

# Mathieu Joseph Bonaventura Orfila (1787-1853): The Founder of Modern Toxicology

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## ABSTRACT

Mateu Joseph Bonaventura Orfila i Rotger was a prominent Spanish chemist and scholar of the 19<sup>th</sup> century whose experimental work has enormously contributed to the progress of toxicology. Being a pioneer with his research on the effects of toxins and antidotes on live animals, he established basic principles of modern medicine and pharmacology. Orfila improved the accuracy of several chemical techniques such as the Marsh test. He served as an expert and well-known scientific investigator in important legal trials involving alleged poisonings with arsenic and other chemical substances. In 1840, he was asked to investigate the notorious case of Charles Lafarge's death, whose wife had been accused with murder by poisoning his food with arsenic. After four failed chemical analyses, Orfila was finally able to detect arsenic in the victim's body, leading the court to convict Madame Lafarge. Due to his overall contribution to the field, Orfila is considered the father of modern toxicology.

**Keywords:** chemistry, animal experiments, Marsh test, Lafarge trial, arsenic, forensic medicine.

## INTRODUCTION

**M**ateu Joseph Bonaventura Orfila i Rotger (mentioned as Orfila hereafter), was a 19<sup>th</sup> century Spanish chemist (Figure 1). He is considered the founder of modern toxicology due to his indisputable contribu-

tions to the field, which is rapidly evolving in modern times (1-2). As a scholar of the Junta de Comerç de Barcelona (i.e., Barcelona Commercial Association), Orfila initiated his medical studies first in Valencia and Barcelona, and later on in France. Early in his scientific career, he published several treatises on medical chemistry,

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including a textbook of toxic substances entitled *Traité des Poisons Tirés des Règnes Minéral, Végétal et Animal ou Toxicologie Générale* (A treatise on poisons found in the mineral, vegetable and animal kingdoms, or, a general system of toxicology), which was published in 1814. In addition to lecturing on chemistry and other scientific topics, Orfila's research on poisonous substances using live animals contributed to the advancement of medical knowledge and education.

Orfila has also received musical training as a singer in a church choir. He would later use these talents in the Parisian salons and social gatherings where intellectual elites were discussing topics such as religion, politics, and science. He became famous for his musical skills, which allowed him to interact with many notable French society members, several of whom became key supporters during crucial moments of his life. He soon began hosting his own salons and continued to garner support from various physicians and politicians.

With encouragement from his influential contacts of the French society and his medico-legal expertise, Orfila gained numerous high positions, culminating in his appointment as dean of the Faculty of Medicine in Paris, France. He often served as an expert in criminal and legal investigations, such as the trial of Marie Lafarge, who had been accused with the murder of her husband in 1840. He captivated the courts with his various chemical analyses and tests on corpses, and his testimony often led the jury's verdict.

### **Orfila's life and career**

Mateu Joseph Bonaventura Orfila i Rotger, also known as Mateo José Buenaventura Orfila or Mathieu Joseph Bonaventure Orfila, was born on April 24, 1787, in Mahon, in the outskirts of Minorca on Spain's Balearic Islands. His mother, Susana Rotger Serra, was of English descent. His father, Antonio Orfila Villalonga, was a wealthy merchant. Antonio wanted his son to pursue a maritime career and, in March 1803, enlisted him as a second pilot on a merchant ship heading to Egypt. Orfila spent most of the voyage studying. After being released from a pirate capture, he expressed his desire to study medicine. With his father's permission, he was enrolled at the University of Valencia's Faculty of Medicine

in 1804 at the age of 17. There, he studied physics, chemistry, and mathematics (3-10).

Orfila studied Spanish, English, French, German, Latin, and Greek as well as the theory and discoveries of Lavoisier, Berthollet, and Fourcroy. He was therefore able to read virtually all the scientific literature of his time. Disappointed by the intellectual offerings of the University in Valencia, Orfila transferred to the University of Barcelona in 1805 or 1806, where he studied chemistry with Francesc Carbonell (1768–1837). He also studied anatomy and internal medicine on both cadavers and live patients (3-9).

After two years in Barcelona distinguishing himself as a promising student, the Catalanian Barcelona Commercial Association granted Orfila a scholarship (*pensión*) to travel to Madrid and then France to continue his studies on chemistry and mineralogy. In exchange for 1500 francs *per year* for four years, Orfila would occupy the chair of chemistry in Barcelona. However, when the war between France and Spain broke out, Orfila was detained as a Spanish citizen and threatened with imprisonment. Fortunately, the esteemed chemist Louis Nicolas Vauquelin (1763–1829) helped to get him released, but the Barcelona Commercial Association had ceased its financial support. Orfila then turned to his uncle, a wealthy merchant in Marseilles, who offered him a pension to continue his studies in France (3-11).

In July 1807, he arrived in Paris, where he met another scholar (*pensionado*), Francesc Lacoma i Fontanet (1784–1849). In 1808, he started his first year at the Faculty of Medicine, attending lectures by Louis Jacques Thenard (1777–1857), a young pharmacist who would become influential in the field of chemistry. Both Vauquelin and another chemist, Antoine-François Fourcroy (1755–1809), invited Orfila to study at their laboratories. In early 1808, he began teaching private courses in August-César Barrat's (1790–1854) chemistry laboratory. Barrat was a student of law who also owned a natural history cabinet. Every day except Sunday, Orfila taught physics, chemistry, anatomy, and forensic medicine to a selected group of students, reproducing the experiments performed at the Collège De France or other institutions. With the significant financial profit from these lectures, he was able to start delivering free, thrice-weekly courses to a smaller group of about

20 students. These courses gained popularity in the French market, laying the foundations for the study of toxicology, a new science investigating illnesses and deaths caused by poisons. After being successful with the required exams in August 1811, he received his medical degree in October 1811. His thesis entitled *Nouvelle Recherche sur l' Urine des Ictériques* (*New Research on the Urine of Icteric*), offered an analysis of urine of patients suffering jaundice (3-12).

Orfila was gifted not only in chemistry and medicine but also in music, a talent he inherited from his mother. Just as his educational lectures were popular among students, his singing performances were in great demand in the Parisian salons. He often performed accompanied by his wife, Gabrielle Lesueur, who was the sister of one of his laboratory assistants. In 1814, he was a special guest at the soirées hosted by Princesse De Vaudémont, who ran one of the most influential salons in Paris. There, he met physicians, politicians, and other influential benefactors, who would assist him in his eventual career as toxicologist (5, 9-11). That same year, he published one of the most important chemistry books of his era, entitled *Traité des Poisons Tirés des Règnes Minéral, Végétal et Animal ou Toxicologie Générale* (*A treatise on poisons found in the mineral, vegetable and animal kingdoms, or, a general system of toxicology*). This treatise was based on his lectures and provided new ideas and novel information on the activities of various toxic substances, their dangerous dosages and their use as potential medical treatments. In 1817, he published *Éléments de Chimie Médicale* (*Elements of Medical Chemistry*), a book on medical chemistry, and in 1818, *Secours à Donner aux Personnes Empoisonnées et Asphyxiées* (*Remedies to be used in cases of poisoning and asphyxiation*), a book of remedies for poisoning; around 1821, one of his most important textbooks on forensic poisoning medicine, *Leçons de Médecine Légale* (*Courses on Forensic Poisoning*), was published (7, 13). During the 1820s and 1830s, he was active with the Société De Chimie Médicale (Medical Chemistry Society), which was responsible for the publication of the *Journal de Chimie Médicale, de Pharmacie et de Toxicologie* (*Journal of Medical Chemistry, Pharmacy and Toxicology*) (3-7, 9, 11).

After becoming a naturalized French citizen in 1816, Orfila was appointed as a Physician in

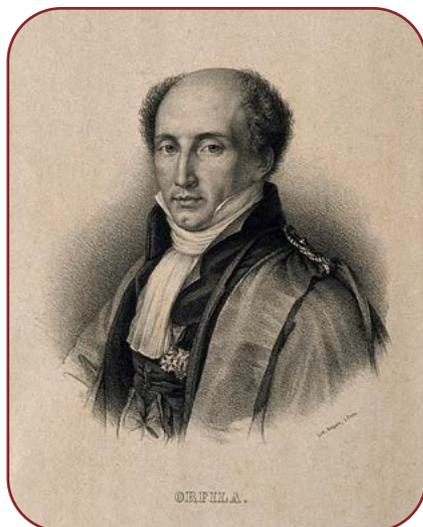
the service of King Louis XVIII. He also taught at "l' Athénée" from 1817 to 1819, when he became professor of forensic medicine at the Faculty of Medicine in Paris, a chair he held until 1822, when he was dismissed amid concerns about liberal ideologies among professors. The culmination of his career was his appointment as Dean of the Faculty of Medicine in Paris during the Orleanist monarchy, a position he kept from 1831 to 1848 (Figure 1). He received various honors, such as membership in the General Council of Hospitals in Paris and Council of Public Instruction of the Department of Seine, as well as eternal president of the Benevolent Association of Physicians. In 1845, he contributed to the foundation of the Museum of Comparative Anatomy in France, dubbed the Musée d'Anatomie Delmas-Orfila-Rouvière (The Anatomy Museums of Delmas-Orfila-Rouvière) in Orfila's honor in 1846 (3-8, 10-11).

In 1846, he visited Barcelona, Valencia, Madrid, and Sevilla, where he received the title of "honorary doctor." In 1848, he was appointed president of the National Medical Academy of France, though he was removed from his position as dean of the faculty of medicine later that same year due to political upheavals (3, 7). On March 12<sup>th</sup>, in 1853, Orfila died of pneumonia with "bilateral foci of hepatization" at the age of 66 and was buried at the Montparnasse Cemetery in Paris (3, 7-8). In his honor and in recognition of his scientific legacy in the fields of chemistry, forensic medicine and toxicology, an eponymous medical prize was established for toxicological surveys (7).

### Orfila's scientific contribution

Orfila's studies on poisons in the early 19<sup>th</sup> century advanced medical, biological, chemical, physiological, and legal sciences. His main contribution to toxicology is his 1814 treatise, *Traité des Poisons Tirés des Règnes Minéral, Végétal et Animal ou Toxicologie Générale* (*A treatise on poisons found in the mineral, vegetable and animal kingdoms, or, a general system of toxicology*), in which he theorizes that arsenic and other mineral poisons are absorbed by the body, causing local inflammation in the digestive tract and ultimately death (4, 11). In this treatise, Orfila presented valuable experimental evidence setting the foundations for the study of the detrimental effects of arsenic on biological systems (14, 15).

**FIGURE 1.** Mateu Joseph Bonaventura Orfila i Rotger. Credit: Pierre Matthieu Joseph Bonaventura Orfila. Lithograph. Wellcome Collection. Public Domain Mark



His contribution in medical education was essential, since he introduced new teaching methods such as animal experimentation. Animal models had been already used experimentally in medical research, but he extended this type of research by detecting and assessing various exposures to poisons as well as the activity of antidotes (7). These methods caused controversy among the scientific community of that time that was questioning the use of animals as analogous substitutes for humans (4, 5, 11, 13). He persisted, however, and eventually demonstrated absorption and elimination of poisons from internal organs using a canine model (Figure 2) (7, 9-10).

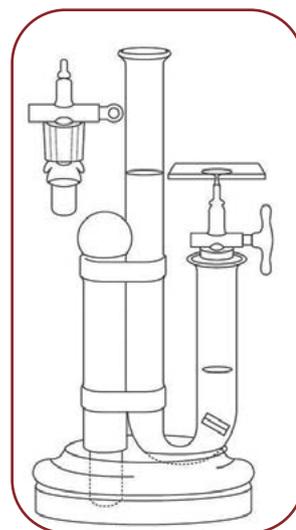
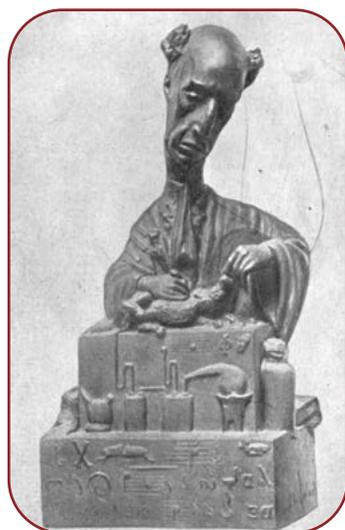
Combining mineralogy with toxicology, Orfila also studied the absorption of different alkalis (e.g., soda, barite, potash, lime) on various mi-

neral or vegetal acids (e.g., oxalic acid, nitric acid, acetic acid, hydrochloric acid, sulfuric acid) and on salts of bismuth, gold, silver, lead, tin, zinc, and mercury, including mercuric chloride. Furthermore, he wrote detailed textbooks about iodine, liver of sulfur (a mixture of potassium sulphides), ammonium chloride, potassium nitrate, and a solution of sodium hypochlorite called eau de Javelle. He administered these substances to dogs and then tried to detect them in the blood, urine, and tissues of the several internal organs (11).

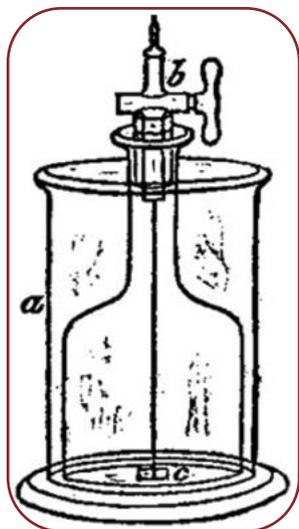
Orfila compiled current data on the clinical symptoms of poisons and their possible antidotes via autopsies, innovative chemical tests, and studying other scholars' work (4, 11). For example, around 1836, the British chemist James Marsh (1794–1846) discovered that arsenic produced arsine (then known as "arsenic hydrogen") when combined with hydrogen. Arsine could then be easily dissected to produce arsenic on a thin metallic foil on the surface of a receptacle. The required hydrogen was provided through a mixture of pure zinc and sulfuric acid (Figures 3 and 4) (13). Orfila adapted Marsh's method in the practice of forensic medicine, using it to detect arsenic in several poisoning trials, including the famous Mercier and Lafarge trials, in which he identified absorbed arsenic in the remains of long-buried corpses (4, 11).

In February 1840, Charles Lafarge, owner of a forge in the small French town Beysac, died after a brief illness characterized by violent vomiting and severe stomach pain. Witnesses de-

**FIGURE 2.** Caricature of Mateu Orfila performing experiments with dogs (ca. 1838). Small bronze sculpture. Musée Carnavalet, Paris. Reproduced in Juan Hernández Mora, "Orfila. El hombre, la vocación, la obra," *Revista de Menorca*, 49 (1953): 1-121, p. 120 (plate XXI). Private collection.



**FIGURE 3.** Marsh equipment for the detection of arsenic. Credit: Marsh James, "Account of a method of separating small quantities of arsenic from substances with which it may be mixed", *Edinburgh New Philosophical Journal* 1836;21:229-236.



**FIGURE 4.** Modification of the Marsh equipment to detect arsenic in large amounts of liquid. Credit: Marsh James, "Account of a method of separating small quantities of arsenic from substances with which it may be mixed", *Edinburgh New Philosophical Journal* 1836;21:229-236.

clared that they had seen a white powder in the drinks and soups that Lafarge's wife, Marie Lafarge, had offered to her husband. Lafarge's connection to Paris aristocracy and the famous Parisian salons helped fuel attention to the case. A group of doctors and pharmacists from the neighboring town of Brive were called to give their opinions and after four chemical analyses, Marie Lafarge was arrested for her husband's murder. The court suspected she had fed him arsenic in a cake, where the poison was identified, but the victim's corpse showed no indication of the toxin. The investigation was further impeded when a test tube broke during the chemical analysis, making it impossible to obtain the arsenic in a metallic state, as required by the protocols of the time (4, 10, 13, 16).

The court then called in additional expert witnesses: Charles Olivier D'Angers from the Academy of Medicine, Alexandre Bussy from the School of Pharmacy, and Orfila. Orfila soon de-

termined that the Marsh Test had been incorrectly performed and that there was indeed arsenic in the corpse. Together, the experts determined that the amount of arsenic detected was neither a product of a natural or chemical process nor from the soil near the grave. Based on these results, Marie Lafarge was sentenced to life imprisonment, though she was released in 1852 (4, 6, 10-11, 13).

Orfila based his work on experimentation and a high degree of competence. Using laboratory resources that were available only to a small group of well-trained physicians and pharmacists, he compiled treatises that introduced new approaches and novel experiments for the study of toxicology. Despite his expertise, however, he faced disapproval from his lay audience and even from colleagues and translators (5).

## CONCLUSION

Orfila is considered the father of modern toxicology. Using laboratory experiments, clinical data, and sometimes post-mortem examination, he developed a reliable and systematic method to detect poisonous substances in the human body. His scientific prowess was well known in his time, and he even served as an expert witness in poisoning trials. Although his work generated controversy, his experimental skills, melodic singing voice, and rhetorical adeptness served him well throughout his life and career. □

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