A Note from History: Two Pioneering Chemists, Three Hundred Years Apart

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The use of chemicals gradually increased from prehistoric time to the fourth century A.D. when alchemy was introduced. Alchemy was a branch of chemistry that attempted to transform base metals (e.g., lead, copper, and zinc) to precious metals (e.g., silver and gold) [1]. Alchemists pursued this futile goal with secretive stubbornness for over a thousand years, to the detriment of chemistry as a whole. The fact that chemistry established its scientific reputation at the expense of alchemy is largely due to one person, Paracelsus (1493-1541) (Fig. 1).

Paracelsus was a contemporary of Nicolaus Copernicus (1473-1543) and was born in the year that Christopher Columbus (1451-1506) returned from his first voyage to the New World. During his student years at the University of Basel in his native Switzerland, Paracelsus’ initial interest was in mining and metallurgy, but he soon developed a serious interest in medicinal chemistry. He was an independent thinker and rejected the Greco-Roman Galenian humoral doctrine [2]. He did not accept authority and never settled long at one place. He crisscrossed Europe under the assumed name, Paracelsus, which means “equal with Celsus” (25 BC-AD 50), the eminent Roman physician [3].
Paracelsus’ real name was Theophrastus Philippus Aureolous Bombastus von Hohenheim. His trips across Europe bought him in contact with midwives, prostitutes, blacksmiths, miners, and sick people. He was always ready to learn, willing to help, and constantly thinking about new chemical remedies.

Paracelsus believed that diseases were caused by the precipitation of chemicals in the body and he conceived that health could be restored by chemical treatments. He is credited with the introduction of mercury, lead, sulphur, iron, zinc, copper, arsenic, iodine, and potassium compounds as medications for internal use [2]. Paracelsus published hundreds of chemical formulas and wrote a monograph on therapeutics [4]. His observations on pulmonary diseases in miners and metallurgists and his descriptions of cretinism and endemic goiter were published long after his death [5]. This book is famous as the first treatise on occupational diseases and on the epidemiology of an endemic disease. His book “De Grandibus” [6], which was also published posthumously, describes most of his innovations in chemical therapeutics, including the internal use of mercurials for the treatment of syphilis (which he termed “French gonorrhoea”).

Paracelsus gave due warning that all chemicals are potentially poisonous and that the dose and concentration are what render them poisonous or non-poisonous [2]. Paracelsus was a pioneer among chemists by introducing chemical remedies into medical practice. He was an innovator in industrial chemistry by his development of processes to make glass, enamels, and imitations of precious metals and stones [7]. However, despite his hard work and earnest attempts, Paracelsus and his chemical remedies were outlawed by contemporary organized medicine.

In 1541, Paracelsus died in Salzburg, Austria, owing to trauma that he suffered in a brawl. During the two centuries after his death, the field of chemistry advanced very slowly. According to Motherby [1], the first Dictionary of Chemistry, published in 1771, declared that chemistry is nothing more than a collection of facts without an understanding of their relations to one another and that chemistry could not yet be ranked as a science. Although the first chemical society was founded in Philadelphia in 1792, it took another hundred years until chemistry, supported by biologists, physiologists, and pathologists, actually became a science [8].

Paul Ehrlich (1854-1915) grew up in Germany at a time when chemistry began to have a major impact on medicine (Fig. 2). The discoveries of Louis Pasteur (1822-1895) in France, Joseph Lister (1827-1912) in England, and Robert Koch (1843-1910) in Germany could not have taken place without the advances and applications of basic chemistry. Ehrlich, a disciple of Koch, was familiar with the Paracelsian concept of using specific chemicals to treat specific diseases. While Ehrlich was a medical student, he discovered by using methylene blue that certain parts of blood cells absorbed the stain while other parts did not [9]. In 1879, Ehrlich named the granular blood cells, which had been discovered by von Recklinghausen (1833-1910) in 1863, “mast cells” [10] and he devised a technique for differential blood cell counting [11]. In 1881, Ehrlich introduced the use of methylene blue as a bacteriological stain [12] and he discovered the blood reticulocytes [13]. In 1891, Ehrlich published the first basic text of hematology [14], which included a description of aplastic anemia and distinguished between the lymphoid and myeloid types of leukemia. His work with blood films and chemical stains bought Ehrlich wide recognition and high renown in medicine. Ehrlich’s collaboration from 1890 in the newly emerging Hoechst Chemical Co. secured him generous financial support [7].

After demonstrating that methylene blue is lethal in vitro for malarial parasites [15], Ehrlich began to experiment with chemicals as therapeutic agents. His discovery that the arsenical compound, salvarsan, was an effective agent against trypanosomiasis and syphilis [16] led to Ehrlich’s receiving the Nobel Prize in 1908. At that time, Ehrlich embarked on large scale experiments in a new direction. He injected rats and mice with eosin, pyocyanase, and selenium in attempts to destroy cancer cells. His observations were summarized in a book [17] that is regarded as the first treatise on chemotherapy. In its book’s conclusions, he pointed out that malignant neoplasms are composed of
chemically sensitive cells and chemically resistant cells. This was a new concept at that time; it was repeatedly reconfirmed after the 1970s. Ehrlich died in 1915, the year that an obscure German physicist, Albert Einstein (1879-1955), introduced his theory of relativity.

Paracelsus and Ehrlich, despite the differences in their eras and personalities, had many things in common. Both spoke German, were physicians by training, and became seriously interested in chemistry while they were medical students. Both experimented with new chemicals and advocated the internal use of chemicals as remedies for a broad spectrum of diseases. Both made important contributions to the chemical treatment of syphilis, Paracelsus by mercurials and Ehrlich by arsenicals. Above all, each contributed, in his own way, to the foundations of biochemistry and medicinal chemistry. They served as exemplars of the productive collaboration by chemists between medicine and industry.

References

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