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Adolf Thierry and the first pharmaceutical factory in Southeast Europe

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The paper explores the beginnings of pharmaceutical industry development in Croatia and the establishment of the first pharmaceutical factory in Southeast Europe. Adolf Thierry de Chateauxvieux (St. Pölten, 1854 – Pregrada, 1920), a nobleman hailing from France, immigrated to Croatia at the end of the 19th century. He bought the *Angjelu čuvaru* (*Guardian Angel*) pharmacy (1892) in the small town of Pregrada and established the first pharmaceutical factory (1894) in this part of Europe. The factory had an equipped laboratory, a production facility, a storage room for raw materials and balsams, a room for packaging and shipping finished products and a commercial office. Production was mainly based on herbal remedies. The most famous were *Thierry's Balsam* and *Thierry's Centifolia Ointment*, both registered and patented in London (1900). By virtue of Adolf Thierry's entrepreneurial spirit and skilful product advertisement, his medicinal preparations were distributed across Europe, America, India and Africa, a testament to which is the well-preserved and researched documentation.

1. Introduction

With the advancement of science in the 19th century, the isolation of active ingredients from herbal drugs began and pharmaceutical chemistry in pharmacy laboratories gradually developed into an independent science. This triggered the development of pharmaceutical industry in pharmacies that were at the time organised for manufacturing large quantities of medicine, which was more cost-effective and ensured medicines of greater quality. Particularly alkaloids (morphine, quinine, papaverine, strychnine) were produced, obtained through isolation from herbal drugs. Apart from alkaloids, galenic preparations, especially fluid extracts, were also industrially produced. Galenic pharmacy includes production of medicinal preparations in pharmacy laboratories and was named after the ancient Greek physician and philosopher Galen (129 AD – c. 210 AD) (Schmitz 1998). Many of today's big pharmaceutical companies, such as *Merck* and *Schering* in Germany, *Hoffmann-La Roche* in Switzerland, *Burroughs Wellcome* in England, *Etienne Poulenc* in France and *Abbott*, *Smith Kline*, *Parke-Davis*, *Eli Lilly*, *Squibb* and *Upjohn* in the USA, started out as manufacturers and suppliers of medicines in 19th century pharmacies (Cowen and Helfand 1990; Corley 2003). In the Czech Republic, a well-known pharmaceutical company is Zentiva, the beginnings of which can be traced back to the 15th century, when the *Black Eagle* pharmacy, one of the oldest ones in the Czech Republic, was opened in Prague. The pharmacy was purchased by the Fragner family (1857), who built a pharmaceutical factory in the suburb of Prague. The company first manufactured medicines in 1930 (<https://www.zentiva.com/>). The state-owned company BB-NCIPD Ltd (National Center of Infectious and Parasitic Diseases) in Bulgaria is also worth mentioning, which began not as a pharmacy laboratory, but as the *Antivariola Laboratory* (1881). Later, it merged with the *Bacteriological Institute* and *Antiplague Institute* in 1898 and started manufacturing antivariola vaccine. The company became independent as late as 2000. Three years later, it joined *The Bulgarian Generic Pharmaceutical Association* (<http://bulbio.com/en/>).

Meanwhile, the development of synthetic organic chemistry ushered in the production of organic compounds (especially dyes), first in university laboratories, and then in chemical factories across Europe and America in the late 19th century. Due to the fact that pharmaceutical chemistry and pharmacology became scientific

disciplines at the end of the 19th century, these chemical companies discovered the medicinal application for their products and grew into a pharmaceutical industry. These are, for example, *Bayer* and *Hoechst* in Germany, *Ciba*, *Geigy* and *Sandoz* in Switzerland, *Imperial Chemical Industries* in England and *Pfizer* in the USA (Drews 1998; <https://cen.acs.org/articles>; Sneader 2005).

The aim of this research was to present the beginnings of industrial production of medicines in Croatia within a European context, i.e. as the first country in Southeast Europe which, through the efforts of certain pharmacists, began manufacturing medicinal preparations in production facilities bearing all of the marks of pharmaceutical industry, relying primarily on galenic products (*specialities*).

2. The development of pharmaceutical industry in Croatia

The beginnings of the industrial production of medicines in Croatia can be traced back to the town of Pregrada in Hrvatsko zagorje and are associated with the Thierry family of pharmacists. Adolf Thierry (1854–1920) opened the first industrial and manufacturing facility for the production of medicines in this part of Europe (1894) (Grdinić 1996). At that time, Croatia was part of the Austro-Hungarian Empire, an imperial and royal dual monarchy (1867–1918) and a multinational state in Central Europe ruled by the Habsburg dynasty. In today's Hungary, which was a part of the former Austro-Hungarian Empire, pharmaceutical industry is thought to have begun in 1901, when pharmacist Gedeon Richter obtained a license to manufacture medicines in his own pharmacy laboratory in Budapest. With the increase in medicine production, primarily of organotherapeutic preparations, Richter moved his pharmacy laboratory into a newly built factory in 1907 (Zajta 1968; <http://www.gyogyszeresztortenet.hu/>).

The success of the pharmaceutical factory in Pregrada encouraged pharmacist Eugen Viktor Feller (1871–1936) to open his *Sveto Trojstvo* (*Holy Trinity*) pharmacy (1899) in Donja Stubica, a town in Hrvatsko zagorje near Pregrada, and to build a medicinal preparations factory and laboratory two years later (1901), where his world famous preparation *Elsa-fluid* was manufactured (Fatović-Ferenčić and Ferber-Bogdan 1997). This was followed by a period during which Croatia saw the development of scientific labora-

tories for chemistry and pharmacy. In Zagreb, the *ISIS d.d.* drug store was founded (1918), a joint stock company for the production and distribution of drugs and chemicals with a view to manufacturing medicines and chemicals and intermediating in the process of procurement of pharmaceutical and chemical preparations (Zagreb National Archives 1918). The company, together with the Hungarian pharmaceutical company *Chinoïn*, established the *Kaštel* factory for the production of chemical and pharmaceutical products in Karlovac, Croatia, which was a precursor to *Pliva*, the most famous Croatian pharmaceutical factory. The first president of *Kaštel* was university professor Gustav Janeček (1847–1929), the founder of Croatian university chemistry and pharmaceutical industry in the contemporary sense. In 1928, *Kaštel* moved to Zagreb, due to a better connection with suppliers and buyers, as well as a more efficient form of collaboration with university professors. Vladimir Prelog (1906–1998), a university professor of organic chemistry and winner of the Nobel Prize in Chemistry (1975), established *Kaštel*'s first research laboratory for medicinal chemistry in 1936. The laboratory was a driving force in further scientific research and development of the scientific institute in the *Pliva* pharmaceutical factory (Kovačević 2002; Milčec 1996).

2.1. Adolf Thierry, the founder of industrial medicine production in Croatia

The Thierry de Chateaufieux family is of noble origin, hailing from France. Adolf Thierry (Fig. 1) was born in St. Pölten, Austria, on 14 June 1854.



Fig. 1: Adolf Thierry with his youngest daughter Adolfinia, undated, Inventory No DVT-396, courtesy of the Pregrada Municipal Museum "Dr Zlatko Dragutin Tudjina", Croatia.

In 1873, he enrolled in pharmacy studies in Vienna, on the basis of his internship exam and two years of internship in a pharmacy. In the winter semester of the academic year 1873/74, he took an experimental physics course with Prof. V. Lang (1838–1921), a botany course with Prof. E. Fenzl (1808–1879), a zoology course with Prof. L. K. Schmarada (1819–1908) and a chemistry course with the renowned Prof. F. Rochleder (1819–1874). In the summer semester (1874), he additionally took a course in mineralogy with Prof. A. E. Reuss (1811–1873) (Vienna University Archives 1874). He took his final exams from 1878 to 1880. He passed his first rigorous exam on 24 May 1878 and his second on 4 July 1878. However, he did not pass the third, which was held on 21 July 1879, and had to retake it on 26 June 1880. Among the examiners were world renowned professors A. Lieben (1836–1914), professor of chemistry, and A. E. Vogl (1833–1909), professor of pharmacognosy (Fig. 2) (Vienna University Archives 1878–1880).

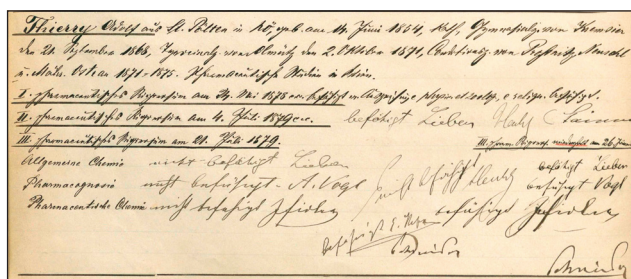


Fig. 2: The register of final exams taken by Adolf Thierry as part of the pharmacy studies in Vienna (1878 – 1880), *Rigorenprotokoll der Pharmazeuten* PH 61.2, p. 96, courtesy of the Vienna University Archives.

In search for work, Adolf Thierry moved with his family to the town of Pregrada, located in Croatia's Hrvatsko zagorje region (around 1887). The first written record regarding his immigration is found in Pregrada's Registry of Birth Certificates, which contains the birth certificate of his oldest daughter Josipa Paula (1887) (Croatian State Archives 1887). The available documentation does not list the reasons for his arrival to this small town in Zagorje, but one can assume that it was much more difficult to open and independently run a pharmacy in Austria than in a rural town in the Austrian-Hungarian Empire. In that period (at the end of the 19th century), there were few educated pharmacists in Croatia because, prior to the establishment of the university pharmacy course in Zagreb (1882), it was necessary for candidates to go to other European university centres to study pharmacy (Memorial book 1958). Thus the immigration of pharmacists from Europe to Croatia was not that uncommon.

With his wife Josefina (Josipa), née Hersch (1860–1933), he had eight children: Alfred (1883–?) (Zagreb University Archives 1908), Adolf Alfons (1885–1897), Josipa Paula (1887–?), Karlo (1889–?), Vilhelmina (1890–1942), Vilim Friedrich (1894–1980), Adolf Gustav (1897 – 1897) and Adolfinia Marija (1899 –?) (Croatian State Archives 1887 – 1942). His son Vilim completed the graduate pharmacy programme at the University of Zagreb (1920) (Pregrada Municipal Museum 1920). After his father's death, (Pregrada, 21 June 1920), he took over the family business and ran it until the end of the Second World War, when their property was nationalised after a new regime was established (Validžija 2008). Having acquired a great reputation in society, Adolf Thierry applied for the recognition of a title of French nobility within the former Hungarian state and submitted his application to the government in 1904 (Croatian State Archives 1904). For this purpose, he submitted his birth certificate, the birth certificates of his father and grandfather and the genealogy of the Thierry family (Croatian State Archives 1910a). After the subsequent addition of other necessary documents, his application was approved in 1910 (Croatian State Archives 1910b). From then on, the family could use its title of nobility, coat of arms and nobiliary particle *de*, as in *de Chateaufieux*, within the Hungarian state (Fig. 3). The following year, the government approved Thierry's request for adding the title of nobility to his children's birth certificates (Croatian State Archives 1911).



Fig. 3: The ring bearing the coat of arms of the noble Thierry family, a facsimile of the photograph belonging to the permanent display of the Thierry Pharmacy Collection in the Pregrada Municipal Museum “Dr Zlatko Dragutin Tujdina”, Croatia.

2.2. Thierry purchases the “Angjelu čuvaru” pharmacy and opens an industrial facility for medicine production

After coming to Pregrada, Adolf Thierry became the manager of the *Angjelu čuvaru* pharmacy (1889), which he purchased and took over (1892) from the successor of the pharmacist Hippolith Bilinski, the first pharmacist in Pregrada (Bilinski et al. 2018; Bilinski et al. 2019). The transcript of a document of the Pregrada District (1893) shows that Thierry received a license to run a public pharmacy and a pharmaceutical craft enterprise in Pregrada on the basis of a reply by the Royal Croatian-Slavonian-Dalmatian Land Government, of 9 November 1892 No 52.906., which was also approved by the Pregrada District on 7 September 1893 (Pregrada Municipal Museum 1893a). In those days, pharmacy was considered a craft enterprise until the new Pharmacy Act was passed in 1894, which distinguished it from a craft. Thus, pharmacies in Croatia became health institutions (Tartalja 1954).

After taking over the pharmacy, the Thierry family relocated to a new building designed by the famous Zagreb architect and builder Gjuro Carnelutti (1854–1928), the construction of which was approved by the Pregrada District on 29 June 1893, a fact also confirmed by plans containing the approval (Fig. 4). The ground floor of the newly constructed building housed the *Angjelu čuvaru* pharmacy, which operates in the original setting even today, with the original inventory preserved. The upper floor housed an abun-

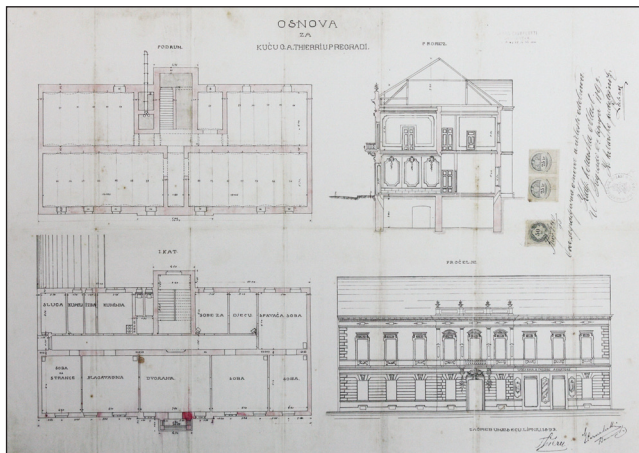


Fig. 4: The 1893 plan of the building which housed Thierry’s pharmacy *Angjelu čuvaru* (*Guardian Angel*), Thierry Pharmacy Collection, showpiece No 484-487, Pregrada Municipal Museum “Dr Zlatko Dragutin Tujdina”, Croatia.

dantly equipped residential area of the Thierry family. Behind the main building, a factory for the production of medicinal preparations was built, the first of its kind in this part of Europe, which began operation in 1894 (Report 1900; Grdinić 1997). In 1899, the factory had 18 employees and its annual turnover amounted to 700 000 forints. After about ten years, the factory had 20 to 25 employees and an annual turnover of 150 000 Krone (Report 1906).

The header of the memorandum of Adolf Thierry’s company states that the headquarters and industrial facility for the production of medicinal preparations is located in Pregrada (Croatia), with a simple address: Thierry, Pregrada. These were mostly galenic preparations (*specialities*) which were dispensed in Thierry’s pharmacy and distributed abroad. Raw material quality testing was performed according to the Croatian and Slavonian Pharmacopeia from 1888, and later according to the second edition of the Croatian and Slavonian Pharmacopeia from 1901, the original Croatian pharmacopeia (Inić and Kujundžić 2012). A *control book* from 1916 regarding the inspection of Adolf Thierry’s pharmacy at the time was preserved as a part of the Thierry family legacy. The *control book* states that the pharmacy was organised and clean, containing all necessary literature (pharmacopeia, Pharmacy Act) and pharmacy instruments (scales, microscope, apparatuses for medicine preparation). The tested reagents, chemicals and pharmaceutical preparations were according to the regulations of the pharmacopeia which was in effect at the time. The inspected medicinal drugs were fresh and valid (Pregrada Municipal Museum 1916). The memorandum illustration shows that the factory area had a laboratory with necessary apparatuses and laboratory glassware (water still, press, funnels, percolators, mortars, graduated cylinders and others), a storage room for medicinal drugs and other raw materials necessary for the production of medicinal preparations, a storage basement for balsams, a production area for the feeding of finished products, a room for product packaging and shipping

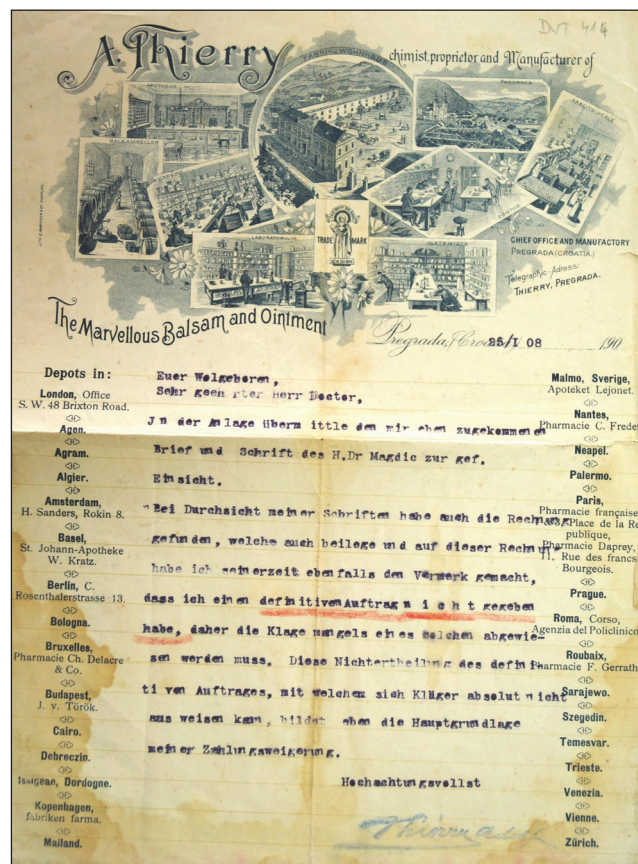


Fig. 5: Thierry’s memorandum letter with the illustration of the entire area and equipment of the pharmaceutical factory in Pregrada, as well as the list of offices around the world (1908), Inventory No DVT 414, courtesy of the Pregrada Municipal Museum “Dr Zlatko Dragutin Tujdina”, Croatia.

and a commercial office where business correspondence was done (Pregrada Municipal Museum 1929).

The products from the Thierry factory could be ordered directly from Pregrada, but Thierry had offices and warehouses for his pharmaceutical products in other European cities as well. Thus, his *specialities* could be procured in London, Agram (Zagreb), Amsterdam, Basel, Berlin, Brussels, Budapest, Copenhagen, Paris, Prague, Rome, Sarajevo, Venice, Vienna, Zürich, Cairo and other cities around the world, as shown in his memorandum letter which contained the list of supply centres (depots) along with the picture of Pregrada, the factory and the recognizable trademark (Fig. 5) (Pregrada Municipal Museum 1908).

Medicinal preparations manufactured in Pregrada were the result of Thierry's versatile expert knowledge of botany and chemistry, combined with his entrepreneurial and marketing prowess. In the Thierry family legacy, specific books were preserved which he used in his work, e.g. J. F. Jacquin, *Lehrbuch der allgemeinen und medicinischen Chymie* (Jacquin 1803), J. F. Jacquin, *Grundzüge der allg. und med. Chemie* (Jacquin 1836) and G. Hell, *Pharmaceutisch-technisches Manuale* (Hell 1898), a pharmaceutical manual that pharmacists used for the purpose of manufacturing medicinal preparations. Adolf Thierry manufactured his well-known specialities mostly from medicinal plants through various physical and chemical procedures. Therefore, phytotherapy was, in fact, the foundation of his pharmacy operation. This comes as no surprise, as Europe saw the introduction of synthetically obtained chemical medicines such as acetylsalicylic acid, acetanilide, acetophenetidin, anaesthetics, chemotherapeutic agents and other medicines during that time (at the turn of the 19th century). Acetylsalicylic acid was synthesized by Bayer's chemist Felix Hoffman (1868–1946) and clinically introduced in 1899 as *Aspirin*[®]. Ehrlich's arsphenamine (*Salvarsan*), introduced as a medicine in 1910, was later replaced with a less toxic chemotherapeutic agent – neoarsphenamine (Valentin 1944; Rubin 2007; Ravina 2011).

2.3. Thierry's Balsam and Thierry's Centifolia Ointment

Of all the Thierry's products, the best-known were certainly the *English Miracle Balsam and Ointment*, and later *Thierry's Balsam* and *Thierry's Centifolia Ointment*. The copy of the 1893 document contains the recipe for the *English Miracle Balsam* containing ten ingredients: *Benzoe opt.*, *Myrrha opt.*, *Olibanum opt.*, *Styrax liquida*, *Bals. peruvianum*, *Rad. angelicae*, *Rad. rhei chin.*, *Rad. anchusae*, *Alcohol 90%* and *Aqua destil. r.e.* The ointment contained: *Flor. rosa centifol. Ver.*, *Ol. olivae opt.*, *Camphora*, *Minium*, *Bals. peruvian* (Fig. 6).

The same document shows that based on the decision *Varaždin County of 21 July 1891 No 6108*, it was found that the balsam does not contain any prohibited, harmful substances (Pregrada Municipal Museum 1893b). The minutes of the Chamber of Commerce and Trade in Zagreb of 1894 include information on important decisions, including the one that *Thierry, a pharmacist in Pregrada, has a government license to sell his Miracle Balsam* (Zagreb National Archives 1894). We learn from the outer packaging that the balsam was said to be most effective in *cases of digestive issues such as belching, heartburn, flatulence, acid build-up, lack of appetite, in cases of stomach cramps, gastric and intestinal catarrh, weakness, cough, hoarseness and lung diseases*. *Thierry's Centifolia Ointment*, named after the species of rose it contained, was, according to its manufacturer, a well-known preparation for a variety of fresh and old wounds, with or without purulent discharge, swelling, cuts, stabs, incisions, cuticles, paronychia and abscess. It alleviated pain and removed foreign bodies of every kind.

To protect his products, Thierry also created a trademark for the balsam, the *zelena opatica* (*Green Nun*), and a pharmacy cross with a rose in the middle and a snake wrapped around the cross for the ointment (Zagreb National Archives 1895; Oglasnik Pariške mode 1895). The trademark for the *English balsam*, which was used on bottle labels, was entered into the register of trademarks on 17 July 1893 at the Chamber of Commerce and Trade in Zagreb. Three years later, Thierry changed the label on the bottle of his

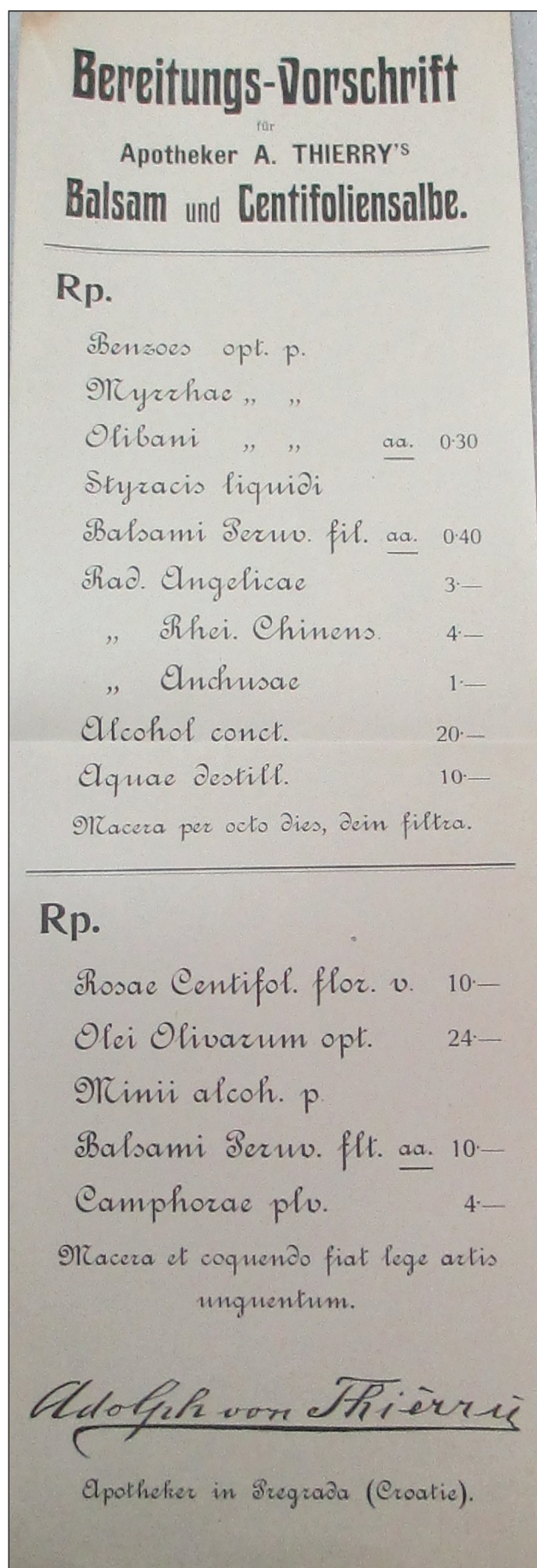


Fig. 6: The recipe for *Thierry's Balsam* and *Thierry's Centifolia Ointment*, courtesy of the Pregrada Municipal Museum "Dr Zlatko Dragutin Tudjina" in Pregrada, Croatia.

product and sold it with a new trademark as *Thierry's Balsam*, as evidenced by the data of the Chamber of Commerce and Trade in Zagreb on cancellation of the old trademark and application of the new one on 8 June 1896 (Zagreb National Archives 1896).

Being a skilled and astute entrepreneur, Thierry registered his best-known products, the *Miracle Balsam* and the *Ointment*, on 20 October 1899 in London. The following year, on 2 March 1900, he protected these products by patent and his trademark, the *zelena opatica* (Fig. 7) (Pregrada Municipal Museum 1900). In 1901, he sold the patent in London for 960 000 Krone, probably for business purposes (Grdinić 1997).

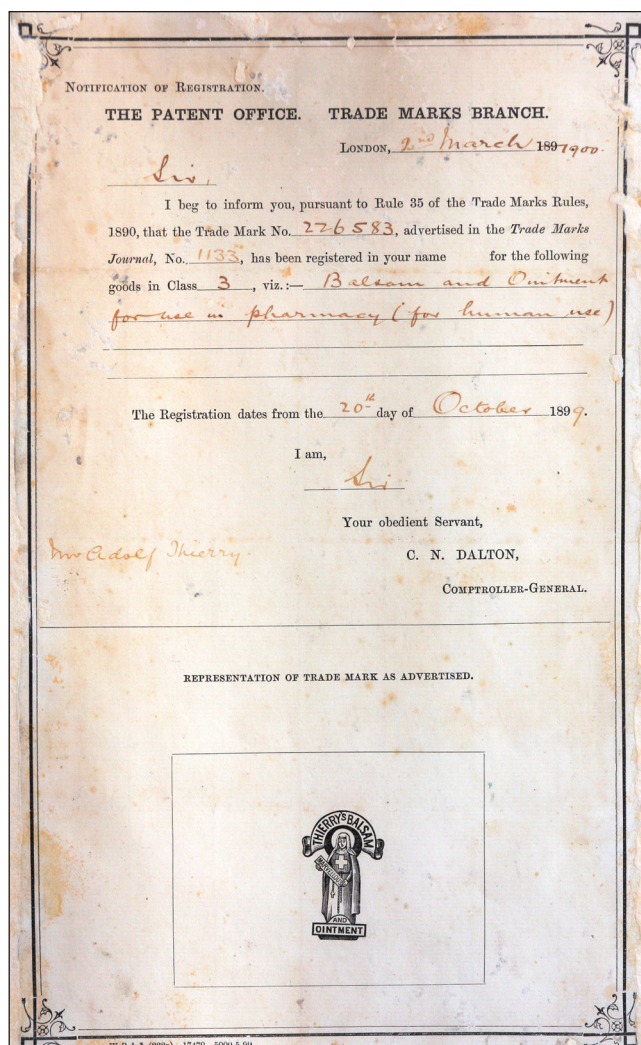


Fig. 7: The patent of *Thierry's Miracle Balsam* and *Ointment* from 1900 with the *zelena opatica* (Green Nun), a trademark for product advertising, Inventory No DVT 357, courtesy of the Pregrada Municipal Museum "Dr Zlatko Dragutin Tudjina", Croatia.

The first patent for a medicine was granted in 1698 in England to manufacturers of *Epsom salt* (magnesium sulphate) (Sakula 1984). Patent laws in the modern sense were introduced in the 19th century in Europe: France (1844), England (1852), Italy (1864), Germany (1877), and later in the United States of America (1870). One of the requirements for obtaining a patent protection was to fully disclose the invention being patented, that is, in the case of pharmaceutical industry, to disclose the composition of a drug. Those drug manufacturers that did not want to disclose information on the composition of their drug could waive the patent protection and protect their product by using a brand name or trademark. This allowed them to use trademark and brand name for advertising purposes. Trademarks and brand names were proprietary rights to pharmaceutical products protected by international agreement

after 1883 (Cowen and Helfand 1990; Appelbe 2005). Thierry's factory laboratory was a place where drugs of different pharmaceutical forms for various health problems were prepared (Fig. 8).



Fig. 8: Pharmacists, apprentices and other employees of Thierry's pharmacy and factory laboratory (undated), facsimile of the photograph belonging to the permanent display of the Thierry Pharmacy Collection in the Pregrada Municipal Museum "Dr Zlatko Dragutin Tudjina", Croatia.

In addition to *Thierry's Balsam* and *Thierry's Centifolia Ointment*, other preparations in his pharmacy included *Thierry's Chest Syrup from Zagorje* (for heavy cough), *Thierry's Blood Cleansing Tea* (for blood cleansing, lack of appetite, for stomach cramps and anaemia), *Thierry's Blood Cleansing Pills* (for blood cleansing and proper digestion), *Thierry's China Ferrous Wine* (for recovery and anaemia alleviation), *Thierry's Haematin Pastilles* (for anaemia, insomnia and for relaxation), *Thierry's Digestive* (to strengthen the stomach and improve digestion), *Thierry's Mirabile Pain-Expeller* or *Rheumatic Fluid* (for external use in cases of rheumatic pain, swelling and inflammation) and numerous other preparations (Pregrada Municipal Museum 1905).

The outer packaging of each product contained a trade (brand) name, pharmaceutical form of the drug (powder, pastille, liquid, balsam),

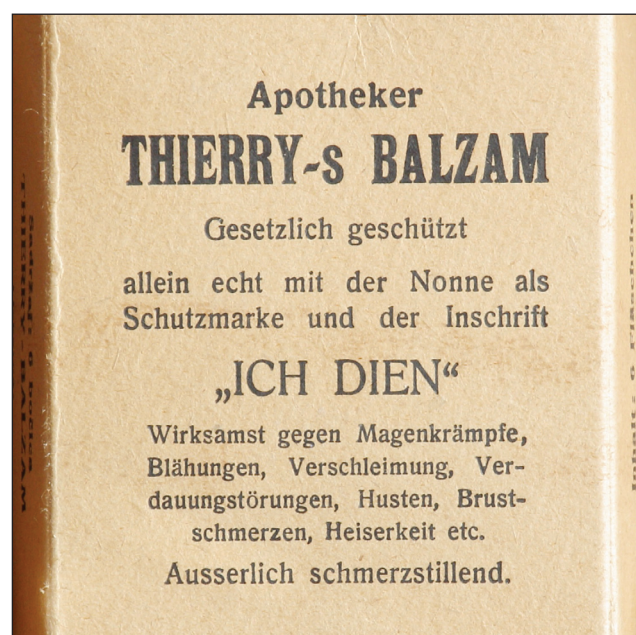


Fig. 9: The outer packaging of *Thierry's Miracle Balsam* in German intended for sale on the European market, Inventory No DVT 410, courtesy of the Pregrada Municipal Museum "Dr Zlatko Dragutin Tudjina", Croatia.

quantity of the drug, drug administration and instructions for use. Some of his products were named after the active ingredient (the *China Ferrous Wine*, *Borax Soap*). In order to protect his patented balsam and ointment from fake preparations sold as Thierry's products, he put an additional warning on the packaging which suggested that the balsam and ointment were *only genuine with a trademark*. The preparations intended for sale in other countries in Europe and the world had names and instructions for use in many world languages (English, German, French, Hungarian and others) printed on the outer packaging (Fig. 9) (Inić and Flegar 2018).

2.4. Marketing and advertising of Thierry's products

Based on the legacy of the Thierry family, especially the business records and preserved correspondence, it is clear that Thierry's products were shipped worldwide. Orders for various pharmaceutical products came from Croatia, but also from other European countries and even other continents (Pregrada Municipal Museum 2012). Upon receiving orders, the drugs were successfully shipped from the factory in Pregrada to different parts of Europe, Africa, America, India. Thierry managed to achieve such business success thanks to well-designed advertising, which is not surprising since he came from Austria where pharmaceutical advertising had already been strongly developed.

In the early twentieth century there were two classes of drugs. The first group included standard medicines, which were later dubbed *ethical* drugs, prescribed by physicians (e.g. digitalis, morphine, quinine, aspirin, ether and others). The other class of drugs was *patent* or *proprietary medicines*, which were made of unknown ingredients under trademarked names (e.g. Lydia Pinkham's Vegetable Compound, Hamlin's Wizard Oil). The main ingredient of such tonics, salves and bitters was water, while some products contained addictive substances such as alcohol or opium. At the turn of the century, patent medicine makers advertised their prod-

ucts in newspapers, spending more than half of their income on advertising. These advertisements made exaggerated claims about the effectiveness of their products and seldom disclosed their ingredients or risks (Donohue 2006). Although many pharmacists advertised their pharmaceutical products in various newspapers and other publications during the 19th century, pharmacists with their own factory production exporting their patented *specialities* had the greatest influence on advertising such products (Fatović-Ferenčić and Ferber-Bogdan 2018).

Thierry advertised his products in various European countries, in foreign languages and in various publications, mostly in newspapers (Fig. 10) (Idun 1899; Varaždinski vjestnik 1900; Il Giornaleto 1903; L'Eco 1896.) and folk calendars (Ožanić 2006; Danica 1907). For that purpose, Thierry designed and issued his own calendar for his most loyal customers (Thierry 1907).

Folk calendars had a significant impact on advertising medicinal products because they were intended for a wide range of people, most often to the rural population, to whom they were the only literature. Initially written in verse, these calendars later included short prose texts with interesting and instructive content (Tatarin 2008). Various matrices for printing advertising material have been preserved as part of the Thierry family's legacy. The *zelena opatica* trademark had also been carefully designed for advertising purposes. By its appearance, the *zelena opatica* was supposed to suggest miraculous powers and miraculous healing when using Thierry's products with the clear aim of attracting the widest possible range of economically weaker and less educated population.

It is interesting that the business success of Thierry's company enabled the introduction of telegraph and telephone (1903) in the small Croatian town of Pregrada, which influenced the faster economic development of this region (Gretić 2017; <https://www.pregrada.hr/povijest>).

3. Conclusion

The pharmaceutical industry in Croatia evolved in line with the development of natural sciences in other European countries at the end of the 19th and beginning of the 20th century. Thanks to Adolf Thierry, the first pharmaceutical factory in Southeast Europe (1894) opened in the region of Hrvatsko zagorje at the end of 19th century. The pharmaceutical factory had a fully developed manufacturing process with the necessary laboratory and warehouse for storage of medicinal raw materials, a room for storage of drugs manufactured, a room for their packaging and shipping, and a pharmacy where the drugs could be purchased. Adolf Thierry, a pharmacist and the owner of the factory, had a successful and well-designed method of advertising and selling his pharmaceutical products that were shipped to all parts of the world. His best-known drugs were *Thierry's Balsam* and *Thierry's Centifolia Ointment*, protected by patent (1900) and the *zelena opatica* trademark. The factory, which was opened in Pregrada, a small town in the region of Hrvatsko zagorje, Croatia, set a good example for modern pharmaceutical factories which later opened in Croatia. It also bears witness to the long-standing pharmacy tradition in Croatia, based on modern, professional and scientific practice.

The preserved *Angjelu čuvaru* pharmacy with the authentic original pharmacy's furniture can be still found today on the same spot in Pregrada, while the Pregrada Municipal Museum "Dr Zlatko Dragutin Tudjina" hosts a collection dedicated to the Thierry family's pharmacy business (Validžija 2009).

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Conflicts of interest: None declared.

Enda äkta engelska

UNDERBALSAM,

pröfvad och godkänd af sundhetskollégium

Denna balsam är: 1) Ett opphunnat verksamt botemedel mot alla sjukdomar i lungor och bröst, lindrar katarrh, stillar slem-afsöndring, lindrar den smärtsammaste hosta och bortar till och med gamla lidanden. 2) Verkar förträffligt vid alla hals sjukdomar m. m. 3) Fördrifver grundligt hvarje feber. 4) Helar öfverraskande alla sjukdomar i lefvern, magen och tarmarne, i synnerhet magkramp, kolik och värk i underlivet. 5) Borttager smärtorna och botar hämorrhoider. 6) Verkar lindrigt afluöande och blodrenande, rensar njuren, borttager hypokondri och melankoli och släpker apiten och matsmältningen. 7) Tjänar förträffligt vid tandvärk, ihåliga tänder, skörbjugg i munnen och vid alla tand- och munsjukdomar och borttager uppstötningar och dålig lukt. 8) Är ett godt medel mot mask, binnikemask och vid epilepsi. 9) Tjänar såsom ett underbart utvärtes botemedel för alla sår, friska och gamla ärr, ros, hethlemmor, listlar, vårtor, brännsår, förfrusna lemmar, klåda, utslag, spruckna, sträfvå händer m. m. och förtager hufvudvärk, surning, reumatism, gikt, örvärk m. m. Detta medel bör, såsom första hjälp, icke saknas i någon familj, i synnerhet under influensa-, kolera- eller andra epidemier. Ett enda prof öfvertygat bättre än någon kungörelse. Äkta är denna balsam endast, om hvarje flaska är tillstuten med en silfverkapsel, som bär min firmastämpel: **Adolf Thierry, Apotheke zum Schutzengel in Pregrada**, och är försedd med ofvanstående gröna skyddsmärke. Hvarst ej depöt finnes torde man beställa direkt under adress: **Schutzengel-Apotheke des A. Thierry in Pregrada bei Rohitsch-Sauerbrunn, Osterreich**, Franko hvarje poststation i Skandinavien kosta 12 små eller 6 dubbelfaskor kr. 8:— . Mindre sändas icke. Sändas mot efterkr.

Kraft och verkan

af den äkta engelska under-salvan.

Med denna salva blef en 14 år gammal för obotlig ansedd benröta fullkomligt läkt, nyligen äfven ett 22-årigt svårt kräftartadt lidande. Engelsk undersalva är ett vid de svåraste, äfven gamla skador med det bästa resultat användt medel med utmärkt dragningskraft. Engelsk undersalva finner användning vid: ondt bröst hos barnsängsvinnor, stockning i mjölkflödet, förhårdnader i bröstet genom ros, vid allehanda gamla skador, öppna fötter eller ben, sår, eksem, svullna fötter, t. o. m. vid benröta, vid hugg-, stick-, skott-, snitt-, krossår; för utdragning af alla främmande ämnen, såsom: glas, träflisor, sand, hagel, törne m. m.; vid alla bulnader, växter, karbunklar, nybildningar, t. o. m. kräfta; mot fuislag, nagelbulnader, blåsor, onda fötter, alla slags brännsår, förfrusna lemmar, vid liggsår hos sjuka, svullnad i halsen, mot spikböldar, mot ösprång, vid hudlöshet hos barn m. m. m. Ju äldre den engelska undersalvan blifver, desto bättre resultat! I hvarje familj bör alltid finnas ett förråd af detta enda hjälpmiddel. Mindre än 2 ösror sändes ej; försändes endast mot förutbetalning af beloppet eller mot efterkr. Kostar med postporto, fraktsedel och inpackning m. m. kr 6:—

Tabrika attester till förfogande.

Jag varnar mot inköp af värdelösa förfalskningar och ber att noga iakttagas att på hvarje degel måste ofvanstående skyddsmärke och firma **Schutzengel-Apotheke des A. Thierry in Pregrada** vara inbrändt.

Enda inköpsställe: **Schutzengel-Apotheke des A. Thierry in Pregrada bei Rohitsch-Sauerbrunn.**

Depöter å de flesta apotek.

Fig. 10: An advertisement for Thierry's *Miracle Balsam* and *Centifolia Ointment* published in the Swedish magazine *Idun* (1899), a practical weekly magazine for women and the home.

References

- Appelbe G E (2005) From secret remedies to prescription medicines: a brief history of medicine quality. In: Anderson S (ed.) *Making Medicines: A Brief History of Pharmacy and Pharmaceuticals*. Pharmaceutical Press, London, pp. 230-236.
- Bilinski V, Biba F, Grdinić V (2018) Hippolit Bilinski, the first pharmacist in Pregrada – the predecessor of Adolf Thierry. *Farmaceutski glasnik* 74: 109–118.
- Bilinski V, Biba F, Grdinić V (2019) The arrival of Adolf Thierry, the successor of Hippolit Bilinski, in Pregrada in 1888. *Farmaceutski glasnik* 75: 135–142.
- Corley TBA (2003) The British pharmaceutical industry since 1851. In: Richmond et al. (eds.) *The Pharmaceutical Industry: A Guide to Historical Records*, 1st ed., Ashgate Publishing, Farnham, pp. 14-19.
- Cowen DL, Helfand WH (1990) *Pharmacy an illustrated history*, Harry N. Abrams Inc., New York, pp. 161–173.
- Croatian State Archives (1887 – 1942) Collection of Registries (copies), ZM-34/588 (DVD- 271), ZM-34/590 (DVD-272), ZM-34E/595, ZM-34E/596 (DVD-272).
- Croatian State Archives (1887) Collection of Registries (copies), ZM-34/588 (DVD-271), p. 366, No 376.
- Croatian State Archives (1904) F 78, box number: 770, Royal Croatian-Slavonian-Dalmatian Land Government's documents No 35.912 of 5 May 1904 and No 2197 of 22 May 1904 whereby Adolf Thierry applies for the recognition of a title of French nobility and family coat of arms
- Croatian State Archives (1910a) F 78, box number: 770, Adolf Thierry's application of 5 January 1910 No 148 for the recognition of a title of French nobility in which the enclosed documentation is specified.
- Croatian State Archives (1910b) F 78, box number: 770, Royal Croatian-Slavonian-Dalmatian Land Government's document No 2134 of 3 May 1910 whereby Adolf Thierry's French nobility title and the noble suffix of *de Chateauvieux* are recognised.
- Croatian State Archives (1911) F 78, box number: 770, Royal Croatian-Slavonian-Dalmatian Land Government's document No 3914 of 19 October 1911 whereby Adolf Thierry was granted permission to enter the title of nobility in his children's birth certificates.
- Danica (1907) *The Calendar of the Society of St. Jerome for 1908*. Društvo Sv. Jeronima, Zagreb, no number.
- Donohue J (2006) A history of drug advertising: the evolving roles of consumers and consumer protection. *Milbank Q* 84: 659–699.
- Drews J (1998) *Die verspielte Zukunft: Wohin geht die Arzneimittelforschung?*, Birkhäuser Verlag, Basel, pp. 37-63.
- Fatović-Ferenčić S, Ferber-Bogdan J (1997) Pharmacist Eugen Viktor Feller. *Medicus* 6: 277–283.
- Fatović-Ferenčić S, Ferber-Bogdan J (2018) Father and sons: Feller family members in the context of the beginnings of advertising in Croatia. *Acta medico-historica Adriatica* 16: 49–84.
- Grdinić V (1996) Pharmacy on Croatian soil: the heritage, visions and achievements, *Nakladni zavod Matice hrvatske*, Zagreb, pp. 115–118.
- Grdinić V (1997) An illustrated history of Croatian pharmacy. *Pharmacy on Croatian soil: the evidence*. Hrvatsko farmaceutsko društvo i Nakladni Zavod Matice hrvatske, Zagreb, p. 363.
- Gretić D (2017) Thierry de Chateauvieux, Adolf, Alfons. *Enciklopedija hrvatskoga zagorja* (ed. A. Vujić), Leksikografski zavod Miroslav Krleža, Zagreb, p. 834.
- Hell G (1898) *Pharmaceutisch-technisches Manuale*. Buchholz und Diebel. Troppau, Czech Republic.
- <http://bulbio.com/en/historical-notes.html>, accessed on 20 January 2020.
- <http://www.gyogyszereszetortenet.hu/wp-content/uploads/2013/08/The-Hungarian-Pharmaceutical-Industry.pdf>, accessed on 20 January 2020.
- <https://cen.acs.org/articles/83/125/EMERGENCE-PHARMACEUTICAL-SCIENCE-INDUSTRY-1870.html>; *Chemical & Engineering news* (2005). Emergence of pharmaceutical science and industry: 1870-1930, Vol. 83, Issue 25, June 20, accessed on 20 June 2020.
- <https://www.pregrada.hr/povijest>, accessed on 25 January 2020.
- <https://www.zentiva.com/who-we-are/history>, accessed on 20 June 2020.
- Idun (1899) 12: 25 (600), 29 Mars, p. 8. Swedish *A Practical Weekly Magazine for Women and the Home* in which Thierry' advertisements for the English Balsam and Ointment were published.
- Il Giornaleto di Pola, (1903) 4 (107), 17 April, p. 2.
- Inić S, Flegar V. (2018) Pharmaceutical families Thierry and Feller – The beginnings of pharmaceutical industrial production in Croatia. *Prirodoslovlje* 17: 129–146.
- Inić S, Kujundžić N (2012) The original Croatian pharmacopoeia from 1901. *Pharmazie* 67: 652–657.
- Jacquin J W (1803) *Lehrbuch der allgemeinen und medicinischen Chymie*. Bd. 1.2. Wappler und Beck, Wien.
- Jacquin JW (1836) *Grundzüge der allgemeinen und medicinischen Chemie*, Bd.1.2: *Allgemeine und specielle Chemie der unorganischen Körper, Mörchner und Jasper*, Wien.
- Kovačević K (2002). Gustav Janeček, one of the founders of Croatian pharmaceutical industry. In: Grdinić D (ed.), *Gustav Janeček (1847–1929), život i djelo*, HAZU, Zagreb, pp. 151–161.
- L'Eco di Pola (1896) 11(41) 10 October, p. 4.
- Memorial book (1958) of University of Zagreb Faculty of Pharmacy. In: Iveković H (ed.) *75 godina farmaceutske nastave na Sveučilištu u Zagrebu 1882–1957*, Zagreb, pp. 9–16.
- Milčec Z (1996) *A history of Pliva*, Pliva, Zagreb, pp. 10–30.
- Oglasnik Pariške mode (1895) 1(1), 15 January, p. 3, Thierry's advertisement for the English Miracle Balsam and Ointment indicating the Government's Decision on the safety of the balsam and the serial number of the ointment trademark, in the territory of the Austro-Hungarian Empire.
- Ožanić S (1906) *Economic and Viticultural Calendar 1906*, Hrvatska knjižarnica Zadar, Zadar, pp. 172–174.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1893a) Thierry Pharmacy Collection, catalogue exhibit No 194, DVT 417, p. 52, a copy of the operating license issued by the Pregrada District No 4785 in 1893 authorising Thierry to run a public pharmacy in Pregrada.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1893b) Thierry Pharmacy Collection, catalogue exhibit No 194, DVT 417, p. 52, a copy of the operating license issued by the Pregrada District, which contains a certificate of safety for the English Miracle Balsam and Ointment.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1900) Thierry Pharmacy Collection, catalogue exhibit No 192, DVT 357, p. 52, patent protection of Thierry's Balsam and Ointment, London, 2 March 1900.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1905) Thierry's recipe book, Inventory No DVT 418, in which various recipes of medicinal products were entered after 1905.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1908) Inventory No DVT 414, Thierry's memorandum letter of 25 January 1908 with an illustration of the factory and a list of depots in which Thierry's products were available.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1912) a letter from Milan of 30 August 1912 sent to Adolf Thierry, which contains an order for Thierry's Balsam.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1916) Thierry Pharmacy Collection, catalogue exhibit No 42, DVT 420, p. 47, control book regarding the inspection of the pharmacy, 12 September 1916.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1920) Thierry Pharmacy Collection, catalogue exhibit No 41, p. 47, Vilim Thierry's diploma in pharmacy from University of Zagreb Faculty of Philosophy, 27 October 1920.
- Pregrada Municipal Museum "Dr Zlatko Tujdina" (1929) Thierry Pharmacy Collection, catalogue exhibit No 196, MGP-1221, p. 52, Thierry's memorandum letter with an illustration of factory premises of 29 November 1929.
- Raviña E (2011) *The Evolution of Drug Discovery: From Traditional Medicines to Modern Drugs*, Wiley-VCH, Weinheim, pp. 24–52.
- Report (1900) of the Administrative Board and the Deputy County Prefect of the Varaždin County on the proper functioning of the said Administrative Board of the County and its Royal Oblasts for the period from 1 January to 31 December 1899, *Platzerova knjigotiskara*, Varaždin, p 132.
- Report (1906) of the Administrative Board and the Deputy County Prefect of the Varaždin County on the proper functioning of the said Administrative Board of the County and its Districts for the period from 1 January to 31 December 1905, *Tiskara Stiflerova*, Varaždin, p. 203.
- Rubin RP (2007) A brief history of great discoveries in pharmacology: In Celebration of the Centennial Anniversary of the Founding of the American Society of Pharmacology and Experimental Therapeutics. *Pharmacol Rev* 59: 289–359.
- Sakula A (1984). Doctor Nehemiah Grew (1641-1712) and the Epsom salts. *Clio Med* 19: 1–21.
- Schmitz R (1998) *Geschichte der Pharmazie*. Bd. 1: Von den Anfängen bis zum Ausgang des Mittelalters. Govi-Verlag, Eschborn, pp. 187-200.
- Sneider W (2005) *Drug Discovery: A History*, John Wiley & Sons, Ltd, Chichester, pp. 3–7.
- Tartalja H (1954) The main pharmaceutical association for Croatia and Slavonia founded in Zagreb in 1858. *Acta Pharm Jugoslav* 4: 1–8.
- Tatarin M (2008) The role of popular calendars in creating Croatian readership, <http://www.hrvatskiplus.org/article.php?id=1893&naslov=uloga-puckih-kalendaru-stvaranju-hrvatske-citateljske-publike>, accessed on 20 June 2020.
- Thierry A (1907) Adolf Thierry's calendar for the year 1907. *Tisak Antuna Scholza*, Pregrada kod Rogatca Slatine.
- Valentin H (1944) *Geschichte der Pharmazie und Chemie*, Wissenschaftliche Verlagsgesellschaft m.b.H. Stuttgart, pp. 77, 87.
- Validžija I (2008) The Thierry pharmacy collection in Pregrada. *Hrvatsko Zagorje* 14: 77–81.
- Validžija I (2009) The Thierry pharmacy collection of the permanent display of the Pregrada Municipal Museum. *Informatica Museologica* 40: 19–25.
- Varaždinski vjestnik (1900) 11(45): 10 November, p. 4.
- Vienna University Archives (1874) Adolf Thierry's faculty form from the winter semester 1873/74 and the summer semester 1874.
- Vienna University Archives (1878 – 1880) Register of final exams (*Rigorošenprotokoll der Pharmazeuten*) PH 61.2, p. 96.
- Zagreb National Archives (1894) F 252, Chamber of Commerce and Trade in Zagreb 1876 – 1925, minutes of the joint meeting of 26 November 1894, p. 36.
- Zagreb National Archives (1895) F 252, Chamber of Commerce and Trade in Zagreb 1876 – 1925, minutes of the joint meeting of 20 April 1895, p. 42. with a notice that two of Thierry's trademarks have been registered with the Ministry in Budapest.
- Zagreb National Archives (1896) F 252, Chamber of Commerce and Trade in Zagreb 1876 – 1925, minutes of the joint meeting of 22 June 1896, p. 62.
- Zagreb National Archives (1918) F 271, ISIS Joint Stock Company for the Industry and Trade in Drugs and Chemicals, *ISIS Rules of operation* adopted on 12 July 1918.
- Zagreb University Archives (1908) Faculty of Philosophy, full-time students of the Faculty of Philosophy in the academic year 1907/1908, Alfred Thierry's faculty form, with date and place of birth, 4 April 1883, Vienna.
- Zajta E (1968) *Drug research, pharmaceutical production and foreign trade*. In: Kempler K(ed.) *Hungarian pharmacy*, Medicina publishing house, Budapest, pp. 59–61.