A DRUG FOR ALL SEASONS MEDICAL AND PHARMACOLOGICAL HISTORY OF ALOE

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ALOE IS A DRIED RESINOUS SAP derived from the leaves of various species of the aloe plant. It belongs chemically to the anthraquionone-producing plants, along with cascara, frangula (alder buckthorn), rhubarb, rumex, and senna.[1] Since earliest times aloe has occupied a prominent place in the materia medica, prescribed in small doses as a tonic to improve digestion and in larger doses as a powerful purgative and an emmenagogue. Other uses include detersive, desiccative, insecticide, antiseptic, vermifuge, and cholagogue. Viewing aloe as one of the more reliable drugs in their armamentarium, physicians employed it as an extract, decoction, tincture, wine, or powder, alone or in composition with iron, myrrh, or asafetida. Its popularity as a therapeutic agent is marked by long antiquity, the considerable number of preparations which included aloe among their constituents, and the tenacity with which the drug held forth in the pharmacopoeias, dispensatories, and medical texts of the world.[2,3,4]

VARIETIES OF ALOE

The aloe plant belongs to the Lily family (family *Liliaceae,* tribe *Aloineae*) and comprises more than 180 species and hybrids native to sunny, arid areas in Southern and Eastern Africa, and subsequently introduced into Northern Africa, Spain (Valencia and Granada), Gibraltar, China, and the West Indies. The plants are succulent perennials that secrete a watery juice from tubular cells that run lengthwise through the stout, fleshy leaves. In areas of South Africa and Natal, certain species of the aloe plant attain a height of 30 to 60 feet, with stems more than 12 feet in circumference. The juice is collected from wild plants (typical in South Africa) or from aloe extensively cultivated in rows 18 inches apart (in the West Indies). Juice collection begins the second year from planting and continues for some 12 years. In March or April, following the rainy season, the leaves are cut and their ends placed in a

trough or container to collect the juice. In Aruba cultivators evaporated the juice over an open fire or steam-jacketed vacuum pans while in Africa the juice was allowed to ferment before evaporation in the fresh air. The thick residue was then poured into gourds, tins, boxes, kegs, goat or monkey skins, or other containers, and allowed to harden before export.[5,6]

Of the many species and hybrids of aloe, only a few have been of importance to the materia medica. The 1843 *Dispensatory of the United States* (1882) mentions Socotrine, Barbadoes, Cape, Mocha, Caballine and Natal aloe.[7-10] English apothecary Jonathan Pereira (1804–1853), in his *Manual of Materia Medica and Therapeutics* (1866), noted numerous varieties of commercial aloe in the mid-19th century. These included Socotrine aloe brought originally by way of Smyrna (thus called Turkey aloe) and later through Bombay in the skins of gazelles; Hepatic aloe, which came to the London markets via Bombay and called Bombay or East-Indian aloe; Barbadoes aloe, transported in 60 and 70 pound gourds; Cape aloe, which came in chests or skins; fetid, horse, or caballine aloe, which were thought to be a cheap and impure grade of aloe without specific origin; Mocha aloe, also a cheap grade, adulterated with sand and other impurities; the black and brittle Indian aloe, which came from northern India; Guzerate aloe, which resembled Indian aloe; the dark and gummy Salem aloe; Trichinopoli aloe, known for its brittleness, odor, and opaque color; and Curacao aloe, popular in Holland and which resembled Cape aloe.[11] However, by the 20th century three species predominated within the various materia medicas: *Aloe ferox,* Mil., Cape aloe; *Aloe perryi,* Baker, Socotrine, and Zanzibar aloe; and *Aloe baradensis,* Mil., Mediterranean, Curacao, or Barbados aloe. The formerly important Socotrine and Zanzibar varieties are no longer official in the *British Pharmacopoeia,* having been replaced by the Cape and Curacao varieties.[12,13]

Socotrine aloe grew in eastern Africa and on the island of Socotra in the Indian Ocean. Imported from Bombay and Zanzibar, the commercial drug was reddish-brown and was translucent in thin segments.[14] According to Engler and Prantl, who elaborated on its production in 1887, natives of Socotra made a hole in the ground and lined it with goat or sheep skins. Aloe leaves were then cut and laid around the depression so that the juice from the leaves would flow into the hole. As the watery juice evaporated, it left a thick residue known as *Jayef Gesheeshah.* After further evaporation the residue hardened and was called *Jayef Kasahul.* Interestingly, most 19th century authors believed that very little of the Socotrine aloe was actually exported from Socotra to Europe. Instead, exporters shipped inferior aloe such as Mocha through the ports of Bombay, Muscat, Aden, and Zanzibar and identi-

fied it as Socotrine aloe.[10,15,16] However, because of the impurities in Mocha aloe, federal authorities in the United States rejected the variety in 1911. By 1912 Mocha aloe had disappeared from the market.[17]

Cape aloe, produced in the Cape Colony since 1773, remains an important article of commerce today. Early references to the aloe of South Africa include descriptions by Clusius in 1605, followed by the works of Emanuel Swertius in 1612 and Johannes Bodaeus in 1644. The Dutch East India Company, formed in 1602 from an amalgamation of private Dutch trading companies, developed a company garden devoted to native African plants. Here, during the 17th century, many species of aloe were collected and identified. The first mention of the commercial use of the Cape variety was by Frances Masson, sent to the Cape by the Royal Gardens at Kew to collect seeds and plants. During his two-year visit he described how the local "peasants" (Hottentots) gathered the gum aloe from the sap of the leaves and sold the juice for two to six pence per pound.[18]

Cape aloe was gathered in much the same way as Socotrine aloe, its cultivators leaving the juice to evaporate either naturally or over an open flame, and the concentrated liquid poured into boxes to harden. In these containers merchants shipped the aloe to Cape Town and from there to Europe and America. Although recognized in the Swiss, German, and Austrian pharmacopoeias, Cape aloe was dropped from the *U.S. Pharmacopoeia* in 1880. Nevertheless, it remained popular among physicians with European training (especially German) who preferred the Cape aloes as a more reliable drug. It became official in Britain in 1932.[10,13,19,20]

Traders first brought Barbadoes aloe to the London Market in 1693, but it did not become a regular commercial article until a half century later. By 1843 London was importing 4,227 gourds annually. The production of the Barbadoes aloe differed markedly from the technique used in the Cape aloe. Instead of digging a hole in the ground, cultivators placed the dripping ends of the cut leaves in wooden troughs, which carried the juice to collecting vessels. From there the juice was taken to the boiling house where the liquid thickened and darkened in color. When the aloe reached the right consistency, workers poured the residual mass into 60 to 70 pound gourds to dry. By the end of the 19th century, however, the cultivation of Barbadoes aloe virtually stopped and, in its place, a local crop exported from the island of St. Vincent was sold under the Barbadoes designation. In addition, exporters sold Curacao or Bonaire aloe under the Barbadoes name.[6,21]

Although sometimes called Bonaire or West Indian aloe, the Curacao aloe was cultivated on the islands of Aruba, Bonaire, and Curacao in the Dutch West Indies and appeared on the European market about 1817. Cultivated in

much the same manner as Barbadoes aloe, the Curacao variety sold principally in the United States and often under the guise of Barbadoes and Cape aloes. Manufacturers imported 96,500 pounds into the United States in 1876 and 230,634 by 1882. By 1898 drug manufacturers were importing 640,658 pounds into the United States and 841,130 pounds by 1901.[10,13]

Other unofficial varieties such as Natal, hepatic, fetid, and caballine or horse aloe received less favorable commentaries, criticized for their impurities and lack of market availability. Around 1900 a variety known as Uganda aloe appeared on the London market. Only afterward did druggists learn that this new variety was really Cape aloe prepared in a different manner. Instead of evaporating the juice over an open fire, the growers partially fermented it before evaporation in the sun.[10]

ALOIN

Although physicians had prescribed aloe for more than 2,000 years, not until 1851 did T. and H. Smith of Edinburgh discover the active principle of the plant. In the preparation of a quantity of the aqueous extract of aloe, the two chemists separated from the commercial Barbadoes aloe a crystalline substance that, upon trial action on the body, yielded a cathartic action which they regarded as the active principle. They gave the substance the name "aloin." Subsequent experiments extracted a similar crystalline substance from the Socoterine and Cape aloe.[22] The Smiths concluded that aloin possessed all the properties of the crude drug. In small doses it acted as a tonic, assisting digestion, giving tone to muscular tissue, and exerting a special influence on the liver. In larger doses it became a strong purgative, acting especially on the large intestine, increasing the intestinal secretions and the peristaltic action of the bowels. In combination with strychnine and belladonna, aloin became one of the most effective and popular laxatives for chronic constipation.[23,24]

More than a decade after the Smiths' discovery, William Craig of Edinburgh questioned the validity of their claim, suggesting instead that the purgative power of aloe was due to the resin. Craig, a lecturer on materia medica at the Edinburgh School of Medicine, carried out experiments in 1872 on the properties of "changed aloin," "modified aloin," or so-called resin of aloe. Having first administered the drug to rabbits and later to men and pregnant women, he concluded that the resin of aloe possessed "all the activity of crystallized aloin."[25]

In research carried out in 1875 and in a subsequent paper read before the Medico-Chirurgical Society of Edinburgh in 1877, Craig reversed his earlier

position and admitted that, unless prepared with extreme care, the resin contained enough aloin to confuse the properties of aloin with those of the resin. When aloin was thoroughly removed from the resin, Craig discovered that the resin possessed no purgative properties. "In my first experiments with the resin," he noted, "I obtained similar results, and on communicating these results to Mr. Smith, he immediately examined the resin, and found that it contained a small amount of aloin, and afterwards prepared some which he believed to be as nearly exhausted of aloin as resin can well be; and when I experimented with this resin, I found it perfectly inert even in doses of twelve grains." From these more exacting experiments Craig determined that aloin remained the active principle of aloe and attributed any purgative effect found in the resin to the aloin remaining after impure manufacture.[23]

Having established that aloin differed in physiologic activity as well as chemical properties from natural aloe, industrial pharmacists soon began manufacturing barbaloin, socaloin, zanaloin, and nataloin as a purer and more effective drug substitute, causing little or no griping of the bowels. chemists set out to answer whether the crystalline principles of the various aloes were the same or whether there were differences among them. Craig concluded that the aloin of true Barbadoes aloe was nearly three times more powerful than other varieties.[10,26] Subsequent researchers have determined that the pharmaceutical properties of aloe in its native state are stronger than those in a transplanted condition.[27]

Nevertheless, while some believed barbaloin to be more active than either zanaloin or nataloin, physicians and pharmacists tended to make little distinction in their choice of a purgative. Indeed, they prescribed aloe and aloin almost without discrimination. And although reports in medical and pharmaceutical journals did suggest some differences in their respective strengths, there remained sufficient uncertainty to preclude any definitive statement on which the medical profession could base a substantive change in practice.[14,28]

Modus Operandi and Uses

Physicians could not agree on the exact modus operandi of the drug. William Cullen (1712–1790), and later George B. Wood (1797–1879) and Franklin Bache (1792–1864), believed that the drug had a particular affinity for the large intestine. Others such as Rhazes (865–925) and Aretaeus the Cappadocian (2d to 3d century A.D.) had held that aloe affected the secretion of bile, excited by its specific action on the liver.[29,30,31] Other physicians discounted both the intestinal and liver origins and asserted instead that aloe

acted specifically upon the vena porta system. One such advocate was William Braithwaite, who wrote: "That it acts upon the vena portarum, is fairly to be be deduced from the very peculiar state into which the hemorrhoidal vessels are thrown by the congestions which so rapidly occur after a dose of this drug has been taken, and also by the condition of the uterine vessels, which has led to its employment as an emmenagogue."[29]

Physicians prescribed aloe as a purgative, and considered its effects the same whether administered internally (aloetic pill) or applied externally to an ulcer or excoriated surface (aloetic salve). Pharmacists also concocted a popular children's purgative using one part tincture of aloe and two parts soap liniment or five grains of aloe mixed with lard, which they sold as oleate of aloe. When the mixtures were rubbed with gentle friction on the abdomen of costive children, physicians claimed that they were useful purgatives that did not irritate the intestines or produce hemorrhoids. Physicians also prescribed aloe in the form of enema for dislodging worms from the rectum.[29,32]

As a rule, physicians prescribed aloe as a laxative "tonic" for the lower bowel. Although not recommended to clean out the entire alimentary canal, it did serve to cure chronic constipation. Because of its purgative powers, aloe became the chief ingredient of the popular dinner-pills sold in the eighteenth and nineteenth centuries.[24] While physicians understood calomel to act chiefly upon the upper portion of the small intestines, they believed that aloe acted upon the lower portion of the large intestines. For that reason, physicians prescribed a compound cathartic pill (containing both aloe and calomel) so that the aloe could take over where the calomel left off.[33]

Physicians prescribed aloe for disturbances of the digestion, anorexia, dyspepsia, flatulent distention, habitual costiveness, and obstinate constipation, in jaundice and other diseases of the liver, in affections of the menstrual secretions, and for troublesome affections such as hypochondria, melancholy, and mania. Physicians also believed that aloe affected the genitourinary system, creating hyperemia of the uterus, and augmenting the menstrual flow in women while occasioning erections and increasing the sexual appetite in men.[29] Women saw in aloe a different capability, relieving "almost all classes of bodily ailments...from the age of puberty to the menopause; and there is even a superstition that it will measurably relieve the nervous manifestations which often accompany that interesting period in woman's life."[24]

In 1883 William K. Bowling, professor of medicine in the Medical Department of the University of Tennessee and former president of the American Medical Association, recalled having mistakenly given Cooke's pills containing aloe to a slave suffering from dysentery in 1832. Fearing that he had

killed the slave and that the owner would be seeking retribution for the mistaken prescription, he was relieved to learn that the pills had actually cured the bloody flux. Soon he was prescribing ipecac and Cooke's pills for dysentery and was pleased to see it become a popular remedy in the southern states.[32]

Although not discussed at any length in medical journals, the compound tincture of benzoin, better known as Friar's Balsam, was prescribed as a local sedative for insect bites.[34] Physicians sometimes employed the same compound tincture as an inhalant or vulnerary in bronchitis.[33]

So well known was the reputation for spicata or Socotrine aloe to produce hemorrhoids that many patients simply refused to take it when prescribed.[35] Physicians typically warned that, when repeatedly given, aloe irritated the rectum and encouraged hemorrhoids. Fallopius reported that of 100 persons who used aloe freely, 90 of them became affected with "a hemorrhoidal flux, which ceased when its use was omitted."[29,36]

PHARMACO-THERAPEUTIC HISTORY

The German Egyptologist Georg Ebers (1837–1898) reported aloe to be among the many drugs used in ancient Egypt. Legend suggests that Alexander the Great, after conquering Persia in 333 B.C., and on the advice of his mentor Aristotle, returned by way of the Indian Sea and visited Socotra where he left Ionian Greeks to cultivate the aloe for medicinal purposes.[6,37,38] Aloe was also mentioned in the *Natural History* of Pliny the Elder (23–79 A.D.) and in the *Materia Medica* of Dioscorides (first century A.D.) as well as by later Greek and Arabian physicians. Dioscorides referred to its bitterness and strong smell. Yet, "it hath a power of binding, of procuring sleep, of drying, of thickening of bodies, and of loosening of ye belly, and of cleansing of ye stomach being dranke ye quantity of two spoonfuls with water cold, or warm milk...." He also found it useful in the treatment of skin irritations and promoting the healing of boils and wounds.[39,40,41] In the *Medical Formulary* of Al-Kindi (800–870), *aloe vera* and *aloe perryi* were regarded as effective for strangury and stomach problems in Babylonia. It was also employed in the care of boils, in a drug for abscess, as a dentifrice, in eye medicines, as a remedy for insanity and epilepsy, and in a recipe for excessive perspiration.[42]

John Scarborough notes that while many of the drugs and simples listed by Dioscorides had "local" origins within the Greek oikoumene, nevertheless a number of plants, including aloe, were imported from the east, beyond the extent of Hellenistic influence. From the descriptions provided by Dioscorides and other Greek and Latin sources, Scarborough deduces that the

plant was *aloe perryi,* Baker, the Socotrine aloe, from the island of Socotra in the Indian Ocean. Instead of accepting the legendary origins of its introduction into the Greek world by Alexander's expeditions, he suggests that aloe entered Greco-Roman medicine around the time of the reign of Augustus (27 B.C.–14 A.D.) during trade between India and Roman Egypt. Scarborough recognizes evidence by other scholars who, noting the discovery of the monsoons and their navigational impact, suggest an earlier origin, somewhere between 100 and 70 B.C.[43]

A venerated aloe preparation, known as *hiera picra,* may have been invented by Themison, a Roman physician practicing in the reign of Augustus (27 B.C.–14 A.D.). His concoction consisted of aloe, mastisch, cinnamon, saffron, Indian nard, carpobalsamum, and asarum. Later physicians added honey to make it into an electuary.[33,44,45] Through the centuries, women prescribed for themselves "hicry picry" as an abortifacient.[46]

Rufus of Ephesus, who lived during the reign of Emperor Trajan, introduced a mixture under the name *pilulae pestilentiales,* and the early Edinburgh pharmacopoeias referred to the same mixture under the title *pilulae communes.* Raymond Minderer's (1570–1621) book *Aloedarium marocostinum,* published in 1616, extolled the virtues of the pill as a cathartic and general tonic, which served as a substitute for the compound rhubarb pill.[33,47]

Paracelsus (1493–1541), who was not shy when proclaiming the virtues of the materia medica, extolled the aperient powers of *elixir proprietatus* which he claimed would prolong life by keeping the bowels open. His disciple Oswald Croll (1560–1609) reported that the formula for this elixir contained tincture of aloe, myrrh, and saffron with sulphuric acid. Despite its questionable contents, the elixir sold under a variety of titles, including Elixir of Aloes, Compound Tincture of Aloes, Tincture of Aloes and Myrrh, and Elixir Garus.[46,48,49]

During the late 18th century aloe became an essential part of the so-called Morisonian system of medicine that thrived for a time in England. Its founder, James Morison, "discovered" a series of self-evident truths regarding the human constitution and built his Morisonian pill-shop around the use of his panacea. According to Morison,

> All animals consist of fluids and solids!
> All embryo animals consist entirely of fluids.
> The chief fluid is the blood, from which all others are derived.
> Blood forms the water—air gives it life.
> All constitutions are radically the same.
> All diseases arise from impurity of the blood.

> All diseases arise from one source, and therefore require but one medicine.
> Proper purgation by vegetables is the only effectual way of curing all diseases.
> This vegetable purgative must be capable of being digested and mixing with the blood, so as to rid the body of all superfluous humours (disease).[50]

Morison's Pills No. 1, a mild aloetic pill consisting of equal parts of aloe and cream of tartar, made into a mass with either mucilage or syrup, and his Pills No. 2, a compound aloetic pill of dangerous strength, consisting of colocynth, gamboge, aloe, and cream of tartar made into a mass, formed the basis of his Morisonian system.[50]

Thomas Parr, an Englishman who reputedly lived to the incredible age of 152 years, sold pills that became a household word in the late 18th century. Parr's Life Pills, consisting "purely of vegetable origin," and noted for their "remarkable...efficacy and simplicity," contained a combination of aloe, rhubarb, and jalap made into a pill mass and flavored with liquorice powder, treacle, and sugar. However, not everyone was convinced of the accolades given to Parr's Pills. One cynic provided an especially amusing testimonial:

> I hereby certify and swear to it, that at the age of fifteen years I had the misfortune to fall into the crater of Vesuvius, and was burned to a cinder; but on taking two of Parr's Life Pills, I completely recovered. At Waterloo I was blown to atoms by a Congreve rocket; but after taking one box and a half of the Pills I speedily got well, and with the exception of occasional shooting pains, which a single pill invariably relieves, I have since been a better man than ever. In 1828 I was cut in two by an engine and forty-five ballast wagons; but on taking one box of those life-renovating pills, I became one again. Last year I fell from the Monument, and my head was driven in; but on taking three of thy pills, O Parr! a new head was observed springing up, and the old one sloughed off.
>
> Mit Hochactung,
> Verbliebe ich U.S.W.,
> Munchausen, Ph.D.
> Langerbogenschussprofessor[50]

Throughout the 18th and 19th centuries aloe remained one of the more popular physician-prescribed and self-prescribed over-the-counter medicines. For relief from habitual constipation Wiesbaden Elixir was an especially effective remedy. The elixir contained Spanish saffron, Socotrine aloe, myrrh, rhubarb, gentian, and brandy. Users dosed themselves after each meal with eight or ten drops mixed with brandy or wine. Americans and Europeans took the highly prized dinner-pill to relieve constipation or simply to encourage healthy stools. Because of their relatively slow action (dinner pills required 12 to 18 hours for effective use), they were deemed an especially effective and mild-acting digestive tonic.[24]

Popular aloetic proprietary drugs included Anderson's Scot's Pills, made from Barbadoes aloe, jalap, treacle, and soap; Dr. Baillie's Pills made from

aqueous extract of aloe, compound extract of colocynth and castile soap; Dr. Baillie's Dinner Pills made from powdered aloe, powdered ginger, ipecacuanha, and powdered capsicum; Dixon's Antibilious Pills made from aloe, scammony, rhubarb, and tartar emetic; and Dr. Fairthorn's Mild Provisional Pills made from gamboge, aqueous extract of aloe, sulphate of potash, senna, scammony, and tartar emetic. Other popular nostrums that contained aloe as the principal ingredient included Hooper's Female Pills, James's Analeptic Pills, Lee's Antibilious Pills, Wyndham's Pills, Peter's Pills, Speedman's Pills, Dr. Hugh Smith's Stomachic Pills, Dr. Fothergill's Pills, Lady Crespigny's Pills, Lady Webster's Dinner Pills, Fordyce's Pills, and Thomas Hawkes Tanner's Pure Pepsin.[50]

Because they were cheap and manufactured in a convenient pill form, aloe and aloetic compounds became the most commonly used cathartic and tonic among the working classes in England and on the continent. Aloe remained popular through the 1890s, particularly the dinner pill containing aloin, strychnine, and belladonna. Other drugs that competed with aloe for its cathartic effect included calomel, jalap, quassia, ipecacuanha, and tartar emetic.[35]

In the United States *Pharmacopoeia* of 1820 the number of preparations using aloe included: Pills of Aloes and Colocynth—Cochiae; Pills of Aloes and Myrrh—Rufi; Pills of Aloes, Myrrh and Guaiac; Pills of Aloes; Powder of Aloes and Canella-Hiera Picra; Tincture of Aloes; Tincture of Aloes and Myrrh; and Tincture of Rhubarb and Aloes—Elixir Sacrum.[46,51] By the early 20th century no fewer than 27 different preparations of aloe were in popular use.[46,52]

In Iran today the Socotrine aloe is employed as a purgative; and in Egypt it is regarded as a detersive, desiccative, and emmenagogue.[42,54,55] Both aloe and aloin continue to be used as medicinal laxatives although aloe has lost much of its previous popularity because of its known tendency to cause griping. In veterinary medicine aloe remains a commonly recommended purgative but contraindicated in peritonitis, nephritis, laminitis, advanced pregnancy, lactation, and debility.[56]

Although aloe has lost much of its popularity as a purgative in pharmacotherapeutic practice because of its tendency to cause painful griping, industrial pharmacists have found new uses for this age-old plant.[33,57,58] In 1935 physicians successfully treated a patient suffering from facial x-ray burns with the healing effects of fresh juice from aloe leaves.[59] Physicians and scientists verified the effects of this treatment in subsequent experiments over the following decades.[60,61,62,63,64] Today aloe is used externally for various

dermatitides, radiation burns, and skin ulcers. Experiments by Rovatti and Brennan showed that when aloe was used to treat dermal burns the skin remained soft and the lesions healed.[65] Aloe is also an important ingredient in compound tincture of benzoin. Cosmetic manufacturers have incorporated the stabilized muscilaginous gel of the aloe leaf into various creams, lotions, and ointments to soften, smooth, and moisturize the skin.[66-70] From ancient folklore into the modern era, aloe has continued to hold forth its many virtues.

REFERENCES

1. Viehoever, A.: Evaluation of aloe. *Am. J. Pharm. 107*:47-72, 1935.
2. Freeman, W.G. and Chandler, S.E.: *The World's Commercial Products: A Descriptive Account of the Economic Plants of the World and of Their Commercial Uses*. Boston, Ginn, 1907.
3. Boulos, L.: *Medicinal Plants of North Africa*. Algonac, MI, Reference Publications, 1983.
4. Sibthorp, J.: *Flora graeca; sive Plantarum rariorum historia, quas in provinciis aut insulis Graeciae legit, investigavit et depingi curavit Johannes Sibthorp*. London, Taylor, 1806–1840.
5. Day, W.B.: The botany of aloes. *J. Am. Pharm. Ass. 2*:620-21, 1922.
6. Fluckiger, F.A. and Handbury, D.: *Pharmacographia. A History of the Principal Drugs of Vegetable Origin, Met With in Great Britain and British India*, 2nd ed. London, Macmillan, 1879.
7. Wood, G.B. and Bache, F.: *The Dispensatory of the United States of America*. 5th ed. Philadelphia, Grigg, Elliot, 1843.
8. Maisch, J.M.: *A Manual of Organic Materia Medica*. Philadelphia, Lea, 1882.
9. Farre, F.J.: *Manual of Materia Medica and Therapeutics*. Philadelphia, Lea. 1866.
10. Wilbert, M.I.: Commercial aloes. *Am. J. Pharm. 75*:201-14, 264-73, 1903.
11. Pereira, J.: *Manual of Materia Medica and Therapeutics*. Philadelphia, Lea, 1866.
12. Morton, J.F.: *Major Medicinal Plants: Botany, Culture and Uses*. Springfield, IL, Thomas, 1977.
13. Trease, G.E. and Evans, W.C.: *Pharmacognosy*. 11th ed. London, Baillière Tindall, 1978.
14. Tilden, W.A. and Dobson, N.C.: Therapeutic value of the crystalline principles of aloes. *Med. Times Gaz. 2*:177-78, 1867.
15. Lloyd, J.U.: *A History of the Vegetable Drugs of the Pharmacopoeia of the United States*. Cincinnati, Lloyd, 1911.
16. von Engler, A. and Prantl, K.: *Die Naturlichen Pflanzenfamilien nebst ihren Gattungen und wichtigeren Arten inbesondere den Nutzpflanzen*. Liepzig, Engelmann, 1877–1911.
17. Dennehy, C.J.: Socotrine aloes. *J. Am. Pharm. Ass. 2*:985-86, 1913.
18. Reynolds, G.W.: *The Aloes of South Africa*. Johannesburg, Trustees, 1950.
19. Bornman, H. and Hardy, D.: *Aloes of the South African Veld*. Johannesburg, Voortrekkerpers, 1971.
20. Jeppe, B.: *Aloes*. Cape Town, Purnell, 1974.
21. Ligon, R.: *A True and Exact History of the Island of Barbados*. London, Parker, 1673.
22. Smith, T. and Smith, H.: On aloin: The cathartic principles of aloes. *Monthly J. Med. Sci. 12*:127-31, 1851.
23. Craig, W.: On the therapeutics of aloin. *Edinburgh Med. J. 22*:911-16, 1877.
24. Aulde, J.: Studies in therapeutics—aloes. *Med. Rec. 38*:629-30, 1890.
25. Craig, W.: Notes on "changed aloin" and the resin of aloes. *Edinburgh Med. J. 20*:1002-04, 1875.
26. Leger, E.:Sur les aloines de aloes de Natal. *J. pharm. Chemie 94*:13-17, 1903.
27. Perry, L.M. and Metzger, J.: *Medicinal Plants of East and Southeast Asia*. Cambridge, MA, MIT Press, 1980.

28. Valaer, P. and Mallory, G.E.: A study of aloes and a quantitative determination of some of its constitutents. *Am. J. Pharm. 106*:81-96, 1934.
29. Peters: On the action and use of aloes. *N. Y. J. Med. 4*:161-67, 1845.
30. Cullen, W.: *Lectures on the Materia Medica*. 2nd ed. Dublin, Whitestone, 1781.
31. Wood, G.B. and Bache, F.: *The Dispensatory of the United States of America*. Philadelphia, Lippencott, Grambo, 1851.
32. Bowling, W.K.: Old lights newly snuffed. *Southern Pract. 5*:97-100, 1883.
33. Fantus, B.: Aloes as a medicine. *J. Am. Pharm. Ass. 11*:616-21, 1922.
34. Cock, F.W.: Aloes as a local sedative. *Br. Med. J. 2*:256, 1918.
35. Noeokomoe: On the use and abuse of aloes. *London Med. Gaz. 4*:139-43, 1829.
36. Fallopio, G.: *De simplicibus medicamentis purgantibus, tractatus*. Venetiis, Ziletti, 1565.
37. Dragendorff, G.: *Die Heilpflanzen der verschiedenen volker und zeiten*. Stuttgart, Enke, 1898.
38. Ebers, G.: *Die ereste bis jetzt aufgefundene sichere Angabe uber die Regierungszeit eines agyptischen konigs aus dem alten Reich*. Liepzig, n.p., 1874.
39. Pliny the Elder: *Natural History*, 27.14-22.
40. Gunther, R.T., editor: *The Greek Herbal of Dioscorides*.Oxford, Johnson, 1934.
41. Riddle, J.M.: *Dioscorides on Pharmacy and Medicine*. Austin, Texas, University of Texas Press, 1985.
42. Levy, M., translator: *The Medical Formulary or Aqrabadhin of Al-Kindi*. Madison, University of Wisconsin Press, 1966.
43. Scarborough, J.: Roman pharmacy and the eastern drug trade; some problems as illustrated by the example of aloe. *Pharm. Hist. 24*:135-43, 1982.
44. LeClerc, D.: *A Natural and Medicinal History of Worms Bred in the Bodies of Men and Other Animals*. London, Wilcox, 1721.
45. Galen: *Compounding Drugs by Place in the Body*, 8.3.
46. Snow, C.M.: Pharmaceutical preparations of aloes. *J. Am. Pharm. Ass. 2*:621-23, 1922.
47. Minderer, R.: *Aloedarium marocostinum*. Augustae Vindelicorum, 1616.
48. Paracelsus: *Botanica oculta; las plantas magicas*. Buenos Aires, Kier, 1945.
49. Croll, O: *Bazilica chymica, and Praxis chymiatrica*. London, Starkey and Passinger, 1670.
50. Anony: The anatomy of quackery. *Med. Circ. 10*:25-27, 167-68, 207-08, 1853.
51. *Pharmacopoeia of the United States of America*. Boston, Ewer, 1820.
52. *Pharmacopoeia of the United States of America*. Philadelphia, Lippincott, 1925.
53. *The National Formulary*, 5th ed. American Pharmaceutical Association, 1926.
54. Dymock, W., Warden, C.J.H., and Hooper, D.: *Pharmacographia Indica. A History of the Principal Drugs of Vegetable Origin, Met With in British India*. London, Paul, Trench, and Trubner, 1890-1903.
55. Ducros, A.H.: *Essai sur le droguier populaire arabe de l'inspectorat des pharmacies du Caire. Mem. pres. a l'Inst. d'Egypte 15*:141, 1930.
56. *The Merck Index of Chemicals and Drugs*. 6th ed. Rahway, N.J., Merck, 1952.
57. Claus, E.P., Tyler, V.E., and Brady, L.R.: *Pharmacognosy*, 6th ed. Philadelphia, Lea and Febiger, 1970.
58. Osol, A., Pratt, R., and Altschule, M.D.: *The United States Dispensatory and Physicians' Pharmacology*, 26th ed. Philadelphia, Lippincott, 1960.
59. Collins, C.E. and Collins, C.: Roentgen dermatitis treated with fresh whole leaf of *aloe vera*. *Am. J. Roentgenol. 33*:396-97, 1935.
60. Loveman, A.B.: Leaf of *Aloe vera* in treatment of roentgen ray ulcers. *Arch. Dermatol. Syphilol. 36*:838-43, 1937.
61. Lushbaugh, C.C. and Hale, D.B.: Experimental acute radiodermatitis following beta irradiation. *Cancer 6*:690-98, 1953.
62. Rowe, T.D.: Effect of fresh *aloe vera* jel in the treatment of third-degree roentgen reactions of white rats. *J. Am. Pharm. Ass. 29*:348-50, 1940.

63. Brown, J.: Management of Cancer of the Skin of the Face and Neck. In: *Cancer of the Head and Neck,* Conley, J., editor. Washington, D.C., Butterworths, 1967. Butterworths, 1967.
64. Lewis, W.H. and Elvin-Lewis, M.P.F.: *Medical Botany: Plants Affecting Man's Health*. New York, Wiley, 1977.
65. Rovatti, B. and Brennan, R.J.: Experimental thermal burns. *Ind. Med. Surg. 28*:364-68, 1959.
66. Goff, S. and Levenstein, I.: Measuring the effects of topical preparations upon the healing of skin wounds. *J. Soc. Cosmetic Chem. 15*:509-18, 1964.
67. Morton, J.F.: Folk uses and commercial exploitation of aloe leaf pulp. *Econ. Botany 15*:311-19, 1961.
68. Roboz, E. and Hagen-Smit, A.J.: A mucilage from *aloe vera*. *J. Am. Chem. Soc. 70*:3248-49, 1948.
69. Wells, F.V.: *Cosmetics and the Skin*. New York, Reinhold, 1964.
70. Beedel, S.: *Herbs for Health and Beauty*. London, Sphere Books, 1972.