

Vilnius University Museum¹; Department of Drug Technology and Social Pharmacy²; Lithuanian University of Health Sciences; Museum of the History of Lithuanian Medicine and Pharmacy³, Lithuania; Faculty of Pharmacy⁴, Riga Stradins University, Latvia; Estonian Health Museum⁵; Institute of Pharmacy⁶, University of Tartu, Estonia

The national pharmacopoeias of the Baltic States

R. KONDRATAS¹, V. GUDIENĖ², Z. ŠIMAITIENĖ³, B. MAURINA⁴, K. PAJU⁵, T. HINRIKUS⁶, A. RAAL⁶

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A. Raal, Nooruse 1, Tartu 50411, Estonia
ain.raal@ut.ee

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After Estonia, Latvia and Lithuania proclaimed their independence in 1918 and began to create their national health care systems, one of their stated priorities was the formulation and publication of national pharmacopoeias. In order to accomplish this, working groups as well as commissions composed of pharmacists, medical specialists and even linguists had to be formed. The process was long and difficult. New terminology in native languages had to be created. Sources for the monographs had to be chosen, researched, analyzed and compared. There were organizational and financial problems. Nevertheless, by the late 1930s, all three Baltic States published their national pharmacopoeias. Officially, they were not able to use them for long because during World War II all three were occupied and annexed by the Soviet Union. Pharmacists in those countries were obliged to use the Soviet pharmacopoeias, although unofficially, they also made good use of their national ones. Currently, the European Pharmacopoeia is in use in Estonia, Latvia and Lithuania.

1. Introduction

From the 18th century until 1918, the Baltic States (Estonia, Latvia and Lithuania) were a part of the Tsarist Russian Empire. In 1721, Estonia and part of Latvia were annexed by Tsarist Russia. The former Swedish-Estonian lands, Estonia and Livonia became the Russian provinces of Estland and Livland. In 1772, Tsarist Russia annexed Latgale (Inflanty), and in 1795, as part of the third and last partition of the Polish-Lithuanian Commonwealth – most of Lithuania, the Duchy of Courland, and Semigallia. Estonia, Latvia and Lithuania became independent republics in 1918. From 1940–1990, the Baltic States were occupied and annexed by the Soviet Union.

Russian and German pharmacopoeias and manuals were used in pharmaceutical practice in the Russian Empire. The first Russian Pharmacopoeia, the *Pharmacopoeia Rossica*, was published in 1778, the second in 1871, the third in 1880, the fourth in 1891, the fifth in 1902, and the sixth in 1910. The seventh edition of the *Pharmacopoeia Rossica* appeared in Soviet Russia in 1925, and its supplement in 1933. In 1946, the eighth edition was published.

For several years after the Baltic States regained their independence in 1918, the Russian 6th edition (1910), the Russian Military edition (1913), and the German 6th edition (1926) pharmacopoeias were used as main references by pharmacists in the Baltic republics. Until the new national pharmacopoeias were published in the Baltic republics in the 1930s, the Tsarist Russian 6th edition Pharmacopoeia (1910), rather than the newer and slightly revised Soviet Pharmacopoeia (1925), was officially recognized and used in those countries (Kondratas et al. 2014).

2. Toward the national pharmacopoeias

After Estonia, Latvia and Lithuania proclaimed their independence in 1918 and began to create their national health care

systems, one of their stated priorities was the formulation and publication of national pharmacopoeias of these countries. In order to accomplish this, work groups as well as commissions composed of pharmacists, medical specialists and even linguists had to be formed.

In 1925, at the First Baltic Pharmacy Congress in Riga, the Latvian pharmacy delegate Davis Blumenthal (1871–1937) proposed to create a common pharmacopoeia for Estonia, Finland, Latvia and Lithuania, and translate it into the respective national languages. This proposal was not approved and each country chose its own distinctive path (The speeches... 1927).

The Estonian Pharmacopoeia was published in 1937, the Lithuanian in 1938, and the Latvian in 1940. After the Soviet occupation and annexation of the three Baltic States following World War II, pharmacists in these countries were obliged to use the Soviet Pharmacopoeia (Maurina et al. 2011). However, unofficially, they also made good use of their national pharmacopoeias. Currently, the European Pharmacopoeia is in use in Estonia, Latvia and Lithuania – as in the other member states of the European Union.

In the early 1930s, a decision was made by the Estonian, Latvian and Lithuanian pharmacy organizations, and the respective government agencies regulating their activities, to prepare national pharmacopoeias. Responsible persons were appointed to accomplish this task. Later, funding was provided and the plan was to complete the task in a few years, but it took much longer than anticipated.

Before the appearance of national pharmacopoeias, Estonia and Latvia published pharmacy manuals in their native languages. They appeared as follows: in Estonia in 1923 (with later editions in 1924 and 1937) and in Latvia in 1927 (*Manuale pharmaceuticum*, 1923; 1924; 1937; Maurina et al. 2011).

In 1937, Hugo Lembit Salasoo, editor of the Estonian Pharmacopoeia, introduced the new edition of the Finnish



Fig. 1: Estonian, Lithuanian and Latvian Pharmacopoeia.

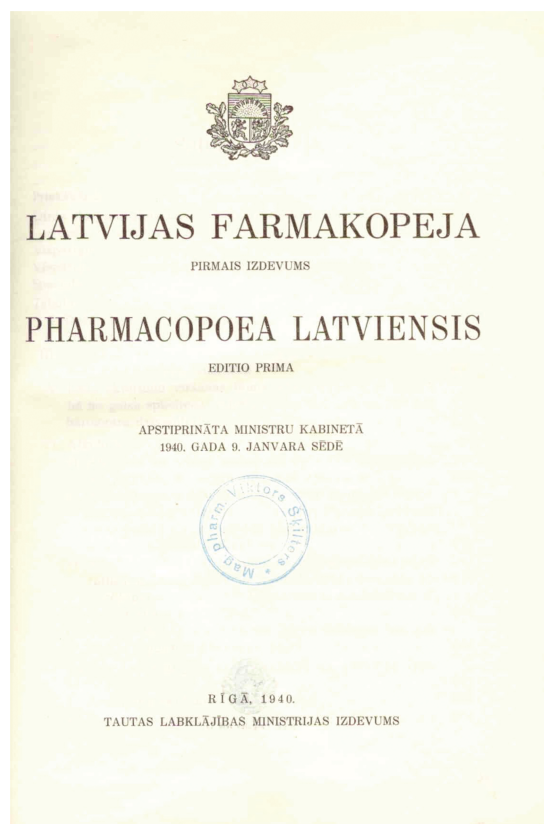


Fig. 3: Latvian Pharmacopoeia.

pharmacopoeia and reviewed the chronology of publication of pharmacopoeias in other countries (*Pharmacopoea Estonica Prima*, 1937: 13). He wrote that: “The *Pharmacopoeia Helvetica V* and the *Pharmacopoeia Jugoslavia* appeared in 1933, the *Pharmacopoeia Hungarica IV* in 1934, the second edition of the *US Pharmacopoeia* and the *Portuguese Pharmacopoeia* in 1936, and finally in 1937– the French, Polish and Finnish



Fig. 2: Hugo Salasoo (1901-1991).



Fig. 4: Janis Maizite (1883-1950).

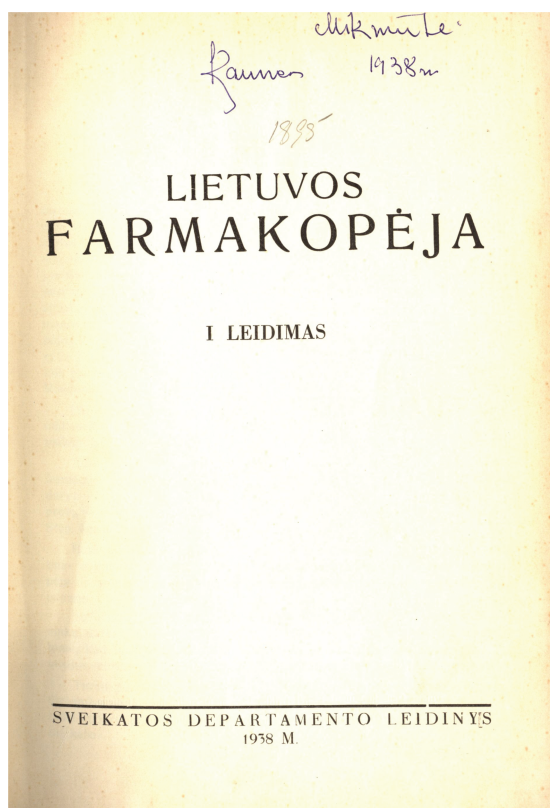


Fig. 5: Lithuanian Pharmacopoeia.

pharmacopoeias. It should be noted that today there are 27 pharmacopoeias in the world. 21 European states have pharmacopoeias of their own.”

2.1. The Estonian Pharmacopoeia

Estonia was the first of the three Baltic countries to publish its own national pharmacopoeia – the *Eesti Farmakopõa*. Effective and fruitful work started in 1933 after H. Salasoo was appointed head of the work group. H. Salasoo was born in 1901 in Tartu



Fig. 6: Steponas Nasvytis (1883-1976).

county and died in Australia in 1991. He received his undergraduate degree in pharmacy (1927), his master's degree in pharmacy (1928), and his doctoral degree in pharmacy (1932) from the University of Tartu. He was a member of the editorial board and the editor-in-chief of the journal *Eesti Rohuteadlane* (Estonian Pharmacist) from 1928–1933. In 1933, Dr. Salasoo became the founder, general manager, and head of the editorial commission established to formulate the *Pharmacopoeia Estonica* (1937) as well as the author of many of its monographs.

The *Pharmacopoeia Estonica* was compiled and published during an extremely short time – from April 1934 to January 1937. In April 1934, six special committees were formed to prepare monographs for the pharmacopoeia. The final manuscript of the pharmacopoeia was presented to the State Health Council (the *Riigi Tervisenõukogu*) in June 1936 and was accepted right away. The work was printed and made ready for distribution in January 1937 (Raal et al. 2006).

Several sources were used to compile the Estonian Pharmacopoeia. They were: the 5th edition of the Swiss Pharmacopoeia (1933), the 6th edition of the Russian Pharmacopoeia (1910), the 6th edition of the German Pharmacopoeia (1926) as well as selected monographs from other national pharmacopoeias, such as the Hungarian Pharmacopoeia (1934) (*Pharmacopoea Estonica Prima*, 1937). Monographs from the 5th edition of the Swiss Pharmacopoeia (*Pharmacopoeia Helvetica*) served as a model for the Estonian Pharmacopoeia. The correspondence between Dr. Hugo Salasoo and Prof. Johannes Stamm lets us surmise that the Swiss pharmacopoeia was chosen as a model in Estonia because it was available and being used at the Department of Pharmaceutical Chemistry of Tartu University (Personal correspondence, 1990).

The most complicated problem was the pharmaceutical terminology. Special terms that did not exist in the Estonian language had to be created. The main task for the editors was to reconcile monographs drafted by different committees terminologically, linguistically, stylistically and structurally.

Estonian pharmacists continued to have heated discussions, even after their pharmacopoeia was published. Soon after its publication, articles appeared in professional journals such as *Pharmacia* and *Eesti Rohuteadlane* (Estonian Pharmacist) pointing out mistakes found in the monographs of the pharmacopoeia, which were later corrected. Specific pharmaceutical problems were discussed in these journals even before the pharmacopoeia was compiled. Since several new analytical methods were described in the pharmacopoeia, H. Salasoo suggested that special courses should be organized for the pharmacists of Tallinn and Tartu in order to better acquaint them with these new methods.

2.2. The Latvian Pharmacopoeia

The compilation of the Latvian Pharmacopoeia took 17 years. While it was being compiled, the 6th edition of the Russian Pharmacopoeia (1910) and the 5th edition of the German Pharmacopoeia (1910) were used by practicing pharmacists in Latvia. These pharmacopoeias did not reflect the rapid progress and innovations of 20th century pharmacy. Latvian pharmacists intended to compile a pharmacopoeia based on current research (Viksna, 1993).

In 1923, the University of Latvia professor Jānis Maizīte (1883-1950) became the head of the pharmacopoeia formulation working group. He began his pharmacy career as an apprentice at the Vjazma Apothecary in Smolensk. In 1901, he passed the exam for pharmacy assistant at the University of Tartu and, in 1908, received his pharmacy degree there. In 1920, he was appointed Assistant Professor of Forensic Chemistry, and a year later Assistant Professor of Pharmaceutical Chemistry at the

Table 1: Scope of the pharmacopoeias

Country	Year of publication	Pharmacopoeia (pages)	General part (pages)	Special part (number of monographs)	Appendices/tables (pages)
Estonia	1937	751	26	805	76 (16 tables)
Latvia	1940	964	41	658	155 (11 tables and 6 drawings)
Lithuania	1938	528	one-page preface	616	47

University of Latvia. He was the Head of the Department of Pharmaceutical Chemistry until his death. His textbook on the introduction to practical pharmacy (1946) is the only book in Latvian on drug manufacturing technology up to the present day. Special committees were set up by J. Maizīte to compile the pharmacognosy, chemical, galenical, and pharmacology monographs. In 1924, he wrote in a Latvian pharmacy journal about the methodology to be used when compiling a pharmacopoeia and quoted the principles proposed by the Swiss pharmacist Alexander Tshirch in his article “Die Pharmakopöe, ein Spiegel ihrer Zeit” (1904): pharmacopoeia methods should be cheap, correct, and use a small amount of substances and reagents, should not require a lot of time and expensive equipment, and should not be too sensitive. Prof. Maizīte recommended that these principles be followed when formulating the Latvian Pharmacopoeia.

Pharmacy graduate students were used to verify and compare the medicinal preparations and analytical methods already in use. Information from German, Russian, British, USA, Belgian, Swiss, Italian, Romanian, Spanish, and Swedish pharmacopoeias was used by these students. Almost all their degree work was supervised by Professor Maizīte (Maizite, 1924).

2.3. The Lithuanian Pharmacopoeia

Compilation of the Lithuanian Pharmacopoeia also took a rather long time. Two working groups were set up (one in 1925 and the other in 1929). Each failed to meet the deadline. Thus, in 1934, a management change was made. Steponas Nasvytis (1883-1976), an adviser (expert) in the Pharmacy Section of the Department of Health, took over the lead of the working group from the pharmacist, researcher and educator Prof. Petras Raudonikis (1869-1950). In 1907, S. Nasvytis graduated from Kharkov University as an assistant pharmacist, and in 1918 received his pharmacy degree from Moscow University. That same year he returned to Lithuania, and together with three other colleagues, established a drug warehouse in Vilnius. He was a founder of Lithuanian professional associations, such as the Society of Lithuanian Pharmacists as well as one of the founders and editors of the journal *Farmacijos žinios* (Pharmacy News). In 1944, Nasvytis and his family fled from the Red Army to the West. They first lived in Austria and Germany, and then emigrated to the USA in 1948. He was active in Lithuanian-American cultural and political activities and died in Cleveland, Ohio.

In order to hasten the preparation of a pharmacopoeia in Lithuanian, Nasvytis proposed to translate the Soviet Pharmacopoeia, whose content he considered appropriate. Thus, the Lithuanian Pharmacopoeia is a translation of the 7th supplemented edition of the Soviet pharmacopoeia (1933). As stated in the introduction to the Russian language pharmacopoeia, the compilers made use of pharmacopoeias from the USA, United Kingdom, Germany, Holland, and Japan, among others. They also took into account the international requirements discussed and approved at the congresses devoted to the international standards for pharmacopoeias held in Brussels in 1902 and 1925 (the Brussels Conventions). In the 7th edition (1933) of the Soviet Pharmacopoeia, 116 new preparations were added, while 112 which were in the 6th edition (1925) were deleted. Comprehensive

articles about quality control, adulterated and counterfeit remedies, and other topics were prepared. It took about five years to translate the Russian text. The Lithuanian Pharmacopoeia was published in 1938. During the course of its preparation, practicing pharmacists actively made suggestions to the editorial group through the press, and did not feign from criticizing their procrastination (Kondratas et al. 2014).

3. Structure of the pharmacopoeias

All three pharmacopoeias were divided into three major parts or sections (Table 1):

[I] General information: standards, measures, descriptions of solutions and reagents, and methods of sterilization, including drawings of various kinds of apparatus/equipment and containers;

[II] Special information: monographs on therapeutic agents arranged alphabetically by their Latin names and next to the Latin names are synonyms and names of those materials in the native languages, standards for their strength and purity and their formulation; and

[III] Appendices/tables: the largest single amount or daily dose of poisonous and strong acting materials, medicines in the A and B lists, the specific gravity of solutions, and so forth.

The Estonian Pharmacopoeia is 751 pages long with 26 pages of general information, 805 monographs, and 76 pages of appendices including 16 tables. The Latvian Pharmacopoeia is 964 pages long with 41 pages of general information, 658 monographs, and 155 pages of appendices including 11 tables and 6 drawings. The structure of the Lithuanian Pharmacopoeia is different not only from the Latvian and Estonian ones, but also from the Soviet pharmacopoeia from which it was translated. The Lithuanian Pharmacopoeia is 528 pages long. There is a short single page preface by the publishers followed by the special part with 616 monographs. The general information is combined with 47 pages of supplements.

In all three national pharmacopoeias, the monographs were similar because they were based on older Russian, German and Swiss pharmacopoeias, which adhered to international standards for pharmacopoeias set at the International Congresses of Pharmacy in Brussels in 1902 and 1925. Even the Soviet Pharmacopoeia, which was translated by the Lithuanians, was based on earlier Russian pharmacopoeias and followed the Brussels Conventions. The Lithuanian Pharmacopoeia differed the most from the others because very little attention was paid to general information. In the Lithuanian Pharmacopoeia, there is a short preface by the publishers followed by the special part. The general part was combined with the supplements (appendices/tables).

It should be noted that the editors of the Lithuanian Pharmacopoeia made changes when translating from the Soviet pharmacopoeia. They radically shortened the general part, not translating and publishing 16 important articles from it, such as those about “Antidotes and first aid for poisoning”, “Biological methods for detecting medicinal properties”, “Biologic research into medicinal serums” and others. The special part was left practically unchanged.

In 1933, the editors of the Soviet Pharmacopoeia made significant changes to the content of the pharmacopoeia issued in

1925. These changes were carried over to the Lithuanian Pharmacopoeia. For example: they followed the recommendation of the Brussels International Congress (1925) and formulated a new monograph about endocrine preparations - *Organoterapeutica*. In this way, the Lithuanian Pharmacopoeia had articles about endocrine preparations and descriptions of such preparations as *Insulinum*, *Pituitrinum*, *Thyreoidinum*.

The Latvian Pharmacopoeia, which was published later, had none of these articles; while the Estonian Pharmacopoeia, which was published earlier, had articles on *Insulinum* and *Pituitrinum*. Lithuanian editors followed the Soviet example and excluded the article *Vinum*. Estonian and Latvian editors devoted several articles to medicinal wines. The compilers of the Soviet pharmacopoeia (1933) omitted over 100 articles on drugs from the previous edition (1925), though some of them are described in the Estonian and Latvian pharmacopoeias.

4. Content of the pharmacopoeias

In these national pharmacopoeias, drugs used for centuries were listed alongside the new discoveries of the 19th and 20th centuries: alkaloids, glycosides, synthesis products, sera, and vaccines. For example, one of the most popular remedies during the 17th-19th centuries was *Dover's Powder*, a mixture of opium and ipecacuanha root powder. One dosage form of that medicine, *Tabuletae opii et ipecacuanhae*, was mentioned in the Lithuanian Pharmacopoeia. *Pulvis Ipecacuanhae opiates* was also included in the Latvian Pharmacopoeia.

The alkaloids quinine, codeine, caffeine, cocaine as well as morphine compounds and the injectable form of morphine were mentioned in the national pharmacopoeias. Heroin, and 10 articles about various drugs containing opium, were described in the Lithuanian pharmacopoeia and an article on *Caput Papaveris* can be found in the Estonian Pharmacopoeia. There were monographs devoted to *Opium*, *Dover's Powder*, *Tinctura Opii crocata* in the Latvian Pharmacopoeia. *Hoffmann's Drops* (spirit of ether), a very popular 19th-century remedy, was mentioned in all three national pharmacopoeias.

Pills, suppositories, and capsules were described in all of the pharmacopoeias. There were separate monographs about each of these dosage forms. There were just a few monographs about tablets and injectable solutions. The Estonian Pharmacopoeia had just one general monograph about these dosage forms [*Compressi (Tabuletae)*] and two monographs about particular drugs: *Compressi Acetosol* and *Compressi Hydrargyri bichlorati*. The Lithuanian Pharmacopoeia described 23 tablet standards, and the Latvian only one (*Tabuletae Hydrargyri sublimati corrosive*). A general monograph about injections (*Injectabilia*) was prepared only by the Latvian compilers. They also wrote two specific monographs about injections: *Morphinum hydrochloratum* and *Solutio Natrii chlorati physiologica*. The Lithuanian Pharmacopoeia described three injections: *Solutio Coffeini natrio-benzoici 10% sterilisata pro injectionibus hypodermicis*, *Solutio morphii hydrochlorici 1% sterilisata pro injectionibus hypodermicis* and *Solutio natrii chlorati isotonica sterilisati*. More injections were presented in the Estonian Pharmacopoeia: *Solutio Natrii chlorati isotonica*, *Solutio Epinephrini hydrochlorici* and others. Tablets and solutions for injections had been prepared for several decades in pharmacy laboratories, but they were described only very briefly or not at all in the pharmacopoeias. For example, in 1920, even the small town druggist Kazys Mazonas was making cocaine, caffeine, and morphine ampoules. But 18 years later, only a few of those injections were described in the Lithuanian Pharmacopoeia. Only the Estonian Pharmacopoeia described *Tuberculinum* [623], smallpox vaccine [637],

Table 2: Chemical analyses in the pharmacopoeias

Country	Physical constants of active substances	Identification methods for cations/anions	Titrimetric solutions
Estonia	5	10/7	19
Latvia	5	–	19
Lithuania	5	–	17

and *Ephedrinum*; and only the Latvian Pharmacopoeia - *Chloraminum* and *Colchicinum*.

In all three pharmacopoeias, next to the newly synthesized drugs of the early 20th century such as the barbiturates (veronal), neosalvarsan, and others, popular 19th century drugs such as the compounds of mercury, arsenic, and antimony were also listed. Nearly 20 monographs in the Estonian, Latvian and the Lithuanian pharmacopoeias were devoted to materials of animal origin such as drugs from the Spanish fly (*Cantharis*, *Emplastrum Cantharidis*, *Emplastrum Cantharidis perpetuum*, *Tinctura Cantharidis*), the beaver's gland (*Castoreum*, *Tinctura Castorei*), from whales (*Spermacetum*) and others. Out of the many types of fat used in the 19th century, only pig fat and beef fat (*Sebum bovinum*) were mentioned. Pharmaceutically active materials extracted from plants did not replace galenic preparations made from hemp, henbane, cinchona bark, belladonna root and other plants.

The number of chemical analyses in the three national pharmacopoeias is given in Table 2. There are different methods for the determination of the main physical constants of active substances, such as melting point, congealing point, boiling point, specific gravity and specific rotation as described in the Estonian Pharmacopoeia. The most characteristic constants were printed in the monographs on active substances. Alongside, some other analytical methods concerning the quality of the active substances (loss on drying, dry residue, alcohol, acid number, iodine number, saponification number, drug extraction, etc) were also described. In the Latvian Pharmacopoeia there was a chapter entitled "General rules for the analysis of medicinal products", which described the determination of the main physical constants of active substances and the analytical methods mentioned above. The same main physical constants of active substances (melting point, congealing point, boiling point, specific gravity and specific rotation) were described only in monographs on active substances in the Lithuanian Pharmacopoeia. Their methods of determination were not described in separate monographs.

The Estonian Pharmacopoeia (Table 2) contained standards for the identification of ten cations (ammonia, hydrargyrum, potassium, calcium, magnesium, sodium, iron, lead, zinc, bismuth) and 7 anions (bromide, phosphate, iodide, carbonate, chloride, nitrate, sulphate). The methods for verifying the absence of the same cations and anions were also described in the specific monographs of the pharmacopoeia. Nineteen solutions for titrimetric analysis of active substances were listed for neutralization reactions, oxidation and reduction reactions, and so forth. In the Latvian pharmacopoeia, identification reactions for ions were described only in specific monographs. The number of titrimetric solutions described (19) was the same as in the Estonian Pharmacopoeia. There were no separate monographs on cations or anions in the Lithuanian Pharmacopoeia. They were only identified in the monographs on active substances. There were 17 titrimetric solutions described in the Lithuanian Pharmacopoeia. There were 131 monographs on galenic preparations in the Estonian Pharmacopoeia (Table 3). Some exotic drugs not native to Estonia, such as *Cortex Cinchonae*, *Cortex Cinnamoni*, *Cortex Condurango*, *Crocus*, *Flos Cinae*, *Flos Koso*, *Folium Sennae*,

Table 3: Galenical preparations in the pharmacopoeias

Country	All extracts	Dry extracts	Thick extracts	Liquid extracts	Syrups	Species	Ointments	Tinctures	Plasters
Estonia	27	15	1	11	17	8	23	47	9
Latvia	32	7	16	9	29	1	17	36	6
Lithuania	32	5	16	11	10	10	19	35	9

Fructus Cardamoni, *Fructus Lauri*, *Fructus Vanilla*, *Herba Lobeliae*, *Radix Senegae*, etc, were also described. There were 121 monographs on galenical preparations in the Latvian Pharmacopoeia and 115 in the Lithuanian Pharmacopoeia. Exotic plants were also described in the Latvian and Lithuanian pharmacopoeias: except for *Flos Kos* and *Fructus Lauri*. The Lithuanian Pharmacopoeia did not have monographs on *Fructus Vanilla* or *Herba Lobeliae* either.

5. Summary

The compilers of these national pharmacopoeias faced a difficult task. One of the most difficult problems was the creation of a new terminology in their native languages. There were also organizational and financial problems. The Estonian and Latvian working groups had to decide which monographs to choose from a number of sources. Also, some of the monographs which they chose from different pharmacopoeias had to be researched, analyzed and compared by graduate students and pharmacy students. The results of their research were used by the compilers. The Lithuanian compilers chose a different path, namely to translate an already published pharmacopoeia, the 7th supplemented edition of the Soviet Pharmacopoeia (1933). Despite all of the difficulties, all three countries managed to compile their own national pharmacopoeias. Even though after the occupation and annexation of the Baltic States by the Soviet Union in 1940, the pharmacists in those countries were obliged to use the Soviet pharmacopoeias, many continued to use their national ones as well.

Note: This work was done as part of a project on history of pharmacopoeias worldwide, initiated by the International Society for the History of Pharmacy under the supervision of Prof. Dr. François Ledermann, Bern, Switzerland.

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