Mediaeval Quality Assurance of Medicines within the Territory of the State of Burgundy

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Abstract: The State of Burgundy from Charles the Bold included in 1477 the Low Countries (comprising large parts of present-day Belgium, the Netherlands, Luxembourg and parts of northern France) as well as the counties of Nevers and Burgundy and the duchy of Burgundy. The quality of mediaeval medicines within the territory of the Burgundian State was assured by four themes in the municipal and governmental pharmaceutical regulations: inspection of the pharmacy, surveillance of medicines preparation, quality prescriptions and the professional education. Uniform prescriptions were a key factor in the QA (quality assurance) of medicines. Based on ordinances and on heritage inventories in nineteen Burgundian towns it became evident that between 1310 and 1540 the Antidotarium Nicolai was usually prescribed or present as a formulary and that from 1568 on, the presence of the Dispensatorium Cordis predominated.

Key words: Middle ages, history of pharmacy, State of Burgundy, mediaeval QA of medicines.

1. Introduction

Most studies on the history of mediaeval pharmacists are country-based. But the State of Burgundy included in 1477 (large parts of) Belgium, the Netherlands, Luxembourg and France (Fig. 1). During the reign of Philip the Good (1419-1467) a further administrative cohesion for the territory was developed with the convocation of the States-General in 1464 in Bruges. After the Act of Abjuration in 1581 the last link between the Low Countries and Burgundy expired. This study is on the various aspects of QA (quality assurance) of medicines in the territory of the State of Burgundy up to 1600.

2. Methods

2.1 Identification of Late Mediaeval Regulations on QA

Based on publications in the Netherlands, Belgium and France, regulations for apothecaries, practicing in thirty-five towns within the territory of the Burgundian State, have been identified over the period 1300-1600. In an earlier study [1] nine common themes were distinguished and four of them have been selected for further analysis in this study.

2.2 Analysis of the Regulations

The towns where the selected themes on late mediaeval QA of medicines were found are in a chronologic order represented and their relative importance has been established as well as their evolution in time and the surveillance of their application.

2.3 Inventory and Analysis of Quality Related Prescription Manuscripts and Books

The obligation to prepare medicines according to general accepted prescriptions was an important issue to warrant the mediaeval medicine quality. An inventory of in the course of time prescribed and in reality found manuscripts and books have been made and analyzed with respect to QA of medicines.

3. Results and Discussion

3.1 Governmental Pharmaceutical Regulations

Between 1200 and 1600 several medical-pharmaceutical
Fig. 1  The territory of the House of Valois-Burgundy in 1477.
regulations have been promulgated by kings and emperors touching the Burgundian State and often based on earlier town proclamations. In Paris for example an extended regulation was already known in the year 1322, while the French king Charles VIII proclaimed not until 1484 a governmental regulation based on the Paris one. The governmental “Placcaert” from Emperor Charles V, addressed to the Low Countries, was almost a copy of the medical-pharmaceutical regulation from Ghent in 1456. Perhaps the “Constitutiones” from emperor-king Fredrick II, being unique, form an exception to this rule.

Frederick II (1194-1250) (Fig. 2) was king of Sicily, Italy and Germany and from 1220 on Holy Roman Emperor. Between 1231 and 1243 he edited the “Constitutiones Regni Siciliae”, a coherent compilation of laws and competences. His 1241 “Edict of Salerno” [2], an appendix of the Constitutiones was the first modern governmental law for the regulation of the apothecary profession with as most important issues:

• separation of the occupations of physician and apothecary to prevent conflicts of interest;
• inspection of the pharmacy by two government jurymen and preparation of medicines under the supervision of a physician;
• taking an oath to certify that the apothecary will deliver products prepared in a capable and reliable way;
• limitation of the number of pharmacies;
• fixation of the prices of various medicinal remedies.

The French king Charles VIII promulgated in 1484 the following ordinance [3]:

• apothecaries own the monopoly for selling medicinal remedies;
• the pharmacy will be visited 2 or 3 times a year and inspected on the quality of the remedies and the exactness of the weights;
• the widow of a master apothecary (“femmes de maistres veufves”) may continue the pharmacy, provided she employs a sworn master servant;
• the master apothecary should have been examined, delivered a masterpiece and should have served his seven years apprenticeship in a qualified pharmacy;
• the son of an apothecary could be exempted from the apprenticeship obligation and could enjoy simplified requirements for the masterpiece preparation.

Emperor Charles V issued in 1540 in Brussels a medical-pharmaceutical decree [4] with the following subjects:

• inspection of the pharmacy each four months by 2 physicians and 2 sworn master apothecaries;
• control of the weights;
• education details for the master apothecary;
• preparation of compounded medicines only according to prescription of a qualified physician;
• obligation to make use of qualified prescription books.

3.2 The Municipal Proclamations

Apothecaries, physicians and municipalities
recognized the necessity for regulations in pharmaceutical education and in keeping a pharmacy. In the small towns of the Low Countries—where usually just one apothecary was established—regulations were formulated in the appointment agreement between the town magistrate and the (town-) pharmacist. In the bigger towns, usually the municipality took the initiative to draw up pharmaceutical regulations like in Anvers (1499), Beaune (1576) and Chalon, but in Dijon (1490) and Autun the apothecaries themselves took the initiative in formulating the regulations [5]. The “Keure” of Ypres—dating from the period 1292-1310—is the first (extended) regulation known in the State of Burgundy (and in Western Europe). It is assumed that Jan Yperman, during his surgeon study in Paris, came across the preparations of the Paris regulation, promulgated in 1322 and he introduced the principles already around 1300 in Ypres, a relatively big town with 30,000 inhabitants at that time [6].

3.2.1 Common Themes in the Pharmaceutical Regulations
In an earlier study 35 pharmaceutical town-regulations within the territory of the Burgundian State have been identified over the period 1300-1600 and the following nine common themes could be distinguished [1]:

(1) Weights and Measures
The necessity to verify weights and measures is already early in the middle ages recognized and it concerns not only the apothecaries but every merchant using balances and measures. In Delft for instance, each merchant was obliged—from 1480 on—to let examine and adjust his weights by two merchants and a tinman [7]. In Gouda (1490) the weights should be gauged free of charge by the bailiff and his servants [4].

(2) Monopoly of the Preparation of Medicines
Like the 1241 Edict of Salerno, the Keure of Ypres states in 1300 the clear separation between medicine preparation and medicine prescription. We meet similar clauses in the regulations of Zutphen in 1387, of Dijon in 1451, of Ghent in 1456, of Maastricht in 1490 [8] and in the 16th century, 23 of such monopoly clauses have been identified.

(3) Price Regulation
In the smaller towns usually just one pharmacist is established. Because of the limited number of potential clients, it concerns often a town-pharmacist, (partly) paid by the magistrate and with additional privileges or a monopolized position. Therefore, price limits are promulgated already early in time, such as in 1355 in Kampen, in 1451 in Zwolle where the prices are fixed by the town-physician, in 1478 in Harderwijk [8] “so men die buten in anderen apteken copen mach” (not more expensive than in other pharmacies), in 1487 in Zutphen “dattet gemeyne volck niet onredelick beschat worde” (reasonable prices for the inhabitants) and in Bergen op Zoom, where each year the prices were evaluated by a physician [8]. Even in larger towns with a real competition we come across price limiting promulgations like in Ypres (1300), in Amsterdam (1519) with reduced prices for poor people and in Leuven where the faculty of the university assesses the value of the medicines.

(4) Position of the Widows and Sons
For 6 towns, clauses are found concerning the position of the widow of a master apothecary. In general, she is allowed to continue the pharmacy. In Dijon, the statutes of 1490 specify that she should employ a capable servant and that her son enjoys reduced demands for obtaining the mastership. In Lille she has in 1586 the choice to employ a master servant or to enter into partnership with another apothecary [9].

(5) Transfer of Poisons
The regulations on selling poison are focused on security assurance. King John II the Good of France (and from 1361-1364 duke of Burgundy as well) promulgated in 1353 the first regulation in France on trade in poison: it is prohibited to sell poison containing products and abortifacients even to a
master apothecary or to a medical scientist without an ordonnance of an official physician [10].

Most municipal regulations on the transfer of poison date from the 16th century and not infrequently in connection with poisoning crimes. The magistrate of Utrecht promulgated in 1529 that selling arsenic and mercury is only allowed in the presence of 2 neighbors of the buyer, after the quadruple poisoning by Geeske Kuypers [8]. In Bruges [11] a regulation was issued in 1585 after the poisoning by a woman of her husband, stating that only married couples are allowed to buy and should declare in the presence of 2 citizens the purpose of the purchase. The council of Autun ordained the apothecaries in 1581 to note the names of clients asking for poison in the presence of 2 witnesses. Some months earlier the servant Blaise Barberet had poisoned his employer Turrelot with aid of Turrelot’s wife and at the same time poisoned his own wife. On January 28 of the year 1581 they were condemned to the stake [5]. Besançon follows an alternative preventive policy: in the statutes from 1530 the apothecaries are obliged to expose a rope in their shop for the sake of clearness what poisoners can expect [12].

The remaining four common themes in the pharmaceutical regulations concern the QA of medicines and are selected for further elaboration and analysis: (6) Quality; (7) Preparation supervision; (8) Inspection of the pharmacy; (9) Education requirements.

3.3 Analysis of the Four QA Regulations

(6) Quality

The quality of medicinal products was assured by the obligation to label the jars, vases, cans and other containers and to mention content and date of preparation, by the commitment to use only fresh products, by the interdiction to falsify medicines and last but not least by the control of these ordonnances. During the period 1300-1500 we met those clauses in ten municipal regulations and in the 16th century in twenty-six municipal regulations. In 1414, prince-bishop John, duke of Bavaria addressed an instruction to the apothecaries and grocers of Liège to deliver not falsified and not color-improved goods: “et marchandes sans estre colorees, tinctes ou soffistikees par faults art ou deception” [11]. Because the quality of imported compounded medicines was difficult to control, import in most towns was restricted or forbidden. In 1490 the Chamber of Dijon issued a prohibition for foreigners to sell herbs and compounded medicines if not inspected by the aldermen and the jurymen of the town [5]. The “Ordonnantie politique nopende het verkoopen van medicynen” (the Decree on selling medicaments) from the town of Ghent mentioned in 1456 that the right to sell medicines is only reserved to the master-apothecaries of the town [13]. A similar promulgation we do encounter in 1518 in the statutes of Valenciennes [14]. The Delft ordonnance from 1520 interdicted to sell “foreign” spices and oily liquids without permission of the town-physician [7]. The “Ordonnantie op de apothecarye bynnen deser stadt Lovene” (Louvain, 1555) mentions that the import of compounded medicines is strictly forbidden [11]. In 1579 in Brielle, the deans of the guilds were in charge to determine whether imported pharmaceutical goods were admitted [8]. Not only the import of medicines was restricted, the access of foreign masters was limited as well.

Deventer restricted the access of foreigners in 1574 as follows: “Itemollen oick ghene vrembde quacksalvers oft andere frembde meisters in deser stat thogelaten worden sunder consent und bewillunge des Rhaedes, und irsten van den doctoren examiniert tho syn” (Foreign masters and quacks are not allowed to sell without permission of the council and after examination by the town-physician) [15]. The magistrate of Oudenaarde published in 1580 an ordonnance in order to keep out swindlers and the decree from Liège interdict in 1592 foreigners to sell drugs and theriac if not inspected by the town-pharmacist [8].
(7) Preparation Supervision
Near half of the pharmaceutical regulations mention a supervision paragraph for the preparation of compounded medicines. Two trends can be distinguished: or the apothecary prepares the medicines in the presence of a physician or he prepares the medicines after the physician has approved the raw materials as was the case in Bergen op Zoom [7] in 1530 and in Brussels [11] in 1540, where the prescriptions of the “Apothekarisboecken” should be followed. Preparation in the presence of a physician was obliged in Zwolle [8] in 1341 and in 1575 in Montbéliard, where the prescription of important compounded medicines should be signed by the physician and the apothecary mentioning date and quantity, on penalty of a “demi teston” [16] (silver coin of 9.5 g).

(8) Inspection of the Pharmacy
From halfway the 15th century on, most municipal regulations require regular inspections of the pharmacy shop like in 1431 in Zwolle, in 1446 in Amiens, in 1456 in Ghent, in 1467 in Kampen, in 1477 in Mechelen, in 1490 in Dijon and in 1497 in Bruges. In Mechelen the visit should be executed by 2 physicians and 2 sworn apothecaries. From the side of the apothecaries apparently little enthusiasm was shown seen the additional clause of 1536: when an apothecary refuses to perform the required inspection, he will be put in prison and stay there until he agrees to perform the inspection [11]. When in 1540 in Brussels medicines were found, not in conformity with the regulations, they were the same day thrown in the streets [17].

(9) Education Requirements
A wide spectrum of education requirements is found in the pharmaceutical regulations of 26 towns. The Chamber of Dijon posed in 1490 the following examination requirements to become master apothecary: the candidate should be examined by 2 apothecaries in the presence of 2 aldermen and one or more physicians [5]. The regulations of the guild of apothecaries, grocers and oil and grease merchants in Tournai mentioned in 1476 that sons of any master are allowed to undergo the master examination without having passed an apprenticeship and if they wish so in another specialization than their father practiced: a son of a grocer could undergo the examination to become master apothecary [18]. When somebody wanted to open in 1530 a pharmacy in Besancon, he should ask the public authority for a license and besides that undergo an examination by the clerks of the town [19].

The Brussels statutes declared in 1540 that it was prohibited to establish a pharmacy if the person concerned had not learned the profession as an apprentice in a pharmacy enjoying a good reputation, if he is not examined and when he is finally certified as a capable applicant by the physicians [17]. In 1576 we met very strict requirements for the master examination in Amiens: the candidate should have passed 4 years apprenticeship in a pharmacy of the town followed by a 6-year period as journeyman in pharmacies elsewhere. The examination starts with a speech in Latin for the physicians and the master apothecaries, followed by a theoretical examination, an examination on his knowledge of medicinal plants, the preparation and delivering of the masterpiece under supervision of 4 master apothecaries and a botanic examination in practice [20].

The towns with pharmaceutical municipal QA-regulations within the territory of the Burgundian State are in a chronologic order represented in Table 1. In Fig. 3, the relative importance of those four QA-regulations is indicated. It can be seen that two regulations—on quality and on education—got the most emphasis in the entire period from 1300 till 1600. Between 1400 and 1500 inspection of the pharmacy prevailed over the surveillance of medicines preparation.

3.4 Evolution of the Regulations in the Course of Time

The pharmaceutical statutes and by-laws evolved in the course of ages through exchange with other towns,
through own experiences and new insights, overruled by governmental decrees and other influences. The statutes of Amiens are a good example of such an evolution [20]:

(1) 1402. Statutes for pedlars, grocers and merchants in fats and wax.

(2) 1446. New statutes for pedlars, grocers and merchants on the:
- correct quality of the goods;
- inspection by the sworn colleagues;
- position of the widow.

(3) 1461. Confirmation of the statutes of 1446 in addition to one new paragraph where the strict surveillance of hawkers is formulated.

(4) 1484. The ordinance of king Charles VIII, regulating the education and duration of the apprenticeship, the inspections of the pharmacy and the exactness of the weights and measures.

(5) 1502. Statutes with the following additional clauses:
- inspection of the pharmacy once a year by the physicians of the town [24];
- examination by the master apothecaries;
- swearing an oath, promising to follow the standards and regulations of the profession;
- presence of a list with stocked herbs.

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<tr>
<th>Town</th>
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Fig. 3 The relative importance of the QA-regulations on education, quality, preparation control and inspection in the period 1300-1600.

(6) 1529. Additional clauses:
- compounded medicines are not allowed to be delivered without order of the physician;
- compounded medicines should be prepared according to the prescription of the antdotarium Nicolai Propositus or according to the physician’s prescription;
- the apothecaries should keep the prescriptions by putting them on a special hook.

(7) 1576. Municipal decree:
- regulation for becoming master apothecary;
- inspection of the pharmacy two times a year by 2 physicians, 2 master apothecaries and several representatives of the town magistrate.

(8) 1582. Supplementary clauses:
- it is prohibited to prepare or stock theriac, mithridate or laxatives made of inferior herbs;
- it is prohibited as well to prepare distillates without prescription.

We can see that in general the number of regulations and themes increases in the course of time and that the subjects are more and more explicitly formulated.

3.5 Surveillance of the Application of the Regulations

Pharmacy inspections were indispensable as is shown by an inspection report of the aldermen of Dijon in 1555 on fourteen pharmacies. They found that nine pharmacies were duly kept, but among those nine, two of them were managed by not examined apothecaries. From the other five pharmacies one was for sale and two others disposed obviously of an insufficient stock. So, in fact only half of the registered pharmacies in Dijon met the regulations of that time.

The regulations on the quality of hawkers’ merchandises and even of official apothecary ones were not superfluous as shows the condemnation in 1550 of the pedlar Pontus, who was banished from the town of Dijon during ten years for selling hay to a poor farmer instead of herbs. And in 1527 the apothecary Michel Josserandot was banished from the town of Chalon-sur-Saone during three years for manipulating powdered herbs [5].

3.6 Inventory of Quality Related Prescription Manuscripts and Books

Uniform prescriptions were a key factor in the QA
of mediaeval medicines. Most directions for preparing remedies are derived from standard treatises dating back to Greek-Egyptian and Arabian sources. In the late mediaeval pharmacist’s library, we come across four kinds of manuscripts and books: herbals, life style books, formularies and technique manuals [25]. Those categories overlap each other sometimes: a life style book may comprise prescriptions or a chapter on medicinal herbs and an herbal may contain technical directions for preparation.

3.6.1 Herbals

Within the territory of the Burgundian State a wide spread of herbal manuscripts and books in Latin, French and Middle Dutch were known. Before 1100 the manuscript De Viribus Herbarum by Odon de Meung was well known in the French parts of Burgundy, which was printed for the first time in 1477. From 1140 on the Livre des simples Mé dicines was frequently copied and a first printed edition came out in 1488.

The famous herbal from Leonhart Fuchs was published in 1542 in Latin entitled De Historia Stirpium, and in 1543 the translations in French and Middle Dutch (Den nieuwen Herbarius) were already printed. The herbal describes 500 plants of which 100 were exotic ones. The plants were drawn true to nature by Albertus Meyer, redrawn on wood by Henricus Füllmaurer and the wood-cutting was done by Veit Rudolf Speckle (Fig. 4).

3.6.2 Life Style Books

Versions of the Garden of Health (Hortus Sanitatis) were very popular in the late middle ages. In 1500 a French version was published in Paris: Ortus sanitatis translate de latin en francois. Another well-known life style manuscript from before 1100 concerns the Regimen Sanitatis, an extensive collection of diet recommendations, advices on the daily hygiene and daily exercises, written down in hexameters.

3.6.3 Formularies

A comprehensive encyclopedic compendium of everything known in nature, entitled Liber de natura rerum, was completed near Leuven in 1245 by Thomas van Cantimpré. De natura rerum depends on earlier sources and had a wide spread diffusion. Some years later a version in rhyme in Middle Dutch appeared and besides chapters on quadrupeds, on monstrous men of the East, on precious stones, chapter ten covers the medicinal and aromatic plants, including preparation and use (Fig. 5).
Two treatises on medicine prescriptions should be especially mentioned in this context: the Antidotarium Nicolai, already well known in the 13th century and the Dispensatorium of the physician and botanist Valerius Cordus. The Antidotarium Nicolai was in fact a sort of compendium with about 120 formulas selected from the Great Salerno Antidotary containing 1,200 formulas. The Dispensatorium Cordus was published in 1546 and can be considered as the prototype of a pharmacopeia, bringing order in the unsystematic corpus of prescriptions by describing only 225 medicinal plants—with their preparations—and which became a thorough guide for apothecaries in the territory of the Burgundian State. Between 1546 and 1670 fifty-three editions were published, most of them in Latin, five in Middle Dutch and another five in the French language [26].

3.6.4 Technique Manuals

Hieronymus Brunswig’s comprehensive book on distillation Liber de Arte Distillandi de simplicibus was in 1500 one of the earliest, devoted exclusively to chemical technology. Due to its in-depth description and detailed illustrations of distillation equipment and techniques, the book was considered to be an authoritative text well into the 16th century (Fig. 6).

![Fig. 6 A bain-marie still from Brunswig’s Liber de Arte distillandi de compositis. A wooden casing holds the alembics and the water, heated by the furnace below.](image-url)
As a follow-up, the *Liber de Arte distillandi de compositis* was published in 1512 with a treatise—entitled *Thesaurus pauperum*—on the preparation of cheap medicines for the poor and for people living in remote settlements.

### 3.7 Prescribed and in Practice Found Books and Manuscripts

Municipal and governmental ordonnances provide us with information on books and manuscripts which should be present in the apothecary’s library. Moreover, inventories of late medieval pharmacies and found prescriptions from apothecaries give us an idea which treatises were present in reality.

An analysis of those documents within the territory of the Burgundian State has been made [25] in chronological order represented in Table 2.

In the towns of Ypres, Antwerp, Amsterdam, Amiens Brussels, Lille, Delft and Middelburg formularies were prescribed by the magistrate. Inheritance inventories from Leyden, Rotterdam and Enkhuizen give us insight which prescription books were present in the pharmacies. And for two apothecaries in Dordrecht and Ghent the presence of prescription manuals is deduced from their prescriptions. Jan Vosse from Dordrecht prepared in 1390 four compounded medicines and their prescriptions are exact copies of those in the Antidotarium Nicolai, so he disposed probably of a manuscript of the Antidotarium. In the archives of Ghent, a collection of prescriptions is found of the apothecary Laurens Boele over the period 1461-1465. Twenty-four of them are copies of the Antidotarium Nicolai, thirty-one of the “Grabadin Mesue” and eighteen of both formularies, so he disposed most probably of both prescription books. Table 2 shows us that between 1310 and 1540 the Antidotarium Nicolai was usually prescribed or present as a formulary and that from 1568 on, the presence of the Dispensatorium Cordis predominates.

### 4. Conclusions

The quality of mediaeval medicines within the territory of the Burgundian State was assured by municipal and governmental pharmaceutical regulations. For thirty-two Burgundian towns, QA themes have been identified within those regulations and it was found that the regulations on education and quality got the most emphasis in the period 1300-1600. Between 1400 and 1500 inspection of the pharmacy prevailed over the surveillance of medicines preparation. In the course of time the number of regulations and themes increases and the subjects are more and more explicitly formulated.

Pharmacy inspections were indispensable as shown by an inspection report of the aldermen of Dijon in 1555 on fourteen pharmacies: in fact, only half of the registered pharmacies in Dijon met the regulations of that time. The regulations on the quality of hawker merchandises and even of official apothecary ones were not superfluous as shows the condemnation in 1550 of the pedlar Pontus and in 1527 of the apothecary Michel Josserandot who was banished from the town of Chalon-sur-Saone during three years for manipulating powdered herbs.

Uniform prescriptions were a key factor in the QA of mediaeval medicines. Within the territory of the Burgundian State we came across four kinds of prescription manuscripts and books: herbals, life style books, formularies and technique manuals. Based on ordinances and on heritage inventories in nineteen Burgundian towns it became evident that between 1310 and 1540 the Antidotarium Nicolai was usually prescribed or present as a formulary and that from 1568 on, the presence of the Dispensatorium Cordis predominates.

### References

[9] Leclaire, E. 1900. History of the Pharmacy in Lille from 1301 up Till the Year XI. Lille: Lefèbre-Ducrocq, pp. 132, 188, 190-1, 197, 319. (in French)