Classical Botanical Pharmacognosy: From Dioscorides to Modern Herbal Medicines

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The following is an excerpt from a soon-to-be published textbook of botanical microscopy by the American Herbal Pharmacopoeia. This chapter, written by AHG founding member and past president Roy Upton, describes the history of pharmacognosy, a history which parallels the history of herbal medicine in Western civilization. The text is designed to help revitalize interest in the once strong and now dying art of botanical microscopy as an assessment tool for the identification of medicinal plants. It was excerpted with permission of the AHP and the publisher, CRC Press, Boca Raton, FL. It is due to be released early in 2011.

"[Pharmacognosy] has been employed throughout the course of man's life on earth – by primitive hunters and warriors who selected specific plants for preparing spear and arrow poisons; by priest-physicians and herbalists who learned by trial and error that some plants produced and others dispelled the symptoms of disease; by apothecaries and chemists who prepared more potent and stable products from crude materials."

Pratt and Youngken, *Pharmacognosy*

Pharmacognosis – knowledge of medicines

In the early 1800s, Johann Adam Schmidt (1759-1809; Figure 1), a professor of General Pathology, Therapeutics, and *Materia Medica* at the Joseph Academy of Medicine in Vienna, Austria, penned a hand written manuscript entitled *Lehrbuch der Materia Medica*, which was posthumously published in 1811. In his *Lehrbuch*, Schmidt, a physician of Beethoven, for the first time in published literature used the term *pharmacognosis*, from the Greek *pharmacon* (*Φαρμακον*), meaning medicine or poison, and *gnosis* (*γνωσις*), meaning knowledge. This described the skills necessary for the development of medicines, from source to finished medical product and its uses. Until these times, these skills were taught under the general heading of materia medica. A few years later in 1815, a medical student in Halle an der Saale, Germany named Christianus Aenotheus Seydler,

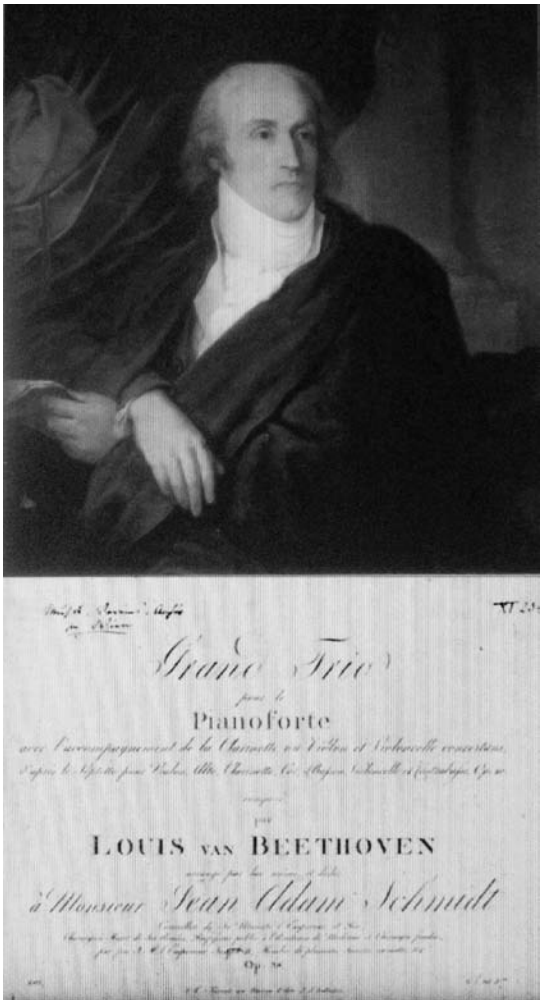

Figure 1
Johann Adam Schmidt (1759-1809). Professor of General Pathology, Therapeutics, and *Materia Medica* at the Joseph Academy of Medicine, Vienna, Austria. Schmidt was a physician to Ludwig von Beethoven who dedicated his Opus 38 (Piano Trio) to Schmidt. Schmidt was the first to coin the term *pharmacognosis* the precursor to *pharmacognosy* in his posthumously published *Lehrbuch* der *Materia Medica* (1811).

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in his doctoral thesis *Analecta Pharmacognostica*, for the first time used the term *pharmacognosy*. This formalized the beginning of a long-practiced but newly emerging scientific discipline dedicated to the development of medicines. At that time, predating the isolation and synthesis of the pure pharmaceutical compounds that are the mainstay of modern drugs, all medicines were derived from natural products, a focus of pharmacognosy that has persisted to this day.

While Schmidt and Seydler represented a formal beginning of pharmacognosy as a scientific discipline, pharmacognostic knowledge had been applied in the trade of medicinal plants for as long as botanicals had been used. Alexander Tschirch (1856-1939), a noted pioneer in the early development of pharmacognosy and professor of pharmacognosy at the University of Bern, Switzerland described pharmacognosy as a discipline that predated any of the departments of pharmacy. He further described herbalists as the first pharmacognosists and Dioscorides (Figure 2), by virtue of his writings on medicinal plants, as the first teacher of pharmacognosy. American pharmacognosists Pratt and Youngken (1956) in their work *Pharmacognosy* stated, "[pharmacognosy] has been employed throughout the course of man's life on earth—by primitive hunters and warriors who selected specific plants for preparing spear and arrow poisons; by priest-physicians and herbalists who learned by trial and error that some plants produced and others dispelled the symptoms of disease; by apothecaries and chemists who prepared more potent and stable products from crude materials."

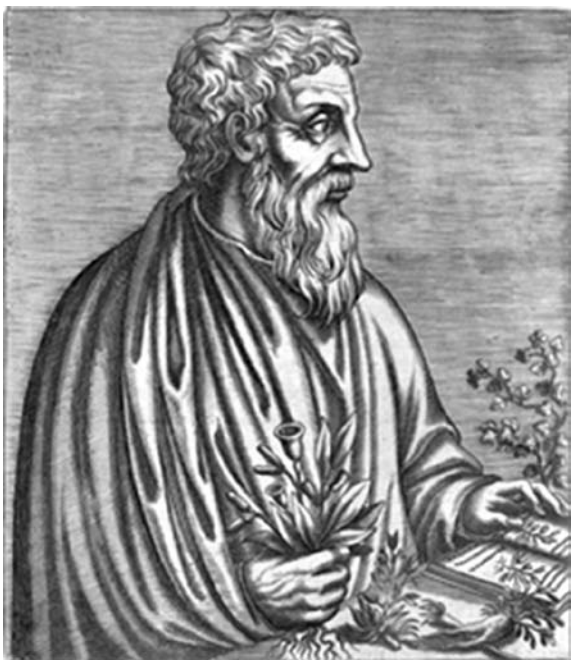

Figure 2
Pedanius Dioscorides (40-90 A.D.). Greek botanist, herbalist, pharmacologist, and physician. Author of De Materia Medica a precursor to all pharmacopoeias in the Western world and one of the most influential medical texts in medical history.

Pharmacognosy – *a descriptive science*

Prior to the advent of modern analytical chemistry, physical description was the primary means of properly identifying medicinal plant parts, and was inextricably linked with botany before the emergence of botany as an independent discipline. Thus, pharmacognosy was predominantly categorized as a "descriptive science." From the earliest records of medical history the knowledge of identifying and cataloguing plants was captured in the many ancient stones, bones, papyri, and texts of herbal medicine and was the domain of herbalists, who were the original physicians. For centuries botany was considered a sub-discipline of medicine, as the identification of plants used in the development of drugs was a pre-requisite for all physicians prior to the rise of pharmacy as a separate discipline. The integration of the profession of medicine and medicinal plants was so strong that still today, graduates of Yale Medical School (US) wear black robes and a green cap, the green in honor of the plants that provide the medicines. The importance of plants in medicine is similarly immortalized in the term routinely used to describe modern medicines; drug; derived from the Dutch *droog* and Old French *drogue*, referring to the drying herbs hanging from the rafters of Old World apothecaries.

Materia medica

Pharmacognosy skills were not limited to only botanical characterization and medicinal uses. In addition, these works included information on the macroscopic characterizations of the plant parts used in medicine (e.g., roots, barks, leaves, seeds, fruits, etc.), country of origin of medicinal plants, specific guidance regarding botanical quality, and potential adulterations. All of these bodies

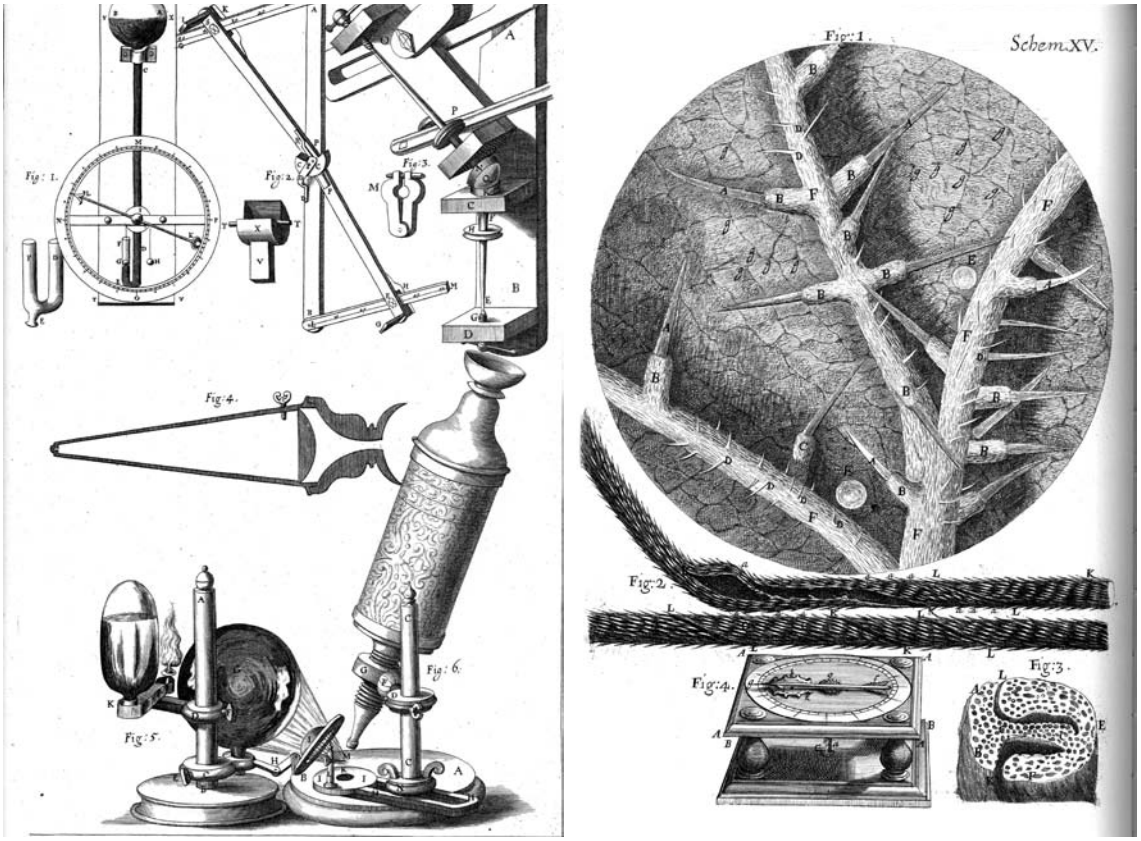

Figure 3
Microscope of Robert Hooke (1667), a contemporary of Sir Isaac Newton, considered by some as the greatest experimental scientist of the 17th century and credited with the invention of the original two-lensed microscope (left). Hooke's microscopic examination of the medicinal plant stinging nettle (*Urtica dioica*) (right). Source: Hooke (1665) *Micrographia*.

of information are of substantial relevance to the quality sourcing of crude medicinal materials, which at one time was the primary domain of the pharmacognosist.

The 19th century was a period of prolific medical writing resulting in the publication of several hundred texts on *materia medica* and medical botany, describing thousands of medicines used worldwide. The early formal *materia medicas* of leading pharmacognosists such as Pereira in 1846 and Flückiger and Tschirch in 1887 provided information regarding plant origin, harvest, chemistry, and the processing and morphological characteristics of the specific plant part to be used as a medicine. Authored works of Pomet (France; 1694), Green (England; 1820), and Cox (US; 1818) discussed the importance of the quality assessment of materials to be used as medicines.

Requirements for quality assessment of medicinal plants were similarly codified in national pharmacopoeias (e.g., London Pharmacopoeia 1618; Paris Pharmacopoeia 1639; Edinburgh 1699; United States Pharmacopoeia 1820). Pharmacopoeias evolved from simple recipe books, to providing detailed descriptions of the macroanatomy of medicinal plant parts. After the application of the microscope to plant morphology, microscopic descriptions were also included, becoming integral to the identity tests provide by pharmacopoeias. Both macroscopic and microscopic descriptions persist in pharmacopoeias today and are accompanied by qualitative and/or quantitative chemical analyses.

Pharmacognosy – *the child of the microscope*

In 1667, Robert Hooke (1635-1703), credited with the invention of the two-lensed microscope (Figure 6a), published his primary work *Micrographia*, in which he described various cells and units of cells as "tissue cells" and further explained that the stinging of nettles (*Urtica* spp.) was due to the flow of a caustic sap from the bristles of the plant (Figure 3). This was among the earliest observations of plant anatomy and physiology at the microscopic level.

Figure 4
Poppy (*Papaver somniferum*). The traditional use of poppy to induce sleep and reduce pain led to the discovery and subsequent isolation of the alkaloid morphine. So named after *Morpheus* the Roman God of sleep and dreams, morphine was the first "active constituent" derived from a plant source. Source: *Medical Botany* Stephenson & Churchill (1836).

In search of the "magic bullet"

In 1805, Friedrich Wilhelm Adam Sertürner, an apprenticed apothecary's assistant in Hannover, Germany with little formal training in pharfimacy, succeeded in isolating the first pure, presumably "active" compound of a plant – the alkaloid morphine from the opium poppy (*Papaver somniferum*) from plant material (Figure 4). In the years following the isolation of morphine numerous other alkaloidal compounds were isolated, including strychnine, caffeine, and quinine (Kapoor 1997). This represented a dramatic departure from the development of whole plants as drugs, to chemical analogues of drugs originally derived from plants. The search for "active constituents" had begun. This change is illustrated in the evolution of the United States Pharmacopoeia (USP). In the 1st edition (1820) there were approximately 150 herbal drugs listed. By 1950, this number had been reduced to approximately 50. Between 1870 and 1970 the total number of botanical drugs in the USP fell from 636 to 68 (Boyle 1991), while increasing to hundreds of relatively pure compounds.

During a similar period in the US (1831-1950), the professions of medicine and pharmacy were also evolving. In the earliest times the herbalists and "rhizomatists" were primarily involved in the collection, distribution, and quality assessment of medicinal plants. As societies became less agrarian and more industrialized, the field of medicine also evolved and commerce in drugs shifted from individual collectors and practitioners to brokers and distributors long disconnected from the source of the plant. This societal change similarly caused a shift away from the herbalists and local "healers" to the emerging academically trained medical profession. The physician's training in *materia medica* began to deemphasize the physical assessment and commercial sourcing aspects of botanical procurement that was evident in early *materia medicas*, and gave greater focus to medicinal activity. Similarly, the focus of the pharmacist became the compounding and dispensing of medicines. Thus, the techniques of pharmacognosy, which had been previously considered a division of botany by some and a distinct science by others, and, which had been dominated by physicians, became an integral but specialized part of pharmacy and the training of pharmacists.

Pharmacognosy – *a shift to "grind and find"*

Pharmacognosy was first formally taught in the US at the Philadelphia College of Pharmacy in 1821 and persisted as part of the curriculum of every pharmacy program in the US until 1940. By the late 1950s in the US most botanical pharmacognosy training was dropped from pharmacy curricula. By this time, plants and the drugs derived from them had largely disappeared from the market, replaced by synthetic or isolated pure chemical entities. The botanical and descriptive aspects of pharmacognosy were supplanted by medicinal and pharmaceutical chemistry as drug quality assurance tools. Continued specialization in analytical chemistry

(e.g., paper chromatography) and structural elucidation, versus the broad organism-based general approach employed by pharmacognosists, was more appropriate for the development of modern drugs. The science of pharmacognosy evolved into the field of pharmaceutical biology with an emphasis on natural products chemistry, molecular biology, biotechnology, and biological and chemical screening. In the US this caused many of the techniques of classical pharmacognosy, including botanical microscopy, to almost completely disappear from academia and practical use, though the quality control aspects of herbal drugs were continuously taught in Europe (e.g., Germany and Switzerland).

Quality assurance of herbal ingredients

Botanical supplements come in various forms, including whole or chopped herbs, powders, teas, capsules, tablets, hydro-alcoholic tinctures, dry extracts, and syrups. In addition to their use as supplements or medicinal agents, botanicals are also increasingly being added to conventional food products such as cereals, beverage teas, potato chips, soups, and juices, as well as to sundry other products such as toilet paper, shampoos, hair conditioners, and skin care products. The quality assurance and assessment of botanical drugs, traditional or modern, requires that every available tool be accessible and applied as appropriate. Each analytical tool has its purpose and utility, and one is only superior to another in terms of the analytical goal. It is a legal requirement of nearly all nations to accurately disclose the identity of ingredients in products. For identification purposes, the highest level of confidence in identity that can be achieved is through morphological analysis. However, generally speaking, formal botanical identification is not widely employed in the trade of medicinal plants. Very seldom will manufacturers find ingredient vendors who can provide an affidavit of botanical authenticity, thus raising the question as to the authenticity of plants in trade. However, botanical identification is only specific for identification and is not appropriate for quality assessment or the evaluation of extracts. The initial set of pharmacognostic tools used for quality assessment of medicinal plant parts is macro- and micro-anatomy and organoleptic analysis (sensory evaluation)—namely size, shape, color, form, texture, taste, and aroma. Morphological and organoleptic analyses offer a suite of tests that, in trained individuals, can provide an assessment of the most subtle of characteristics that contribute to the identification and true quality of a plant, while the microscope allows for the assessment of plant material at a cellular level.

Botanical pharmacognosy – *a phoenix rising from the ashes*

Throughout its long history as both an informal and formal discipline, pharmacognosy has gone through ebbs and flows in its evolution. Pharmacognosy has vacillated between being narrowly defined as a descriptive science focused exclusively on the morphological characterization of drug plants and their adulterants—to being more broadly defined as the body of knowledge needed to understand all aspects of natural products drug development, including pharmacological activity—to being limited to natural products chemistry and structural and molecular elucidation. This latter greater level of specialization represented both the decline of the botanical oriented tools of the pharmacognosist and the birth of a new era of pharmacognosy as noted by renowned pharmacognosist EJ Shellard (UK).

Table 1:	***Eras of pharmacognosy according to Shellard (1983)***
Up to 1890	Pharmacognosy limited to a descriptive science and application of simple chemical assays.
1890-1950	"Halcyon Days": Focus on the macroscopic and microscopic evaluation of crude and powdered drugs.
1959-1980	"The Unfortunate Phoenix": The study of active constituents representing the rebirth of pharmacognosy in the UK.

In name, this identity crisis of pharmacognosy remains daunting to modern pharmacognosists. However, as long as people utilize plant-based medicines, the need for the classical tools of botanical pharmacognosy, including botanical microscopy, will remain. As prophesied by

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Professor Farnsworth (2004), it is unlikely that botanical pharmacognosy will regain its stature in modern pharmacy. However, the day may come when herbal medicines become so integrated into the fabric of modern health care that pharmacists will once again be called upon to do custom compounding and manufacturing of salves, syrups, tinctures, and suppositories. Such practices have reemerged in some pharmacies. Whether, this causes pharmacists to pick up the microscope once again is unknown. Surely, modern physicians, who were once the primary teachers of *materia medica*, will not pick up the botanical skills of pharmacognosy.

At the same time, as noted by Professor Wagner (2004), herbal medicine potentially represents the cutting edge of medicine due to the inherent multi-targeted, multi-component nature of herbal preparations, and the classical tools of the pharmacognosist are very much needed. Perhaps as originally described, botanical microscopy and other observational assessment tools will find their way back into the curriculum of botany programs or into the continued evolution of the training of herbalists. However, it is clear that all the tools of pharmacognosy are important for the continued development and evolution of traditional plant-based medicines. In 1987 Geoffrey Cordell, a professor of pharmacognosy at the University of Illinois-Chicago stated, perhaps prophetically: "Pharmacognosy... is far from dead. It has survived a long, cold winter and presently is awakening as the most high-tech pharmaceutical science." (Kubelka 2004). We need only remember that to ensure the identity, quality, purity, and efficacy of traditional botanical medicines, the tools of classical botanical pharmacognosy are indispensable and therefore must be preserved and cultivated.

Table 2: Evolutionary development of the history of medicine

B.C. 3000	"Here take these herbs with song and prayer."
A.D. 1-1640	"Forget the song and prayer, take willow bark for arthritis and cinchona bark for malarial fevers."
A.D. 1820-1838	"Don't take cinchona and willow bark, take quinine and salicylic acid."
A.D. 1940	"Those herbal potions are snake oil, swallow these pills and antibiotics."
A.D. 1965	"Those pills are unnatural, take these herbs."
A.D. 1995	"Those antibiotics don't work anymore, take echinacea."
A.D. 2000	"Take that snake oil—it's rich in essential fatty acids."
A.D. 2007	"That quinine dosen't work anymore, take wormwood."
A.D. 2525?	"Here take these herbs with song and prayer."

Modified from "the History of Medicine" by anonymous.

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