

# The nineteenth century methodological roots of the Western pharmaceutical industry: A historical perspective

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**Abstract.** The evolution of the pharmaceutical industry is a captivating journey through time. A number of factors have contributed to its birth, both at the cultural-academic, scientific-technical and social-environmental levels. Its historical roots are fascinating and four subsequent major pharmaceutical traditions may be acknowledged in the Western world. The Middle-European line involves countries such as Germany and Switzerland, in which the pharmaceutical tradition derives directly from the existing chemical industry; it emerges in the eighteen hundreds with a typical industrial dimension. The Mediterranean strand originates in Italy and in France. Here the pharmaceutical industry arises from family-based pharmaceutical laboratories that in the course of the nineteenth century flank and then replace the grocers' shops of the Middle Ages. The British pharmaceutical tradition is characterized by UK entrepreneurs who begin producing drugs in the first half of the eighteen hundreds, as also by "foreign" manufacturers who adopt an articulated proactive marketing to sell medicines in Great Britain and in the British colonies. The fourth Western tradition is collocated in the USA, where some nineteenth century pharmaceutical companies were targeted to the elaboration and the marketing of already available drugs, while others began to develop new drugs to sell to physicians and pharmacists. The recent COVID-19 pandemic has clearly highlighted the strategic role of the pharmaceutical industry in ensuring access to and appropriate use of effective, safe and reliable medical products and related services, including vaccines, so as to improve human health. ([www.actabiomedica.it](http://www.actabiomedica.it))

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The evolution of the pharmaceutical industry is a fascinating journey through time whose historical roots date back to various centuries.

Indeed, already in the fifteenth century a first pharmacopoeia appeared in the Western world, given that an Italian book of prescriptions, the so-called "Ricettario Fiorentino", was available in Florence in 1499. The book had been written by order of the authorities so as to indicate both the medicines that were to be present in the apothecaries' shops and the rules to be followed for the correct preparation of drugs. In 1546 a structured list of drugs and medicinal chemicals was also available in Germany (printed by Valerius

Cordus in the city of Nuremberg). A few decades later the London Pharmacopoeia (1618) was to represent the first major paradigm at a national level in England, the country in which the Society of Apothecaries had been established a year before. The foundation of this Society represented a milestone, already in the seventeenth century, in the identification of pharmacy as a stand-alone reality, distinct from grocers. Around the middle of the nineteenth century the birth of the Pharmaceutical Society of Great Britain (1841) closed this historical cycle, also opening a new chapter in the progress of official institutions connected with pharmacy, drugs and their organic study (1,2).

Given this background, the eighteen hundreds may well be considered the period of the rise of pharmaceutical industry as currently understood. A number of factors contributed to this birth, both on cultural-academic, scientific-technical and social-environmental grounds. In effect in this century the scientific faculties of many European universities were stimulated to build a more articulated and comprehensive system of the information available, and in particular medical schools established departments where students could gain updated knowledge regarding fundamental sciences including physics, biology and chemistry (3). In the first half of the nineteenth century the focus of European chemical research was directed first towards the identification and preparation of the most used drugs, such as diuretics, hemetics, laxatives, alkaloids and glycosides and subsequently to their large-scale production by means of industrial equipment. The use of large quantities of raw materials, the risk in the management of the solvents needed for the extraction of active principles and the toxicity of chemical substances led to the building of spacious, functional and well-aired laboratories. In the second half of the century academic and industrial efforts were concentrated on the elaboration of new synthetic substances targeted to the chemistry of dyes. In particular in German-speaking Europe topics such as chemistry and physics were increasingly privileged in academic settings, thus furnishing the rising pharmaceutical companies of countries such as Germany and Switzerland with university-trained personnel fully aware of the newest developments in the fields of medicine, chemistry and technology (4). The case of the German physician Paul Ehrlich (1854-1915) is emblematic in this regard: already interested in structural organic chemistry and dyes when he was a student, later, in search for a specific “magic bullet” to destroy microorganisms, he applied methylene blue to the treatment of malaria patients. With Ehrlich the nineteenth century theoretical concept of a single link, involving the scientific study of human cells, the chemical evaluation of dyes for clinical purposes and the synthesis of molecules targeted to the therapy of infectious and neoplastic diseases, found a unifying practical translation (5).

With this cultural-scientific background and scenario, four major pharmaceutical traditions may be

identified in the Western world in the course of the nineteenth century.

The Middle-European line involved countries such as Germany and Switzerland, in which the pharmaceutical industry arose as a prolongation of the chemical industry, with the common interest for dyes as the starting point. This was consequent to the discovery of the first commercial synthetic organic dye, aniline purple, on the part of the British entrepreneur William Henry Perkin (1838-1907), considered by many historians the founder of the industry of artificial dyer substances and a pupil of the famous German organic chemist August Wilhelm von Hofmann (1818-1892). As a consequence, in the eighteen hundreds, in German-speaking countries the pharmaceutical tradition, since it derived directly from the existing and consolidated chemical industry, emerged from the start with a typical industrial dimension (6). Numerous pharmaceutical industries originated in this period in German-speaking countries constituting trendsetter models and including, to cite some examples, Braun (Melsungen, Germany 1839), Ciba (Basel, Switzerland 1859), Bayer (Barmen, Germany 1863), Hoechst (Hoechst, Germany 1863), Schering (Berlin, Germany 1871), Boehringer-Ingelheim (Ingelheim am Rhein, Germany 1885), Knoll (Germany 1886), Sandoz (Basel, Switzerland 1886), Hoffman-La Roche (Basel, Switzerland 1896). The second great Western pharmaceutical strand was the Mediterranean one, by this mainly indicating Italy and France. As a matter of fact, in these countries the pharmaceutical industry derived from previous family-based pharmaceutical activities that, with their typical domestic dimension, in the course of the century had flanked and replaced grocers' shops deriving from the Middle Ages. This was particularly true for Italy where, for a long time, new-born pharmaceutical firms were, compared to German-speaking ones, smaller and mainly conducted by the descendants of their founders. The pharmaceutical activities of Schiapparelli (Turin 1824), Erba (Milan 1853), Zambelletti (Milan 1866) and Dompé (Milan 1890) are examples of Italian companies born in the eighteen hundreds (7). In the same century in France Poulenc Frères (Paris 1827) and Besins Healthcare (Paris 1885) rose and developed. The third main pharmaceutical tradition of the

Western world was the British one. Many entrepreneurs began producing drugs in the first half of the eighteenth century in Great Britain, among them John Duncan and William Flockhart in Scotland in 1833 (their firm was later called Duncan, Flockhart and Company) and Thomas Beecham (from whom originated the Beecham Group), who began the business of laxative pills in 1842. Some other English firms were founded by “foreign” entrepreneurs; the Wellcome case is illustrative of this. Sir Henry Solomon Wellcome (1853-1936) was the American drug manufacturer who founded the pharmaceutical company Burroughs Wellcome & Company (with his colleague Silas Burroughs) in 1880. They adopted an articulated proactive marketing to sell remedies both in Great Britain and in areas colonized by the British, disseminating in England (1884) medicines among which the - recent for the time - tabloid pills; this was a major achievement since, in previous times, drugs were mainly sold as liquids or powders (8). The fourth Western tradition was collocated on the other shore of the Atlantic Ocean, in the USA. Here a number of pharmaceutical companies were mainly involved in the elaboration and in the marketing of already available drugs, while other firms began to develop new drugs and to produce original chemically based prescriptions to sell to physicians and pharmacists (9). Established as family-sized firms, several US pharmaceutical companies displayed from their beginning, as compared to European ones, more aggressive commercial strategies, which allowed them to achieve rapidly industrial dimensions. Even if many USA companies still at the end of the nineteenth century, and until World War I, largely relied upon the technology of European firms, the history of US pharmaceutical firms indicates that the current industrial giants would not exist without the pioneers of the nineteenth century, among which Frank and John Wyeth, who established Wyeth Laboratories in Philadelphia (Pennsylvania) in 1860, and William McLaren Bristol, who founded his company in Clinton (New York) in 1887 (3,4). Pharmaceutical industries founded in other countries outside of the Western world before the twentieth century, such as the multinational Japanese firm Takeda Pharmaceutical Company Limited, go beyond the scope of this paper, but should be remembered for their historical

roots that, in this specific case, even date back to the eighteenth century (1781). On the other hand, the history of other important European pharmaceutical industries such as the Scandinavian ones still present today (e.g., Janssen-Cilag in Sweden, Novo Nordisk in Denmark) is a typically twentieth century one (10). The pharmaceutical companies that arose in Europe and the United States of America in the eighteenth century have undergone major evolution and progress in the course of the following century, conducting them to their current fundamental role in the global healthcare scenario. The historical journey through time of the Western pharmaceutical industry, with its methodological development in the nineteenth century evidenced in this contribution, is still ongoing and the COVID-19 pandemic has recently demonstrated the asset provided by pharmaceutical companies in ensuring access to and appropriate use of effective, safe, manageable and reliable medical products and related services, including vaccines, for the improvement of human health.

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