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REVIEW

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# Historical Contribution of Pharmaceutics to Botany and Pharmacognosy Development

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## ABSTRACT

**Introduction:** Pharmacy and medicine belong to the oldest human activities, so the development of these sciences is closely related to the socio-economic, cultural and religious opportunities of the nations within which they have been developing. **Goals:** To present the historical influence of pharmacy on the development of the human being from its very beginning; To present the historical link between pharmaceutical and medical activity, as well as early development of independent pharmaceutical activity; To present the historical influence of pharmacists on the development of botany and pharmacognosy and to present the historical influence of the first written herbarium and incunabula on the development of pharmacognosy. **Material and Methods:** The article has a descriptive character, and represents a systematic review of the literature dealing with this topic. **Results:** The roots of pharmacy started to the very beginning of human civilization, when people collected various medicinal herbs and try to alleviate their health problems, pain and suffering. The scientific foundations of the pharmacy were set up in the antique period by the books of Dioskurides and Galen, and its further development continued in the mid-century, at the beginning by rewriting famous parts of ancient literature, and later by writing new discoveries (the base of this development was represented by South Italy) so that in 1240, for the first time in history, came the separation of doctors and pharmacists, and at the beginning of the 13th century the opening of the first pharmacy. **Conclusion:** The effort to maintain knowledge of medicinal herbs and its practical application has led to the writing of a large number of recipes books, the forerunners of today's pharmacopeia, while the aspiration to classify medicinal herbs, and the desire to present medicinal herbs to ordinary people, has led to a large number of herbaria, making the knowledge and descriptions of plants available to many, not just the nobility. Descriptions of plants in herbaria

and later in incunabula lead to the development of pharmacognosy, and to the opening of the first Department for pharmacognosy, 1545 in Padua.

**Keywords:** pharmacy development, botany, pharmacognosy.

## 1. INTRODUCTION

Pharmacy and medicine are one of the oldest human activities. The history of these sciences is closely related to the socio-economic, cultural and religious opportunities of the peoples within which they developed (1). Pharmacy as a science can be defined in two ways: as a field of human activity and as a science. It is a profession responsible for the proper and adequate production and application of pharmaceuticals as well as for providing services that achieve the best results in treatment, or it ensures both the individual and society to use the medicines in the best possible manner. Pharmacy is, in essence, a knowledge system that provides healthcare services by using knowledge about drugs and their effects. Botany is a science of plants. Pharmacodynamics is a scientific discipline in which medicinal substances from nature (drugs) and their medicinal ingredients are studied. Today in pharmacy, the most attention is given to drugs of biological origin-healing herbs, and much less to animals. Medicinal properties of minerals are less and less used. The majority of information and data in pharmacognosy refers to natural resources and ingredients that are pharmacologically active, or to drugs used in the therapy of certain diseases and states of impaired health, and may be used preventively to preserve normal functioning of the organism (1, 2). The name itself for all scientific disciplines is derived from the Greek words "pharmakon" (medicine, poison) and "gnosis" (knowledge), so that this science represents "medicine knowledge" or "knowledge of drugs" (2, 3, 4).

## 2. GOAL

The goal of the article is to present historical influence of pharmacy on the development of the human being from its very beginning, to present the historical link between pharmaceutical and medical activity and to start the development of independent pharmaceutical activity. To present the historical influence of pharmacists on the development of botanics and pharmacognosy and to show the historical influence of the first written herbaria and incunabula on the development of pharmacognosy.

## 3. MATERIAL AND METHODS

The article has a descriptive character, and it represents a systematic review of the literature dealing with this topic.

## 4. RESULTS

For the first time, the term “pharmacognosy” was used by a Viennese pharmacist, **Adam Smith** (1759-1809), in his book „Lehrbuch der Materia Medica“, which was printed after his death in 1811. Several years later, in 1815, the Polish pharmacist Enoteus Sedler used it in his book „Analecta Pharmacognostica“. Otherwise, there are more names in the world today for this scientific discipline. Thus, in the French speaking area, the term „Materia Medica“ is often encountered, and in Germanic countries, pharmaceutical biology. Sometimes this is called the chemistry of plants, chemistry of the drugs, or phytochemicals (3). The use of plants in the treatment originates from the distant past. The herbage cultivation skill developed in all nations and has been preserved, somewhere more, somewhere less, as traditional or folk therapy, as popularly called, to this day (5, 6, 7). Pharmaceutical activity exists since there is a man. The oldest tribes were dealing with it. **Old-Slavic nations** treated the patients with broken hands and feet with the root of a forest tree (it is not known which wood bark was used). Old Slavic folk “doctors” knew the oak (*Quercus*), the birch (*Betula*), the beak (*Salix*), the beech (*Fagus*), the ash (*Fraxinus*), the jasper (*Populus tremula*), the thousand (*Taxus*), the pine (*Pinus*), the spruce (*Abies*), thuja (*Juniperus*), elm plant (*Ulmus*), joha plant (*Alnus*), linden (*Tilia*), maple (*Acer*), etc. They collected the fruits of wild, wild trees (2). Evidence on the use of hazelnuts, apples and sweet cherries was found in discovered Neolithic European mansions (5, 6). Basics of **Babylonian-Assyrian** pharmacotherapy written in cuneiform were herbal drugs for internal use and ointments for exterior use. The oldest recipe book in the world is excavated in Iraq—a clay tile printed with Sumerian cuneiform (contains twelve recipes for ointments and internal medicines, and on the plate are listed the kitchen salt, myrrh, thyme, figs, dew, milk, leather and turtle armor). The peoples of **Mesopotamia** knew the culture of figs from which they made wine. Figs juices were used for grooming and coating of drugs. They also raised the onion, which was eaten for hygienic reasons. The flax seeds were used as a cure. Barley was used to prepare beer. Cypress, cedar and oak leaves were also used as a medicine. In ancient Egypt, the cult of respect for the dead and the baptismal process of the dead have developed, which have remained preserved to this day. Written medical documents from old-European medicine are papyri. They carry the names of the discoverer, the owner or the place where they are located. *Kahunas*

*Papyrus* (circa 1850 BC) is fully dedicated to female illnesses and contains: instructions for diagnosing female illnesses, pregnancy prognosis guidelines, and prescriptions for facilitating conception and treating sterility. *Edwin Smith papyrus* (circa 1550 BC) is a transcription of the book from 3000 BC and is actually the oldest surgical text and the oldest source of neurological phenomena. It contains instructions for diagnosis and treatment of head, neck and stomach injuries. *Papyrus Ebers* (Georg Ebers) is a kind of encyclopedia of medical knowledge. It is considered as an internistic compilation. It contains anatomic and physiological discussions of the heart and blood vessels, prescriptions for the treatment of all organs and data on malignant tumors and their treatment. The largest medical papyrus is both written and kept in Leipzig. Egyptian doctors treated the disease as divine punishment and/or the consequence of natural factors. They considered the harmful substance is produced by rotting and entering the blood vessels, and that the causes of the disease can be worms and insects. Old Egyptian doctors used magic and herbal drugs to treat the disease, and they put fresh animal flesh on the wounds. In ancient Egypt it was prescribed: eating and drinking moderation, hygiene, sexual hygiene, removal of feces, burial of the dead, drinking water control, nutritional control, body care and dressing. The founder of **Old Chinese Medicine** was Emperor **Huang-Ti** (about 2500 BC). It is believed that he has written a book *Neijing* (*Corpus of Medicine*). In *Neijing*, all the knowledge and experiences of previous centuries or millennia are compiled, and can be divided into two parts: “Huang ti so ven”, where simple questions and answers try to come to life truths and “*Lingshu*” on acupuncture. The first book, *Pent-Sao*, describes herbs and medicines (3000 years old), and is practically the first known pharmacopoeia in the civilization of mankind. In this pharmacopoeia, systematization of medicinal plants and other medicinal substances was performed. The earliest period of **Indian medicine** (about 1500 to 500 BC) is the Vedic period, as all the knowledge was contained in the sacred poems *Vedas*. In the oldest *Ring-Vedi* and somewhat younger *Atharva-Vedi* is reflected the religious-magical medicine: illnesses are considered devils that need to be expelled with a magical ritual. Dietetics in practical medicine were at a high level. Indians were well aware of the effects of many herbs. Among medicines the most commonly used were medications for: vomiting, sneezing and cleansing the bowels. **Greek and Roman culture** has provided the basis for the development of all sciences, including pharmacy. The ancient Greek empiricism was closely related to religion. The priests of *Asclepius* were both doctors and pharmacists. Respect for God’s doctors spread from *Trike* to *Tesalia* to all of Greece, and in 293 BC, during the plague, also to Rome. Its temples were called “*Asklepieon*”, and there were around 185 of them. They were usually associated with a hospital and a health resort where the treatment was performed by prayers, sacrifices, religious rites, suggestions, diets, and medicines. The most famous Greek representative of pharmacy and medicine development is *Hippocrates*. He provided the principles of medical practice and laid the foundations for further development of medicine, but also wrote on the healing properties of beans (*Phaseolus*), peas (*Pisum*), millet (*Panicummiliaceum*), lentil (*Ervumlens*), linseed (*SemenLine*), sage (*Salvia*), lupine (*Lu-*

pinus), cucumber seed (Semen Cucumissativi), sesame, wild saffron (Carthamus) and poppy seed (Papaver). Hippocrates used in its practice of treatment the garlic (Alliumsativum), mustard (Sinapis), the mountain clover, sheep's sorrel (Rumex acetosella), the cabbage (Brassica), mint (Mentha pulegium), the origano (Origanum vulgare) and the radish (Raphanus sativus) (5).

**Theophrastus (Eufraustos)** is the "father of botanics". He has written many books, two of which are the most important "Decausisplantarum" and "Dehistoriaplantarum" (a collection of ten books), which contain description and morphology of plants. Theophrastus first mentions fern (Filix) as medicine against worms (5).

Among the doctors who contributed to the preservation of the Greek heritage in Roman healthcare are also Asclepiades, who was a supporter of natural methods of treatment. His main remedies were: heat, cold and the sun. He studied various types of Greek and Roman wines and their therapeutic effect. He knew balms, vaginal suppositories, medicines for the eye and ears, various bitter drugs (picrate, amaro) and other plants. He opposed the use of superstitious remedies.

Many more medicinal substances compared to Hippocrates school are described by Greek pharmacologist **Dioskurides** (1<sup>st</sup> century AD). His book, "Materia Medica", or the science of healing substances, is the greatest book on drugs of the entire old century. It describes healing drugs and their effect. It also describes preparations prepared or obtained from abroad, as well as signs of their credibility and the way they are used. In particular, he described the significance of very strong substances, and he also mentioned anti-inflammatory drugs. "Materia Medica" is written in Greek language and consists of five parts describing fragrant substances, oils, ointments, trees and their juices, resins and fruits, animals, wax, milk of various animals, grains, vegetables, grass, roots, seeds, wine, mineral and metal materials.

Dioskurides has also used various types of fruits (such as plum-tree resins used against stones) as a medicine. It also used the darnel (*Lolium temulentum*), Fenugreek (*Foenum graecum*), mallow, trumpet, water mint, coriander, garlic, red pepper, mustard, anemone, ivy, rosewood (*Chelidonium*), agaric (*Agaricusalbus*), Liquiritia, *Erythraea centaurium*, akantus, ononis, tragacanth, sage (*Salvia*) and many others. Sea squill (*Scallamaritima*) was already known as a "waterborne drug", or diuretic. Dioskurides used stone mills to grind the medicines. During the reign of Goth in Italy (493-553) Dioskurides "Materia Medica" was translated into barbarian Latin.

**Galen** based on the knowledge of ancestors, continued to improve health care in the Roman Empire. Galen used Dioskurides "Materia Medica", which he supplemented and wrote 11 books on "Mixing and Characteristics of Simple Medicines". About 20 years later he wrote the book "Compilation of drugs according to their nature" and "Compilation of medicines by site on the body". These books later on came through the Vizant to Arabs, and they served them as a basis for their pharmacology. With Galen begins a new chapter not only in the medicine and pharmacy of old Rome, but also in the history of medicine and pharmacy in general. With Galen is marked the highest and ultimate developmental level of ancient medical-pharmaceutical thoughts.

The period from 8th to 15th century was period of "**Golden age of Arabic Medicine**" with a lot of discoveries and a lot of great books about medicine and pharmacy written by great Arabian scientists (1, 8, 9, 21-27), like: Yuhann ibn Masawayh (777-857), Hunayn bin Ishaq (809-873), Sabur bin Sahl (died 869), Ali ibn Sahl at-Taberi (808-861), Muhammad ibn Zakarya al-Razi (865-925), Ali ibn Abbas al-Majusi (925-994), Abu-l-Kasim al-Zahrawi (936-1013), Abu ar-Rayhan al-Biruni (975-1048), Abu Ali ibn Hussayn ibn Abdullah ibn Sina (980-1037), Ibn Jazlah (died 1100), Ibn al-Tilmidh (1073-1165), Rabbi Moses bin Maimon (1135-1204), Ibn al-Baitar (1197-1248), Kohen al-Baitar, Alauddin ibn al-Nafis (1210-1277), etc. (19-26). **Rhazes**, the largest Arab physician, contributed to the development of **Arabic medicine** and pharmacy (16). His full name is Abu Bakr Muhammad ibn Zechariah al-Razi (850-923). He allegedly wrote over 200 books. Among them are books from biology and medicine. His book "Liber medicinalis Almansoris" and his large encyclopaedia book "Continens", in which the texts of antique and Arabic doctors are collected, is important for the history of pharmacy. His significant book is also "Antidotarium", a doctrine of compilation and preparation of medicines. By extracting medicinal herbs, he got the extract and called it a "slave" and used it to make the pills. They called **Avicenna** the "Prince of doctors" (12, 16). His Arabic name was Abu Ali al-Hussein ibn Abdulah ibn Sina. Avicenna has drawn his knowledge from Indian medicine. His most important book is known in the world as "Canon Medicinae" "Al-Qanun Fit-tib". This book describes simple and complex medications, general therapy, cleansing agents, enemas, lining, blood discharge and leeches. His books are also translated into Latin. He also wrote "Kitab Al-Shifa" ("Book of Healing"), "Al-Adwa Al-Kalbija" ("Medicines for the Hearth") and "Kitab Al-Kulandz" ("Book of Pain in the Intestines"). In his books, he mentioned about 760 drugs and medicinal preparations, their properties, manner of action and indications (1). Already in that period he described the iris, eye skin, eye adjustment mechanism as well as the position of the muscle in the occipital pit. It is also believed that he was to first to perform distillation. He was also involved in the production of rose essence, whose extracts were widely used as drugs against various diseases (5).

The most famous Arab botanist was **Ibn al-Bajtar** (died 1248 in Damascus) (12). The results of his studies and travels have been collected in a large book that in the Latin edition is titled "Corpus simplicia medicamentorum et ciborum continens". In this book, simple drugs are listed in alphabetical order, and the number of substances described is 1,400. Of this, 300 new drugs, that he mentioned for the first time (12, 19).

The Arabs have a great deal of credit because they enriched *Materia Medica*, which, according to Steinschneider's estimate, covers more than 2000 substances. In the Greek therapeutic arsenal they introduced precious medicines, primarily camphor, sena, tamarisk, cinnamon, mirobena, mueska, root of galanga, sugar, lemon and other types of citrus, jasmine, pepper and many others. Also, they prepared many agents for staining. They also introduced the use of tannins. Today, some medicines known to the Arabs are re-used, just in a modern manner (19).

In Spain, the Arab pharmacology had its peak. The Arabs occupied Spain at the beginning of the 8<sup>th</sup> century. Under

their rule, which lasted almost 8 centuries, they contributed to the cultivation and use of many useful plants (persimmon, sugarcane, cotton, oranges, etc.), and in Andalusia they also cultivated medicinal herbs.

The development of comprehensive science was largely neglected in the *Middle Ages*, but there were still certain persons that continued the ancient development of pharmacy. Among them are **Kasiodor** (dealing with the rewriting of ancient literature), **Walafrid Strabo** (wrote a book "Hortulus" describing plants used for healing), **Constantinus Aphricanus** (introduces Europe with an Arabic culture of treatment by translating their books) and **Valerius Cordus** (written the first textbook of medicine and deals with the creation of the first pharmacopoeia).

The development of medicine and healthcare, during the early Middle Ages, was based on book in churches and monasteries, and later the medical schools (most notably in Salerno) are being opened where doctors and pharmacists were trained. It is important to note the year 1240 in which was prohibited to a doctor from performing a pharmaceutical duty, which separates the doctors and pharmacists for the first time. The authority has begun to monitor the medication, and the price for a particular medicinal product was determined for the first time. For the first time such a provision was made in the area of southern Italy (at the beginning of the 13th century the first pharmacy was opened in this area), and later similar provisions were implemented throughout Europe.

Since the middle of the tenth century, Arab medicine has come into contact with Europe and has a strong influence on it. Many scientists have become interested in alchemy. In the coming centuries, Italy continues to be the center of development of both health care and pharmacy, and in 1488 the first book of pharmacy was published by **Saladin**.

The *Renaissance* is one of the most creative periods in literature and art that marked the break with the Middle Ages. It dates from the 14<sup>th</sup> century in Italy to the 16<sup>th</sup> century in the rest of Europe. At the beginning of the sixteenth century a new era of medicine began, it is considered that the flowering of medicine in Italy occurred. Medicine is back to the study of the books of medical classics such as Galen and Hippocrates. The first botanical gardens are founded in Italy. In 1545, the first department of pharmacognosy was established in Padua, while in Germany **Brunfels, Bock and Fuchs** published a "New Kreuterbuch" book containing illustrations of German flora plants. These three authors are considered to be founders of pharmacobotany ("fathers of botany").

With the expansion of the conquest of America, **Monardes** has issued a decree of American soil flora. **Clusius**, one of the founders of European botany (Leiden, Germany), has founded a botanical garden that has been preserved within the oldest botanical garden in Europe.

Pharmaceutical botany continued in the 17<sup>th</sup> century as well. Scientists were interested in plants primarily as in drug. Various books on flora have been written in some provinces, usually with pictures. Botany terminology and systematics developed. **Joseph Pittonde Tournefort** (died 1708), a botanist professor in Paris, systematically organized plants in 22 groups. This system was valid until Linne's era. **Basilius Bessler**, a pharmacist from Nürnberg (died 1629), issued the first botanical atlas. **Marcello Malpighi**, a professor in Bo-

logna, published his herbal anatomy in 1675 (5).

In 1638, Count de Cinchon, a woman of the Peruvian pothole, was cured of malaria after using the crust of quinine. When her personal physician brought this drug to Europe, it had great success as a drug for malaria and fever. Many new pharmaceutical dispensations have been released in Europe, mostly new editions of older books. The pharmacy laboratory has changed very much. Pharmacist had to purchase many devices of old alchemist laboratories for making chemical remedies. In the pharmaceutical laboratories of major cities, natural scientists often met. For example, in Oxford, England, naturalists, who met at the home of the pharmacist **Cross**, founded a scientific society. The Academy of Sciences in Paris has its beginning (1666) at the home of pharmacist **Geoffroy** where French naturalists gathered. Fish oil, which the people in the northern regions have for long used for medicinal purposes, was introduced in 1782 by English physicians in textbook medicine.

At the end of the 18<sup>th</sup> century pharmaceutical laboratories expanded. They were not only used for drug production, but for scientific research and learning. They were a pharmaceutical and chemistry generator. Getting smaller quantities in pharmaceutical laboratories has become increasingly difficult for economic and technical reasons. For this reason, the authorities have allowed the pharmacist to buy such a drug also in factory labs, which have been designed to produce large quantities of chemicals. The founders of these companies were usually pharmacists. So, Pelletier soon, after discovering quinine, established a first factory in Paris for the manufacturing of this highly used antipyretic and antimalarial agent. Later, quinine was also produced in large quantities by pharmacists **Riedel** in Berlin and **Zimmer** in Frankfurt (5).

Industrial production in the coming years has become one of the industry's leading industries and a very lucrative business. The progress of pharmacy continues, and in the 20<sup>th</sup> and 21<sup>st</sup> centuries many new compounds have been discovered that successfully treat many diseases, but we cannot escape the impression that plants and nature itself are the basis of every treatment.

The word pharmacopoeia is based on words from the ancient world, such as Pharmacopoeiae (name for pharmacists in old Rome already during the emperor August) and Pharmacopoei (pharmacist), and Pharmacotritae or Pharmacotribae. Until the beginning of the term pharmacopoeia (until 16<sup>th</sup> century) pharmacopoeia books were called: Antidotarium, Dispensarium, Dispensatorium, Lumen, Luminaire, Receptor, Codex, Formularium, Compendium, etc. (3).

Greek word "pharmacopoeia" means drug making, consisting of two words φαρμακου-poison, good drugs and ποιειν-to do, prepare.

The first definition for the pharmacopoeia was given by **Gustav Vulpus** in 1890. His definition was "The Pharmacopoeia is a law book on medicines that regulates the composition of a number of medicines in a particular area of validity" (3).

**August Falck** defines the pharmacopoeia in 1920 as a "Medicine Book, which was handled by experts at the request of the state and which has the power of law" (3).



Figure 1. Herbarius, Latin manuscript from the 14th century, originated from the late 4th century (probably the book of Dioskurides) (3)

**Georg Edmund Urdans** in 1950 defines the pharmacopoeia as a “pharmaceutical standard book whose task is to uniquely determine the type, quality, composition and strength of the drugs”. “That book should be recognized by a medical practitioner within a particular political entity, or at least should be somewhat accepted, and it should be prescribed as compulsory for the whole of the government“ (3).

**Willem Frans Daems and Leo Jules Vandewiele** defined the pharmacopoeia as a book “No matter how it was called, who is the author (himself or herself) for the purpose of the official preparation of medicines it cites instructions and regulations, if the following of it is mandatory to pharmacies or doctors prescribed by their superiors, even when that obligation is not mentioned in the title of the book” (3).

In his book, **Alfons Lutz** “Nuovo Receptario” (Florence, Italy), called it the “Book of Laws, which regulates the composition of a number of essential ingredients of medicines and preparations within a certain area of validity.” Statutory validity should be proved by state acts. books (and) in dedication or in the foretold, has proved to be in practice, does not possess credibility, until the evidence itself fails to be impeccable” (3).

Pharmacopoeia is a book in which the publisher publishes instructions and regulations for the purpose of (official) preparation of medicines, and for following of which the authority prescribed to the pharmacists and the doctors, even when this obligation is not expressed in the title of the book, must be accepted in its entirety. The development of pharmacopoeia books cannot be shown only through the pharmacopoeia in the narrow sense of the word because of the fact that for such books there were more diverse contents and names that were used and were the characteristic of the time and environment in which such books arise. A list of pharmacopoeias shows that at least thirty different names have been used to designate these collections and/or these scientific papers on drugs. Characteristics of these books used by pharmacists and pharmacists candidates for obtaining the necessary knowledge to gain access to the final exam are the following: guides, guidon (rudder), lumen, luminaire, and thesaurus (thesaurus, treasury, glossary) and thresors (treasure).

The naming of plants with certain names dates back to the earliest times (pre-ancient and antique period). The exact descriptions of herbal drugs did not exist, but many

names from different languages have been recorded. In the 19<sup>th</sup> century existed pharmacopoeias which did not include drugs descriptions. Most commonly, pharmacopoeias ended with the lists of drugs, and these lists containing and still contain the name of the basic plant and the name of the drug. Among such pharmacopoeias from the 19<sup>th</sup> century the most significant are:

- Codex Medicamentarius Gallicus from 1818, 1839 and 1884;
- Pharmacopoeia Londinensis from 1809, 1824, 1836 to 1851, and
- United States Pharmacopoeia from 1820, 1831, 1842, 1851, 1863 and 1873.

At that time was created the most advanced pharmacopoeia of that time, Pharmacopoeia Borussica, also featured plant descriptions. Dual or binary drug names were a common thing, and they consisted of the name of the main plant species and of the herbaceous part of the plant that was used, e.g. Herba digitalis and/or Digitalis Folia. This practice was common in Germany and the UK. It responded very well to the needs of pharmacists, as at a time when hundreds of herbal drugs were still in the pharmacy, which were partially derived from the same plant, greatly facilitated differentiation. Drug names that consisted of one word had the advantage of a short name, but they were less specific. Most commonly they were identical to the name of the basic plant. Hence, Digitalis in this case had the meaning of “Digitalis purpurea leaves”. These abbreviated pharmaceutical names were first used in the United States Pharmacopoeia in the year 1820 and have been retained until today. With drastic reduction of herbal remedies at the beginning of the 20<sup>th</sup> century, pharmacologi-



Figure 2 Kräuterbuch (Hieronymus Bock) (3)

cal abbreviated names became increasingly receptive because there was no risk of substitution (3).

**Herbarius** means everything that can be obtained from medicinal herbs from the “nature garden” and for the purpose of restoring health. While related to medieval burial and lapidary related animals, or rocks (minerals), herbars were treated the herbs (herbae), or parts thereof, but often also individual animals and minerals that possessed drug characteristics (3).

Early Middle Ages Herbaris are defined by short texts and text collections, among which „**Herbarius**” (**Pseudo-Apuleius**) (4<sup>th</sup> century) occupies an important place. An unknown author of this illustrated herbal book (the title *De herbarum virtutibus* and/or *De medicaminibus*), called Apuleius Barbarus or Apuleius Platonicus, was mistakenly linked with the Platonic and Sophist Apuleius of Madaurae (2<sup>nd</sup> century) in the middle ages. The oldest preserved manuscript containing figurative depictions of plants and animals originates from the late 4<sup>th</sup> century.

Large number of Pseudo-Apuleius manuscripts, preserved by surrender, show the unusual popularity enjoyed by Herbarius in the Middle Ages. Approximately 130 chapters, each of which were dedicated to the painted plant, with the addition of synonyms, also include habitat data, collection time, preparation and application, and often there are prayers or magic phrases and formulas. The first printed edition appeared in 1481 in Rome (3) (Figure 1).

The real beginning of herbarium in the middle ages is the book of **Hortulus** (circa 840) of **Walafrid Strabo** (about 808-849).

The application of new empirical research methods has led to many useful notions about pharmacognosy, and indirectly also in the field of therapy. The first botanical gardens (Padua, 1545, Bologna, 1567), which are part of the university, have begun to be used for the practical education of students and scientific book. In 1545 the first Department of Pharmacodynamics was established in Padua (5)

Success stories in medicinal herb therapy have been recorded in many books called **billiards (book of herbs)**, most often written in monasteries. The authors of these books are mostly theologians who also deal with medicine and pharmacy. Billiards have gradually lost their characteristics as book of plants and become pharmacopoeias on their way to development. Hieronymus Bock published his first billiard under the German name “**Kräuterbuch**” (Figure 2)

**Otto Brunfels** also begins with classification attempts. He also publishes a billiard with illustrations of German flora plants.

In Germany, **Brunfels, Bock and Fuchs** have published “**New Kreuterbuch**”, a billiard (containing illustrations of German flora plants). These three authors are considered to be founders of pharmacobotans (“fathers of botany”).

With the expansion of the conquest of America, **Monardes** issued a collection of American soil flora. **Clusius**, one of the founders of European botany (Leiden, Germany), has founded a botanical garden that has been preserved within the oldest botanical garden in Europe (3).

The foundation of botanical gardens has led to the publication of books in which authors described such a garden, as well as to the expansion of knowledge gained by collect-



Figure 3. Johann Wonnecker, the *Gart der Gesundheit* (*Hortus sanitatis germanicae*), woodcut, the first printed book on a medicinal plant in German, which was prepared and published in 1485 by Peter Schoffer, a printer from Mainz (3).

ing and cultivating herbs. In all countries of the world where science has been developed, pharmacists have contributed to the knowledge of local flora. **Theophrastus Bombastus von Hohenheim (Paracelsus)** (1494-1541), a Swiss-German physician, a naturalist and a Renaissance philosopher, wrote that healing herbs in each country were growing for treating their patients. Botany was not yet an independent discipline at that time but was in the service of medicine and pharmacy. In the sixteenth century, the pharmacy gardens grew more and more, and somewhere were prescribed by law.

The pharmaceutical practice and botanical experience of pharmacists gave a great combination of chemical and botanical knowledge, which led to the book of most of these people having a special character. In addition to writing botanical books, examining, determining and classifying plants, they also studied their contents, and so they developed into plant hemmers (phytochemics). For example, the isolation of alkaloids for decades was the sole domain of pharmacists. Only the name “alkaloid” (as alkali) for these “herbal base” was given in 1818 by pharmacist **K.F.W. Meissner** (3).

All the books printed since the invention of the printing machine, from 1455 to 1500, are gathered under the name **incunabula**. In the 15<sup>th</sup> century one type of herbarium was created (printed herbarium or incunabuli) whose key representative in the literature was the *Gart der gesuntheit* (The garden of healing) of the Frankfurt city doctor named **Johann Wonnecke Von Cub** (or Kaub, around 1430-1503/04). *Gart der gesuntheit* was published in 1485 by **Peter Schoffer** (around 1425-1502/03) from Mainz, as the first German incunabula on

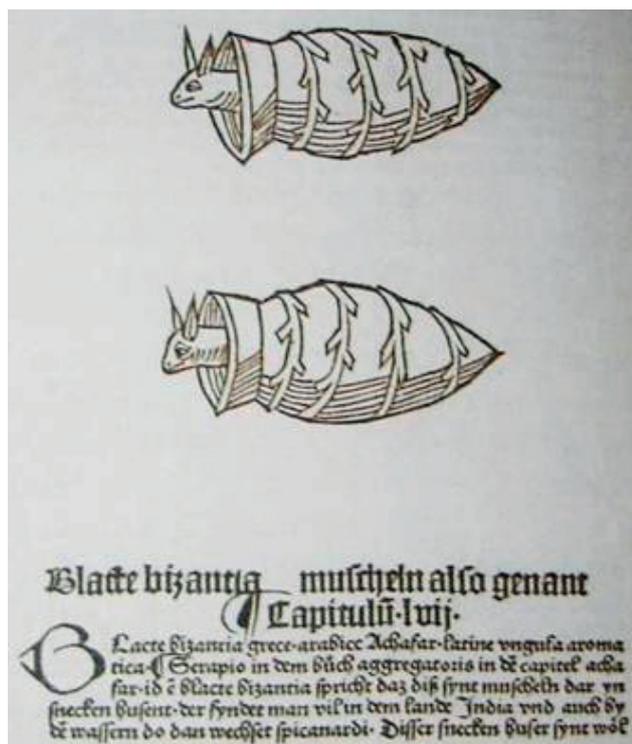


Figure 4. Peter Schoffer, Hortus sanitatis, woodcut of animal origin drug Blacte Byzantine (3)

healing plants. The book was prepared and the press release was given by **Bernhard von Breidenbach** chief clerk. In 1435 rough alphabetical order and according to the Latin names of ordered chapters, Gart der gesuntheit describes 382 plants, 25 animal-like drugs as well as 28 minerals, illustrated with 379 wood engravings (Figure 3) (3).

Since the completion of the book "Gart der gesuntheit" took a very long time, and the publishing of an illustrated plant book was announced for the Frankfurt Spring Fair in 1484, **Peter Schoffer** decided to launch the corresponding Latin-language book on the market within a reasonable time. Thus, on April 11, 1484, a year before the incunabula Gart der gesuntheit (1485), Herbarius Monguntinus was introduced in Frankfurt (Figure 4) (3).

"Gart der gesuntheit" took over the Herbarius Monguntinus register of drug groups and the list of indications. Following the style of the book Gart der gesuntheit, and the Herbarius Alonguntinus pattern, another incunabulum appeared, a book of medicinal herbs, a Latin Ortus sanitatis or Hortus sanitatis made by a printing company **Jakob Meydenbagh**. It is based primarily on a manuscript of 1072 monographs of drugs, of which the 530 monograph deals with medicinal herbs, and the material was probably compiled by a German author around 1450 from easily available, mostly encyclopedic sources. The content is divided into half-alphabetic order, divided into five segments: herbae, animalia in terris, aves, pisces and lapidespretiosi. After the first edition there were several Latin copies (1497-1538) (3).

Herbars, except in Latin and German, were soon printed in Dutch, French and Italian. Gart der Gesuntheit was also known as Herbarius zu Teutch (1485). In the year 1491, the extended version of Gart der Gesuntheit appeared under the title Hortus sanitatis. The French translation, called Arbolary, was published in Bensanon only in 1787/88. Le grand Herbar

en francois, published in Paris around the year 1500, took over the paintings of Hortus sanitatis. In England, Hortus sanitatis appeared as Grete Herbal, and was published in 1526 in London. In the 16<sup>th</sup> century started massive writing and printing of a large number of herbariums (3).

The most well-known list of medieval synonyms was Clavis sanationis or Synonyma medicinae (around 1290) of the Italian botanist and pharmacist **Simon** of Genoa (Simon Januensis), who lived in the second half of 13<sup>th</sup> century.

In 13<sup>th</sup> century or the beginning of the 14<sup>th</sup> century an anonymous medical and botanical dictionary called Alphita (from the Greek alphabet, barley, medical mash), named after the initial word, was created as another important list of drugs and synonyms in Salerno's lexicographic tradition.

In some cases synonyms lists also have Quid pro quo rules, or substitute lists (Succedane, Antiballomena, Quidproquo), Incipit tractatus quid pro quo, followed directly by the basic text of Antidotarium Nicolai in printed form from 1471, encompasses 12 page and is sorted alphabetically. These substitution lists were completely justified, as it could easily be assumed that some drugs, prescribed for centuries by prescriptions, were no longer known and most importantly unavailable so that they had to find a way to replace these drugs with others, equally valuable drugs.

#### 4.1. History of medicines use

##### 4.1.1. Materia medica

In the antique world Materia Medica represents the book of Dioscuri, and refers to the ancient "pharmacopoeia". The Materia Medica of the Renaissance is a generic collective term created especially for pharmaceutical and medical purposes for a set of medically usable substances from all three natural empires: Vegetables, Animals and Minerals. (3)

##### 4.1.2. Antique use of medicines, and the appearance of the first pharmacopoeia

Greek philosophers indirectly had a decisive influence on antique matter medicine. They were not content with just observing nature but were looking for explanations and fundamental causes of things.

**Dioskurides** is the most famous representative of the Greek tradition (19). His book "De materia medica libri quinque" is a copy of the ancient "pharmacopoeia" and is the greatest and best book of medicine of the entire old century. Diocytosis has described more than 750 drugs, of which about 600 plants. In addition to synonyms, these "pharmacopoeias" provide a morphological description and data on the geographic distribution of certain plants, instructions on how to prepare and preserve certain drugs, and therapeutic indications, dosage and pharmacological effects. Various chemical processes and methods have been described to demonstrate the correctness of certain drugs. Liquid drugs obtained by cooking or plunging the drug have easily become misguided. Namely, the Greeks were not yet familiar with spirits, which allows the preparation of permanent alcoholic preparations (today called tinctures), and sugar from the trunk, which in the form of syrups can conserve the drug. That was brought by Arabs into the pharmacopoeia. The only slightly stable preparations were those with wine. From the preserved manuscripts of Dioskurides book, the most valuable are the Constantinople and Naples Codes. Both manuscripts are now in the National Library in Vienna (12, 19).

Dioskurides advises practitioners to study each plant with due regard to the differences between the sites and the annual time, to make each drug with precision. Particularly recommended are the recommendations for keeping most medicines in silver, glass or tin-thick containers, often with opaque and rigid walls. There were descriptions of the preparation of maceration extracts followed by evaporation, preparation of juices by the process of draining and their concentration by exposure to sunlight (3).

After the year 146 BC, after Greece became a Roman province, pharmacopoeia books gradually began to move toward Rome. In Rome, in the 1<sup>st</sup> century, **Scribonius Largus** wrote the Pharmacopoeia "Compositiones medicae". He made this book in rough language and the book contained 271 recipes.

**Galen** (129-199 or 200) was the greatest and at the same time the last great Greek Roman pharmacist. He was a great expert in the use, preparation and compilation of medicines. The best source of knowledge of his pharmacology is the book "De simplicium medicamentorum temperamentis et facultatibus". But other books can be considered an ancient "pharmacopoeia". These are the ones from the year 160 "De compositione medicamentorum secundum genera" and "De compositione medicamentorum secundum locos". About 500 herbal drugs and a considerable number of mineral and animal drugs are described in the aforementioned books. He also wrote the book "De Antidotis". Galen's books are preserved in a series of Greek, Latin and Arabic medieval manuscripts. They are then often published, so the number of printed editions is great. The first printed edition was published in Latin in Venice 1490. The first Greek edition of the books is Venetian Aldina in five volumes from 1525. The Latin edition of the Giunta printing in Venice (nine editions, 1541-1625) and the Froben Basel (three editions, 1542-1562) (3).

The famous Roman writer **Pliny the Elder** (Gajus Plinius Secundus, 23-79) wrote many books, but only his "Historia naturalis", the great encyclopedia of natural science and art in 37 books, was preserved. Though it is an inexhaustible treasure trove of all kinds of medications with the manual of their use, this book cannot be considered an ancient "pharmacopoeia". This Pliny book had a strong influence on medieval medicine and pharmacy, and so on the development of the pharmacopoeia. For fourteen centuries it was *Historia naturalis* not only the most important scientific encyclopedia but also one of the most important medical books. In 1492 **Niccolò Leonigeno** corrected Pliny's misconceptions in the botanical field (3).

Valuable advances in the knowledge of herbs in the 4<sup>th</sup> century. An interesting book is one of **Marciellus Empiricus** (born 379), the Latin book of medicines "De medicamentis empiricis, physicis ac rationalibus liber" (3).

Therapy was particularly enriched by the introduction of a large number of medicinal herbs thanks to the strong growth of botany and pharmacognosy. But until that time Dioskurides was the highest pharmaceutical authority, now new methods of research are beginning to apply in this area as well. The application of these new empirical methods has led to botany and pharmacognosy to many useful discoveries, and indirectly also in the field of therapy (3).

With botanics were mostly dealing the physicians at that time, so it was not surprising that the botany paid special

attention to the study of medicinal herbs. **Concordie Apothecariorum** (Barcelona) from 1511 and 1535 may be included in the receptions from that period, or in books whose validity is based on the association's decision (guild) or on the agreement between doctors and pharmacists (3).

The pharmacopoeia of that period, which are based on the legislative act of government, can be counted as **Dispensatorium Noricum** (Nurnberg, 1546) and the book of medicines from Barcelona from 1587. Both Spanish books dating from 1511 and 1535 are based on the agreement between pharmacists and doctors, so their legal force has not been proven (3).

#### 4.1.3. The book of Valerius Cordus

**Valerius Cordus Simesius** born 1515 in Erfurt as the son of Eurosis Cordus, a Marburg professor of medicine. He studied in Marburg and Wittenberg. At the last university in Wittenberg in 1540 he read about Dioscuri. Scientific literature on the life and book of Valerius Cordus is very extensive. Georg Edmund Dann has specifically explored this area of pharmacy history. He argues that Dioskurides approach was not just based on reason or well-conceived and practical (rational), as well as based on experience, or knowledge gained (empirical). It is also critical, or it rests on a strict observation of specific criticism and its criteria. He therefore deserves to be recognized as the beginning of the science of pharmacognosy and pharmacology. His drug classification was based on their expected physiological effect and this activity was largely responsible for determining the modern plant names (3).

**Valerius Cordus** is the author of the first official medical book. He also wrote the pharmacopoeia "Historia Plantarum". He was a professor at the University of Leipzig. He talked about the character and book of Dioskurides and presented the most important features of Dioskurides classification and all his lectures on Dioskurides, which he held to students, were published after his death (3).

The Dioskurides describes for each listed drug its habitat, provides botanical description, explains its properties or mode of action, describes its medical use and side effects, provides quantities and dosages, provides instructions on collection, treatment and preservation of plants, describes methods of destruction and testing for detecting defects, providing veterinary, magical and non-medical use, and pointing to where the plant can be found (3).

## 5. MEDICINE BOOKS ("LJEKARUSAS") AS A ROOTS OF PHARMACY IN BOSNIA AND HERZEGOVINA

Since the population of Bosnia and Herzegovina in the past was exposed to various illnesses, almost any branch of medicine had its own specialists (14, 19). Their medicine was mostly based on superstition, and there was no regulated medical care. However, during 400 years of Ottoman period, some professions proved to be more skilled. For example, Djerrahs, or wounders, were hired as the military doctors in Ottoman army (19, 24, 26). Hapars, were barbers who made salves. Most important however were Attars who made medicines from oils and herb. During that time existed medical books called "Ljekaruše" that contained a lot of folk medicine, but also some of the more refined Sina's medicine. They were copied by the folk and were the main source of folk medicine (27-40). Official literature, however was written in Turkish and Arabic languages and therefore was available

only to the highest members of the society. Even though “Ljekaruša”s had useful knowledge, they were also filled with superstition. They were using amulets, fetishes, and scrolls, as well as parchments of Qur’an, which was contrary to Islamic principles.

Attars were drug specialists that operated in Bosnia and Herzegovina in 16th century. They can be held responsible for development of the folk and traditional medicine (19, 28). Their arrival coincides with arrival of sefardJews from Spain in 1492. Their knowledge stemmed from the Arabian medicine. Attars were mostly situated in bigger cities. Attar practices are being soon picked up by the local Muslims, and they soon outnumbered the Jews. They supplemented their attaric knowledge from the official literature, and they formed unions, while Jews continued working independently. Their stores held a variety of merchandise, from plants to oils and potions. Attars were so significant that even with the prohibition of their work, they still had more profit than official pharmacy, founded during that time (20-30).

Some people would travel far from Bosnia to receive an education from famous universities and then upon return would return to heal the population. Some were even from outside the Empire, but they treated only the nobles. They did however played an important role in the suppression of epidemics. Also, since leading cause of death, besides the epidemics were artificial abortions, doctors and pharmacists had to swear an oath not to perform these procedures.

Earliest records of a pharmacy date to the 16th century. In 1515, a pharmacy was founded and it is considered to be the beginning of attar work. First official pharmacy opened in 1852 but it was closed soon after. Same happened in 1854. After Austro-Hungarian occupation, new pharmacies are being opened (28).

In 17th century there were three types of pharmacies (14, 28, 29). Attar shops, travelling doctor’s pharmacies, and a public pharmacy that was held by educated doctors and pharmacists from Europe and Istanbul (32). Most important were Vilajet pharmacy and GaziHusrev-bey hasthana (house of the ill).

## 6. CONCLUSION

The roots of pharmacy reach the very beginning of human civilization. The effort to maintain knowledge of medicinal herbs and its practical application has led to the writing of a large number of recipes books, the forerunners of today’s pharmacopeia, while the aspiration to classify medicinal herbs, and the desire to present medicinal herbs to ordinary people, has led to a large number of herbaria, making the knowledge and descriptions of plants available to many, not just the nobility. Descriptions of plants in herbaria and later in incunabula lead to the development of pharmacognosy, and to the opening of the first Department for pharmacognosy, 1545 in Padua.

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