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The original Croatian pharmacopoeia from 1901

"Ein vorzügliches Buch!"
("A first-rate book!")
A. Tschirch
(after reading the Croatian Pharmacopoeia)

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The second edition of the *Croato-Slavonian Pharmacopoeia* was published in Zagreb in 1901. As the original scientific work of two university professors, Gustav Janeček and Julije Domac, the *Pharmacopoeia* had strong scientific foundations and introduced a number of innovations. For the first time, a pharmacopoeia prescribed optical rotation for the examination of essential oils, introduced the quantitative analysis of active ingredients in galenic preparations, standardized the boiling points at the atmospheric pressure of 760 mm Hg, and was the only one to prescribe antidotes for herbal drugs and preparations which may cause poisoning. It received extremely positive reviews from the most prominent European pharmaceutical experts. It was written in two languages, Latin and Croatian, and had a wider significance, since it reflected the aspirations of the Croatian people for independence.

1. Introduction

Pharmacy has an exceptionally long tradition on Croatian soil. The first pharmacies were opened in Croatia shortly after the well-known edict of Emperor Frederick II sanctioned the separation of pharmacy from medicine in 1240. The oldest pharmacies were opened in Trogir (first mentioned in 1271), Dubrovnik (1272), Split (1282), Zadar (1289), Zagreb (1355) etc. (Tartalja 1959). The most famous is the *Pharmacy of the Friars Minor* in Dubrovnik, which has been continuously operating at the same place for more than 600 years. As a unique case in the history of pharmacy, this pharmacy survived all the development phases from the Dark Ages to modern pharmacy (Grdinić 1997). Another interesting fact worth noting: at the turn of the 14th and 15th centuries, Dante's great-grandson Nicolò Alighieri was a pharmacist in Zagreb. Dante himself was a member of a pharmaceutical guild in Florence (Grdinić 1998).

The establishment of the *Yugoslav* (today Croatian, CASA) *Academy of Sciences and Arts* (1861), the *Croato-Slavonian Pharmaceutical Association* (1858) and the pharmacy studies at the *Royal University of Franz Joseph I* in Zagreb (1882) created the conditions for the strong development of scientific pharmacy in Croatia, including the publishing of the relevant pharmacopoeia.

2. History of the pharmacopoeia

The oldest pharmacy records as the precursors of pharmacopoeia originated in China (around 2700 BC) and ancient Egypt (between 2000 and 1500 BC). The oldest collection of recipes written in Sumeran cuneiform originated in Iraq (around 2100 BC). Medical practice and pharmacy in ancient India were described in *Ayur-veda,* the holy book of medicine (1600 BC). Various documents about drugs were discovered in today's Israel and Iran.

Collections of pharmaceutical instructions were also written by the ancient Romans and Greeks (Hippocrates, Theophrastus, Heraclides, Dioscorides). Galen (2nd century) is particularly important, as his pharmaceutical prescriptions were the foundation of future pharmacopoeias. In the Middle Ages, after the fall of the Roman Empire, medical texts of Arab physicians (Rhazes, Albucasis, Avicenna etc.) were very influential.

Along with the provisions separating pharmacy from medicine, Frederick II issued the first official regulations on the preparation of drugs which had to be observed by pharmacists. It was the beginning of the publication of the pharmacopoeias that were not official yet. They had a variety of names: *Dispensatorium, Antidotarium, Ricettario, Luminare, Pharmacopoeia*. The oldest among them include *Antidotarium Nicolai* from Salerno (c. 1150), *Antidotarium* of Guglielmo da Saliceto and *Dispensatorium medicum seu de recta medicamentorum praeparatione* of Nicholas Myrepsi from the 13th century. The pharmacopoeia called *Nuovo Receptario composito* was published in Florence (1498) and later became known as *Ricettario Fiorentino* etc. (Grdinić 2001; Tartalja 1960). The first official German pharmacopoeia, is considered to be the *Dispensatorium* by Valerius Cordus (1515–1544). After a positive expert opinion of Nuremberg physicians, the Nuremberg Town Council approved its printing in 1546 (Friedrich 2000).

2.1. First pharmacopoeias in Croatia

At the time when Croatia was part of the Habsburg Monarchy (1527–1918), the following official pharmacopoeias were used: *Pharmacopoeia Augustana* (1581–1729 eds.), *Dispensatorium Pharmaceuticum Austriaco-Viennense* (1729–1770 eds.), and special pharmacopoeias published by Austria for its provinces, *Pharmacopoea Austriaco-Provincialis* (1774–1794 eds.) and *Pharmacopoea Austriaca* (1812–1869 eds.). Some provinces

used *Venetian Pharmacopoea* from 1781 and *Pharmacopoea Hungarica Editio I* from 1871. The military pharmacopoeia, *Pharmacopoea Austriaco-Castrensis* (1820), was the official pharmacopoeia of the Military Frontier (*Militärgrenze* - the area governed by the Austrian military authorities) (Grdinić 1999).

2.2. Hungarian pharmacopoeia in Croatian

The resistance of Croatian intellectuals, including pharmacists, to the use of Hungarian in the cultural, political and economic realms of Croatia was particularly intense in the late 19th century. This resulted in the publication of the first pharmacopoeia in Croatian and Latin in 1888. It was called *Pharmacopoea Croatico-Slavonica* (Croato-Slavonian Pharmacopoeia). (In this context, "Croatia" denotes the historical crown land of "Croatia proper", which corresponds to today's northern Croatia). However, it was only a translation (with minor modifications) of the Hungarian pharmacopoeia, *Pharmacopoea Hungarica Editio II,* from the same year. The pharmacopoeia in Croatian greatly facilitated the work of most pharmacists, their assistants and students whose native language was Croatian (Tartalja 1954). Early pharmacopoeias were written exclusively in Latin. The Romance nations (France, Spain, Italy) were the first to break this tradition and write their pharmacopoeias in vernacular, which was more suited to the needs of pharmacists and physicians. Aside from Croatia, multilingual pharmacopoeias were printed in Hungary, Japan, Greece, Switzerland and several other countries (Moeller 1921).

2.3. The first original Croatian pharmacopoeia

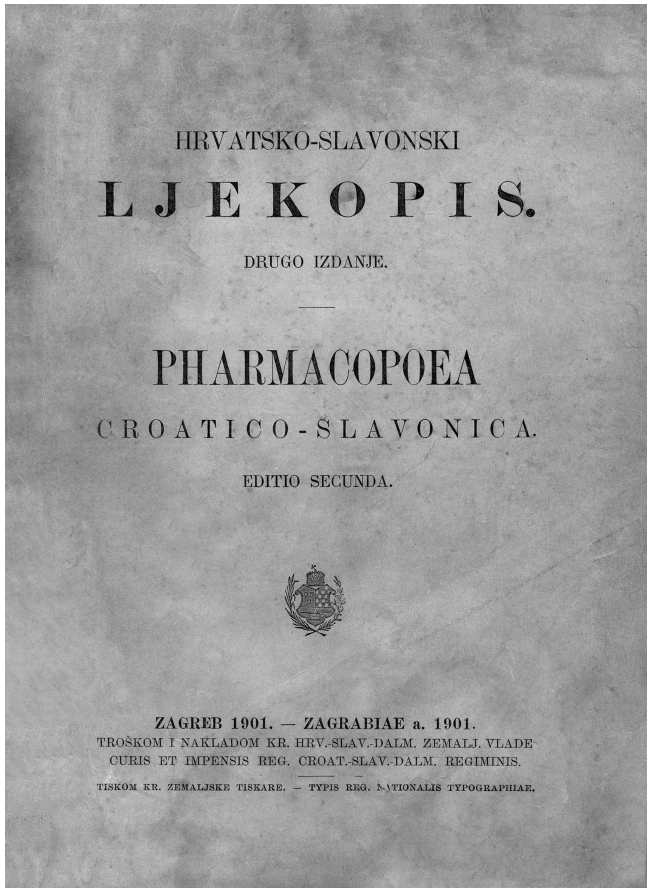
The original Croatian pharmacopoeia was published a decade later, in 1901. It was written in two languages, Croatian and Latin. Its title was *Hrvatsko-slavonski ljekopis. Drugo izdanje. / Pharmacopoea Croatico-Slavonica. Editio secunda.* (The Croato-Slavonian Pharmacopoeia. Second Edition.) (Fig. 1).

The *Croato-Slavonian Pharmaceutical Association (gremios)*, with the support of the *Croatian Pharmaceutical Society "Aesculap"*, made a survey among pharmacists about the medicines that should be included in the new pharmacopoeia. On the basis of that survey, Prof. Janeček compiled the general, chemical and galenic sections of the pharmacopoeia, while Prof. Domac compiled the pharmacognosy section of the new pharmacopoeia (Grdinić and Stefanini-Orešić 2001; Tartalja 1958).

The survey was initiated by the government in 1897, when they sent a letter to Antun Kögl, the president of the *Association*, inviting pharmacists "*to state which medicines and herbal drugs should be dropped in the new pharmacopoeia as obsolete and which new medicines and herbal drugs should be introduced*" (Archives 1897). The introduction of the survey was a new approach to the creation of pharmacopoeias.

The new pharmacopoeia contained 522 monographs, five of them general (*Elaeosacchara, Extracta, Syrupi, Tincturae, Unguenta*). Compared to the previous pharmacopoeia, it left out 69 monographs, for various reasons: unreliable therapeutic effects (*Aconitum* and *Cholchicum* and their preparations, *Aqua chlori* etc.), the possibility of replacement with other drugs and preparations (*Anisum stellatum, Mel crudum* and *rosatum, Vinum malagense* etc.), toxicity of preparations (*Hydrargyrum cyanatum*), nonstandard composition of preparations (*Stibium sulfuratum rubrum, Sal thermarum carolinarum* etc.).

The new pharmacopoeia contained 75 new monographs: *Acidum aceticum bis dilutum* (because of consistent quality), *Codeinum hydrochloricum* (because of better solubility than *Codeinum*), *Belladonnae folia* (most European pharmacopoeias had monographs with preparations of plant leaves instead of plant roots),


HRVATSKO-SLAVONSKI

LJEKOPIS.

DRUGO IZDANJE.

PHARMACOPOEA

CROATICO-SLAVONICA.

EDITIO SECUNDA.

ZAGREB 1901. — ZAGRABIAE a. 1901.

TROŠKOM I NAKLADOM KR. HRV.-SLAV.-DALM. ZEMALJ. VLADE

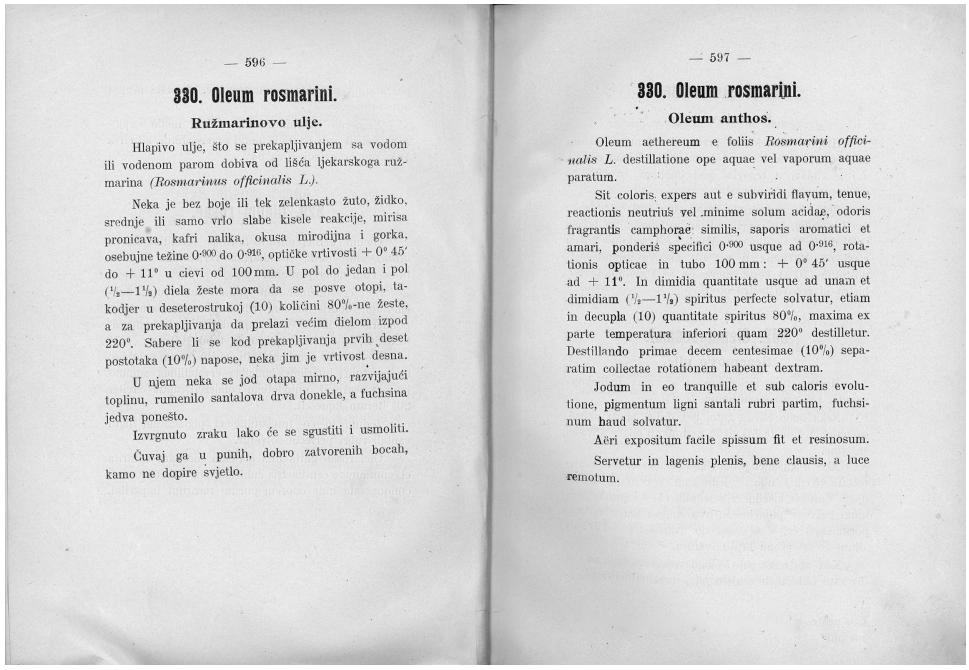
CURIS ET IMPENSIS REG. CROAT.-SLAV.-DALM. REGIMINIS.

TISKOM KR. ZEMALJSKE TISKARE. — TYPIS REG. N-VTIONALIS TYPOGRAPHIAE.

Fig. 1: Cover page of the Croato-Slavonian Pharmacopoeia published in Zagreb in 1901

Oleum pini pumilionis (more pleasant taste than *Ol. pini sylvestris*) and others.

The chemical part of the new pharmacopoeia introduced new analytical methods for the testing of the quality of chemical preparations (e.g. testing of organically bound chlorine for *Acidum benzoicum*, acidimetric determination of *Acidum phosphoricum* with phenolphthalein as indicator, testing for sucrose and dextrin in *Saccharum lactis*, determining the amount of iron in *Ferrum natrio-pyrophosphoricum*, testing for arsenic in *Zincum oxydatum* and *Zincum sulfuricum* etc.). It set new requirements for the purity of preparations that applied to: *Acidum boricum*, *Acidum chromicum*, *Acidum sulfuricum, Aether purus*, *Atropinum sulfuricum*, *Pilocarpinum hydrochloricum*, *Kalium chloricum*, *Spiritus*, *Chloroformium,* quinine preparations etc. It corrected some older values of physico-chemical constants (e.g. the relative density of *Oleum cacao*, *Oleum aurantii corticis,* the melting point and relative density of *Sebum ovile*, the melting point of *Cetaceum* etc.). Some monographs introduced additional constants, such as the saponification value and iodine value for all fats. For some fats and oils (such as *Axungia porci, Oleum amygdalarum dulcium*, *Oleum olivarum, Oleum ricini, Oleum lavandulae, Cera,* etc.), it introduced additional tests for purity and the possibility of adulteration with other substances. Essential oils (*Oleum anisi, Oleum citri, Oleum rosmarini* etc.) already included relative density, but the new pharmacopoeia introduced a new chemical constant, optical rotation, which was used as a supplement test for the quality of a preparation. It was the first time that a pharmacopoeia included optical rotation to test the purity of galenic preparations (Fig. 2).



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330. Oleum rosmarini.

Ružmarinovo ulje.

Hlapivo ulje, što se prekapljivanjem sa vodom ili vodenom parom dobiva od lišća ljekarskoga ružmarina *(Rosmarinus officinalis L.)*.

Neka je bez boje ili tek zelenkasto žuto, židko, srednje ili samo vrlo slabe kisele reakcije, mirisa pronicava, kafri nalika, okusa mirodijna i gorka, osebujne težine 0·900 do 0·916, optičke vrtivosti + 0° 45′ do + 11° u cievi od 100 mm. U pol do jedan i pol ($^1/_2$—$1^1/_2$) diela žeste mora da se posve otopi, takodjer u deseterostrukoj (10) količini 80%-ne žeste, a za prekapljivanja da prelazi većim dielom izpod 220°. Sabere li se kod prekapljivanja prvih deset postotaka (10%) napose, neka jim je vrtivost desna.

U njem neka se jod otapa mirno, razvijajući toplinu, rumenilo santalova drva donekle, a fuchsina jedva ponešto.

Izvrgnuto zraku lako će se sgustiti i usmoliti.

Čuvaj ga u punih, dobro zatvorenih bocah, kamo ne dopire svjetlo.

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330. Oleum rosmarini.

Oleum anthos.

Oleum aethereum e foliis *Rosmarini officinalis L.* destillatione ope aquae vel vaporum aquae paratum.

Sit coloris expers aut e subviridi flavum, tenue, reactionis neutrius vel minime solum acidae, odoris fragrantis camphorae similis, saporis aromatici et amari, ponderis specifici 0·900 usque ad 0·916, rotationis opticae in tubo 100 mm : + 0° 45′ usque ad + 11°. In dimidia quantitate usque ad unam et dimidiam ($^1/_2$—$1^1/_2$) spiritus perfecte solvatur, etiam in decupla (10) quantitate spiritus 80%, maxima ex parte temperatura inferiori quam 220° destilletur. Destillando primae decem centesimae (10%) separatim collectae rotationem habeant dextram.

Jodum in eo tranquille et sub caloris evolutione, pigmentum ligni santali rubri partim, fuchsinum haud solvatur.

Aëri expositum facile spissum fit et resinosum.

Servetur in lagenis plenis, bene clausis, a luce remotum.

Fig. 2: Monograph *Oleum rosmarini* from the Croato-Slavonian Pharmacopoeia (1901), which introduced optical rotation as a new physico-chemical constant

It also prescribed a quantitative analysis of active ingredients not only for preparations with strong effects, such as extracts and tinctures containing alkaloids (e.g. *Extractum* and *Tinctura belladonnae*, *Extractum chinae*, *Extractum* and *Tinctura opii*, *Extractum strychnii*, *Extractum hyoscyami foliorum,* etc.) but consistently for other preparations (determination of: mercury in *Emplastrum hydrargyri*, iron in *Pilulae ferratae*, total amount of potassium in *Sapo kalinus albus* etc.).

For *Extractum* and *Tinctura belladonnae*, it introduced the determination of total alkaloids by extracting them with chloroform from an alkaline solution. Its identification was performed by Beckman's reaction (with $NaNO_2$, H_2SO_4 and KOH), and the reaction with ammonia in an aqueous solution after evaporation of the chloroform extract. For *Extractum* and *Tinctura opii*, morphine was determined by extracting with ethyl acetate from an ammonia solution. The reagents for the qualitative analysis were $FeCl_3$ and $K_3[Fe(CN)_6]$ (Janeček 1899).

Furthermore, the boiling points are standardized to a pressure of 760 mm Hg (Polašek 1906).

In the pharmacognosy section of the pharmacopoeia, the macroscopic descriptions of herbal drugs are more detailed (e.g. *Absinthium, Lichen islandicus, Mentha, Quercus, Salvia, Valeriana* etc.). Most herbal drugs have not only a macroscopic, but also an original microscopic/anatomical description (e.g. *Althaea, Linum, Taraxacum, Valeriana* etc.). A particularly important contribution was the introduction of antidotes in the monographs on herbal drugs with strong effects, such as *Digitalis*, *Ipecacuanha, Scilla, Secale cornutum* etc., which may cause poisoning. Such antidotes are emetics, tannins and black coffee for *Folia digitalis*, alkaline agents and laxatives for *Radix ipecacuanhae*, purgatives, tannins, wine brandy and camphor for *Secale cornutum*. Antidotes were also introduced for all other preparations with strong and very strong effects, such as: *Atropinum sulfuricum, Morphinum hydrochloratum, Extractum scillae, Extractum secalis cornuti siccum pro pulvere* etc. (Fig. 3.) (Janeček 1902).

For some herbal drugs (*Anisum vulgare, Arnica, Senna, Rheum, Tilia* etc.), it makes special mention of the possible admixtures and replacements with other plants and how to recognize them.

The comparison with the German pharmacopoeia, *Pharmacopoea Germanica, Ed. IV,* from 1900, which was created at the same time, clearly shows that the Croatian pharmacopoeia was not inferior to the German one concerning the modern scientific approach of the time. The German pharmacopoeia was published before the Croatian one, but only because of the better printing capabilities.

The new Croatian pharmacopoeia was ready and approved for publication in January 1900 (Croatian Archives 1900) in the print run of 600 copies, which was financed with 9,000 crowns from the government. However, because of low printing capacities, the printing was finished only in November 1901 (Croatian Archives 1901).

As a commentary to the pharmacognosy part of the pharmacopoeia, Domac wrote *Uputa u farmakognoziju* (Introduction to Pharmacognosy) in 1899, which made it easier for pharmacists to use the pharmacopoeia and served as an excellent textbook on pharmacognosy to generations of pharmacy students.

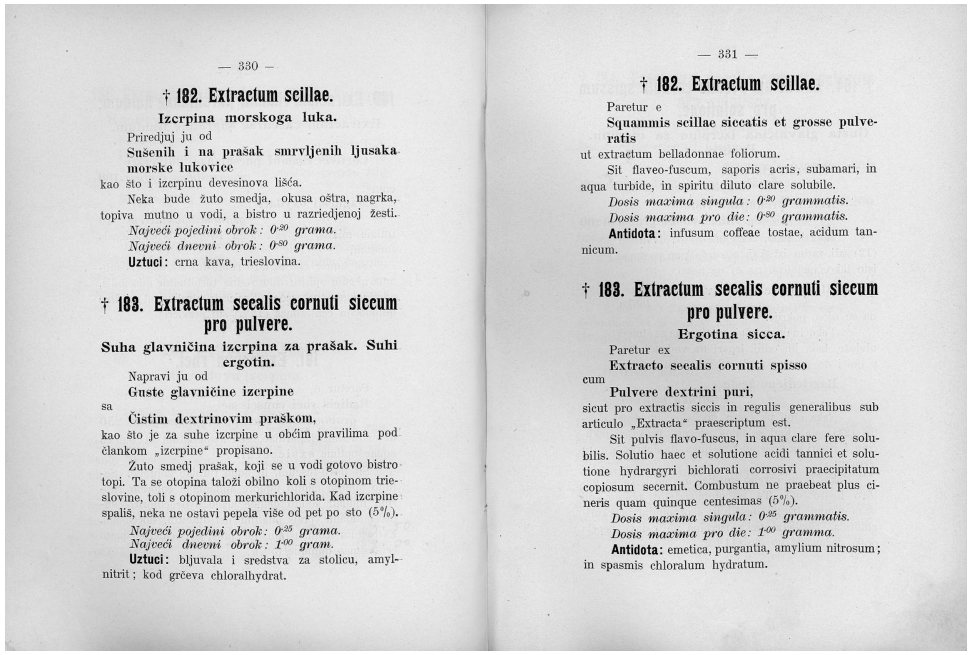
Since the pharmacopoeia had particularly rigorous requirements for the purity of medications, Croatian pharmacists ordered medications of highest purity from Austrian and Hungarian wholesale pharmacies. The price lists of those wholesale pharmacies used special labels for such preparations: "*for the Croato-Slavonian Pharmacopoeia, Second Edition*" (Vrgoč 1943).

All the pharmacies in Croatia were reorganized in order to meet the requirements of the new pharmacopoeia. The reorganization and adaptation of pharmacies to operate in the new conditions was personally supervised by Prof. Domac for several years.

2.4. Original Croatian pharmacopoeia as seen by European pharmacy

The new Croatian pharmacopoeia was mentioned by the most respected pharmaceutical experts and scientists of the time.

Alexander Tschirch (1856–1939), one of the most respected pharmaceutical experts of the age, a professor of pharmacognosy and the director of the Pharmaceutical Institute of the University of Bern, who was the author of the Swiss pharmacopoeia, Ed. IV, from 1907 (Friedrich and Schmidt 1990), commented after reading the Croatian pharmacopoeia: "*Ein vorzügliches Buch!"* (*A first-rate book*!) (Vrgoč 1921).



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† 182. Extractum scillae.

Izcrpina morskoga luka.

Priredjuj ju od

Sušenih i na prašak smrvljenih ljusaka morske lukovice

kao što i izcrpinu devesinova lišća.

Neka bude žuto smedja, okusa oštra, nagrka, topiva mutno u vodi, a bistro u razriedjenoj žesti.

Najveći pojedini obrok: 0·20 grama.

Najveći dnevni obrok: 0·80 grama.

Uztuci: crna kava, trieslovina.

† 183. Extractum secalis cornuti siccum pro pulvere.

Suha glavničina izcrpina za prašak. Suhi ergotin.

Napravi ju od

Guste glavničine izcrpine

sa

Čistim dextrinovim praškom,

kao što je za suhe izcrpine u obćim pravilima pod člankom „izcrpine“ propisano.

Žuto smedj prašak, koji se u vodi gotovo bistro topi. Ta se otopina taloži obilno koli s otopinom trieslovine, toli s otopinom merkurichlorida. Kad izcrpine spališ, neka ne ostavi pepela više od pet po sto (5%).

Najveći pojedini obrok: 0·25 grama.

Najveći dnevni obrok: 1·00 gram.

Uztuci: bljuvala i sredstva za stolicu, amylnitrit; kod grčeva chloralhydrat.

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† 182. Extractum scillae.

Paretur e

Squammis scillae siccatis et grosse pulveratis

ut extractum belladonnae foliorum.

Sit flaveo-fuscum, saporis acris, subamari, in aqua turbide, in spiritu diluto clare solubile.

Dosis maxima singula: 0·20 grammatis.

Dosis maxima pro die: 0·80 grammatis.

Antidota: infusum coffeae tostae, acidum tannicum.

† 183. Extractum secalis cornuti siccum pro pulvere.

Ergotina sicca.

Paretur ex

Extracto secalis cornuti spisso

cum

Pulvere dextrini puri,

sicut pro extractis siccis in regulis generalibus sub articulo „Extracta“ praescriptum est.

Sit pulvis flavo-fuscus, in aqua clare fere solubilis. Solutio haec et solutione acidi tannici et solutione hydrargyri bichlorati corrosivi praecipitatum copiosum secernit. Combustum ne praebeat plus cineris quam quinque centesimas (5%).

Dosis maxima singula: 0·25 grammatis.

Dosis maxima pro die: 1·00 gramma.

Antidota: emetica, purgantia, amylium nitrosum; in spasmis chloralum hydratum.

Fig. 3: Monographs *Extractum scillae* and *Extractum secalis cornuti siccum pro pulvere* from the Croato-Slavonian Pharmacopoeia (1901) in which antidotes were prescribed for the first time

Josef Moeller (1848–1924), the well-known professor of pharmacognosy at the University of Innsbruck and the University of Vienna, wrote in a private letter to Professor Domac in 1902: "*Ich habe das Buch mit wahrem Genuss durchgelesen und teile Ihnen mit, dass die kroatische Pharmakopoe besser ist als das deutsche Arzneibuch, wenigstens in dem meiner Beurteilung zugänglichen pharmakognostischen Teile. Besonders sind mit grossem Geschick die mikroskopischen Karaktere herangezogen soweit dieselben nötig sind*" (*I read the book with particular pleasure and I can tell you that the Croatian pharmacopoeia is better than the German book of remedies, at least in respect to the pharmacognosy parts that I am familiar with. The microscopic descriptions are presented especially well to the necessary extent*) (Vrgoč 1924).

The Austrian pharmacochemist Alois Kremel published an extensive review of the Croatian pharmacopoeia in the *Pharmaceutische Post* (Kremel 1902), where he said: "*... Während die erste Auflage dieses Arzneibuches eine nahezu wortgetreue Anlehnung an die ungarische Pharmakopoe war, ist das neue Arzneibuch eine ganz selbständige Arbeit. Wenn sie auch, wie alle neueren Pharmakopoen eine gewisse Uebereinstimmung mit dem Deutschen Arzneibuche zeigt und sich in pharmakognostischer Hinsicht an die österreichische Pharmakopoe anschliesst, so weist sie doch eine solche Fülle von selbständiger Arbeit und soviel des Interessanten und Bemerkenswerten auf, dass man dazu die Autoren der Pharmakopoe sowohl, als auch die croatischen Apotheker nur beglückwünschen kann, welche, durch den hohen Grad von Vollkommenheit der an sie gestellten Anforderungen, mit diesem Werke in die ersten Reihen der Standesgenossen aller Länder treten*" (*While the first edition of this book of remedies almost literally relied on the Hungarian pharmacopoeia, the new book of remedies is a completely independent work. Like other recent pharmacopoeias, it shows certain similarities with the German book of remedies and relies on the Austrian pharmacopoeia from the aspect of pharmacognosy, yet it shows so much independent effort, as well as many interesting and noteworthy things, that we have only words of praise for the authors of this pharmacopoeia and the Croatian pharmacists. The high degree of perfection with which they met the requirements of this book puts them in the first rank among their peers from all countries*). At the end, he concludes: "*Im Ganzen ist die neue croatische Pharmakopoe eine in jeder Beziehung auf der Höhe der Zeit stehende, den Verfassern zur Ehre gereichende Arbeit, welche rückhaltlose Anmerkung verdient*" (*As a whole, the new Croatian pharmacopoeia stands at the pinnacle of its age in every respect; this work honors its authors and deserves the highest recognition*).

Professor Bocquillon-Limousin (1856–1917), doctor of pharmacy and chemist from the Pharmaceutical School of Paris, pointed out that the Croatian pharmacopoeia was a leader in the field and that other countries should see it as a role model for many aspects of new pharmacopoeias (Batistić and Mirković 1924).

G. M. Forrester, the editor of the reputable London journal *The Chemist and Druggist*, wrote to Domac in 1925, expressing his interest in the Croato-Slavonian Pharmacopoeia and asking where he could obtain a copy for his library (Archives 1925).

During the EU accession negotiations (2008), the Croatian pharmacist profession was evaluated by a team of experts from the EU Member States: "*The team found that the Croatian pharmacy system was at a high level with respect to the standards of education, practice and regulation*" (EC 2008). It is a distant reflection, we believe, of the high standards of the Croatian pharmacopoeia in 1901.

2.5. Political significance of the original Croatian pharmacopoeia

When the Croato-Slavonian Pharmacopoeia was published, Croatia was ruled by Count Károly Khuen-Héderváry, who was the Croatian *ban* (ruler) from 1883 to 1903. He was a Hungarian, pushing anti-Croat policies to turn Croatia into a Hungarian province. It was the time of student protests against the Hungarization of Croatia. On the other hand, Croatian intellectuals participated in a powerful movement for statehood. In October 1895, the students of the University of Zagreb burned the Hungarian flag during the visit of the Emperor Franz Joseph I to Zagreb, clearly showing the Croatian public mood towards the policies of *ban* Khuen-Héderváry (Gross 1969; Racko 1990).

Under such political circumstances, in which Prof. Domac was appointed dean of the Faculty of Philosophy (1901/02), the

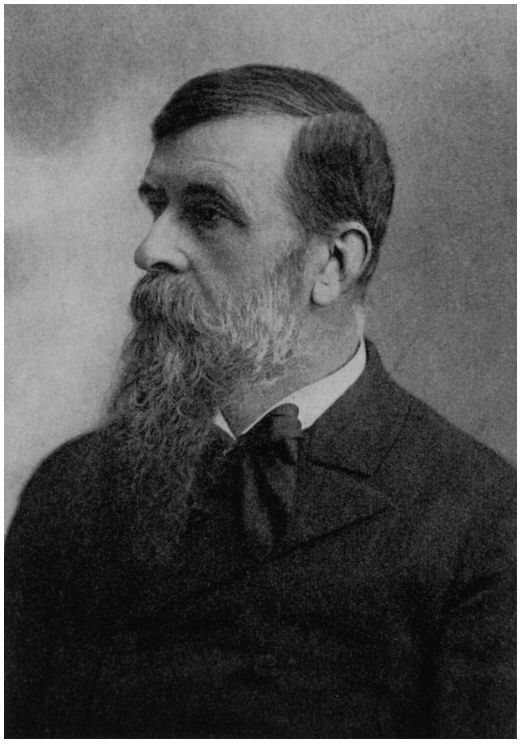

Fig. 4: Gustav Janeček, author of chemical and galenic sections of the Croatian pharmacopoeia from 1901. Photo (before 1924), Zagreb, from: Gustav Janeček (1848–1929), Life and Achievements. Grdenić D (ed.), Croatian Academy of Sciences and Arts, Zagreb, 2002, p. 2.

Fig. 5: Julije Domac, author of the pharmacognosy section of the Croatian pharmacopoeia from 1901. Portrait of J. Domac as Rector of the University of Zagreb (1924), located in the University of Zagreb administration building

original Croatian pharmacopoeia in Croatian and Latin was published. Therefore, the Croato-Slavonian Pharmacopoeia had not only scientific value, but also expressed the intellectual resistance of the academic community faced with the Hungarization of Croatia. Since only those nations with a high degree of sovereignty had their own pharmacopoeias, the Croato-Slavonian Pharmacopoeia can be seen as a reflection of the aspirations for independence of the Croatian people and a sign of their relatively high degree of sovereignty.

2.6. The authors of the original Croatian pharmacopoeia

Gustav Janeček (1848–1929) was born in Konopište, Czech Republic. He graduated pharmacy from the University of Prague (1871) and obtained his PhD in chemistry (1875) from the Charles University, where his mentor was Prof. A. Lieben, with a thesis on the electrolysis of water. He lived in Vienna from 1875 to 1879, first as an assistant at the University of Vienna and later as an assistant and assistant professor at the Technical High School in Vienna, making a name for himself in forensic medicine. He became associate professor of chemistry at the University of Zagreb (1879). Two university chemistry institutes of the University of Zagreb were built according to his instructions (in 1884 and 1919). Gustav Janeček was one of the founders of the study of pharmacy at the Faculty of Philosophy in Zagreb (1882) and the first professor of general and pharmaceutical chemistry (1882–1924). As the first legal expert, he was the founder of Croatian forensic chemistry. Janeček mentored 17 PhD theses in chemistry at the University of Zagreb. He was Dean of the Faculty of Philosophy (1885/86, 1895/96, 1906/07) and the Rector of the University of Zagreb (1908/09), a full member of the Yugoslavian Academy of Sciences and Arts (YASA) from 1887 and its president from 1921 to 1924, and a member of the Czech Academy of Sciences and Arts in Prague. He founded the wholesale pharmacy *Isis* (1918, later *Medika*) and the drug factory *Kaštel* (1921, later *Pliva*), becoming one of the main drivers of Croatian pharmaceutical industry.

He published most of his scientific papers in Croatian, in the journal *Rad* (published by YASA). Janeček wrote the first university chemical manual in Croatian (1883, revised edition in 1907), a textbook on general chemistry (1919), and the second edition of the Croato-Slavonian Pharmacopoeia (1901) together with Prof. Domac.

He founded the *Society for Landscaping and Embellishing the Plitvice Lakes and their Surroundings* (1893) and encouraged activities which made it possible to declare the Plitvice Lakes a national park (1949) (Grdenić 2002; Grdinić 2002) (Fig. 4).

Julije Domac (1853–1928) was born to a family of pharmacists in Vinkovci, Croatia. He graduated pharmacy in Vienna (1874) and continued his scientific work under the chemistry professor A. Lieben. When his father fell ill, he left the University of Vienna (1876) and took over his father's pharmacy in Vinkovci. He returned to science upon the invitation of Prof. Lieben. Upon his recommendation, Domac went to Graz (1879) to work under Prof. L. Pebal, where he obtained his PhD (1880) with a thesis on the structure of hexene and mannitol. He was the first Croat whose scientific works in chemistry were published in an international chemistry journal. After returning to Croatia (1882), he worked as a chemistry teacher at the Royal Great Gymnasium in Zemun and later in Zagreb (1882–1896). At the University of Zagreb, he was appointed honorary professor (1887), associate professor (1896), and full professor of pharmacognosy (1899–1924).

Julije Domac founded the first independent *Institute of Pharmacognosy* in the world (1896) and Croatian scientific pharmacognosy. He was Dean of the Faculty of Philosophy (1901/02) and Rector of the University of Zagreb (1911/12). He published high-school textbooks on organic chemistry, which had three editions (1893, 1899, 1906), inorganic chemistry (1901), a university textbook on pharmacognosy (1899), and numerous professional and popular scientific papers on chem-

istry and pharmacognosy. He co-authored the second edition of the Croato-Slavonian Pharmacopoeia (1901). The annual award of the Croatian Pharmaceutical Society for exceptional achievements in pharmacy is called after Julije Domac (Inić and Kujundžić 2011)(Fig. 5).

3. Conclusion

The Croato-Slavonian Pharmacopoeia was published in Zagreb in 1901 as the original work of university professors Gustav Janeček, who wrote the chemical and galenic parts, and Julije Domac, who wrote the part about pharmacognosy.

The pharmacopoeia had strong scientific foundations. It was the only pharmacopoeia to prescribe optical rotation for the examination of essential oils. It introduced the quantitative analysis of active ingredients in galenic preparations and standardized the boiling points at the pressure of 760 mm Hg. It was the only one to prescribe antidotes for all herbal drugs and preparations which may cause poisoning (preparations with strong and very strong effects). It received extremely positive reviews from the most prominent pharmaceutical experts: A. Tschirch, J. Moeller, A. Kremel and others. Its significance was not only scientific, but also political, as it reflected the aspirations of the Croatian people for independence.

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