



THE PHARMACEUTICAL HERITAGE OF THE NETHERLANDS

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With the realization of a Europe without boundaries, which most associate with the magical year of 1992, and which surely must signify much more than a mere joining together of nations, it is worthwhile to examine the past and see along which paths the pharmacy of the Southern and Northern Netherlands developed; paths which were sometimes shared by both and at other times diverged. Contemporary pharmacy is founded on a common heritage, which took shape over the centuries.

It is therefore useful to review a number of historical facts which affected the practice of pharmacy in the Netherlands.

At the end of the Middle Ages, the Netherlands formed part of the great Habsburg Empire of Charles V, who often resided at Brussels and initiated a significant centralization process. In the 16th century these '17 United Netherlands' revolted against the Spanish-Habsburg rule. The centre of rebellion in the South was the resistance against Phillip II, which began with the iconoclastic outbreak in 1566. But unity, so splendidly depicted by the 'Leo Belgicus' map in 1559, was destroyed after 1578 by the secession of the North.

As the 'Republic of the 7 United Netherlands', the North enjoyed considerable economic prosperity and cultural affluence well into the 18th century, especially after the fall of Antwerp in 1585, when many Southern refugees made new lives in the Republic. These immigrants brought with them their energy, capital, skills and commercial ties, qualities which had made the South so great.

Before the outbreak of the Eighty Years' War, Southern towns such as Brussels, Ghent, Leuven, Bruges and Antwerp had been far more prominent than those in the North. The emigration, however, caused a serious economic crisis in the South.

So Antwerp, which in 1560 could boast a population of 100,000, had but 40,000 inhabitants in 1590, and its flourishing herb and spice market was shifting little by little to Amsterdam.

Until 1713 the South remained under Spanish domination, when it fell under Austrian rule. In 1795 these 'Austrian Netherlands' were annexed by France and subjected to French legislation. In the North the 'Batavian Republic' came into existence after the arrival of the French. After 1806 French influence in the 'Kingdom of the Netherlands' gradually increased, particularly after the annexation by France in 1810. As in the Southern Netherlands everything was done along French lines.

After the liberation in 1813 North and South were united in the 'United Kingdom of the Netherlands' over which the Netherlands King William I assumed sovereignty. From the start this reunification stood little chance of success. Barely 16 years later, in 1830, the Netherlands and Belgium separated and became independent countries.

Following this brief historical introduction, let us go back in time to get an impression of the pharmaceutical heritage of the Netherlands. We will concentrate on the 16th and 17th centuries, in which ordinances were issued, books of prescriptions were published and sciences such as botany and chemistry came to be developed. This was all of enormous importance to the practising pharmacist.

It began long ago with the 'Constitutiones', issued by Frederik II von Hohenstaufen for the medical profession in 1240, in which guidelines were laid down for an independent and protected pharmacy practice. So in the Netherlands the first pharmacists set up practice from the 13th century.

The independence of these pharmacists demanded that guidelines, inspections and ordinances were established in accordance with which the profession was to be practised. The oldest pharmaceutical ordinance in the Netherlands was issued around 1300 at Ypres, a town then just as important and well known as Paris.

Later, regulations in the fields of medicine and dispensing were promulgated in the very affluent Southern Netherlands towns of Bruges, Ghent, Leuven, Brussels and Antwerp. At that time there were only a few pharmacists established in the Northern Netherlands, and it was not until the beginning of the 16th century that local pharmaceutical ordinances became effective in places like Maastricht, Amsterdam, Delft and Bergen op Zoom. A study of the texts of these ordinances shows that the Southern Netherlands regulations served as a model for those of the Northern Netherlands (1).

About 1300 a number of important basic principles for the practice of the pharmacy profession were laid down in the 'Keure van Yper' (2). A pharmacist was required to take an examination and swear an oath. The 'Antidotarium Nicolai', a book of prescriptions which had originated from Salerno, was declared binding. It is obvious then that another prerequisite was that the pharmacist or his assistant had to be able to read.

The 'Ordonnancie politique nopende het verkoopen van medicynen' (3), promulgated one and a half centuries later on 16th October 1456 at Ghent is, according to its modern publisher Leo Vandewiele, one of the oldest pharmacy ordinances which sets out fundamental principles for the practice of the profession. This ordinance served as a model for later regulations. Southern Netherlands towns had been in the lead as far as the development and execution of these local regulations was concerned. Their great economic strength in various areas gave them the edge over the Northern Netherlands towns.

Interesting too is the 'Placcaert op 't stuck der medecyne' (4), which was issued by the Emperor Charles V on 8th October 1540 at

Brussels. For the most part this edict resembles the 'ordonnacie' of Ghent which was published a century earlier.

What is important is that although this proclamation was issued at Brussels, it was intended for 'all the provinces of the Netherlands'. It was a national ordinance which fitted exactly with Charles V's centralization policy, and can be regarded as the first central regulation of pharmacy in the Netherlands. This decree could have had great influence if the regulations and special tribunal it promised had been forthcoming.

This official document originated in a time of renewal and rebirth — 'Renaissance' which, under the influence of Italy, also manifested itself in the Netherlands.

In the Netherlands, scientific influence emanated mainly from the university town of Leuven, while administrative decisions were taken in Brussels, and economic and cultural development was concentrated in the towns of Bruges, Ghent and Antwerp. The Northern Netherlands were actually still apart of the outlying provinces of Europe. The North Netherlands humanist, Desiderius Erasmus (1466-1536) often stayed in Antwerp. Most of his books were published there by the famous printer, Michiel Hillenius van Hoogstraten, including his oration 'Lof der Geneeskunst' (Encomium artis medicae). This he dedicated in 1518 to his friend, 'insigni Medico', the accomplished physician from Lier, Dr. Henricus Afinius (5). Erasmus had this to say about medicines :

"There are so many differences between so many thousands of herbs, each growing in a different place, not to mention the rest of the medicines. And so much extensive study is necessary to be able to extract from all of the herbs, bushes, trees, animals, precious stones and even from poisons, curative medicines for all human ailments".

He refers to the range of medicines in the late Middle Ages, for which at least 80% of the medicinal materials were derived from

plants. Botanical knowledge of these medicines was primarily based on 'De Materia medica' in five volumes by the Greek physician Dioscorides (55 A.D.).

During the Renaissance Dioscorides' work enjoyed considerable esteem. For a long time it served as a model for later herbals, in which simple botanical materials, the 'simplicia', were described.

A printed book which described and illustrated medicinal plants, a 'Herbarius', was published for the first time in Europe in the Netherlands. Of the edition in Netherlands, the 'Herbarius in Dyetsche', three Southern Netherlands publications are known, one from Leuven in 1484 and two from Antwerp in 1500 and 1511. The illustrations which appear in these books, however, show little resemblance to their natural counterparts. This made the identification of herbs difficult.

This changed a lot during the renaissance. The illustrations in the herbals of the three German 'fathers of botany', Brunfels, Bock and Fuchs, had already improved and were truer to nature. The work of the physician and humanist Leonhard Fuchs was especially impressive and indisputably superior to those of his predecessors Brunfels and Bock.

In his book 'Six Wings : Men of Science in the Renaissance', Sarton adds Valerius Cordus (1515-1544) to the three influential German botanists (7). Correctly, he thinks that Cordus surpassed the others in his botanical research. This young German physician wanted to study plants in their natural habitat before he described them.

Cordus travelled a lot and was the first to take the initiative in organizing botanical excursions for medical students. Botany was, after all, a supporting science to medicine. He also took knowledge of the simplicia in a totally different direction by introducing, alongside theoretical academic tuition — 'Lectura simplicium' — the practical demonstration : 'Ostensio simplicium'(8).

With his father — Euricius Cordus — a humanist, physician and botanist and his uncle a pharmacist, Valerius Cordus was involved with the *materia medica* from childhood. Alexander Tschirch (1856-1939), the well-known German pharmacognosist, even includes him among the 'fathers of pharmacognosy', together with Monardus and Clusius.

Although Cordus' *materia medica* is still firmly rooted in the Middle Ages, we can already see the spirit of the new age, the Renaissance, in his botanical research, where he described countless new and rare plants.

In the field of practical dispensing Cordus created order out of the chaotic state that this occupation was then in (9). In 1534, encouraged by his uncle who was a pharmacist at Leipzig, he began to compile a book of prescriptions, which included a number of standardized preparations. This 'Dispensatorium' testifies to his profound practical pharmaceutical knowledge and possesses great scientific value, because Cordus, led by personal observation and research, not only described the characteristic features of nearly 225 different *simplicia*, but also noted the origin of raw materials and possible adulterations.

Unfortunately, Valerius Cordus died in 1544, not yet 30 years old. After his death, in 1546, the 'Dispensatorium' was published at Nuremberg and became the first official pharmacopoeia in Germany.

For the practising pharmacists in the Netherlands, this book of prescriptions was to become exceptionally important.

In the Southern Netherlands, the followers of the German botanists were Dodonaeus, Clusius and Lobelius, who during the Renaissance wrote important works in which a systematic classification and detailed description of many plants can be found.

These Flemish botanists became famous, but would never really have won recognition without their publisher, Christoffel Plantijn (10).

Partly thanks to him an important part of this pharmaceutical heritage has remained intact. In 1548 Plantijn came from Paris to Antwerp, the most important commercial town north of the Alps, and a centre of humanism and science.

No less than 66 printers of books were at work there, and Plantijn started his printer's 'De Gulden Passer' in 1555. This firm became one of the most important publishers in the Netherlands. Plantijn had scientific sympathies, and he was interested above all in the development of the natural sciences, especially botany.

It was just at this period that much research was being done on new material that had been brought back from long journeys to other parts of the world, and which had to be examined, described and illustrated.

Among these were a large number of medicines which until then were completely unknown here, such as Kina, ipecacuanha, sarsaparilla and tolbalsem. The Flemish botanists contributed greatly to the knowledge of these medicines.

The 'Cruyde-boeck' (11) by the physician and botanist Rembert Dodoens, which appeared in 1554, had an enormous influence on practical pharmacy.

Dodoens gave details of origin, collection, preservation, natural features, smell, taste, colour and other specific characteristics of a large number of simplicia. These are what we would refer to today as 'quality requirements'. It removed much of the insecurity that pharmacists often had concerning the processing of the 'opregte simplex'. More than anything the true to nature illustrations in this Cruyde-boeck were of great value. Moreover, the book was not written in Latin, but in the 'ghemeyne Neerduytse tale' (common Dutch language), so that anyone could consult it.

The Antwerp humanist, Carolus Clusius (12), known as the wisest man of his time, was the first to describe the flora of particular regions such as Spain, France and Austria. In addition, being the polyglot he was, he translated botanical works of other authors into Latin.

He translated the Spanish books of Da Costa and Monardus, and the Portuguese works of Garcia D'Orta, and so doing contributed to a growing knowledge of medicines from other parts of the world.

Clusius maintained close relations with pharmacists, especially with those who possessed their own herb gardens. They corresponded on exotic plants and exchanged botanical material. His friend, the Antwerp pharmacist Peeter van Coudenberghe, urged him to translate the Italian antidotarium 'Ricettario utilissimo' which appeared in Venice in 1560. Plantijn published Clusius' translation in 1561 (13).

In 1581 the 'Kruydtboeck' by Mathias de L'Obel (Lobelius) came off the Plantijn presses (14). Lobelius too had connections with various pharmacists, whom he mentions by name in his 'Kruydtboeck'. He elaborates on his friendship with the pharmacist Peeter van Coudenberghe, whose garden he considered to be the richest, most well-tended in the world. In 1548 this Antwerp pharmacist planted a herb garden of two hectares, which became one of the sights of Antwerp famous throughout Europe, not least for its exotic plants derived from Africa, Asia and America (15).

Dodonaeus, Clusius and Lobelius frequented Van Coudenberghe's garden and respected him as a scientist and scholar. Just as Cordus stands in the line of the German botanists, so Van Coudenberghe can be counted among the outstanding Flemish botanists of the Renaissance.

Plantijn asked Van Coudenberghe to thoroughly revise and supplement Valerius Cordus' 'Dispensatorium', because he wanted to publish it. This 'Dispensatorium', which came out at Nuremburg two

years after Cordus' death, had not been edited by Cordus himself. Plantijn, who recognized the great value of this work, rightly feared that the 1546 edition would no longer suffice. Hence his request to Van Coudenberghe who supplied the 'Dispensatorium' with comments and corrected more than 400 inaccuracies. The book was published by Plantijn in 1568.

The great influence that Cordus' 'Dispensatorium' had in the Netherlands is evident from the numerous reprints, including several Dutch translations. The 1614 translation, entitled 'Den Leydsman ende onderwyser der Medicynen', was completely revised by Lobelius.

Because Cordus' book of prescriptions was entirely based on the classical, ancient Arab medicine and pharmacy, it mentions nothing of the chemical medicines that were propagated in the early 16th century by the Swiss physician Paracelsus. Paracelsus, who was both maligned and applauded, roamed all over Europe, visiting battlefields, universities and hospitals to gain experience (16).

So in 1519 he came to Antwerp and visited the market for herbs, spices and new, often exotic, medicines. He wrote that here he had learned more than at all the universities he had visited. Paracelsus frequently worked with mercury, antimony, arsenic and iron compounds. This led to new insights into medicine and the preparation of medicines. Pharmacists began to prepare medicines in their own laboratories.

Paracelsus' ideas for reform were further developed by others, and propagated as 'iatrochemistry'. In 1650 iatrochemistry reached its peak in the Northern Netherlands.

In the North, to which many Southern Netherlands had emigrated after the fall of Antwerp in 1585, Amsterdam became an international centre for trade and culture within a few decades (17). The flourishing Antwerp herb and spice trade shifted to Amsterdam,

because many Southern Netherlands spice and herb merchants had moved there.

In Leyden, the intellectual bulwark in the liberated area, where in 1575 the Leyden university was established by Prince William of Orange, the population doubled between 1580 and 1610 to 30,000, and the number of pharmacies increased from 5 to 10. Round about 1620, 67% of the Leyden population was Southern Netherlands.

This mass emigration was not solely the results of religious difficulties : it was also occasioned by the very serious economic crisis which originated in the South. Not only did confectioners, herbalists, teachers, printers and carpet weavers leave, but also scholars, after the Leuven university began to decline. After all, isn't prosperity in a way also necessary for scientific study and growth ?

Furthermore, the curators of the Leyden University went to all lengths to attract famous scholars, such as the Leuven humanist Justus Lipsius in 1578, who was dubbed the second Erasmus. In 1582 Dodonaeus came to Leyden on account of his appointment as professor of medicine, and in 1593 Clusius became professor of botany at the University of Leyden. By 1578 Lobelius already resided in Delft, where he was court physician to prince William of Orange, to whom he dedicated his 'Kruidtboeck', published in 1581.

Plantijn had also emigrated to the North for economic reasons. It was probably a well-considered move on his part in order to gain control of the Northern Netherlands book trade (18). In the Spring of 1583, still prior to the fall of Antwerp, he opened his 'Officina Plantiniana' at Leyden. On 14th May 1584 he was appointed as university printer, and thus Leyden acquired a scientific publisher, a development which marked the beginning of an age-old tradition.

Although Plantijn had many friends in Leyden — Lipsius, Dodonaeus, Douza and Jan van Hout, the latter two curator and secretary of the university respectively — he still returned to Antwerp

after its fall. He left his Leyden business in charge of his son-in-law, Frans van Raphelingen.

Among the numerous publications which saw the light of day through this establishment from 1583 to its closing in 1619, were a number of pharmaceutical works (19).

Besides the books on chemistry, alchemy and pharmacology, the writings of Paracelsus, Fuchs, Clusius and Dodonaeus above all supplied the large demand from practising pharmacists for books on prescriptions. These were the works of Cordus, Jacobus Sylvius, Renodaeus and Augsburg's pharmacopoeia, to mention but a few. These prescription books had a great influence on the composition of the Northern and Southern Netherlands town pharmacopoeias, which had been published since 1636, beginning with that of Amsterdam. When the trading relations between the North and South gradually became more difficult as a result of the war, the Leyden publishing house set up by Plantijn in the 'Republic of the 7 United Netherlands' contributed considerably to the spread of these pharmaceutical manuals.

Despite the fact that many of the Flemish intelligentsia emigrated to the Northern Netherlands, the South did retain some of its appeal. Plantijn went as quickly as possible to Antwerp once the peace was somewhat restored. Lipsius, the Leyden 'Lumen academiae', returned to Leuven in 1592.

In 1594 Clusius wrote from Leyden to his friend Lipsius: "If I'd known that this would happen, I never would have set foot here" (20). Clusius was already 66 years old when he was appointed by the University of Leyden to supervise the setting up of a Hortus botanicus.

Owing to invalidity, he was unable physically to do the job and so a deputy was appointed, the Delft pharmacist Dirk Cluyt, who in a short time laid out and planted the university garden.

Until his death in 1609, Clusius held only an honorary position at Leyden university, free of all duties. He devoted himself entirely to the publishing of his collected works and to his voluminous correspondence with many of his acquaintances, especially international ones. Because of his great interest in exotic plant products which he came across in pharmacies, he never passed up an opportunity to procure these.

Thus in 1601 he wrote a 'Memorie', which the commanders of the ships that sailed to Africa and the East Indies were to pass on to the ships' pharmacists and surgeons. It stated which plants, fruits and seeds had to be taken along on the journey (21). Dodonaeus lived in Leyden for only a short period. He died in 1585 at the age of 68, just three years after his arrival.

Following the death of Prince William of Orange in 1584, Lobelius was appointed town physician of Middelburg. From 1596 until his death in 1616, Lobelius lived in England, where he supervised of a medical herb garden.

In the 16th-century there was still no university garden in the Southern Netherlands. It did, however, have the pharmacist Peeter Van Coudenberghe's private garden, mentioned earlier, which was visited by renowned botanists such as Garcia d'Orta and Conrad Gesner (22).

During the siege of Antwerp Van Coudenberghe's life's work was destroyed overnight. He died around 1599. By then the Leyden Hortus botanicus was completed, the first university botanical garden in the Netherlands.

The question of how many pharmacists actually emigrated to the North after the fall of Antwerp is difficult to answer because the archives give little information on this. It is conceivable, however, that a pharmacist does not readily abandon his pharmacy since the preparation and dispensing of medicines is necessary always and under all conditions. As far as Leyden is concerned, we know that by 1610 half

of the 10 Leyden pharmacists were emigrants or descended from emigrants.

One family which had left the Southern Netherlands for religious reasons and settled in the German Hanau near Frankfurt, was that of the merchant Deleboe. Later, in 1658, his son Franciscus was appointed professor of medicine at Leyden (23).

Franciscus Deleboe, or Sylvius, as this descendant of a Southern Netherlands emigrant called himself, considered chemistry one of the main components of medicine. He was convinced that the functioning of the human body could be explained in terms of the chemical processes which happen within it. The period until 1672, in which Sylvius was active at Leyden, can be regarded as the height of 'iatrochemistry'.

Not only did his library include many medical texts, but also various botanical and alchemistic-chemical works (24). In addition, he also possessed pharmacopoeiae, such as the 'Pharmacopea Augustana'. In 1653, at Gouda, an edition of this book appeared, in which the rise of iatrochemistry is clearly apparent in a separate appendix of more than 100 chemical preparations.

The 'pharmacopoea spagyrica' by Johann Glauber also belonged to the library of Sylvius, who in his home on Leyden's Rapenburg had two rooms equipped as laboratories to carry out his own chemical-pharmaceutical experiments. There he prepared mixtures, amongst which his volatile salts became especially well-known. These were alkaline products which he prescribed to 'neutralize the acidity in the body'.

But however much Sylvius propagated iatrochemical thinking, it is obvious that the preparations linked with his name are for the mostpart composed of traditional, galenic materials. His 'Diascordium Sylvii', a classic recipe, related to the Theriak, is mentioned in the final edition of the Leyden pharmacopoeia in 1770.

We have to realise, however, that chemistry in the 18th century was still at the beginning of its development. In the different publications of books of prescriptions from North and South Netherlands towns, appearing between 1636 and 1795, the breakthrough of chemistry is evident from the increase in the number of chemical preparations, and by the titles of these pharmacopoeiae in which the supplement 'Galenico-chymicum' gets more prominence. Such a supplement occurs for the first time in a Southern Netherlands pharmacopoeia which appeared in Antwerp in 1661.

Only under French rule did the publication of town pharmacopoeiae finally come to an end in both the Southern and Northern Netherlands.

During the regime of the Batavian Republic, the Northern Netherlands witnessed the introduction of a national book of prescriptions, the 'Pharmacopoea Batava' which appeared in 1805. The publication of a national pharmacopoeia was never realized in the Southern Netherlands, despite the plea of the Brussels pharmacist Van Mons, who in 1800 even spoke of a European pharmacopoeia (25).

In November 1813, the Northern and Southern Netherlands united in the 'Kingdom of the Netherlands'. Pharmacists fervently hoped for the long-awaited reform of their training. To their great dismay, however, no mention was made of a university education in the medicine Act of 12th March 1818. This act even gave country physicians permission to dispense medicines, which pharmacists considered a violation of their long-standing monopoly in the sale of medicines. The pharmacists were not even consulted in the compilation of the new book of prescriptions, the 'Pharmacopoea Belgica', which was published in 1823. We can assume therefore that they were not too well-disposed towards King William I.

In 1822 the University of Ghent, established by William I in 1817, appointed a Dutchman as Professor of botany, zoology and comparative anatomy, namely Jacobus Gijsbertus Samuel van Breda (26). He was also in charge of the Hortus Botanicus and under his

management the Museum of Natural History was radically expanded. Van Breda was a highly dedicated teacher and an important natural scientist. The national upheaval of 1830 put an abrupt end to his Ghent career and he returned to the Netherlands.

After the separation of the Netherlands and Belgium, a university education for pharmacists finally became reality : in Belgium as early as 1849, and in the Netherlands after 1865. Both countries went their separate ways, and this also applied to the area of pharmacy. Nevertheless, the pharmaceutical heritage left behind by great scientists and preserved in the excellent work of the printers, has in part fallen to us.

In this historical review, most attention has been given to the 16th and 17th centuries, the age of Humanism and the Renaissance, in which scholars and scientists diligently contributed to our inheritance and thus laid the foundations for our common pharmaceutical past. Particularly the Southern Netherlands contributed in large measure to this.

In the near future, after 1992, we will see again the pursuit of harmonization in the field of pharmacy (28).

As early as 1969 the first part of the European Pharmacopoeia was presented to the secretary-general of the European Council. In 1987 mutual recognition of our pharmacists' diplomas was achieved. Training will also aim at meeting common standards, and a European registration system is to result in the uniformity of medicines.

The Belgian and Dutch Societies for Phytotherapy are already part of the European umbrella organization, the ESCOP (29). And thus our paths converge again. It seems advisable therefore to remain aware of our common heritage as we proceed together.

For the last 40 years the 'Kring voor de Geschiedenis van de Pharmacie in Benelux' (Society for the History of Pharmacy in Bene-

lux) has been studying the pharmaceutical past, in which the pharmacist, the preparer of medicines from way back, occupies an important place.

This historical study supplies some unexpected views of the past and the future.

Sarton also pointed this out to us in his 'new humanism' (30). In his own words : "The present without its past is insipid and meaningless; the past without the present is obscure. The life of science, like the life of art, is eternal".

His new humanism did not result in narrow specialism, but in what he refers to as a 'double Renaissance', which also incorporates nature, culture and man.

In this way an inspiring influence emanates from the past and thus our common pharmaceutical heritage can form a link between our nations.

In turn this can contribute to the process of evolution which is necessary to realize harmonization within the framework of the European Community.

Notes

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