Rev. CENIC Cienc. Biol.; vol 51. (no.2): 149-163. Año. 2020. e-ISSN: 2221-2450

REVISION BIBLIOGRAFICA

# WILLIAM GREGORY
# Morphine, chloroform, and hippuric acid

# *WILLIAM GREGORY*

# *Morfina, cloroformo y ácido hipúrico*

**Jaime Wisniak**

Department of Chemical Engineering, Ben-Gurion University of the Negev, Beer-Sheva, Israel, 84105

**Recibido**: 28 de enero de 2020; **Aceptado**: 12 de marzo de 2020;

## ABSTRACT

William Gregory (1803-1858), an English physician turned chemist, carried extensive research on a wide variety of subjects in inorganic, organic, and biochemistry. His most important contribution was the development of a new method for separating morphine from opium, based on extraction with water, precipitation with ammonia, and treatment with HCl. This method was faster, had a very high yield, and avoided the use of alcohol, an expensive reagent. Therapeutic tests showed that Gregory's morphine hydrochloride was more efficient and economical than the painkillers used at that time. Gregory studied uric acid and the preparation and properties of several of its derivatives, among them alloxan, alloxantin, ammonium dialurate, dialuric acid, ammonia acid thionurate, and alloxanic acid. Gregory developed also a very efficient process for preparing glycocoll, for purifying chloroform and making it a safer anesthesia, based on washing it with sulfuric acid. He also proved that lead sulfite, used for extracting sugar cane, was not toxic to humans, and developed an efficient modification of Baup's procedure for preparing potassium iodide.

**Keywords:** chloroform; hippuric acid; iodides; morphine;sugar; uric acid.

## RESUMEN

William Gregory (1803-1858), médico inglés convertido en químico, llevó a cabo una amplia investigación en temas de química inorgánica, orgánica, y bioquímica. Su contribución más importante fue el desarrollo de un nuevo método para separar la morfina del opio, basado en la extracción con agua, precipitación con amoníaco, y tratamiento con HCl. Este método era más rápido, tenía un rendimiento muy alto, y evitaba el uso de alcohol, un reactivo muy caro. Ensayos terapéuticos demostraron que el hidrocloruro de morfina de Gregory era más eficiente y económico que los calmantes de aquella época. Gregory estudió el ácido úrico y la preparación y propiedades de varios de sus derivados, entre ellos, aloxano, aloxantina, dialurato de amonio, ácido dialúrico acid, tionurato ácido de amonio, y el ácido aloxánico. Gregory desarrolló también procesos muy eficientes para preparar glycocoll y para purificar el cloroformo, basado en lavados con ácido sulfúrico, y así convertirlo en un anestésico más seguro. También probó que el sulfito de plomo, usado en la extracción del azúcar de caña, no era nocivo para el uso humano y desarrolló una eficiente modificación del proceso de Baup para preparar ioduro de potasio

**Palabras clave**: ácido hipúrico; ácido úrico; cloroformo; morfina; yoduros.

# INTRODUCCIÓN

## Life and career

William Gregory (Figure 1) was born on December 25, 1803, in Edinburgh. He was the fourth son of Isabella Macleod and James Gregory (1753-1821), a professor of medicine in the University of Edinburgh. In 1820 he had an attack of fever that resulted in sporadic swelling of one of his legs and eventually would seriously restrict his movements. In 1821, after completion of his basic education, he begun medical studies at the University of Edinburgh and received his degree od doctor of medicine in 1828 after successfully defending a dissertation entitled *De Principiis Vegetabilium Alkalinis* (The principles of alkaline vegetables) (Gregory, 1828). After graduation he moved for one year to Giessen, Germany, to study under Justus von Liebig (1803-1883).

Upon his return to Britain (1828) he was appointed assistant to Edward Turner (1796-1837) at the University of London and in 1829 he returned to Scotland to begin a successful academic and research career that would continue until his death. He was appointed extra academical lecturer on chemistry in Edinburgh, professor at the Andersonian College in Glasgow (1837), succeeding Thomas Graham (1805-1869), lecturer at the Park Street School of Medicine in Dublin (1836-1837), professor of medicine at King's College, Aberdeen (1839), and chair of chemistry at the University of Edinburgh. In 1830 Gregory married Lisette Scott; one son (James Crawford Gregory) was born of this union.

In his later years his disabling disease became more acute and restricted him to a sedentary life. During this period he devoted much his effort to the study of diatomaceous earths and propagation of phrenology, hypnotism, and animal magnetism, much to the chagrin of his colleagues (Gregory, 1851b; Kaufman, 2008). Gregory died on April 24, 1858, and was buried in the Canongate Churchyard.

Gregory was one of the founders of the Aberdeen Philosophical Society and its first secretary. In 1832 he was elected a Fellow of the Royal Society of Edinburgh and served as its secretary from 1844 to 1858.

## Scientific contribution

Gregory wrote about 55 papers and books (Gregory, 1842, 1845c, 1851b) on the subjects of inorganic, organic, and biochemistry, etc. In addition to the topics described below, he analyzed a substance found among the products of the eruption of Vesuvius (Gregory, 1832b) and a coprolite from Burdiehouse (Gregory & Walker, 1835); studied some particular chrome chlorides (Gregory, 1834), the petroleum of Rangoon (Gregory, 1836c), and the action of potassium ferrocyanide on sulfovinates and sulfomethylates, (Gregory, 1841); described an economical procedure for preparing potassium permanganate (Gregory, 1836b); discovered two new compounds of sulfur (Gregory, 1845ab); conducted extensive research on the Diatomaceæ present in waters of England (i.e. Gregory, 1853 1854ab, 1855, 1856, 1857ab, 1859, etc.); etc.

## Morphine

Gregory wrote that in the last edition of Berzelius's *Lehrbuch* (Berzelius, 1825-1831) the translator Friedrich Wöhler (1800-1882) had added a description of the several processes given by Carl Wittstock for separating opium from narcotine (noscapine) (Gregory, 1831a). In one of them, for example, the morphine crystals, assumed to contain narcotine, were dissolved in an excess of HCl and the solution concentrated by evaporation until precipitation of the morphine as chlorhydrate, and the narcotine chlorhydrate remaining in solution. The precipitate was pressed between pieces of paper to separate as much as possible the attached liquid and the morphine purified by extraction and recrystallization with alcohol (Gregory, 1831a). Gregory investigated the possibility of separating the morphine from the opium without the use of alcohol, and thus, in a more economical manner. The process he developed began cutting the opium in small pieces, exhausting them with cold water or water at 32 °C, concentrating the extract to a very small volume and precipitating it with a small excess of ammonia. The filtered precipitate was washed with water, dried, crushed to powder, humidified with water, and treated with dilute HCl until it became slightly acid. The resulting solution of morphine and narcotine was filtered, evaporated to a syrupy state, and left to crystalize. The process continued as described by Wittstock. The whole was now pressed between papers to eliminate the attached solution of narcotine hydrochlorate. The crystallized morphine was purified by successive recrystallization from water. The pure morphine appeared as white crystals, almost completely soluble in boiling water. Gregory reported that the yield depended on the quality of the opium, with most of the loss occurring in the paper pressing and recrystallization steps. Nevertheless, the new process was undoubtedly cheaper that the older versions (Gregory, 1831a).

Gregory asked his friend, the physician Robert Christison, to conduct therapeutic tests with a solution of morphine prepared by his procedure, and containing 1.143 g of the hydrochloride to 100 g of water. According to Christison this portion induced profound calm, much dreaming, and a pleasant feeling, followed by a refreshing sleep. The after effects were minor and occasional: dry brown tongue and headache. More important, they were entirely exempt of the bad effect produced by opium on the stomach. Christison believed that use of the new preparation offered great advantage over the other preparations of opium. Gregory wrote that several other practitioners that had tested his preparation had reached similar conclusions. He also mentioned that for 20 shillings a pharmacist could prepare 295 doses of Battley's sedative solution (containing opium), 1,700 doses of laudanum, and 1,840 of morphine chlorhydrate, proving clearly the economical advantage of his medicine (Gregory, 1831a).

Some time later Gregory asked Pierre Jean Robiquet (1780-1840) to test his new procedure for preparing morphine from opium that allowed manufacturing it in larger quantities and at a lower cost (Robiquet, 1833). Gregory provided Robiquet with a sample of the raw material he had employed, in order to make the test more reliable, and explained that he had not manufactured morphine but its chlorhydrate, because that was the way morphine was employed in Scotland. Robiquet divided the sample in two equal parts and treated one part by the standard method and the other by Gregory's procedure. Robiquet followed the new procedure and in his report he added more details than those present in Gregory's publication. The evaporation of the water extract was carried in a tinned flask and the neutralization of the excess of HCl was done with broken calcium carbonate, iron-free, to avoid coloring the extract with iron meconate. The precipitated calcium meconate was separated by filtration. The resulting morphine hydrochloride was slightly brown and was discolored with animal carbon at below 88 ºC to avoid the decomposition of the chlorhydrate. Robiquet stressed the need that all neutralizations be carried with calcium carbonate in order not to decompose the hot liquid, that all evaporations be carried to the highest temperature before being crystallized and always under mixing, and that the expression of the crystals between papers or cloth be carried as much as possible. The experimental results convinced Robiquet of the goodness of Gregory's procedure; not only it produced morphine in higher yield, it also contained less narcotine than the one manufactured by the standard methods (Robiquet, 1833).

## Uric acid and derivatives

In 1837 Liebig and Friedrich Wöhler (1800-1882) reported that the reaction between uric acid and lead dioxide yielded oxalic acid, allantoin, and urea, and assumed that the urea was present in uric acid combined with urilic acid (Liebig & Wöhler, 1837). Gregory found that urea, unlike other organic substances, resisted the action of strong oxidants like potassium permanganate. This led him to assume that if urea could be obtained from uric acid under the influence of potassium permanganate, then this result would support Liebig and Wöhler's assumption. In practice, oxidation of uric acid with the above oxidant produced a large amount of urea, together with oxalic acid, and another new acid originating from the oxidation of allantoin. This result confirmed Liebig and Wöhler's supposition (Gregory, 1840a).

## Alloxan

Liebig and Wöhler prepared alloxan mixing uric acid with nitric acid of specific gravity 1.42 and separating the resulting crystals by means of a porous brick, without recuperating the additional substance remaining in the mother liquor (Liebig & Wöhler, 1837). Gregory improved the yield of the process by using acid of specific gravity 1.35, filtrating the liquid, and purifying the crystals by recrystallization. The mother liquor was treated successively for five times in the same manner and the crystals gathered as before. This series of steps allowed collecting 65 g of anhydrous alloxan from 100 parts of uric acid. The residual liquid yielded a large amount of parabanic acid or ammonia oxalurate (Gregory, 1840b). Treatment of alloxan with hydrogen sulfide yielded alloxantin and boiling it with a solution of ammonium sulfite and ammonia produced ammonia thionurate. Uramil (dialuramide, murexan) was obtained by boiling the thionurate with an excess of dilute sulfuric acid (Gregory, 1840b).

In a following publication, Gregory described in great detail his process for preparing alloxan in larger quantities, and correcting some mistakes he had previously made, particularly the one related to the concentration of the nitric acid to be used in the first stage (Gregory, 1846). The modified method involved mixing colorless nitric acid of specific gravity 1.412, with uric acid, with continuous agitation to avoid the formation of lumps. Effervescence and generation of heat accompanied the solution of the uric acid. Overheating had to be avoided otherwise no alloxan was produced. The whole was then left to stand overnight in a cool place and the next day the alloxan precipitated was separated by filtration. The mother liquor was subjected to the same process, to recuperate as much as possible of alloxan. All the mother liquors collected were employed to prepare alloxantin and dialuric acid, as indicated above. Gregory reported now that he had obtained 102 g of hydrated alloxan from 100 g of uric acid, against the theoretical 128 g. He did not believed that it would be possible to increase this yield significantly, considering the difficulty of separating the whole alloxan from the acid liquid in which it was formed (Gregory, 1846).

**Alloxantin (uroxin)** Gregory wrote that this substance could be prepared by treating a dilute solution of the mother liquor of alloxan with hydrogen sulfide until no further reaction was detected. As a result, sulfur was first deposited followed by alloxantin. The separated precipitate was washed with a little of cold water and then boiled with water acidulated with HCl. The solution was filtered while hot and then left to cool; the resulting precipitate was pure alloxantin (Gregory, 1843-1845).

### Ammonium dialurate

Gregory reported that the salt ammonium dialurate could be obtained from the mother liquor of alloxan, as well as from that of alloxanthine (Gregory, 1843-1845). For this purpose, cold ammonia was added to the mother liquid until a slight excess of acid was left. An excess of ammonium sulfide was now added so as to redissolve any amount of sulfur that may precipitate. The resulting thick solution of dialurate was first heated and then cooled to allow precipitation of the salt. The filtrated solid was washed first with ammonia sulfide, then with alcohol, and finally pressed between papers and dried. Pure ammonium dialurate appeared as small almost colorless prismatic crystals, packed together in light bulky masses (Gregory, 1843-1845).

### Dialuric acid

According to Gregory, this acid was easily prepared by dissolving pure ammonium dialurate in an excess of warm dilute HCl. The liquid, on cooling deposited crystals of dialuric acid. This acid formed sparingly salts with KOH and with baryta. Gregory analyzed dialuric acid and found that the composition corresponded to the same formula reported by Liebig and Wöhler, $C_8H_2N_4O_8$ (Gregory, 1843-1845).

### Ammonia acid thionurate

This salt was prepared by treating a hot aqueous solution of 1 equivalent of neutral ammonia thionurate with a solution containing 1 equivalent of HCl. Upon evaporation, the product of the reaction deposited small prismatic crystals of ammonia acid thionurate (Gregory, 1843-1845).

### Alloxano sulfurous acid

Gregory obtained this compound by dissolving alloxan in the smallest possible amount of water and then adding a slight excess of a saturated sulfur monoxide solution, followed by aqueous KOH until the liquor became slightly alkaline. The resulting precipitate was a salt in hard brilliant crystals, which were purified by recrystallization from water. Gregory was unable to separate the acid but it seemed to be composed of two atoms of sulfur monoxide and one of alloxan (Gregory, 1843-1845).

## Alloxanic acid

According to Gregory, an aqueous solution of alloxantin left to stand, lost the property of giving a violet precipitate with baryta water, and finally produced a white precipitate. Evaporation to dryness of the filtrate left a crystalline residue, which was very soluble in water and in alcohol. At the request of Gregory, Liebig analyzed this residue and declared it to be alloxanic acid. Gregory was not sure that this was true; he believed that his product was isomeric with alloxantin (Gregory, 1843-1845).

## Hippuric acid

In 1799 Antoine François Fourcroy (1750-1809) and Louis Vauquelin (1763-1829) discovered a new acid in the urine of certain animals, which they assumed to be benzoic acid (Fourcroy & Vauquelin, 1799). According to Liebig, mixing the urine of horse with an excess of HCl resulted in the precipitation of a yellow brown crystalline substance, having a foul odor, which could not be removed by water washes (Liebig, 1829). To do so it was necessary to boil it with quicklime and water, to filter the liquid, and then treat it with calcium chloride until the liquid that passed the filter did not smell like urine. Mixing the hot odorless liquid with HCl and leaving it to cool by itself resulted in the separation of long prismatic crystals, white and transparent, which differed from benzoic acid not only by being less soluble in water but also by its salts being different from benzoates, and by not containing nitrogen. When heated, it melted and then decomposed turning black. It was named *hippuric* acid to identify its origin: *hippo* = horse and *ouron* = urine. Sulfuric acid at 120 ºC dissolved it without change and water precipitated it. HCl also dissolved it but crystallized out upon cooling (Liebig, 1829).

Many chemists had tried to determine its composition, with conflicting results. According to Liebig, the divergences were due to the fact that the nitrogen content had been determined by difference, and hence it carried the accumulated error from the analysis of the other elements. This indirect analysis was due to the lack of a control substance generating a sufficiently large amount of nitrogen dioxide by combustion (Liebig, 1834). After much seeking, Liebig found that the procedure proposed by Friedrich Kodweiss (1802-1866) was the most appropriate for determining the composition of hippuric acid (Kodweiss, 1830). Kodweiss discovered that the gas mixture obtained by combustion of uric acid contained (by volume) 7 parts of $CO_2$ per 2 of nitrogen, meaning that after its analysis, uric acid contained 4 atoms of nitrogen for 5 of carbon. Liebig verified this proportion by burning ammonium urate and potassium urate. The pertinent gases were found to contain 22 volumes of $CO_2$ per 10 of nitrogen, indicating with certainty that uric acid contained 4 atoms of nitrogen for 5 of carbon. Burning hippuric acid carefully by means of cupric oxide yielded a mixture of $CO_2$ and nitrogen in the ratio 100 to 5. Burning ammonia hippurate gave 2 volumes of nitrogen and 27 of $CO_2$, confirming the previous ratio. The full analysis indicated that hippuric acid contained, by weight, 62.9% carbon, 4.96% hydrogen, 24.8 of oxygen, and 7.36% nitrogen, corresponding to the formula $C_{20}H_{10}O_6N$ (C = 6, oxygen = 8) (Liebig, 1834).

Liebig added that hippuric acid dissolved most of the metallic oxides. The soluble compounds produced with iron a rusty color and with the nitrates of silver and mercury(I), white flocculent precipitates. The hippurates of potassium, sodium, and magnesium were soluble and crystallizable. Liebig also mentioned that he had been unable to extract the smallest trace of benzoic acid from the food of horses of which he examined the urine (Liebig, 1834).

Gregory discussed the above information and added that in 1845 Victor Dessaignes (1800-1885) had shown that hippuric acid was a combination of glycocoll (glycine) and benzoic acid, which split into its components when heated with strong acids (Dessaignes, 1845; Gregory, 1847). A year after, Eben Norton Horsford (1818-1893) determined the formula of glycocoll as $C_4NH_4O_3$ and confirmed the results of Dessaignes (Horsford, 1846). Gregory added that the usual procedure for preparing glycocoll was to concentrate by evaporation the urine of the horse or cow and then add HCl to precipitate the hippuric acid in an impure state. Gregory believed that the best procedure for purifying this product was the one proposed by H. Schwarz (Schwarz, 1845). It consisted in boiling the impure acid with an excess of limewater and straining the alkaline liquid from the undissolved lime. Addition of acid caused the precipitation of hippuric acid nearly white. Gregory noticed that all these steps did not decompose hippuric acid and for this reason decided to use them directly upon urine, and thus, shorten the process. Hence, he boiled a mixture of horse urine and an excess of limewater, strained the solution, and concentrated it by evaporation. Addition of HCl produced a large amount of crystals, which Gregory discolored using Schwarz procedure. Repetition of the process yielded snow-white crystals of highly pure hippuric acid. According to Gregory, his method allowed preparing large quantities of hippuric acid in a very short time (Gregory, 1847).

## Chloroform

Gregory wrote a long paper about chloroform, its properties, and purification (Gregory, 1850).

In the first part he stated that chloroform was manufactured from ethanol and from methanol; the latter was used because it was cheaper but in practice it was a mixture of several substances, all of which did not yield chloroform. It was an impure product that was less effective than the one prepared from ethanol. Anyhow, the *pure* chloroform prepared from these two sources had the same properties (smell, density, boiling point, and physiological action). The peculiar impurities attached to both kinds of chloroform were not identical, but had similar constitution and properties. Eugène Souberain (1797-1859) and Louis Mialhe (1806-1888) had examined both kinds of product and reported that they contained chlorine, had an obnoxious smell, and when inhaled, they caused headache and sickness. It was a known fact that many persons *after* the use of chloroform had experimented side effects such as headache, nausea, and vomiting (Gregory, 1850).

According to Gregory, perfectly pure chloroform did not produce disagreeable effects, hence it had to be accepted that these originated from the presence of impurities. Good manufacturers avoided this problem by washing chloroform with sulfuric acid. This reagent destroyed the common impurities and at the same time released $SO_2$. For this reason the chloroform was afterwards neutralized with calcium carbonate or barium carbonate. Anyhow, even the best commercial products available still contained minute amounts of the pernicious impurities, which could be easily detected with sulfuric acid: The tested chloroform assumed a yellow or brown tint. According to Gregory another very simple and fast test was to pour the chloroform on the hand or a handkerchief: The volatile chloroform evaporated rapidly while the less volatile oil was left behind. Gregory believed that truly pure chloroform should have specific gravity 1.500 at 15.6 ºC (Gregory, 1850).

All the above considerations led Gregory to develop a new method for purifying chloroform that had been found to contain impurities: The impure chloroform was mixed with half its volume of sulfuric acid, agitated, left in contact until the acid stopped getting darker in color, drained, and then mixed with a little of manganese to eliminate the $SO_2$. A sample poured in the hand should evaporate without leaving a disagreeable odor. Gregory made the comment that in London and elsewhere, chloroform was not used extensively as it should, in consequence of the occurrence of some fatal cases where the cause of death was attributed to the drug. This was probably true because the chloroform employed was not the required degree of purity. It was also possible that although the correct degree of purity had been used the cause of death was human error due to a wrong manner of administering the drug as a vapor into the respiratory system, carried on by persons not qualified for performing this delicate treatment. Gregory ended his paper with a table describing the properties of 10 commercial samples of chloroform, indicating their specific gravity, the result of the action of concentrated sulfuric acid, evaporation on the hand, and general remarks (Gregory, 1850).

## Lead in sugar

James Scoffern (1814-1882) wrote the extraction of sugar, as practiced in the colonies, was an extremely inefficient process, as shown by the following figures: The actual amount of pure and crystallizable sugar present in the sugar cane juice varied between 19 and 23% and the amount of juice contained in the cane was about 90%. Of this amount only an average of about 60% was extracted and of latter, only one-third was recovered as dark sugar instead of white and pure. The extraction process involved the use of calcium carbonate and this chemical was responsible for most of the loss (Scoffern, 1849). Several unsuccessful attempts had been made to overcome this obstacle; one of them was using lead basic acetate, known to be very potent, although hard to eliminate its excess. Scoffern found that this problem could be solved successfully by bubbling hydrogen sulfide into the liquor and converting the acetate to insoluble sulfite. This alternative permitted extracting all the sugar instead of the two-thirds by the standard method. In addition, the process was faster and the sugar recovered was now pure white instead of dark (Scoffern, 1849).

The results of Scoffern led Gregory to study in detail the properties of lead sulfite, a salt that was known to be totally insoluble in water (Gregory, 1851a). Gregory mentioned that from the physiological point of view, lead sulfate was considered to be inert and for this reason, sulfuric acid was considered the proper antidote for cases of lead poisoning. This suggested the possibility that lead sulfite was also physiological inert. Gregory prepared pure lead sulfite and gave it in the moist state to rabbit and dogs with their food, in large daily doses, for three to six weeks. The results confirmed his assumption: the animals showed no signals of poisoning or deleterious physiological effects. Consequently, Gregory concluded that the sugar prepared by the method of Scoffern should be considered safe, even if it contained minute amounts of lead sulfite (Gregory, 1851a).

## Eblanine

On August 1836 R. Scanlan reported to the British Association for the Advancement of Science the discovery of a new substance (eblanine) from the distillation of wood. Eblanine was described as a yellow solid, insoluble in water but soluble in alcohol from which it separated as long rectangular prisms. Elemental analysis indicated that it contained 10 atoms of carbon, five of hydrogen, and 2 of oxygen (Scanlan, 1836).

A year later, Gregory and the chemist James Apjohn (1796-1886) reported more details about eblanine (Apjohn & Gregory, 1837). Scanlan had named the new substance eblanine, as a derivative of *eblana*, the old name of Dublin. Eblanine was contained in pyroxylic spirit; it fused at 193 ºC, volatile in a current of air at 149 ºC, and heated in a closed tube did not sublime or decompose. It was insoluble in water and alkalis, and soluble in alcohol, ether, concentrated acetic acid, and concentrated sulfuric acid, yielding a yellow solution. It reacted with strong sulfuric acid producing a deep bluish purple color that afterwards turned brownish black. It was soluble in strong HCl generating an intense purple red color that afterwards also turned brownish black. It dissolved in nitric acid; treatment of the solution with water deposited a yellow solid that decomposed suddenly with a weak explosion while releasing bright vapors. Elemental analysis indicated that it contained, by weight, 75.275% carbon, 5.609% hydrogen, and 19.116% oxygen, corresponding approximately to the formula $C_{21}H_9O_4$ (assuming C = 75) (Apjohn & Gregory, 1837). Robiquet, who presented the French version of this paper, suggested naming it *pyroxanthin*, instead of eblanine.

## Phosphoric acid from bones

Gregory wrote that the usual method of preparing phosphoric acid by oxidation of phosphorus with nitric acid or combustion seemed to be wasteful since the phosphorus was obtained from phosphoric acid. A simpler procedure seemed to be preparing phosphoric acid directly from bones. In practice, phosphorus was prepared from calcium superphosphate, a water-soluble substance obtained by treating bones with sulfuric acid and water. It seemed reasonable to check the possibility of using the same starting material for preparing phosphoric acid (Gregory, 1845c, 1849). In the usual procedure, the solution of calcium superphosphate was neutralized with ammonia or ammonium carbonate, which precipitated all the calcium in the solution and left the phosphorus as a mixture of bone phosphate and ammonia phosphate in the ratio 1: 3. The filtrate, upon evaporation, deposited crystals of ammonia phosphate. Heating the crystals in a crucible drove away the ammonia and most of the water, leaving a residue of metaphosphoric acid. This process had several shortcomings, for example, the need of crucibles of very large size and their corrosion by the phosphorus produced as by-product, and the presence of carbon in the final product caused by carbonization of foreign organic material (Gregory, 1845c, 1849).

Gregory described another process, which he believed was suggested by Liebig, based on the fact that addition of sulfuric acid to the concentrated solution allowed the complete elimination of lime. As a result, the large amount of calcium sulfate produced turned the liquid very thick. This process was repeated several times until addition of sulfuric caused no more precipitation. In this stage, the liquid contained all the phosphoric acid, the magnesia always present, and the excess sulfuric acid. Gregory suggested preparing phosphoric acid by the following procedure: The solution of phosphoric acid from which the lime had been separated by excess of sulfuric acid, was evaporated to syrup and heated to eliminate the sulfuric acid. The resulting transparent and colorless glass was totally soluble and contained only phosphoric acid, water, and magnesia. It could be dissolved in boiling water and concentrated by evaporation in a crucible to about 315 °C, without alteration. At a higher temperature it became turbid and started precipitating in large amount a powder containing, according to Gregory's analysis, 15.87 % magnesia and 84.13% phosphoric acid, corresponding, approximately, to the formula $3P_2O_5 + 2MgO$, an unusual combination for phosphorus, The syrupy mass was left to cool, afterwards digested in cold water, and the liquid filtered. The filtrate was a solution of pure phosphoric acid (Gregory, 1845c, 1849).

Robert Maddrell repeated the experiments of Gregory and found that Gregory's acid was not absolutely pure but retained traces of magnesia and soda, obviously derived from the bones themselves. A more delicate analysis of the white precipitate indicated that it contained about 8 % of sodium, and was in fact a double metaphosphate of sodium and magnesia: $3\,(MgO,PO_5) + NaO,PO_5$. Nevertheless, Gregory's acid appeared to be sufficiently pure for nearly all purposes (Maddrell, 1845).

## Iodides

### Preparation of potassium iodide

Gregory wrote that elementary chemistry books described three procedures for preparing potassium iodide (Gregory, 1831b): (1) neutralization of HI with potassium carbonate. This method was unsatisfactory because HI had a very short shelf life, decomposing spontaneously, (2) decomposition of ferric iodide with potassium carbonate, followed by filtration to eliminate the ferric oxide, and crystallization [the Baup process (Baup, 1821)]. According to Gregory, the solutions in this process were bulky and it was difficulty to locate the exact saturation point to avoid an excess of iron or of potassium carbonate; (3) addition of an excess of iodine to a solution of pure KOH, with formation of both potassium iodide and potassium iodate by decomposition of water. The potassium iodate was converted into iodide by means of a stream of hydrogen sulfide [the Turner process (Turner, 1825)]. According to Gregory, in addition to the disagreeable last step, sometimes, part the sulfur adhered to the KI and turned it impure.

Gregory went on to describe a new process he had developed, which was a modification of the one by Turner: Iodine was dissolved in enough KOH pure (with the help of heat) to produce a strong yellow color solution. The solution was then evaporated to dryness and the resulting mixture of potassium iodide and potassium iodate heated gradually until red heat, for about one hour, in a closed platinum or silver crucible. This converted the potassium iodate into potassium iodide, while releasing oxygen. The resulting cold salt was dissolved in hot water, filtered, and the filtrate evaporated to dryness and converted into a snow-white crystalline salt. A small amount of the salt was treated with alcohol to detect the presence of unconverted potassium iodate, which was insoluble in alcohol. The resulting pure KI was white and crystalline, deliquescing slightly in air and easily soluble in water and alcohol. The solution with lead acetate yielded a yellow precipitate of lead iodine. According to Gregory, his process was simpler and much faster then the one of Turner (Gregory, 1831b).

## Lead iodide

In 1832 Gregory announced the discovery of a new lead iodide (Gregory, 1832a). While treating a boiling solution of diluted lead acetate with another of diluted potassium iodide, he noticed the formation of a precipitate of yellow flakes of the ordinary lead iodide, accompanied by a considerable amount of small acicular crystals, dirty yellow, mixed with microscopic orange yellow crystals. The latter were easily dissolved by boiling water, leaving the other untouched. The remaining crystals were dried and analyzed by means of sulfuric acid and found to contain, by weight, 62.10% lead and 37.90% iodine. Hence, they were a lead sub-iodide containing two atoms of lead and one of iodine (Gregory, 1832a).

## Pure silver

Gregory wrote that metallurgists used nitric acid to purify silver, particularly from copper, because silver chloride was insoluble in water while the chlorides of other metals were soluble (Gregory, 1843). Unfortunately, silver chloride was very difficult to handle, particularly in the moist state. Silver chloride could be reduced to silver under the action of aqueous HCl and zinc or iron, but usually some zinc adhered to the silver and was difficult to eliminate. Dry silver chloride could also be reduced by potassium or sodium carbonate at red heat but only under very careful conditions. The silver could also be reduced by the direct action of copper on the impure silver nitrate or sulfate, although there was always the possibility that traces of copper would attach chemically to the silver (Gregory, 1843). Gregory believed that the best procedure was to reduce the silver chloride without the help of a reguline metal. It was known that a diluted or concentrated solution of KOH had no action on silver chloride; Gregory found that a hot solution of KOH, of specific gravity 1.25 to 1.30, was able to decompose, almost immediately, the moist silver chloride converting it into heavy jet-black powder of pure silver oxide. This oxide was completely soluble in diluted nitric acid yielding a solution of colorless and pure nitrate. The oxide, under the action of the alcohol burner, was reduced completely to pure silver. Gregory used these facts to develop the following practical procedure to reduce silver chloride: In the first step, the cuprous solution of silver was precipitated by means of sodium chloride. The precipitate of silver chloride was separated and washed with water and, while moist, mixed with a solution of KOH, specific gravity 1.25 or more, and then boiled under agitation. Within 5 to 10 minutes the power turned black; the black oxide was separated and washed several times with water. This oxide was very dense and has a pure black color (Gregory, 1843).

## Pure HCl

According to Gregory it was very difficult to prepare HCl pure for chemical purposes (Gregory, 1841-1843). The available commercial material contained a variety of impurities originating from the raw materials used to prepare the acid; hence, preparation of a pure acid required employed pure starting materials. Gregory found that using one equivalent of salt and two of sulfuric acid diluted in a certain amount of water allowed expelling the HCl without a trace of sulfuric acid and two-thirds of the acid distilled over before water was volatilized (Gregory, 1841-1843).

## Pyrolysis of caoutchouc (natural rubber)

Gregory mentioned that years ago the entrepreneur Mr. Enderby had taken a patent for the production of a volatile inflammable liquid obtained by the pyrolysis of caoutchouc (Gregory, 1836a). Enderby has described his product as a colorless and tasteless liquid with an ethereal smell, having specific gravity 0.680 and boiling below 38 ºC. These unusual properties led Gregory to study the new solvent in detail. Gregory distilled this oil more exhaustively; he successively rectified it, without or with boiling, at about 27º to 32.2 ºC and separated a liquid of specific gravity 0.666 at 15.6 ºC. This fraction approached closely the fraction *eupion* (0.655) that Carl Reichenbach (1788-1869) had obtained by distillation of the same oil (Reichenbach, 1832), but was not eupion because it boiled at 32.2 ºC and was instantly decomposed by sulfuric acid. Anyhow, the liquid separated by Gregory was not pure because its boiling temperature changed; it began boiling at 35 ºC and continued up to 76.7 ºC. A surprising result was that analysis of the liquid indicated a composition very close to ethylene. Upon treatment with a large amount of sulfuric acid it decomposed immediately; the reaction was exothermic and accompanied by vaporization. The residue was a black semifluid liquid. Slow addition of the acid resulted in the formation of a colorless liquid floating above the black sediment. This new liquid had an aromatic smell similar to turpentine and boiled at 227 ºC. Nevertheless, its elemental composition remained similar to that of ethylene (Gregory, 1836a).

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