Medicinal Plant Exploration—Past and Present

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The Arnold Arboretum, in collaboration with the U.S. National Cancer Institute and the Indonesian Herbarium Bogoriense, is exploring the tropical forests of Asia for potential treatments for AIDS and cancer.

Since prehistoric times, the fields of botany and medicine have enjoyed an enduring and fruitful relationship. Whether in the sophisticated setting of a modern pharmaceutical laboratory or an herbalist’s hut on the banks of the Amazon River, plants provide a critical source of treatments for the myriad diseases that afflict humans. In either setting, the principal challenge of the medical practitioner is to distinguish plants that possess pharmaceutical properties from those that are toxic or medicinally inert. Although methods used to screen the plant kingdom for bioactive compounds have changed considerably over the course of human history, the invaluable selection of cures and therapeutics available to modern medicine is the product of a long history of pharmaceutical experimentation.

The Past

We can only conjecture as to when and where the search for herbal remedies began. Archeological remains dating back sixty thousand years reveal that Neanderthals laid their dead to rest with plants that later became staples of ancient pharmacopoeias, such as millefoil (Achillea), St. Barnaby’s thistle (Centaurea), and joint fir (Ephedra). Whether these plants were actually used as medicines or simply served as a farewell gesture to the deceased may never be established with certainty. We do know, however, that most contemporary preliterate cultures, whose lifestyles closely mirror those of our distant ancestors, maintain oral traditions of medical practice that depend primarily on native vegetation.

By the time literacy developed into a basic means of human communication, the application of botanical lore to the practice of medicine was firmly established and systematized. Sumerian clay tablets and Egyptian papyri (2000 B.C.) describe ancient prescriptions and pharmacopeias in considerable detail. Many of the plants that appear in these early records are now known to possess highly bioactive constituents, evidence for which can be found in our own medicine cabinets. Codeine, derived from the opium poppy and used as a narcotic analgesic in Nyquil®, appears in medical traditions that predate modern pharmacology by thousands of years. Similarly, salicylate (aspirin) was originally extracted from willow bark, and ephedrine, the flu remedy in Vicks®, was derived from Ephedra. Approximately twenty-five percent of all modern prescriptions contain natural plant extracts, most of which were used in traditional medicine. Moreover, a significant number of synthetic medicines are derived from plant products whose therapeutic qualities have only recently been improved by chemical tinkering.

The first records of the systematic application of scientific methods to traditional medicine are found in Greece. Hippocrates (fifth to fourth century B.C.) systematically explored the pharmacology of plants and their therapeutic properties. The use of herbs in traditional medicine continues today, with many modern synthetic drugs derived from plant sources. The exploration of tropical forests for potential medicinal compounds is a continuation of this long history of human-plant interaction.
century BC), for example, earned his title “father of medicine” by subjecting folk remedies to open and critical discourse. From the Corpus Hippocraticum, written twenty-three hundred years ago, we know that practitioners of his school of thought paid limited attention to the spiritual source of disease and focused on the effects of diet and weather on health. Cures were based on the regulation of diet and the use of pills, potions, poultices, gargles, ointments, and inhalations derived from a variety of native and foreign plant products.

Four hundred years later (first century AD), Dioscorides acquired his medical knowledge while travelling throughout Europe and Asia Minor as a surgeon to the Roman army of Nero. De Materia Medica describes his medical practice and illustrates the use of over five hundred plant species. Among these, the use of mandrake (Atropa mandragora) as a sedative and castor oil (Ricinus communis) as a purgative are known to have descended from guilds of priests and seers in Egypt and Mesopotamia. Dioscorides also outlined the natural history of drug plants, specified the parts of plants that contain bioactive properties, and described the methods for preparing medicines. The encyclopedic breadth and utility of De Materia Medica ensured its survival for more than a millennium; scholastic monks throughout medieval Europe copied and made use of the work until the Renaissance. By 1655, an English translation of the work provided a model from which emerging European schools of pharmacology developed.

While Spain was exploring tropical America, England and France were discovering new and useful drug plants in temperate North America. De Bry (1593) provided early descriptions and illustrations of medical treatments in Florida that paralleled those used at the time of Hippocrates (i.e., herbal potions, vapors, smoke). In Boston, works such as New-Englands Rarities Discovered by John Josselyn, published in 1672, described the “physical and chyrurgical reme"edies wherewith the Natives constantly use to cure their distempers, wounds and sores.” Many of these native North American drug plants were assimilated into the comprehensive English Herbal of 1633 by John Gerard, including sassafras (Sassafras albidum) from Florida, employed “to comfort the weake and feeble stomacke, to cause good appetite . . . stay vomiting, and make sweet a stinking breath,” and

*Frontispiece from the Spanish treatment on Aztec medicine, Rerum Medicarum Novae Hispaniae Thesaurus, seu Plantarum, Animalium, Mineralium Historia (1651). The bizarre mixture of Greco-Roman and Latin American images indicate anachronistic and exotic influences on the practice of European medicine during the Renaissance. The upper portion portrays a pillar in the form of a medieval castle turret flanked by two winged serpents, suggesting elements of the caduceus of the Greek god of healing, Asclepius. Just below sit two female figures, one holding in her lap a symbol of the Latin goddess Fortuna, life’s horn of plenty, the other with a globe of the world, suggesting the Grecian concept of Mother Earth. The globe does not represent, however, the world of antiquity; rather, it portrays a contemporary view of the world with the American continents in their proper geographic positions. Underneath is a detailed map of central Mexico flanked by two native Americans, one standing by a bundle of medicinal herbs.*
sarsaparilla (*Smilax* spp.) from Virginia, providing "a remedie against long continuall paine of the joynts and head, and against cold diseases." To supplement drug materials from temperate regions, the Society of Apothecaries in Chelsea, England, tried to circumvent the Spanish monopoly in tropical America. In 1729 the Society commissioned the British surgeon William Houstoun to procure drugs and dye plants from the New World tropics for introduction into the mild climate of Georgia. Priority was given to such products as the popular jalap root, the cochineal beetle and its host plant, *Opuntia*, and "Jesuit bark" (quinine, *Cinchona officinalis*). Although this particular project was cut short by the premature death of Houstoun, the global search for new medicines was by this time firmly established as a worthy scientific and commercial enterprise.

During the seventeenth and eighteenth centuries, American medicinal plants and their byproducts were exported to Europe by the tons. Major exports from Mexico included the purgative jalap root (*Ipomoea purga*) and tobacco (*Nicotiana tabacum*), valued for its stimulating, anti-infectant, and anthelmintic properties. Coca leaves (*Erythroxylum coca*) were shipped from South America to be sold as a stimulant and local anesthetic, while ipecac (*Cephaelis ipecacuanha*) was marketed as an emetic and antidysenteric. Apothecaries throughout Europe began dispensing New World medicinal plants and their extracts on a commercial scale. At the same time, society's expectations for improved health care and the desire to increase trade helped justify yet more exploration.

To facilitate the study of pharmaceutical botany, former palace retreats such as the *jardin
du Roi in Paris were transformed into educational and scientific establishments. Both living and preserved plant collections were assembled by trained naturalists who were commissioned to accompany trade ships around the world. European physicians and botanists such as Sir Hans Sloane of England, Paul Hermann of the Netherlands, and Carolus Linnaeus of Sweden received large shipments of specimens originating from Asia, Africa, and the Americas. These extensive collections allowed Linnaeus to attempt the first global inventory of the earth's flora. He estimated the total number of species at ten thousand, a number that probably errs by a factor of at least twenty-five. Yet, even with this limited view of the size and complexity of the plant kingdom, eighteenth-century botanists required a lifetime of dedication to cover the full breadth of their subject. As a consequence, the focus of botanical science shifted away from medicine, leaving practitioners of medical botany to establish their own specialized discipline, known today as pharmacology.

The Present

Over the course of the following two centuries, the science of medicine became more sophisticated and specialized than any Renaissance herbalist could have imagined. Indeed, recent developments in the use of laser beams, ultrasonic waves, and genetic engineering continue to challenge the imagination of modern innovators. Surprisingly, this rapid progress in the medical sciences has also reaffirmed the continuing relevance of botany to medicine. Technical innovations have accelerated the search for medicinal substances in natural products by providing increasingly simple and economical methods for screening massive quantities of plant samples. During the last few decades, discoveries of plant products with anti-tumor, antimalarial, antibiotic, and immunostimulating properties have demonstrated that we are far from exhausting the medicinal potential of botanical resources. With our increased access to the full range of the earth's biological diversity, the possibilities for finding effective treatments for human diseases have never been better.
identified by exposing crude extracts of plant tissues to living cultures of cancerous or HIV-infected cells. If an extract exhibits an effect on diseased cells, the active constituent of the sample is isolated, chemically characterized, and subjected to clinical analysis. Up to ten years of study and hundreds of millions of dollars are required to demonstrate that a promising chemical agent is effective, safe to use, and economically producible.14

The success of these efforts in drug development depends, however, on a critical first step: a program to collect and screen samples of potentially useful plants. This program requires teams of botanists and the collaboration of a worldwide network of botanical institutions.15 Medicobotanical explorations focus primarily on the floristically diverse regions of tropical America, Africa, and Asia, and are led by botanical institutions that specialize in these regions: the New York Botanical Garden, the Missouri Botanical Garden, the Arnold Arboretum, and collaborative research institutions of host countries. As one of the leading institutions in the study of Asian floristics, the Arnold Arboretum is responsible for securing plant material from Indonesia, a tropical country with an exceedingly rich flora (about 37,000 species). Over the past seven years, botanists of the Arnold Arboretum have conducted numerous drug plant expeditions in collaboration with the Herbarium Bogoriense, Indonesia’s national plant collection facility located in Bogor, on the island of Java. Study sites have included the other major islands of the country—Kalimantan (Borneo), Irian Jaya (New Guinea), Sulawesi (Celebes), Java, and Sumatra—as well as the lesser islands of Bali, Kabaena, Sumba, and the Moluccas.

Just to reach these sites presents the first of many challenges that confront the modern plant explorer. While air transport greatly facilitates travel between the larger islands, moving about the smaller islands can require anything from chartered missionary airplanes to fishing boats. Inland transport depends largely on tropical river systems, with each island presenting a distinctive set of obstacles. In Borneo, for example, only large boats with powerful motors can navigate the island’s swift and rocky rivers. The waterways of Irian Jaya, on the other hand, are littered with sunken hardwood trees that permit only small pontooned boats with shallow drafts.

At each site, the plant explorer gathers bulk samples of leaf, stem, bark, and fruit material from about 350 species for analysis at the NCI pharmaceutical laboratories. In addition, up to 1,000 herbarium specimens are collected to identify and document the screening samples and inventory the regional flora. Since 350 bulk collections can weigh more than 1,000 pounds,
A small, pontooned craft with provisions for two months departs the northern coast of New Guinea. Three days of ocean and river travel will be required to reach the planned destination.

A team of workers is needed to help collect, transport, and process plant materials. At least four young men with a talent for tree climbing are engaged to sample material suspended up to 150 feet above the forest floor. A knowledgeable resident provides the research team with local names and traditional uses of plants. As samples are brought into camp, other workers process the plant materials as quickly as possible to prevent fungal contaminations. Fresh bulk samples are chopped into small pieces to facilitate drying, while herbarium specimens are pressed and preserved in alcohol in plastic bags. Miscellaneous tasks required to live and work at the camp—gathering fresh vegetables or hunting meat from the forest, sending messages to neighboring villages, or scouting out routes to nearby collection sites—often occupy the entire population of a small village.

After two months in the field, dried bulk collections and preserved herbarium specimens are brought back to the Herbarium Bogoriense. Indonesian staff members carefully press and dry the voucher material in small ovens to finish preparation of herbarium specimens for future study and reference. Screening samples are shipped immediately to NCI laboratories in the United States, where they wait in cold storage for further processing.

During the early phases of testing, up to five percent of the samples exhibit some degree of efficacy against AIDS or cancer. Subsequent investigations by toxicologists will eliminate most of these possibilities, however. Since 1986,
New Guinean villagers help prepare plant materials for drying in northern Irian Jaya. The dried samples provide a broad range of plant products that will be screened for antitumor and anti-AIDS activity.

over 50,000 plant extractions have been screened at the NCI, of which fewer than ten have been identified as potentially useful drugs.\textsuperscript{16} Success rates have been particularly low in the search for antitumor agents. By comparison, the more recently initiated anti-AIDS research has been more promising: after only a decade, a number of potential anti-HIV compounds have been extracted from plants collected in distant continents (\textit{Ancistrocladus} in \textit{Africa}, \textit{Calophyllum} in Malesia, \textit{Conospermum} in Australia; \textit{Homolanthus} in Samoa).\textsuperscript{17} All of these promising discoveries are presently under study by clinical physicians and toxicologists.

Although modern medicine has yet to identify cures for AIDS, many cancers, and a host of other human maladies—arthritis, obesity, schizophrenia, parkinsonism, depression, to name just a few—potential pharmaceutical treatments for many of these conditions undoubtedly reside in the rich chemical diversity of the plant kingdom. Modern tools of pharmacology have greatly improved on the methods of the forest shaman, the Egyptian seer, and the Aztec herbalist, but we have yet to discover or invent a richer selection of chemical possibilities than that which nature has already provided. So long as the natural diversity of the earth's vegetation remains accessible to scientific inquiry, the tradition of medicinal plant exploration is likely to continue for centuries to come.

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Endnotes


5. T. De Bry, *Grands Voyages* [Frankfort, 1593].

6. J. Josselyn, 1672.

7. J. Gerard, 1633.


The winter habit of a mature Eucommia ulmoides growing near the Hunnewell Building in the Arnold Arboretum. The plant was received from the Veitch Nursery of England in 1907 and was probably grown from seed collected by E. H. Wilson on an early expedition to China.