicine from the Faculté de Médecine de Paris, after successfully defending a thesis on some new ideas about human abilities envisaged from a phrenological viewpoint (Millon, 1836). In 1837 he read to the Académie des Sciences his first scientific memoir, describing the preparation of two new compounds, the bromides of nitrogen and cyanogen (Millon, 1838, 1845b); this work was done while Millon was working in the laboratories of Théophile-Jules Pelouze (1807-1867). The following year he was assigned to the hospital of Gros-Caillou, where he now decided to follow a career of pharmacist, instead of surgery. In 1841 he postulated and won the competition as *professeur de chimie* at the Val-de-Grâce school. He was then transferred to Toulouse, Lunéville, Metz, Versailles, and back to Val-de-Grâce (1847). At the end of 1847 he left the school at Val-de-Grâce to move to Lille to become chief pharmacist and first professor at the city's instructional military hospital, where he published his first work about wheat (Millon, 1848c). The revolution of 1848 led to his transfer to Flandres after being promoted to *pharmacien major de 1^e classe*. Again, he was transferred to Algiers in 1850 and in 1852 he was promoted to *pharmacien principal de 1^e classe* and in 1859 to *pharmacien en chef de la division de Alger*. Millon served in this top ranking position of the hierarchy of the health corps of the army until his retirement in 1865. In 1853 the government recognized his many achievements by appointing him *chevalier* to the Légion de Honneur, followed by a promotion to *officier* in 1862. Eugène Millon

passed away on October 22, 1867, at St.-Seine-l'Abbaye, after suffering for many years of intestinal problems.

Scientific contribution

Millon wrote over 80 papers, booklets, and books (i.e. Millon, 1842b, 1843ab, 1845b, 1845-1848, 1846, 1854c) about his research activities in the areas of inorganic, organic, mineral, and analytical chemistry, physiology, toxicology, botany, etc.. As customary for all candidates to the Académie des Sciences, Millon published a booklet describing his researches and achievements (he failed in all his attempts) (Millon, 1844a). In addition to the subjects described below Millon also investigated the nitrides of bromine, iodine, and cyanogen (Millon, 1838, 1845b) and the preparation of HBr and HI (Millon, 1842c); the nature of catalytic reactions (Millon and Reiset, 1843); the chemical constitution of acids and bases (Millon, 1844i); the reaction of mercury salts with ammonia (Millon, 1845c); the composition and classification of wheat (Millon, 1848c, 1849c, 1854ab); extraction of perfumes from Algerian flowers (Millon, 1856b); the analysis of mineral water (Millon, 1856a); the chemistry of nitrification (Millon, 1860); milk (Millon and Commaile, 1864abc, 1865ab); alcoholic fermentation (Millon, 1864); etc.

Chlorine compounds with oxygen and sulfur

Millon mentioned that it was commonly accepted that the bleaching compounds obtained by the reaction between chlorine and alkalis were mixtures of metallic chlorides and salts, produced by a particular acid named *hypochlorous acid*. Although this assumption had been supported by Antoine-Jerôme Balard's (1802-1876) finding of the existence of a peculiar compound formed of one equivalent of chlorine and one of oxygen, it did not provide a satisfactory explanation of his results on the action of these mixtures of chlorine and hypochlorites upon salts of a lower grade. For example it was known that mixing a fresh solution of lime chloride with another of lead nitrate produced a precipitate, which turned from white to yellow and then to brown, while the liquid was found to contain only calcium oxide nitrate. The white precipitate was considered to be a lead chloride, which additional decomposition of hypochlorite turned into lead dioxide (Millon, 1839).

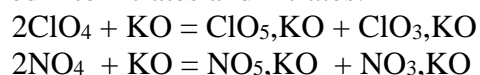
According to Millon, if the fresh white precipitated was filtrated immediately it was found that it was not lead chloride and that it continued to change its color in spite of not being in contact with lime chloride. The white and brown forms were found to be isomers of $PbOCl$, that is, of a compound where one of the oxygen atoms had been replaced by one of chlorine. Similar results were found by passing a current of dry chlorine over litharge obtained by calcining lead carbonate; by substituting the lead nitrate with ferrous nitrate, manganous salts, salts of cupric oxide, etc. To Millon, these results suggested that the alkali bleaching compounds should be considered to be compounds corresponding to the peroxides, in which one equivalent of chlorine had replaced the corresponding amount of oxygen. In these two series of corresponding compounds, the analogy in composition would reflect in an analogy in properties: similar instability and similar oxidizing and bleaching power. Millon believed that comparing the composition of the bleaching compounds of sodium and potassium could prove his theory.

According to him, the composition of the potassium peroxide corresponded to KO_3 ($KO + O_2$) and that of sodium to Na_2O_3 ($Na_2O_2 + O$). Hence the bleaching compound of potassium should contain four times more chlorine as that of sodium. Experience proved that KOH absorbed double the quantity of chlorine than NaOH, proving that the actual formula of sodium peroxide should be

NaO₂. In other words, the potassium compound should, as was demonstrated by experiment, to have twice the bleaching power of that of sodium (Millon, 1839).

In Millon's words, "the bleaching compounds should not be considered as salts, but rather combinations corresponding to the peroxides, in which all the oxygen, which was added to the lower oxide to form a higher one, was replaced by its equivalent of chlorine. It could also be stated that the compounds considered as mixtures of chlorides and hypochlorites, are actually simple compounds; while the hypochlorites, considered as simple salts, and without mixture, are mixtures of peroxides and peculiar bodies corresponding to peroxides" (Millon, 1839). Millon added "it was logical to assume that bromine, iodine, sulfur, and, perhaps, other metalloids, formed analogous compounds. Oxygenated water, therefore, promised to become the type of numerous and parallel series, which would expand considerably the field of mineral chemistry, without introducing any complication" (Millon, 1839).

Millon also described the results of his research on the synthesis and properties of the compound ClO₄, which Joseph-Louis Gay-Lussac (1778-1850) had named *chlorine deutoxide* (Millon, 1841b; Gay-Lussac, 1814). He mentioned that this compound was a liquid up to the temperature 20 °C, which reacted with alkaline oxides generating chlorates and chlorites, in the same manner that hyponitric acid, NO₄, transformed into nitrates and nitrites:



For these reasons he suggested changing its name of the compound from chloride deutoxide to *hypochloric acid*.

The chlorites existed in the same manner as the nitrites and constituted by themselves a new series of salts, stable enough to transfer their acid to metallic oxides and generate their salts in a crystalline state. The action of HCl upon potassium chlorate did not generate a particular gas but a mixture of various gases composed mainly chlorine and hypochloric acid. The compound, known as hypochlorous acid, did not react with alkalis as an acid; it converted them into peroxides and chlorine oxides and continued the series beginning with oxygenated water, showing the importance that this compound could play in science (Millon, 1841a).

In a following publication Millon wrote that he had proven that the combination of oxygen and chlorine named chlorine deutoxide was a complex acid incapable of forming salts, and convertible into chlorate and chlorite by alkaline bases. He believed that the latter result suggested the existence of a new chlorine oxide of formula ClO₃. He was now happy to announce that he had succeeded in isolating this compound, which he named *chlorous acid*, as well as developing several simple processes for preparing it in large amounts (Millon, 1842a).

Millon stated that chlorous acid was always formed when deoxidizing chloric acid. It was the most stable oxygenated compound of chlorine, remaining as such even in the presence of a deoxidizing agent, as long as it was maintained below the temperature at which the acid or its salts were destroyed. The experimental results indicated that chlorous acid resisted the reducing action of nearly all organic and metallic substances, and was a product of the calcination of potassium perchlorate, which became chlorite before it turned chloride (Millon, 1842a).

In this publication Millon described in detail the following process for preparing chlorous acid: A mixture of one part of tartaric acid and four of potassium chlorate was introduced into a flask of the capacity of 300 or 400 cubic centimeters, followed by addition of a solution

1. Million wrote his formulas according to the prevailing custom and using 6 as the atomic mass of carbon.

containing six parts of nitric acid of relative density 1.327, and eight parts of water. The ensuing reaction was spontaneous at room temperature (25 °C) and could be accelerated by heating the bottom of the flask first with a single piece of lighted charcoal and afterwards with any other heating medium, while taking the care not to exceed the temperature of 45° to 50 °C. The reaction ended when the mixture became colorless. The gas released was a mixture of chlorous acid and CO₂, which could be dried over calcium chloride, or absorbed by passing through a washing bottle containing water. Chlorous acid was a gas of a very deep greenish yellow, strongly irritating the throat and lungs, and easily confounded with hypochloric acid. It bleached the tincture and paper of turnsole and indigo sulfate, was converted by cold water into a red liquid, and decomposed at 57 °C with production of a slight shock (Millon, 1842a). The aqueous solution of chlorous acid had a caustic taste; it was colored green when the gas was diluted, and very deep golden yellow when the water had absorbed five or six times its volume of the gas, which appeared to be the limit of its solubility. At 20 °C the solution stained the skin yellow almost instantly.

Millon determined the composition of chlorous acid by streaming its gas through a small glass tube containing metallic copper. Repeated analysis of the resulting products indicated that chlorous acid contained, by weight, 60.15% of chlorine, corresponding to the formula ClO₃ (59.65 % chlorine). This formula was verified by analysis of the chlorites having the general ClO₃MO, where M is a metal, and measurement of the density of the gas: the experimental result was 2.616, against the calculated one 2.733. These values proved that two volumes of chlorine combined with three of oxygen to form three volumes of gaseous acid (Millon, 1842a).

Gaseous chlorous acid was found to be highly non reactive with certain metals. For example, copper, lead, tin, antimony, zinc and even iron, reduced in very fine filings, remained an hour or more in its atmosphere without the least sign of alteration. Mercury formed an exception; it absorbed the gas at room temperature without leaving a residue. The behavior of an aqueous solution varied with the nature of the metal; with mercury it produced oxichlorides; with copper, a mixture of chlorate and chloride; with zinc and lead, chlorides, and chlorites, etc. It did not react with antimony, gold, and platinum (Millon, 1842a).

Millon mentioned that the hydroxides of potassium and sodium formed acid chlorites strongly colored red and non-crystallizable. The chlorites of lead, silver, barium, and strontium gave crystalline salts, which were easily analyzed. Treatment of all these chlorites with dilute nitric acid resulted in the disengagement of a strongly colored yellow gas with a powerful odor, which was no other than chlorous acid itself (Millon, 1842a).

In a more detailed publication Millon reviewed the information available for the properties of chlorine and its oxides, since the discovery of the element and summarized it as follows:

ClO₇, discovered by the count of Stadion

ClO₅, discovered by Berthollet and isolated by Gay-Lussac

ClO₄, discovered simultaneously by the count of Stadion and Davy

ClO, discovered by Davy and confirmed by Gay-Lussac

The oxides ClO₅ and ClO₇ were the basis of all the researches that followed (Millon, 1843b).

Millon went on to summarize the results of his research about (a) the action of sulfuric acid upon potassium chlorate, chlorine oxide, chlorine deutoxide, chlorous acid, and hypochloric acid (ClO₄); (b) the action of HCl upon potassium chlorate, chlorine protoxide (ClO); Davy's euchlorine, and chlorochloric acid (Cl₃O₁₃ = 2ClO₅, ClO₃); and chloric acid (ClO₃); (c) the preparation and properties of chlorous acid; (d) the chlorites of sodium, barium, strontium, lead, and silver; (e) the action of light upon the oxygenated derivatives of chlorine; (f) the thermal decomposition of potassium chlorate and perchlorate; (g) determination of the composition of chlorous acid (ClO₃), hypochloric acid (ClO₄), chlorochloric acid (Cl₃O₁₃), chloric acid (ClO₅), chloroperchloric acid (Cl₃O₁₇), and perchloric acid (ClO₇). He expressed his belief that his results could be generalized very easily: Perchloric acid, being composed only of chlorine and oxygen, was modified by the replacement of one equivalent of oxygen by one of oxygen, yielding chlorous acid, ClO₆Cl = 2ClO₃; all the series of oxygen derivatives of chlorine could be expressed by the union of several molecules of perchloric acid where some were characterized by oxygen replacing chlorine, and the others remaining unchanged. These principles could be easily extended to the acids of nitrogen and sulfur, having for primitive combination NO₅ and SO₃, respectively. Accepting these ideas suggested the existence of many combinations of sulfur, chlorine, or nitrogen with oxygen, yet to be discovered (Millon, 1843b).

In 1844 Millon reported that during his search for a chloride of sulfur higher than the one known so far (disulfur dichloride, S₂Cl₂) he had noticed the formation of a crystalline product, which he supposed contained only sulfur and chlorine (Milton, 1844b; 1850b). Further experiments showed him that this compound appeared only when the chlorine was wet and in great excess. This finding led him to suspect that this derivative also contained oxygen. The new derivative was easily prepared by adding a few drops of disulfur dichloride to a wet flask containing some chlorine moistened by its passage through a washing bottle. In these circumstances, a layer of colorless transparent crystals covered rapidly the sides of the flask. Removal of the crystals by scratching resulted in their immediate decomposition by the moist air. The same effect was noticed when using chlorine with a high content of water. Millon avoided this problem by filling a flask with 4 or 5 liters of moist chlorine, followed by addition of 20 to 30 g of sulfur chloride saturated with chlorine, and 2 or 3 g of water. After agitation the flask was immersed in a refrigerating mixture of ice and salt for 4 or 5 hours. During this period a great disengagement of HCl took place. The flask was again filled with moist chlorine, placed in the refrigerating mixture, and the process repeated until most of the sulfur chloride had solidified to a crystalline mass, which floated in the excess of sulfur chloride. The formation of the crystals was preceded by the production of a yellowish liquid, heavier than the sulfur chloride, from which it separated as oil (Millon, 1844b).

Millon found that it was almost impossible to analyze these crystals immediately after their formation because they decomposed violently and were thrown in every direction when contacted with water, alcohol, or weak acids. After numerous experiments he found that when the crystals had been freed as much as possible from the accompanying sulfur chloride and stored in a very dry glass tube for 2 or 3 months, they had become soft, pasty, and moist, and after 7 or 8 months they had converted into an extremely fluid liquid, which did not solidify even when cooled to -18 °C. This process had transformed the original material into an isomer, as shown by the change in physical and chemical properties, for example, the liquid thrown into water did not produce the

sound of red-hot iron suddenly extinguished, and treated with weak acids, water, and alcohol, it deposited at the bottom and eventually decomposed into SO_3 , SO_2 , and HCl . According to Millon, this transformation agreed very well with the chemical analysis which indicated that it was a compound of sulfur, chlorine and oxygen, in the proportion $\text{S}_2\text{O}_3\text{Cl}_2$, as determined by its transformation into barium sulfate and silver chloride. Millon named it *hypochlorosulfuric acid*; this acid was clearly a different compound from the combination discovered by Victor Regnault (1810-1878) (Regnault, 1836) (SO_2Cl), and analyzed by Heinrich Rose (1795-1864 ($\text{S}_2\text{O}_3\text{Cl}$) (Millon, 1844b; Rose, 1833).

Millon also studied the action of hypochlorous acid on sulfur chlorides (Millon, 1849b, 1850a). He observed that an aqueous solution of chlorine did not change when kept in the dark, but after being under the influence of solar light it was able to precipitate lead dichloride as lead dioxide (PbO_2) and manganese dichloride as manganese dioxide (MnO_2); reactions that did not take place with the solution kept in the dark. He assumed that the action of chlorine on water was identical to the one it exerted on most organic substances where it substituted a hydrogen atom by one atom of chlorine. He thought that this simple concept could be extended to disulfur dichloride, which corresponded to the system H_2S , where chlorine had replaced hydrogen on the basis of one equivalent per equivalent. On the one hand, this arrangement suggested that sulfur chloride contained an equal number of equivalents of chlorine and sulfur, in spite of the fact that chemists had been unable of combining one equivalent of sulfur with one of chlorine. On the other hand, it was very easy to combine several equivalents of sulfur with one of chlorine. This suggested the following correspondence between hydrogen sulfides and chlorine sulfides (Millon, 1849b, 1850a):



Iodine and its derivatives

In his first publication on the subject Millon remarked that Gay-Lussac, in his extensive paper about iodine and derivatives, had mentioned that chlorine was unable to decompose chlorates (Gay-Lussac, 1814). This outstanding result remained unnoticed until discovery of the considerable analogy that existed between the series of chloride derivatives and the corresponding series of iodides. This finding led Millon to ponder the opposite possibility, that is, the reaction between iodine upon potassium chlorate. In this first publication he reported that the results justified his assumption: No reaction took place when treating potassium chlorate with iodine at room temperature, but a clear one occurred when adding iodine into a boiling solution containing one part of potassium chlorate and three or four of distilled of water. The iodine disappeared almost completely, although the solution remained colorless until the iodine added was about equivalent to the chlorate present. Afterwards the solution became colored more and more yellow. The resultant mixture was found to contain potassium iodate and iodine chloride more or less iodated. Evaporation to dryness led to disengagement of iodine chloride, leaving a residue of pure potassium iodate (Millon, 1841a). Ending the reaction before reaching this limit indicated that the iodate was already present as well as most of the iodine chloride.

Millon found that addition of a few drops of nitric acid were sufficient for causing a significant increase in the rate of the reaction. It was enough to slightly heat the mixture of iodine and potassium chlorate to originate a self-standing reaction, which was accompanied by an abundant release of chlorine. The process ended when the solution had acquired a slight dark color; evaporation to dryness left a residue of pure potassium iodate. Millon believed that in this case the oxidation of iodine was determined by the amount of chloric acid liberated by the nitric one. The

iodic acid formed acted over a new portion of chlorate and the process repeated until the total decomposition of the chlorate. In this situation, the iodine chloride, which was an essential product of the reaction between iodine and potassium chlorate, become an accidental byproduct. Its formation could be almost completely avoided by adding the iodine drop wise (Millon, 1841a).

In the following publication Millon gave a very detailed description of the preparation of iodic acid (actually I_2O_5), its hydration (to true iodic acid), and the preparation of a large number of iodates (Millon, 1843c). He reported that the best method for preparing iodic acid required using iodine in his purest form, particularly free of iron. A mixture of 80 g of purified iodine, 75 g of potassium chlorate, 400 g of water, and 1 g of nitric acid were boiled until it began releasing chlorine; heating was then stopped and the solution treated with 90 g of barium nitrate. The precipitated barium iodate was separated, washed with water, boiled with 40 g of sulfuric acid and 150 g water for half an hour, filtered, and evaporated to crystallization. Millon remarked that the results of these experiences indicated that iodic acid (IO_5) could be prepared in three different forms: (1) combined with one equivalent of water (HO), IO_5,HO , soluble in all proportions of water, soluble in alcohol, and losing $2/3$ of an equivalent of water when heated to $130\text{ }^\circ\text{C}$; (2) combined with one-third equivalent of water, $IO_5,(1/3)HO$, soluble in water while decomposing to IO_5,HO , and insoluble in alcohol; and (3) anhydrous, IO_5 , originating from the previous two forms by heating to $170\text{ }^\circ\text{C}$ or more (Millon, 1843c). Millon provided a detailed description of the procedure for preparing potassium iodate, silver iodate, potassium biiodate ($IO_5,KO + IO_5HO$), potassium triiodate ($IO_5,KO + 2IO_5,HO$), calcium iodate (IO_5,CaO), barium iodate (IO_5,BaO,HO), strontium iodate (IO_5,SrO,HO), sodium iodate, magnesium iodate ($IO_5,MgO,4HO$), four different forms of cupric iodate, ammonium iodate, and ferric iodate (Millon, 1843c).

Millon found that the action of nitric acid upon iodine depended on the degree of hydration of the acid (Millon, 1844c). Thus nitric acid combined with 4 or more equivalents of water was unable to oxidize iodine; the element dissolved in hot acid yielding a violet color solution, which deposited on cooling without forming iodic acid. Similarly, iodic acid dissolved in this particular nitric acid without any apparent reaction, but by passing a small amount of nitric oxide gas through the solution resulted in the reduction of the iodic acid and precipitation of iodine. Nitric acid dissolved in two to three equivalents of water, oxidized iodine with the assistance of heat. The nitrous products formed did not react with the iodic acid; iodic acid was formed as long as the acid was sufficiently concentrated. The acid separated in white mammillated crystals, which were always found to contain one third of an equivalent of water, having for formula $3IO_5 + HO$. They were completely insoluble in alcohol and absolutely exempt of any combination with nitric acid (Millon, 1844c). Millon reported that triturating a mixture of 10 to 15 g of iodine with 120 to 150 g of nitric acid containing 1 or 2 equivalents of water, resulted in the formation of a voluminous yellow powder composed of iodine, oxygen, and nitric acid, which decomposed easily upon heating or addition of water into iodic and nitric acids, and iodine. From this yellow powder Millon was able to separate a new oxide of iodine having the formula IO_4 , which he named *hypoiodic acid* (Millon, 1844c).

In a following work Millon reported that the action of sulfuric acid on iodic acid depended on the temperature level. The different heating stages, which begun with the dissolution of iodic acid and ended with its complete decomposition, were accompanied by the appearance of a variety of compounds that were stable only in a completely dry atmosphere or in solution with concentrated sulfuric acid (Millon, 1844d). At a temperature close to its ebullition, sulfuric acid was able to dissolve about 20% of its weight of iodic acid. Further heating resulted in an abundant generation

of very pure oxygen, without showing the presence of iodine, while the solution became strongly colored yellow and afterwards green; at this stage iodine began to appear and continued to do so until no more oxygen was generated. Millon indicated that stopping the reaction at these different stages showed that they were accompanied by the separation of many combinations of (a) sulfuric and iodic acid, (b) of three acids iodic, hypoiodic, and sulfuric), (c) of hypoiodic and sulfuric acids, and (d) of sulfuric acid with an iodine acid less oxidized than hypoiodic acid, represented by the formula I_5O_{19} ($IO_7 + 4IO_3$), which could be named *sub-hypoiodic acid* (Millon 1844d). Millon was able to separate and analyze about a dozen of these intermediates, among them, $3(SO_3,HO) + IO_5,HO$; $4IO_5 + IO_4 + SO_3,HO$; $2IO_5 + IO_4 + SO_3,HO$; $I_5O_{19} + 10SO_3,HO$, etc. (Millon, 1844d).

Millon went on to give a detailed description of the procedure for preparing the two new iodine oxides he had discovered (hypoiodic acid and sub-hypoiodic acid), as well as their properties. Hypoiodic acid appeared as an amorphous yellow powder, stable under strong sunlight and dry or humid air. It decomposed into iodine and iodic acid when heated to about 170 °C or in contact with boiling water or hot nitric acid. It was stable in contact with cold water, cold nitric or sulfuric acids, and alcohol. Hydrogen chloride decomposed it into iodine chlorine while releasing chlorine. Sub-hypoiodic acid appeared as a yellow ochre solid, stable under sunlight and dry or humid air, and slowly decomposed by cold water. Alcoholic solutions of alkalis were colored violet (Millon, 1844ef). Millon also studied the oxidation of many substances by means of iodic acid, for example, sugarcane, tannin, starch, fibrin, gelatin, gums, hydrogen cyanide, oxalic acid, etc. (Millon, 1844gh, 1845a).

Nitric acid

Millon wrote that his work about chlorine oxides had led him to realize that the complete purification of nitric acid was yet an unresolved problem (Millon, 1842b). The usual procedures were mostly devoted to eliminating the small amounts of hydrogen chloride and sulfuric acid present (using the nitrates of silver, barium, or lead) without consideration to the residues of hyponitric acid. The latter was found to be present even when the acid was highly diluted and colorless; as shown by the fact that it was able to precipitate the iodine of alkaline iodides, of sulfur from an aqueous solution of hydrogen sulfide or of an alkaline sulfide, to color ferrous salts brown and potassium ferrocyanide green, and decolorize a solution of indigo, at a degree of dilution at which pure nitric acid ceased to have any effect on it. Finally, the decomposition of urea that took place when preparing this compound from urea chlorides was attributed also to the nitric acid employed, when it was actually caused by the direct action of hyponitric acid (Millon, 1842b).

In his 30-page long memoir Millon described in detail the procedure he had developed for preparing highly pure nitric acid devoid of hyponitric acid. He recommended using an aqueous solution of hydrogen sulfide as the best reagent for detecting the presence of this impurity. The nitric acid to be tested was first diluted with once or twice its volume of water and then mixed with a few drops of the reagent. The presence of traces of hyponitric acid was signaled by the liberation of sulfur, which gave an opalescent appearance to the liquor. This opalescence was normally accompanied by formation of a small amount of ammonia. Basically, Million's process involved distilling the acid and discarding the first third that passed over, which contained the whole of the hyponitric acid. The best procedure, even in the case that the nitric acid contained organic matter, was to add 1% of potassium dichromate to the acid to be purified. This transformed the impurity into nitric acid at the expense of the oxygen of the chromic acid. Millon

found that distillation of nitric acid to increasing degrees of concentration signaled the presence of at least the following hydrates of nitrogen pentoxide (Millon 1842b):

NO_5, HO

$\text{NO}_5,$

2HO

$\text{NO}_3, 4\text{HO}$

$\text{NO}_5, 4\text{OH}, 0.5\text{HO}$

Millon wrote that in spite of all the efforts done by chemists, they had failed to prepare ethyl nitrate (ether nitrate), although they had synthesized all the other members of the alkyl nitrate series (Millon, 1843a). His previous work on the negative action of hyponitric nitric on the reactivity of nitric acid led him to suspect that this impurity might be behind the failure of the efforts. The results of his experiments proved him to be true. Addition of a few crystals of urea nitrate to a mixture of nitric acid and alcohol led to a quiet reaction and the synthesis of ethyl nitrate accompanied by a little of water and alcohol. Millon added that the nitric acid should also be free of HCl because it neutralized urea and made it inactive. In addition, it was important to carry the reaction using a 1:1 (molar) proportion of acid and alcohol (Millon, 1843a).

The experimental procedure was very simple; the reagents were put in a distillation apparatus and the mixture heated slowly. The first fraction that passed over was essentially diluted alcohol, followed by the ethyl nitrate, easily identified by its particular smell. Addition of water to this fraction resulted in the separation of two phases, the lower one being the alkyl nitrate. The urea nitrate was little consumed by the reaction; at the end of the distillation it deposited in a white crystalline state, even if in its original state it was yellow and very much colored. The crude ethyl nitrate was purified using standard procedures: washes with alkaline water and then with distilled water, drying with calcium chloride, and finally distillation. Elemental analysis indicated that pure ethyl nitrate contained, by weight, 26.53% carbon, 5.81% hydrogen, 15.20% nitrogen, and 52.46% oxygen, corresponding to the formula $\text{NO}_5\text{C}_4\text{H}_5$ (at that time the atomic mass of carbon was taken as 6) (Millon, 1843a).

Millon described ethyl nitrate as a soft and sweet smelling and tasting liquid, having relative density 1.112 at 17 °C, boiling at 85 °C, burning with a very white flame, and decomposing at temperature somewhat above its boiling point. It was totally insoluble in water and completely soluble in alcohol. It was not decomposed by an aqueous solution of KOH, but an alcoholic solution destroyed it even in the cold, depositing a large quantity of crystals of potassium nitrate without a trace of nitrite. It was also destroyed by nitric, hydrochloric, and sulfuric acids, as well as by chlorine. Iodine dissolved in it producing a violet colored solution (Millon, 1843a). According to Millon hyponitric acid decomposed instantly urea into equal volumes of nitrogen and CO_2 ; therefore urea prevented the formation of this acid at the expense of the nitric one (Millon, 1843a).

Metals in Human Blood

In 1848 Millon read to the Académie a memoir describing the result of his experiments on the presence of different metal and salts in human blood (Millon 1848a). For his purposes he diluted the blood issuing from a vein in about three times its volume of water and introduced it into a jar of full of gaseous chlorine. As a result, the fluid coagulated, turned brown, and then became a grey amorphous mass, in which the organization of the sanguineous globules had completely disappeared. Millon separated the liquid part by squeezing the mass with a piece of fine cloth, and

noticed that it remained completely limpid. According to Millon, his process had led to a peculiar, almost complete separation of the elements of the blood: The organic substances were concentrated almost completely in the coagulated portion while all the salts had collected in the liquid. On the one hand, washing the coagulum and then calcinating it resulted in its complete destruction, without leaving any residue. On the other hand, the liquid, after evaporation to dryness and burning in a tube, generated so little CO₂ that it was possible to determine the proportion of the organic matters of the blood, which the chlorine did not coagulate, as 1% (Millon, 1848a).

Millon wrote that it was easy to accept that the coagulum provided by the organic principles did not contain the fixed salts of the blood and encircled a quantity only proportionate to the quantity of water, which impregnated it. In other words, weighing the water in which the blood was to be collected, and weighing it again after mixture with the blood, allowed us to operate upon a known weight of filtered liquid, as on a given weight of blood. Millon believed his procedure could be easily extended to the investigation of other tissues and other liquids employed for economical purposes (Millon, 1848a).

Isolation of the salts allowed their qualitative and quantitative analysis. Thus Millon found that this fluid always contained silica, manganese, lead, and copper, and these were present in enough quantity to determine them by the standard analytical procedures. For this purpose the clear liquid phase was evaporated to dryness and then calcined for a short time to eliminate any possible organic impurity. The insoluble part of the ashes was treated in the same way as a mineral was treated to determine the amounts of silica, manganese, lead, and copper. Thus Millon found that 100 parts of the insoluble residue contained between 1 to 3 parts of silica, 1 to 5 of lead, 0.5 to 2.5 of copper and 10 to 24 of manganese (Millon, 1848a).

It was now very easy to determine if copper and lead were disseminated throughout the all mass of blood, or whether, like the iron, they were assembled in the red globules. His results indicated that 1 kg of coagulated blood carefully separated of the serum of numerous bleedings, contained 0.083 g of lead and copper, while 1 kg of serum separated from the preceding coagulum contained only 0.003 g of these two metals. Millon believed that the 3 mg of lead and copper contained in the serum should be ascribed to the red globules dissolved or suspended in the lymph. In other words, the copper and the lead were not diffused in the blood but fixed with the iron in the globules (Millon, 1848a).

In a following note Millon described the analytical procedure he suggested for the quantitative determination of the amount of copper and lead present in the blood (Millon, 1848b). For this purpose, about 500 g of serum were introduced in a platinum capsule and heated over very hot burning coal. After elimination of all the volatile matter and the remaining carbon having constant weight, distilled water was added to the residue and the mixture boiled for a minute or so and then filtered over paper. The filter and the retained residue were again calcined inside the platinum capsule and the whole process repeated for a third time. The new residue was dissolved in HCl, evaporated, and dissolved in water acidulated with HCl. The resulting solution was now treated with a stream of hydrogen sulfide to precipitate the lead and the copper as their sulfides (Millon, 1848b).

Millon's reagent

In 1849 Millon reported that the very acid liquid obtained by dissolving mercury in water containing nitric acid in a concentration equal to 4.5 times the weight of the element, was an extremely sensitive reagent for all albuminoidal substances and related compounds. This solution tinted these substances strong red even when present in the amount of 1 per one hundred thousand parts. Millon gave a long list of the substances that could be detected with his reagent and the color assumed by the mixture. For example, cotton, starch, and Arabic gum acquired a quite distinct rose coloration; a mixture with urea became rose after it had been heated and the urea destroyed, blood albumen, fibrin, casein, legumin, feathers, epidermis, gelatin, became colored intense red, etc. (Millon, 1849a).

The reagent was prepared by adding over pure mercury a weight equivalent to 4.5 equivalents of nitric acid. A lively reaction took place at room temperature and could be accelerated by slight heating until all the metal had disappeared. The resulting solution was diluted with an equal volume of water and filtered after about four hours. The reagent acted upon all the substances mentioned but the reaction became complete only when the mixture was heated to 60 to 70 °C, or boiled. Millon indicated that an excess of reagent did not affect the result and that its active component was not mercurous or mercuric nitrate, as shown by the fact that a solution of these salts did not produce coloration (Millon, 1849a).

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