

The History of the Norwegian Pharmacopoeias and Formularies

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Norway was rather slow to develop proper national pharmacopoeias to aid the pharmaceutical and medical profession, the result being that the pharmacists relied upon several foreign pharmacopoeias for their *composita* and *simplicia*, which often caused confusion.

Between 1380 and 1814 Denmark and Norway were in a close union with the same king. The first Danish pharmacopoeias as described by Poul Kruse were also authorized for Norway.

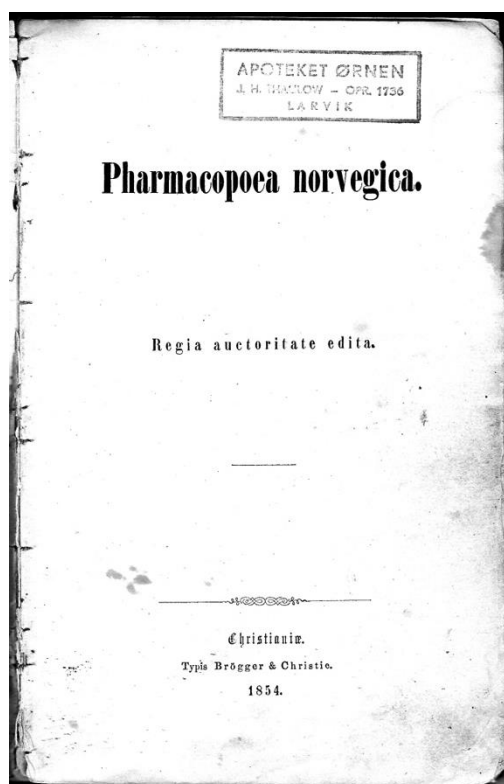


Fig 1: Title page of Ph.Norv.I. Some editions had a blank page for private comments after every printed page. It also gave the book a more proper size.

The pharmaceutical service in Norway developed slowly from the

establishment of the first retail pharmacy (The Swan) in Bergen 1595. Due to the union with Denmark, procuring, preparation and storage of medicines followed partly the Danish rules and partly the experiences of the owners of the retail pharmacy privileges. The first pharmacy owners came from different countries i.e. Denmark, Germany, The Baltic States and The Netherlands. It was the king that granted the privilege to open a pharmacy and from 1672 the owner had to be examined by the Faculty of "Medicae Doctoribus oc Apotheckerne" in Copenhagen.

Medicines were brought to Norway often directly from Bremen and Hamburg due to the shipping trade routes. By time it became necessary to implement a better standardization of the pharmaceutical service offered in Norway. The lack of a proper up-to-date pharmacopoeia implied that pharmacists and members of the medical profession used the German and English pharmacopoeias as their reference books. Especially the Württemberg and the Augsburg pharmacopoeias and later the German Pharmacopoeia were in common use. This was parallel with the development in Denmark.

The first pharmacopoeia in official use in Denmark and Norway was *Dispensatorium Hafniense* from 1658, which was authorized for the whole kingdom in 1672. At that time there were 20 pharmacies in Denmark and 6 in Norway. *Pharmacopoeia Danica I* appeared in 1772. In 1814 the following books were authorized in Norway: *Pharmacopoeia Danica II* from 1805, *Pharmacopoeia pauperum Danica* from 1799 and *Pharmacopoeia*

militaris from 1813. All of them were issued in Copenhagen.

Denmark ended up on Napoleons side during his wars, and in 1814 the Congress of Vienna decided that Norway should come under Swedish rule. Norway obtained a more independent status concerning internal affairs during this union, and wanted its own pharmacopoeia.

Pharmacopoeia Norvegica I

There were 24 pharmacies in Norway in 1814. The University of Oslo (Det kongelige Frederiks Universitet) had been established in 1811, and it took some time before the country was able to produce an official pharmacopoeia. The first independent Norwegian pharmacopoeia commission was appointed in 1820 with members from the medical faculty and three professors, one of them being professor and apothecary Hans Heinrich Maschmann (1775 – 1860). The work proceeded very slowly and in 1842 they realized that what they had produced so far, did not satisfy the requirements of that time and many alterations had to be done. The members of the commission felt too old or too occupied with other tasks to start again, so a new commission was appointed with only three members: Professor of Medicine Frederik Holst (1805 – 1866), professor of Physiology and Veterinary Medicine Christian Boeck (1798 – 1877) and apothecary Peter Møller (1793 – 1869).

“Pharmacopoeia Norvegica I” was finally printed in 1854. It was a pretty little book, and received a “mention honorable” at the Industrial Exhibition in Paris. But the content was not well received at all, and the discussions delayed the authorization until January

1. 1856. It had become customary to use other foreign official pharmacopoeias (i.e. the German Pharmacopoeias).

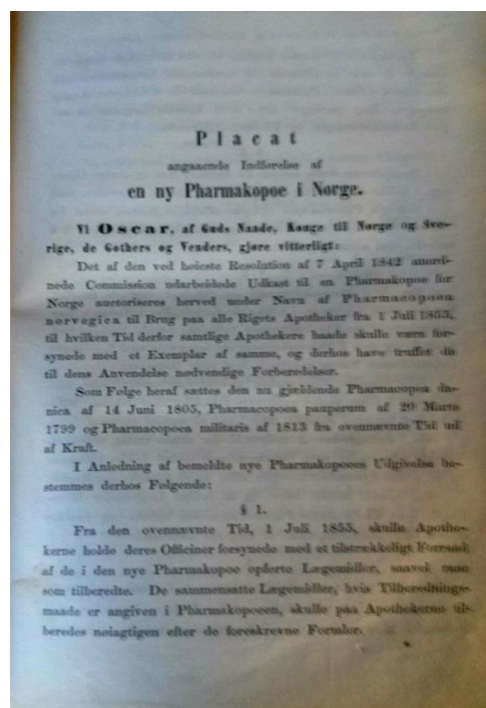


Fig. 2: The Swedish and Norwegian king Oscar I wrote the introduction to *Norvegica I*.

After all, the publication of the first Norwegian pharmacopoeia meant progress: Many obsolete drugs of plant- and animal origin were not given a monograph and new chemicals like morphine acetate and strychnine acetate had been added as well as physical constants like boiling points, molecular- and specific weights, solubility properties and chemical formulas. For poisons, a *Dosis media* and *Dosis particularis* were given in units following the old Norwegian medicinal pound, and there was a table converting the old medicinal weights to the metric system. The *Pharmacopoeia Norvegica I* was printed in Latin.

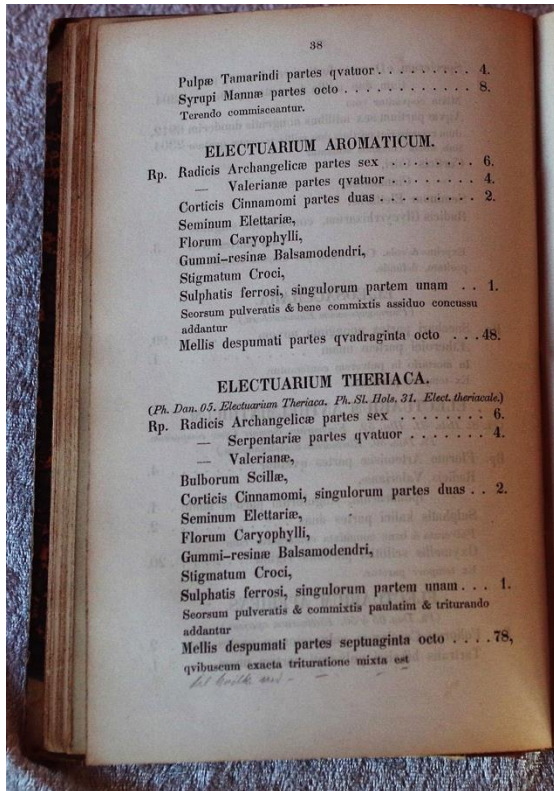


Fig. 3: *Electuarium theriaca*
Ph.Norv.I. One ingredient, *Opii pulverata pars una* follows on the next page.

Nordic Cooperation

At a meeting in Stockholm in 1865 between Denmark, Sweden and Norway, new principles for apothecary standards were agreed upon for the participating countries.

It reflected the development in the pharmacies from mainly handling plant-drugs to using more isolated active ingredients and chemicals. The pharmacies had to ensure the quality with chemical analysis. This meant quite large investments for each pharmacy, but this was possible in the Nordic countries because the privilege system ensured there were not too many pharmacies (each pharmacy had to have an official permit regulating the number of privileges). In small places, the pharmacies were often

allowed to have other incomes, e.g. being the local post-office. From 1865 and onwards collaboration between the Nordic countries with official and unofficial meetings resulted in the gradual modernization of the Norwegian pharmacopoeias up to the issue of the *Pharmacopoeia Nordica* in 1963.

Pharmacopoeia Norvegica II

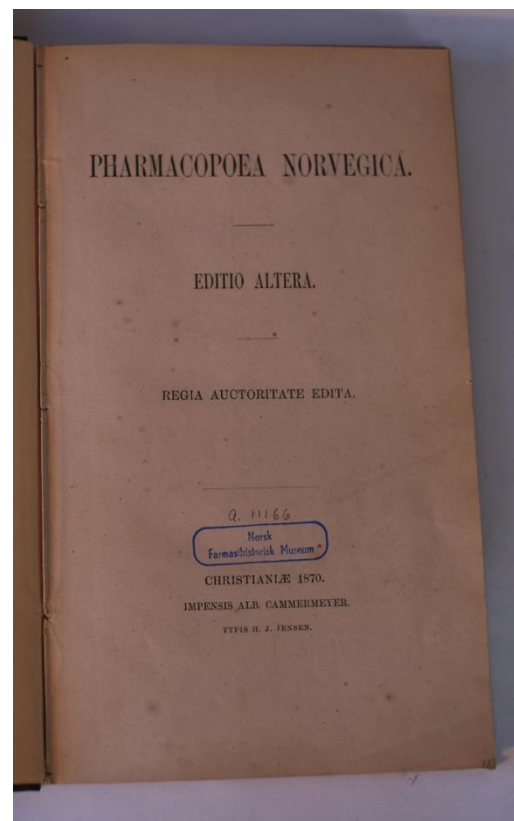


Fig. 4: Title page of *Ph.Norv.II*

A Norwegian commission for producing a new pharmacopoeia was appointed by king Carl IV in 1867, and *Pharmacopoeia Norvegica editio altera* was authorized from July 1. 1871.

This pharmacopoeia was also written in Latin, but Norwegian names of *Simplicia* and *Composita* were added. The metric system for volumes and weights were implemented. Of 687

agents in *Norvegica I*, 250 had been removed, among them *Electuarium Theriaca*. 60 new agents were added, like atropine, glycerin, phenol, santonin and glacies (!). The nomenclature was also somewhat different: *Essentia* became tinctures and *pingvolea* became *olea*. Some chemical tests for purity were introduced and even a quantitative analysis of the morphine-content in *Opium*. All pharmacies were required to have the necessary equipment for measuring specific weight, titration and for performing some chemical analysis. To compensate for the new expenses, the profit allowed on all medicines was increased, for some medicines from 50% to 100%. When a new edition had to be printed in 1879, there was also an *Additamenta ad Pharmacopoeia Norvegicae, editionem alteram*. It renewed the text for several chemicals like Chloroform and Glycerol and added new ones e.g. salicylic acid.

Pharmacopoeia Norvegica III

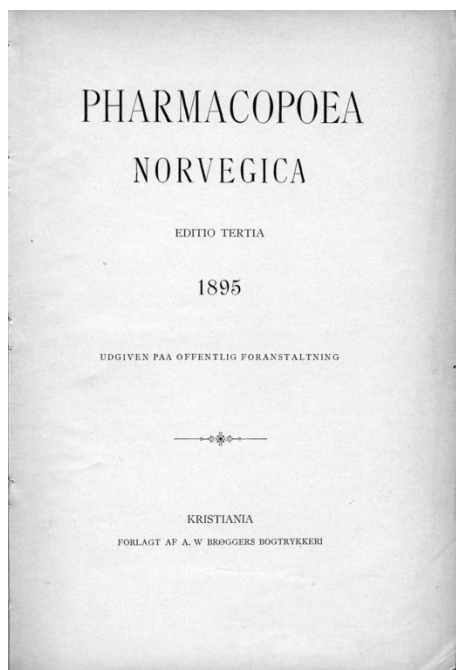


Fig. 5: Title page of *Ph.Norv. III*

In the fall of 1890, there was a meeting in Copenhagen between delegates from Denmark, Sweden and Norway, agreeing on new principles for the pharmacies. In Norway, a commission was appointed in 1891 for preparing a new pharmacopoeia, and *Pharmacopoeia Norvegica III* was authorized from April 1.1896. It was written in Norwegian, a fact that caused a lot of discussion and described as a very radical change. 110 *composita* from *Pharmacopoeia Norvegica II* were removed and 89 were added. 40 *simplicia* were removed and 14 were added. A new nomenclature was used: *Flos* for *Flores*, *Semen* for *Semina* etc, which was not well received by the pharmacies since old apothecary jars had to be marked with the new names. There were new regulations for cutting, pulverizing, preparing drug extracts and for storing light-sensitive drugs.

23. June 1906, Norway joined the international agreement of harmonization on standard production procedures and names for strong-acting drugs based on the principles adopted by the Conference in Brussels 1902. This was officially authorized when the Addendum to the *Pharmacopoeia Norvegica III* was issued in 1902.

Pharmacopoeia Norvegica IV

June 4. 1898, a permanent Norwegian pharmacopoeia commission was appointed, and it should cooperate with the other Nordic countries. Professor dr. med Poul Edvard Poulsson (1858 – 1935) was chairman, with dr. med Hagbarth Strøm (1854 – 1912), dr. med. Søren Block Laache (1854 – 1941), apothecary dr. Hans Henrik Hvoslef (1831 – 1911), apothecary Arnulf Bernhard Schøyen (1837 – 1902) and apothecary Claus Gustav Hansen (1850 – 1911) as members. Strøm,

Hvoslef and Schøyen had also been on the commission preparing *Norvegica III*.

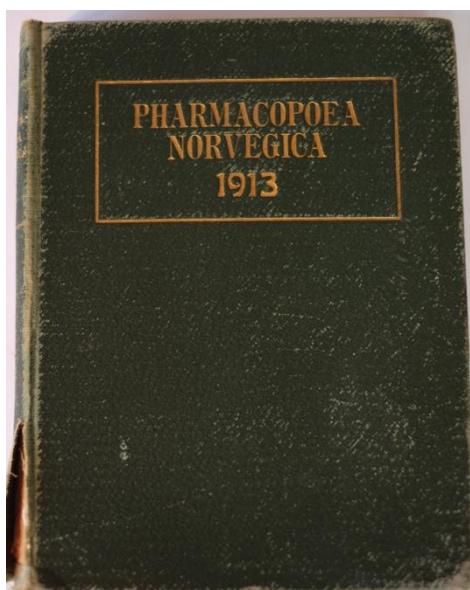


Fig. 6: Front page of Ph.Norv. IV

Pharmacopoeia Norvegica IV was printed in 1911, but was not authorized until 1914. The nomenclature was not much altered from *Norvegica III*, and it added 85 new medicines and removed 40. New preparation methods like percolation was described and the analytical part improved. The use of microscope for quality control was mandatory.

Pharmacopoeia Norvegica V

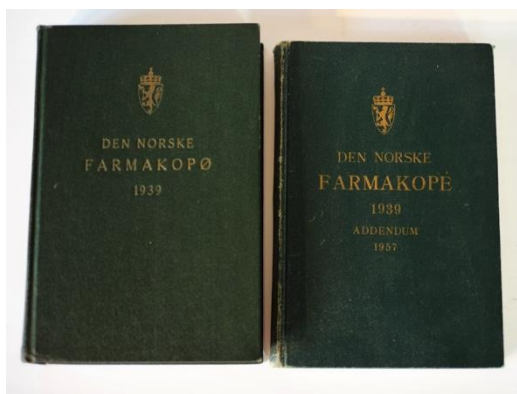


Fig. 7: Front pages of Ph.Norv. V and Ph.Norv. V Addendum

Pharmacopoeia Norvegica V was ready for print in 1937 but the Ministry ordered it to be printed with the new official Norwegian orthography – a mixture of the traditional written language and Norwegian dialects. It had to be translated and was finally printed in 1939, but then came World War II and it was not authorized until 1949.

The nomenclature was much changed. The chapter on collecting, drying and storage of plants was removed – maybe prematurely: The regulation that plant drugs had to be imported uncut, was still valid. Exceptions were *Cortex Qvillajae*, *Lignum Qvassiae* and *Lignum Guajaci*. Regulations on sterilizing were more extensive as was the chapter on melting points, boiling points and polarization. All pharmacies were required to have autoclave and tablet machine. At that time most medicines were still produced in the pharmacies, in the laboratory or *ex tempore* after an individual prescription from the physician. *Norvegica V* was criticized for not being up-to-date and it was even suggested to authorize the Danish Pharmacopoeia of 1948 instead! A supplement (Addendum) was edited in 1957 with many new monographs, e.g. 35 for new tablets. *Norv V* had only 11 monographs on tablets.

Pharmacopoeia Nordica I

The tradition of Nordic cooperation was strong and at a meeting in Stockholm in May 1946, a joint committee for a Nordic pharmacopoeia was discussed. The governments of Sweden, Denmark and Norway agreed and three members from each country were appointed. The Nordic Pharmacopoeia Council was established November 1948. Finland participated with an observer. The

result was a common pharmacopoeia for Denmark, Finland, Iceland, Norway and Sweden of 1963: Pharmacopoeia Nordica I. A special volume, dedicated to biological methods, was the first of its kind. Annual supplements finally brought the number of Nordic Pharmacopoeia standards up to 1200.

The European Pharmacopoeia

During 1975, the Nordic countries successively acceded to the Council of Europe Convention on the European Pharmacopoeia, and in 1978 the European Pharmacopoeia was authorized in Norway.

Formularies

Before 1900, almost all medicines were produced in a pharmacy. Then came new, patented medicines and the retail pharmacy owners were worried about losing the production of medicines to the medicinal industry. What we may call the NAF-movement (NAF was the Association of Proprietor Pharmacists) was started in 1927 to ensure that some production in the retail pharmacies was kept. The proposal was that the retail pharmacies should prepare the most used medicines themselves. At this time Norwegian and foreign pharmaceutical industry seemed to take over the medicines market in Norway, and the pharmacy-production would be limited to “orphan drugs” that were not profitable. The NAF-preparations should be prepared in the same way and sold in identical packaging from all pharmacies. The same ideas were implemented in Denmark at that time.

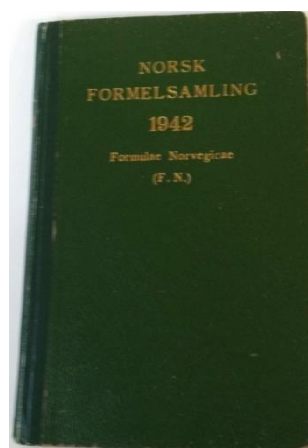


Fig. 8: This Formula was intended for physicians and included the medical indications and normal doses as well as the ingredients of the preparations

Although the NAF-movement was not an immediate success it kept the local production of medicines alive in the Norwegian pharmacies for a long time. Tablets had become very important at that time, and from 1930, all pharmacies had a tablet machine.

A special NAF- Formulary 1st edition was published in 1927 with additional issues in 1937, 1942, 1948, 1952, 1964 and 1980.

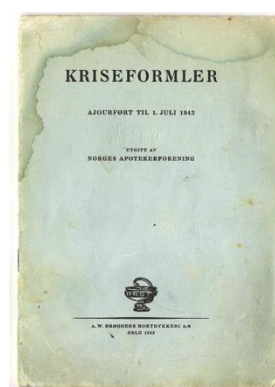


Fig. 9: During the Second World War there were shortages on some raw materials, and a leaflet with substitutes was published. This is the front page.

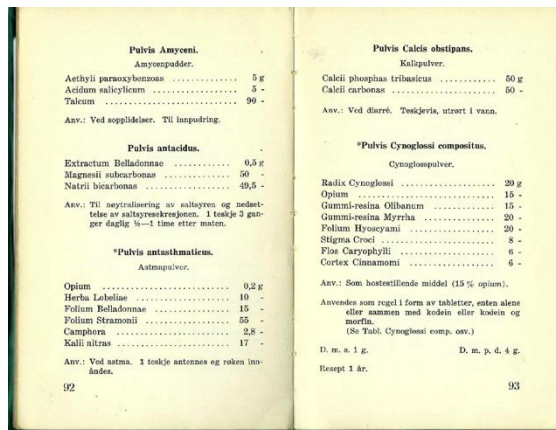


Fig. 10: Pages from the *Formulae Norvegicae (F.N.) 1947*. The asterisk means these recipes are from *Norvegica IV*

To ensure the quality, the Association of Proprietary Pharmacists employed a pharmacist from 1938 and established its own test laboratory in 1952. As late as 1960, almost 50 % of the medicines sold in pharmacies were produced by the pharmacy. Some pharmacies had specialized on production and got a license to sell to other pharmacies. At that time, there was a cheaper pharmacy-made alternative to many of the most important prescription-medicines too.



Fig. 11: The 1964 edition was a ring binder for easy replacement or addition of new pages.

A book by Ramstad and Christiansen on *simplicia* (published in 1943)

described products needed by the Norwegian pharmacies that were not described in the official pharmacopoeia. As an example of the variation in preparations on offer it was noted that one Norwegian industry (Apothekernes Laboratorium for Specialpreparater AS) in 1927 produced 1307 different products. The idea behind the NAF-movement was to compete in the market with guaranteed products well described by the official pharmacopoeia or the NAF-formulary. It will be understood that it was not easy to compete with the pharmaceutical industry with their contact with members of the medical profession. However, the official pharmacopoeia and the NAF-formulary continued to be used as references for medicines production in the pharmacies until the introduction of the *Pharmacopoeia Nordica*. During the 1970ies the production disappeared when new quality regulations moved the production to the pharmaceutical industry for good. But the NAF-formularies had been a great support for the production of medicines in the pharmacies and kept the interest of formulation alive among pharmacists. For many young pharmacists this was the introduction to drug formulation.

In 1975 there was a clear statement from the Health Authorities that both economic and practical circumstances made it difficult to establish fully satisfactory conditions for routinely production of medicines in all retail pharmacies. Therefore, centralization of the production of medicines would be necessary.

By the end of the century, a new law concerning pharmacies stated that production facilities were no longer needed in all pharmacies. In 2012 only 1 – 2 % of the medicines were produced in a pharmacy.

Bibliography

Kruse P. R.: The History of the Danish pharmacopoeias.

www.histpharm.org/ISHPWG Denmark

Sverre N. A.: Et studium av farmasiens historie, 2. edition by Y. Torud; Norges Apotekerforening, Oslo 1982.

Johannessen F. E. og Skeie J.: Bitre piller og sterke dråper. Norske apotek gjennom 400 år 1595 – 1995. Norsk farmasihistorisk Museum Oslo 1995.

Backe-Hansen K.: Farmakopékommisjonen 100 år. Cygnus 1998, hefte 2.

Christiansen T. & Ramstad E.: Usammensatte lægemidler; Norges Apotekerforening, Oslo 1943

Torud Y., Reizer S. og Hopstock A.: Apotekfarmasi gjennom 100 år. Norges Apotekerforening, Oslo 1981