

Medicinal plants

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Medicinal plants have been identified and used throughout human history. Plants make many chemical compounds that are for biological functions, including defence against insects, fungi and herbivorous mammals. At least 12,000 such compounds have been isolated so far; a number estimated to be less than 10% of the total.^{[2][3]} Chemical compounds in plants mediate their effect on the human body through processes identical to those already well understood for the chemical compounds in conventional drugs; thus herbal medicines do not differ greatly from conventional drugs in terms of how they work. This enables herbal medicines to have beneficial pharmacology, but also gives them the same potential as conventional pharmaceutical drugs to cause harmful side effects.^{[2][3]} Moreover, plant material comes with a variety of compounds which may have undesired effects, though these can be reduced by processing.

The use of plants as medicines pre-dates written human history. Ethnobotany, the study of traditional human uses of plants, is recognized as an effective way to discover future medicines. In 2001, researchers identified 122 compounds used in modern medicine which were derived from traditional plant sources; 80% of these have had a traditional use identical or related to the current use of the active



The bark of willow trees contains large amounts of salicylic acid, which is the active metabolite of aspirin. Willow bark has been used for millennia as an effective pain reliever and fever reducer.^[1]



Medicinal plant garden

elements of the plant.^[4] Some of the pharmaceuticals currently available to physicians are derived from plants that have a long history of use as herbal remedies, including aspirin, digoxin, quinine, and opium.^[5]

The use of herbs to treat disease is widespread in non-industrialized societies. The annual global export value of pharmaceutical plants in 2012 was over US\$2.2 billion.^[6]

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History

The use of plants as medicine predates written human history. Many of the herbs and spices used by humans to season food also yield useful medicinal compounds.^{[2][3]} The use of herbs and spices in cuisine developed in part as a response to the threat of food-borne pathogens. Studies show that in tropical

climates where pathogens are the most abundant, recipes are the most highly spiced. Further, the spices with the most potent antimicrobial activity tend to be selected.^[7] In all cultures vegetables are spiced less than meat, presumably because they are more resistant to spoilage.^[8] Angiosperms (flowering plants) were the original source of most plant medicines.^[9] Many of the common weeds that populate human settlements, such as nettle, dandelion and chickweed, have medicinal properties.^{[10][11]}

Some animals such as non-human primates, monarch butterflies and sheep are also known to ingest medicinal plants to treat illness.^{[12][13][14]}

Plant samples gathered from prehistoric burial sites are an example of the evidence supporting the claim that Paleolithic peoples had knowledge of herbal medicine. For instance, a 60 000-year-old Neanderthal burial site, "Shanidar IV", in northern Iraq has yielded large amounts of pollen from 8 plant species, 7 of which are used now as herbal remedies.^[15] The deliberate placement of flowers has been challenged. Paul B. Pettitt has stated that the "deliberate placement of flowers has now been convincingly eliminated", noting that "A recent examination of the microfauna from the strata into which the grave was cut suggests that the pollen was deposited by the burrowing rodent *Meriones tersicus*, which is common in the Shanidar microfauna and whose burrowing activity can be observed today".^[16] Also a mushroom was found in the personal effects of *Ötzi the Iceman*, whose body was frozen in the Ötztal Alps for more than 5,000 years, which was probably used to treat whipworm.^[17]

Ancient times

In the written record, the study of herbs dates back over 5,000 years to the Sumerians, who created clay tablets with lists of hundreds of medicinal plants (such as myrrh and opium).^[22] In 1500 BC, the Ancient Egyptian Ebers Papyrus, contains information on over 850 plant medicines, including garlic, juniper, cannabis, castor bean, aloe, and mandrake.^[22]



The essential oil of common thyme (*Thymus vulgaris*), contains 20-54% thymol.^[18] Thymol, is a powerful antiseptic and antifungal that is used in a variety of products.^[19] Before the advent of modern antibiotics, oil of thyme was used to medicate bandages.^{[20][21]} Thymol is also used to treat respiratory infections. A tea made by infusing the herb in water can be used for coughs and bronchitis.^[18]

In India, Ayurvedic medicine has used many herbs including turmeric possibly as early as 1900 BC.^{[23][24]}

Earliest Sanskrit writings such as the Rig Veda, and Atharva Veda are some of the earliest available documents detailing the medical knowledge that formed the basis of the Ayurveda system.^[22] Many other herbs and minerals used in Ayurveda were later described by ancient Indian herbalists such as Charaka and Sushruta during the first millennium BC. The *Sushruta Samhita* attributed to Sushruta in the sixth century BC describes 700 medicinal plants, 64 preparations from mineral sources, and 57 preparations based on animal sources.^[25]



The Ebers Papyrus (c. 1550 BC) from Ancient Egypt has a prescription for *Cannabis sativa* (marijuana) applied topically for inflammation.

The mythological Chinese emperor Shennong is said to have written the first Chinese pharmacopoeia, the "Shennong Ben Cao Jing". The "Shennong Ben Cao Jing" lists 365 medicinal plants and their uses - including Ephedra (the shrub that introduced the drug ephedrine to modern medicine), hemp, and chaulmoogra (one of the first effective treatments for leprosy).^[26] Succeeding

generations augmented on the *Shennong Bencao Jing*, as in the *Yaoxing Lun* (*Treatise on the Nature of Medicinal Herbs*), a 7th-century Tang Dynasty treatise on herbal medicine.^[27]

The earliest known Greek herbals were those of Diocles of Carystus, written during the third century BC, and one by Krateuas from the first century BC. Only a few fragments of these works have survived intact, but from what remains, scholars have noted that there is a large amount of overlap with the Egyptian herbals.^[28] Greek and Roman medicinal practices, as preserved in the writings of Hippocrates (e.g. *De herbis et curis*) and - especially - Galen (e.g. *Therapeutics*), provided the pattern for later western medicine.^[29] Sometime between 50 and 68 AD, the Greek physician Pedanius Dioscorides wrote *Περὶ ὕλης ἰατρικῆς* (commonly known by its Latin title *De Materia Medica*), a compendium of more than 600 plants, 35 animal products, and ninety minerals. *De Materia Medica* remained the authoritative reference of herbalism into the seventeenth century.^[30] Similarly important for herbalists and botanists of later centuries was Theophrastus' *Historia Plantarum*, written in the fourth century BC, which was the first systematization of the botanical world.^{[31][32]}

Middle Ages

Benedictine monasteries were the primary source of medical knowledge in Europe and England during the Early Middle Ages. However, most of these monastic scholars' efforts were focused on translating and copying ancient Greco-Roman and Arabic works, rather than creating substantial new information and practices.^{[34][35]} Many Greek and Roman writings on medicine, as on other subjects, were preserved by hand copying of manuscripts in monasteries. The monasteries thus tended to become local centers of medical knowledge, and their herb gardens provided the raw materials for simple treatment of common disorders. At the same time, folk medicine in the home and village continued uninterrupted, supporting numerous wandering and settled herbalists. Among these were the "wise-women" and "wise men", who prescribed herbal remedies often along with

spells, enchantments, divination and advice. It was not until the late Middle Ages that women and men who were knowledgeable in herb lore became the targets of the witch hysteria. One of the most famous women in the herbal tradition was Hildegard of Bingen. A twelfth-century Benedictine nun, she wrote a medical text called *Causae et Curae*.^{[36][37]}



Dandelion (*Taraxacum officinale*) contains a large number of pharmacologically active compounds, and has been used for centuries as an effective laxative and diuretic, and as a treatment for bile or liver problems.^[33]



Dioscorides' *Materia Medica*, c. 1334 copy in Arabic, describes medicinal features of cumin and dill.

Medical schools known as Bimaristan began to appear from the ninth century in the medieval

Islamic world among Persians and Arabs, which was generally more advanced than medieval Europe at the time. The Arabs venerated Greco-Roman culture and learning, and translated tens of thousands of texts into Arabic for further study.^[38] As a trading culture, the Arab travellers also had access to plant material from China and India. Herbals, medical texts and translations of the classics of antiquity filtered in from east and west.^{[39][40]} Al-Dinawari described more than 637 plant drugs in the ninth century.^[41]

Baghdad was an important center for Arab herbalism, as was Al-Andalus between 800 and 1400. Abulcasis (936-1013) of Cordoba wrote *The Book of Simples*, an important source for later European herbals, while Ibn al-Baitar (1197–1248) of Málaga wrote the *Corpus of Simples*, the most complete Arab herbal which introduced 200 new healing herbs, including tamarind, *Aconitum*, and nux vomica.^[38] Avicenna's *The Canon of Medicine* (1025) lists 800 tested drugs, plants and minerals.^[42] Book Two is devoted to a discussion of the healing properties of herbs, including nutmeg, senna, sandalwood, rhubarb, myrrh, cinnamon, and rosewater.^[38] Other early pharmacopoeias include Abu-Rayhan Biruni's in the eleventh century,^[43] Ibn Zuhr's in the twelfth century,^[44] Peter of Spain's *Commentary on Isaac*, and John of St Amand's *Commentary on the Antedotary of Nicholas*.^[45]

Early modern era

The 15th, 16th, and 17th centuries were the great age of herbals, many of them available for the first time in English and other languages rather than Latin or Greek.

The first herbal to be published in English was the anonymous *Grete Herball* of 1526. The two best-known herbals in English were *The Herball or General History of Plants* (1597) by John Gerard and *The English Physician Enlarged* (1653) by Nicholas Culpeper. Gerard's text was basically a translation of a book by the Belgian herbalist Dodoens and his illustrations came from a German botanical work. The original edition contained many errors due to faulty matching of the two parts. Culpeper's blend of traditional medicine with astrology, magic, and folklore was ridiculed by the physicians of his day, yet his book - like Gerard's and other herbals - enjoyed phenomenal popularity. The Age of Exploration and the Columbian Exchange introduced new medicinal plants to Europe. The *Badianus Manuscript* was an illustrated Mexican herbal written in Nahuatl and Latin in the 16th century.^[46]

The second millennium, however, also saw the beginning of a slow erosion of the pre-eminent position held by plants as sources of therapeutic effects. This began with the Black Death, which the then dominant Four Element medical system proved powerless to stop. A century later, Paracelsus introduced the use of active chemical drugs (like arsenic, copper sulfate, iron, mercury, and sulfur).^[47]

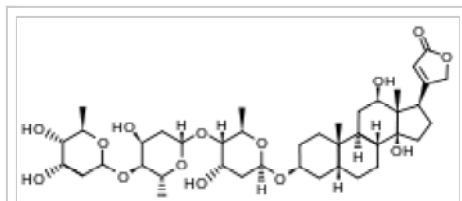
Modern study of plant medicines

The use of herbs to treat disease is almost universal among non-industrialized societies.^[48]

Many of the pharmaceuticals currently available to physicians have a long history of use as herbal remedies, including opium, aspirin, digitalis, and quinine. The World Health Organization (WHO) estimates that 80 percent of the population of some Asian and African countries presently use herbal medicine for some aspect of primary health care.^[49]

Pharmaceuticals are prohibitively expensive for most of the world's population, half of which lives on less than \$2 U.S. per day.^[48] In comparison, herbal medicines can be grown from seed or gathered from nature for little or no cost.

The use of, and search for, drugs and dietary supplements derived from plants have accelerated in recent years. Pharmacologists, microbiologists, botanists, and natural-products chemists are combing the Earth for phytochemicals and leads that could be developed for treatment of various diseases. In fact, according to the World Health Organisation, approximately 25% of modern drugs used in the United States have been derived from plants.^[50]



Digoxin is a purified cardiac glycoside that is extracted from the foxglove plant, *Digitalis lanata*. Digoxin is widely used in the treatment of various heart conditions, namely atrial fibrillation, atrial flutter and sometimes heart failure that cannot be controlled by other medication.

Among the 120 active compounds currently isolated from the higher plants and widely used in modern medicine today, 80 percent show a positive correlation between their modern therapeutic use and the traditional use of the plants from which they are derived.^[4] More than two thirds of the world's plant species - at least 35,000 of which are estimated to have medicinal value - come from the developing countries. At least 7,000 medical compounds in the modern pharmacopoeia are derived from plants.^[51] In many medicinal and aromatic plants (MAPs), significant variations of plants characteristics have been ascertained with varying soil traits, and the selective recovery and subsequent release in food of certain elements have been demonstrated. Great attention must be paid to choose soil and cropping strategies, to obtain satisfactory yields of high quality and best-priced products, respecting their safety and nutritional value.^[52]

Phytochemistry

All plants produce chemical compounds as part of their normal metabolic activities. These phytochemicals are divided into (1) primary metabolites such as sugars and fats, which are found in all plants; and (2) secondary metabolites—compounds which are found in a smaller range of plants, serving a more specific function.^[53] For example, some secondary metabolites are toxins used to deter predation and others are pheromones used to attract insects for pollination. It is these secondary metabolites and pigments that can have therapeutic actions in humans and which can be refined to produce drugs—examples are inulin from the roots of dahlias, quinine from the



The carotenoids in primrose produce bright red, yellow and orange shades. People consuming diets rich in carotenoids from natural foods, such as fruits and vegetables, are healthier and have lower mortality from a number of chronic illnesses

cinchona, morphine and codeine from the poppy, and digoxin from the foxglove.^[53] Toxic plants even have use in pharmaceutical development.^[9]

Plants synthesize a bewildering variety of phytochemicals, but most are derivatives of a few biochemical motifs:^[54]

- Alkaloids are a class of chemical compounds containing a nitrogen ring. Alkaloids are produced by a large variety of organisms, including bacteria, fungi, plants, and animals, and are part of the group of natural products (also called secondary metabolites). Many alkaloids can be purified from crude extracts by acid-base extraction. Many alkaloids are toxic to other organisms. They often have pharmacological effects and are used as medications, as recreational drugs, or in entheogenic rituals. Examples are the local anesthetic and stimulant cocaine; the psychedelic psilocin; the stimulant caffeine; nicotine; the analgesic morphine; the antibacterial berberine; the anticancer compound vincristine; the antihypertension agent reserpine; the cholinomimetic galatamine; the spasmolysis agent atropine; the vasodilator vincamine; the anti-arrhythmia compound quinidine; the anti-asthma therapeutic ephedrine; and the antimalarial drug quinine. Although alkaloids act on a diversity of metabolic systems in humans and other animals, they almost uniformly invoke a bitter taste.
- Polyphenols (also known as phenolics) are compounds contain phenol rings. The anthocyanins that give grapes their purple color, the isoflavones, the phytoestrogens from soy and the tannins that give tea its astringency are phenolics.
- Glycosides are molecules in which a sugar is bound to a non-carbohydrate moiety, usually a small organic molecule. Glycosides play numerous important roles in living organisms. Many plants store chemicals in the form of inactive glycosides. These can be activated by enzyme hydrolysis, which causes the sugar part to be broken off, making the chemical available for use. Many such plant glycosides are used as medications. In animals and humans, poisons are often bound to sugar molecules as part of their elimination from the body. An example is the cyanoglycosides in cherry pits that release toxins only when bitten by a herbivore.

- Terpenes are a large and diverse class of organic compounds, produced by a variety of plants, particularly conifers, which are often strong smelling and thus may have had a protective function. They are the major components of resin, and of turpentine produced from resin. (The name "terpene" is derived from the word "turpentine"). Terpenes are major biosynthetic building blocks within nearly every living creature. Steroids, for example, are derivatives of the triterpene squalene. When terpenes are modified chemically, such as by oxidation or rearrangement of the carbon skeleton, the resulting compounds are generally referred to as *terpenoids*. Terpenes and terpenoids are the primary constituents of the essential oils of many types of plants and flowers. Essential oils are used widely as natural flavor additives for food, as fragrances in perfumery, and in traditional and alternative medicines such as aromatherapy. Synthetic variations and derivatives of natural terpenes and terpenoids also greatly expand the variety of aromas used in perfumery and flavors used in food additives. Vitamin A is an example of a terpene. The fragrance of rose and lavender is due to monoterpenes. The carotenoids produce the reds, yellows and oranges of pumpkin, corn and tomatoes.

A consortium of plant molecular researchers at Washington State University, the Donald Danforth Plant Science Center, the National Center for Genome Resources, and the University of Illinois at Chicago began an NIH-sponsored study of over thirty medicinal plant species late 2009. The initial work, to develop a sequence reference for the transcriptome of each, has led to the development of the Medicinal Plant Transcriptomics Database.

Clinical tests

Many herbs have shown positive results in-vitro, animal model or small-scale clinical tests,^[55] while studies on some herbal treatments have found negative results.^[56]

In 2002, the U.S. National Center for Complementary and Integrative Health of the National Institutes of Health began funding clinical trials into the effectiveness of herbal medicine.^[57] In a 2010 survey of 1000 plants, 356 had

clinical trials published evaluating their "pharmacological activities and therapeutic applications" while 12% of the plants, although available in the Western market, had "no substantial studies" of their properties.^[58]

According to Cancer Research UK, "there is currently no strong evidence from studies in people that herbal remedies can treat, prevent or cure cancer".^[59]

Some herbalists criticize the manner in which many scientific studies make insufficient use of historical knowledge which has been shown useful in drug discovery and development in the past and present.^[4] They maintain that this traditional knowledge can guide the selection of factors such as optimal dose, species, time of harvesting and target population.^[60]

Prevalence of use

A survey released in May 2004 by the National Center for Complementary and Integrative Health focused on who used complementary and alternative medicines (CAM), what was used, and why it was used. The survey was limited to adults, aged 18 years and over during 2002, living in the United States. According to this survey, herbal therapy, or use of natural products other than vitamins and minerals, was the most commonly used CAM therapy (18.9%) when all use of prayer was excluded.^{[61][62]}



The bark of the cinchona tree contains quinine, which today is a widely prescribed treatment for malaria, especially in countries that cannot afford to purchase the more expensive antimalarial medications.

Herbal remedies are very common in Europe. In Germany, herbal medications are dispensed by apothecaries (e.g., Apotheke). Prescription drugs are sold alongside essential oils, herbal extracts, or herbal teas. Herbal remedies are seen by some as a treatment to be preferred to pure medical compounds which have been industrially produced.^[63]

In India, the herbal remedy is so popular that the Government of India has created a separate department - AYUSH - under the Ministry of Health & Family Welfare. The National Medicinal Plants Board was also established in 2000 by the Govt. of India in order to deal with the herbal medical system.^[64]

Avid public interest in herbalism in the UK has been recently confirmed by the popularity of the topic in mainstream media, such as the prime-time hit TV series BBC's *Grow Your Own Drugs*, which demonstrated how to grow and prepare herbal remedies at home.

Safety

A number of herbs are thought to be likely to cause adverse effects.^[65] Furthermore, "adulteration, inappropriate formulation, or lack of understanding of plant and drug interactions have led to adverse reactions that are sometimes life threatening or lethal."^[66] Proper double-blind clinical trials are needed to determine the safety and efficacy of each plant before it can be recommended for medical use.^[67] Although many consumers believe that herbal medicines are safe because they are "natural", herbal medicines and synthetic drugs may interact, causing toxicity to the patient. Herbal remedies can also be dangerously contaminated, and herbal medicines without established efficacy may unknowingly be used to replace medicines that do have corroborated efficacy.^[68]

Standardization of purity and dosage is not mandated in the United States, but even products made to the same specification may differ as a result of biochemical variations within a species of plant.^[69] Plants have chemical defense mechanisms against predators that can have adverse or lethal effects

on humans. Examples of highly toxic herbs include poison hemlock and nightshade.^[70] They are not marketed to the public as herbs, because the risks are well known, partly due to a long and colorful history in Europe, associated with "sorcery", "magic" and intrigue.^[71] Although not frequent, adverse reactions have been reported for herbs in widespread use.^[72] On occasion, serious untoward outcomes have been linked to herb consumption. A case of major potassium depletion has been attributed to chronic licorice ingestion,^[73] and consequently professional herbalists avoid the use of licorice where they recognize that this may be a risk. Black cohosh has been implicated in a case of liver failure.^[74]

A 2013 study published in the journal BMC Medicine found that one-third of herbal supplements sampled contained no trace of the herb listed on the label. The study found products adulterated with filler including allergens such as soy, wheat, and black walnut. One bottle labeled as St. John's Wort was found to actually contain Alexandrian senna, a laxative.^[75]

Few studies are available on the safety of herbs for pregnant women,^[76] and one study found that use of complementary and alternative medicines are associated with a 30% lower ongoing pregnancy and live birth rate during fertility treatment.^[77] Examples of herbal treatments with likely cause-effect relationships with adverse events include aconite, which is often a legally restricted herb, ayurvedic remedies, broom, chaparral, Chinese herb mixtures, comfrey, herbs containing certain flavonoids, germander, guar gum, liquorice



Datura stramonium has been used as a treatment for asthma symptoms when smoked, because it contains atropine, which acts as an antispasmodic in the lungs. However, datura is also an extremely powerful hallucinogen and overdoses of the tropane alkaloids in it can result in hospitalization or death.

root, and pennyroyal.^[78] Examples of herbs where a high degree of confidence of a risk long term adverse effects can be asserted include ginseng, which is unpopular among herbalists for this reason, the endangered herb goldenseal, milk thistle, senna, against which herbalists generally advise and rarely use, aloe vera juice, buckthorn bark and berry, cascara sagrada bark, saw palmetto, valerian, kava, which is banned in the European Union, St. John's wort, Khat, Betel nut, the restricted herb Ephedra, and Guarana.^[66]

There is also concern with respect to the numerous well-established interactions of herbs and drugs.^[66] In consultation with a physician, usage of herbal remedies should be clarified, as some herbal remedies have the potential to cause adverse drug interactions when used in combination with various prescription and over-the-counter pharmaceuticals, just as a patient should inform an herbalist of their consumption of orthodox prescription and other medication.

For example, dangerously low blood pressure may result from the combination of an herbal remedy that lowers blood pressure together with prescription medicine that has the same effect. Some herbs may amplify the effects of anticoagulants.^[79] Certain herbs as well as common fruit interfere with cytochrome P450, an enzyme critical to much drug metabolism.^[80]

Topics

Topics concerning medicinal plants include:

- Herbalism
- Phytotherapy
- Botanical Ethnopharmacy
- Ethnobotany, the scientific study of the relationships that exist between humans and plants
- Bach flower remedies

See also

- Ethnomedicine
- European Directive on Traditional Herbal Medicinal Products
- History of pharmacy
- List of herbs with known adverse effects
- List of plants used in herbalism
- Medicinal mushrooms

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