

JABORANDI: AN INTERDISCIPLINARY APPRAISAL

BO HOLMSTEDT

*Department of Toxicology, Swedish Medical Research Council, Karolinska Institutet,
S-104 01 Stockholm (Sweden)*

S. HENRY WASSÉN

Gothenburg Ethnographic Museum, S-411 14 Gothenburg (Sweden)

RICHARD EVANS SCHULTES

Botanical Museum, Harvard University, Cambridge, MA 02138 (U.S.A.)

(Received August 31, 1978)

Summary

In spite of many references to *Pilocarpus Jaborandi* Holmes in ethnological and botanical sources and suggestions of its employment for a variety of diseases, it has not been possible to pin down the use of its leaves to any particular purpose amongst South American Indians. While the medically important *jaborandis* are species of *Pilocarpus*, it is true that this vernacular name is commonly applied to other rutaceous and numerous piperaceous plants as well.

The introduction of *jaborandi* leaves to western medicine goes back to 1873, when Symphronio Coutinho went to Europe, taking with him samples of the leaves. The copious sweating and salivation brought about by the leaves attracted the attention of French physicians. Soon *jaborandi* leaves were being employed in the treatment of many diseases. In 1875, Hardy and Gerrard independently discovered the alkaloid pilocarpine.

Most therapeutic applications of *jaborandi* leaves and pilocarpine fell into disuse and were discontinued. What remained was the use of the latter in ophthalmology, where it had been introduced as a miotic by Weber in 1876. The mixture of pilocarpine and another natural product, physostigmine, remains to this day one of the mainstays in ophthalmology.

Introduction

Pilocarpine, an alkaloid obtained from several species of *Pilocarpus*, has retained medicinal significance only in ophthalmology as a miotic and to decrease intraocular pressure. All of its other uses have gradually disappeared from modern medicine. Yet pilocarpine and *folia jaborandi* were formerly of appreciable importance in our pharmacopoeias.

The literature shows that there exists much confusion in the use of the vernacular term *jaborandi* in Brazil. It is applied apparently to a number of species of piperaceous plants as well as to members of the rutaceous genus *Pilocarpus*.

In contrast to such drugs as curare and coca, it has not been possible to pin down the use of leaves of *Pilocarpus Jaborandi* Holmes to any particular purpose amongst South American Indians. There appears to be no ethnopharmacological body of information on its use. In spite of many references in ethnological and botanical sources and suggestions of its employment for a variety of diseases, there is no indication that it was extensively valued by the natives primarily for any one purpose.

It would appear, therefore, that a new appraisal might serve at least partially to clarify some of the doubts and uncertainties that surround the history and identification of this drug.

Etymology of the term jaborandi

The confusion surrounding the use of the name *jaborandi* has come, in part, from some of the etymologies that have been proposed for the term in Brazil. The etymon is supposed to be *yabyrandy*. The interpretation offered by Maia (in Edwall, 1901) that *yaúrandyi*, corrupted *jaguarandi*, means "plantes dont le suc guérit les plaies" is without foundation. The most acceptable explanation of the Tupí word *jaborandi* (*iaborandy*, *yaborandi*, *yabyrandi*) was proposed as early as 1918 by Sampaio. He explained that *ya-mbo-r-endi* (for *Pilocarpus microphyllus* Stapf) translated as "what causes slobbering". He has been followed by others, especially by Pio Corrêa in his *Dicionario das Plantas Uteis do Brasil*, who identified *ia-mbor-endi* with *jaborandi legítimo* (Corrêa, 1969).

Since there have been attempts to explain *jaborandi* as *laguar-edy* ("slobber of the jaguar"), it is appropriate to devote a few words to this suggestion. According to Afrânio do Amaral, former Director of the Institute Butantán and a native of the Amazon who, for many years, was in contact with Nheêngatú-speaking Indians, the phytonym *iaborandy* should not be confused with the zoonym *laguarundy/jaguarundi**. The late Brazilian linguist Antenor Nascentes has shown that *jaguarundi*, for "wildcat" or "woodcat", comes from Tupí *yáwar(a)* for "dog" and *údi* for "black-powdered". Cadogan (1955), for example, translates *jaguarundi* (a "piperaceous plant") as "pequeño perro negro" ("small black dog") or "monstruo" ("monster"). do Amaral summarizes the problem in these words: "...the most acceptable interpretation is the following: *jā* (*yā* or *fā*, as a pronominal particle indicating the subject) - *bu/bo* (*mbo*, as a verbal prefix indicating transitivity: "to make, to cause") - *r* (plastic or euphonic letter) - *andf* (*edy*, as meaning "saliva"); the word *jā-bu-r-andf* signifies "what causes saliva(tion) or produces saliva". Consequently, in agreement with Stradelli in his *Voca-*

*A. do Amaral, Etymology of the word "jaborandi". Manuscript with personal communication, São Paulo, April 6, 1975.

bulários da língua geral português-nheêngatú (Stradelli, 1929), do Amaral believes that "the name applied to the sialagogue plants is exclusively *jaborandi*".

As to the denominative Indian use of the same words for "jaguar" and "dog", Nordenskiöld (1930) explained it by the fact that the whites during the conquest introduced "European dogs, including bloodhounds, and in wide areas the native dogs were before long completely exterminated by the European dogs", and that the comparison "must be connected with references to dogs of European breed. The undersized and barkless American native dog would have been accorded too much honour by any comparison with the monarch of the primeval forest". In his list of corresponding words for "dogs" and "jaguars", Nordenskiöld misses the Tupí word, but he has the Guaraní word for "dog" (from Paraguay) as *yagua*. Métraux (1948) wrote that "when the Tupinamba received their first dogs from the Portuguese, they called them "jaguars".

Bertoni employs the Guaraní word *ihvirá-tái* for *Pilocarpus Selloanus* Engl. (Bertoni, 1927). The meaning must be "shrub-acrid". *Ihvirá-tái* is used for treating catarrh, asthma, uremia and malaria. According to Bertoni, it is an *árbol bravo* ("wild tree"). Here wild means "dangerous", since the Indians took the drug with caution. Pardal likewise translates *jaborandi* as *árbol bravo*, stating that the Guaraní knew of the dangers attendant upon its use (Pardal, 1937).

Do Amaral attributes *ivirá-tái* and another term, *kaa-tái* ("herb acrid"), to misleading Indian phytonyms. "Whilst in Brazil, throughout the Tupí zone of prevalence," he maintains, "there has been but one way of naming the typical sialagogue plant, i.e. *jaborandi* (with *jabyrandi* as variant); in Paraguay, there are four names with that approximate meaning: (a) *jaborandi*, as used by scholars and the cultivated class; (b) *kāatai*, still prevailing among Guaraní Indians and meaning "yerba picante"; (c) *artante* (or "pimienta matico"), as employed technically (the Spanish equivalent of the Latin generic name *Artanthe*); (d) *jaguarundi*, a term with a popular use in two fields: zoology — for the brown or moorish cat (*Felis yaguarundy*); and botany -- for the plant known as *artante*, one of the false *jaborandis*. As a matter of fact, there seems to have been a phonetic convergence in Paraguay between *jaborandi* and *jaguarundy*."

First descriptions by Soares, Piso and Marcgrave

The three earliest references to *jaborandi* in the Brazilian literature seem to have been those of the Portuguese Soares de Souza (1587), and of two other European authors: Piso (1648), a Dutchman, and Marcgrave (1648), a German. The following notes concerning these authors and their works may, therefore, be of interest.

Gabriel Soares de Souza worked during the last half of the 16th century. Born in Portugal, he went to Bahía in 1570. He stayed in Brazil for 17 years,

according to F. A. de Varnhagen, as *Senhor de engenho da Baía* and colonist at a locality between Jaguaripé and Jequiriçá. When he left the country to return to Europe, he went to Madrid. There, on March 1, 1587, he signed a letter to D. Christovam de Moura, one of the favourites of Philip II, in which he offered manuscripts for publication, noting that, during his long residence in Brazil, he had written many memorable observations.

It was not, however, until 1825 that the first complete edition was published by the Royal Academy of Sciences in Lisbon. This edition was followed in 1851 by the much improved one published by the Brazilian Institute of History and Geography in Rio de Janeiro. The modern and complete edition quoted here was published in 1974 as Vol. 7 of *Brasiliensia Documenta*.

Soares' work has been highly praised. In 1909, the Argentinian anthropologist Samuel A. Lafone Quevado described it as irreplaceable, and, with regard to the Guaraní, complete.

Willem Pies, Latinized as *Gulielmus Piso* or *Pisonis* (his first name was written also as *Guilielmi*, *Guilherme*, etc.), was born in Leyden in 1611. He died in Amsterdam in November 1678 at the age of 67, only one year before the death of his royal master, Johann Moritz, Prince of Nassau, whom he had been serving since his youth.

Having studied medicine in Leyden and Caen (Normandy), he graduated at the age of 22, after which he set himself up as a physician in Amsterdam in 1633. During the Dutch occupation of parts of Brazil, the Governor, Prince Moritz, supported the first European scientific expedition to Brazil, instigated by the West Indian Company founded in 1621. The royal governor landed in Recife in January 1637. His physician, Willem van Milaenen, died soon after; whereupon, Piso was invited to go to Brazil. Now only 26, he was appointed scientific chief of the expedition and resident medical attendant of the governor. Piso seems to have arrived in 1637. He remained in the country about eight years. By March 1645 he was back in Holland, where he continued his career.

In the 1948 Brazilian edition of Piso's work *De Medicina Brasiliensi* (Piso, 1948), Herminio Conde published an article entitled "Piso, Patriarca da oftalmologia americana". Piso contributed much to ophthalmology, curing the poor who suffered from nyctalopia by prescribing that they should eat fish liver. He had observed that they were eating miserably and discovered that night blindness was due to what is now called avitaminosis. Conde further enumerated no fewer than nine discoveries by Piso, either alone or in collaboration with Georg Marcgrave, all in the fields of medicine and natural history. The sialagogue and diaphoretic qualities of jaborandi are listed as number one.

Georg(e) Marcgrave (Latinized as *Georgi Marcgravi*) was born in Liebstadt, Saxony, on September 10, 1610. Regarding the numerous forms of his name in the literature, Gudger stated, in 1912, that the naturalist himself always signed his name as Marcgrave (Gudger, 1912). According to Affonso de E. Taunay's biographical sketch in the Brazilian edition of

Marcgrave's *Natural History of Brazil*, Marcgrave started his university studies at the age of 17. He went to sundry places in Europe (Marcgrave, 1942). In September 1636, he enrolled as a student of medicine in Leyden, where he studied for two years, until, together with another German, Hendrich Gralitz, he was invited to join the Dutch scientific expedition in Brazil. Marcgrave was 27 years of age when he arrived in the country early in 1638. Gralitz had died during the passage. They have been described as "Medicinae et Mathesos candidatos", that is, qualified students of medicine and astronomy (astrology).

Marcgrave appears to have been an all-round naturalist. During his six years in Brazil, he studied especially the coastal region from Rio Grande de Norte to Pernambuco. Leaving in 1644, he did not return to Europe but went directly to West Africa to continue his research there. He died shortly afterwards in Luanda in July or August 1644, not yet 34 years of age. When his famous *Historiae Rerum Naturalium Brasiliae* appeared in 1648, he had been dead for four years (Marcgravi, 1648).

Marcgrave's biographers, especially Taunay, have cited many of the eulogies bestowed on this member of the expedition. Henry Lichtenstein, who between 1814 and 1826 remarked on the original drawings of the expedition (at that time at the Royal Academy of Sciences in Berlin), considered Marcgrave one of the greatest heroes of science. In 1973, Olympio da Fonseca Filho stated that Marcgrave had noted the vernacular names, nearly all of them in Tupí, on the drawings of his plants and animals, reputedly kept in Berlin, and he evaluated Marcgrave's work as fundamental to our present understanding of the flora and fauna of Brazil (Fonseca Filho, 1973).

The collection of contemporary drawings and paintings of the animals and plants used for the woodcuts in the *Historia Naturalis Brasiliae* of Piso and Marcgrave had to be evacuated from the Preussische Staatsbibliothek of Berlin during World War II. According to the expert on the history of this material, Dr. P. J. P. Whitehead of the Department of Zoology of the British Museum, the collection was lost, officially, "but recent investigations suggest that these precious pictures are now in Poland and that, with persistence, they can once more be made available to scientists and scholars" (Whitehead, 1976). If this happens, it is possible that the *laborandi* specimens referred to by Piso and Marcgrave may be more accurately identified.

There are several kinds of *laborandi* illustrated in Marcgrave's work. On page 36 of the 1942 Brazilian edition, a drawing (Fig. 1) of what seems to be a species of *Pilocarpus* is found, with the following notes.

"*laborandi*. (There are several kinds of this plant.) The first (we publish a drawing of it) is two feet tall. It has a woody stem, round, noded at intervals, twisted and unequal, greyish. One, two, or three stems which branch arise from the root. The root is not stout but has many rootlets; it is clear yellow externally, whitish within, with a strong odour and a taste as sharp as pyrethrum. A peduncle an inch long and with three leaves in the form of a cross, resembling the leaf of *Tilia*, soft, slightly pilose, with a prominent

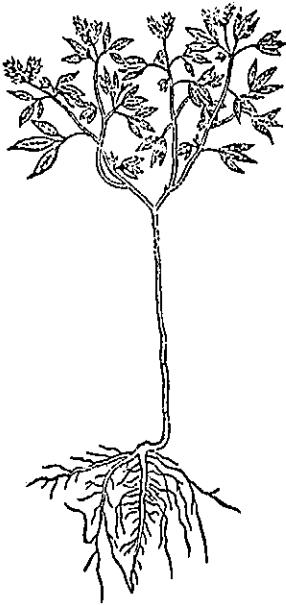


Fig. 1. *Jaborandi* illustration on page 36 in Marcgrave's work (1942). This *jaborandi* appears to be a species of *Pilocarpus*.

midrib and oblique veins, one to five inches long, some longer: they do not have a standard shape; they are pale green, somewhat whitish beneath. At the extremity of the branches, there are numerous bractlets bunched together to form a little spear but forked in the shape of two horns: these contain white florets made up of four sepals (?); then the seed comes, covered by two small, brownish, cordiform paleas which seem to lack one side and resembling those of the hemp plant. The root is used to counteract poisons which the Poio use when toxic mushrooms have been eaten."

Immediately following this description, there is another one which refers apparently to another kind of *jaborandi*.

"A plant resembling *Verbena* (the author gives no illustration). It has a straight root, not stout, with many white, lateral rootlets; it is bitter and arises from an angled and noded stem about a foot and a half in height. Two opposite leaves are borne at each node; they are an inch and a half long, serrated in the upper half. At each node also arise two opposite branchlets bearing leaves, also opposite, but not with only two but with three or four small leaflets united. On these nodal branchlets there are many tiny pedicels, at the most four at each node, each with a rounded capitulum each one of which has a minute projection like the point of a needle: upon opening, it produces a milky floret of four sepals (?) with many small erect stamens in the middle, resembling a feather and giving the floret a plumose appearance."

Later in Marcgrave's volume (page 69), there is mention of another *jaborandi*, with an illustration (Fig. 2) indicating that it is probably a species

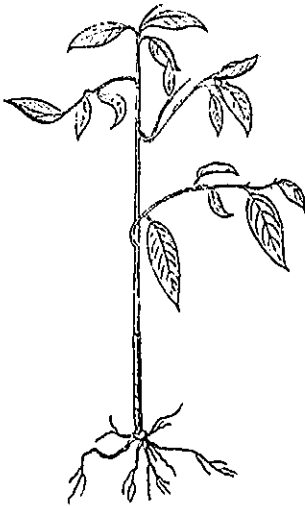


Fig. 2. *Jaborandi* illustration on page 69 in Marcgrave's work (1942). This *jaborandi* is a species of *Piper*.

of *Piper*. It follows a discussion of *manaca*, one of the important native Brazilian medicinal plants and a species of the solanaceous *Brunfelsia*.

"*Jaborandi* (native name). It is another kind of a stem the thickness of a small finger or somewhat thinner. The internodes are long and the stem is round and dark green; the branches that arise at the nodes are likewise noded and green. The leaves arising from both may be either alternate or opposite, measure six to ten inches long, are dark green, shiny and feel rather like parchment, incurved near the apex, with one central nerve and oblique lateral ones. The root is woody, brown, neither large nor fleshy but thin and long. It has little odour or taste when bitten, but if it be chewed a little it burns the tongue and is stronger than pellitory. It draws out quantities of phlegm from the tongue, thus clearing the head of colds, and relieves toothache. Macerated, soaked in water, then boiled and drunk in the morning, the root is a rapid cure for gonorrhoea. It is good against poison, faulty urination and for stones."

A *jaborandi* illustration (Fig. 3) is also found on page 108 of Piso's work in the Brazilian edition of 1948 (Piso, 1948).

Indian medicinal use of *jaborandi*

In comparison with other medicinal elements of the flora of South America, *jaborandi* figures insignificantly in ethnobotanical documents. The extensive literature offers only a few first-hand observations on the use for actual healing of any plant called *jaborandi*. Piso, who mentioned its medicinal applications, described specifically how an Indian was cured of poisoning through sweating and urination induced by drinking "wine"

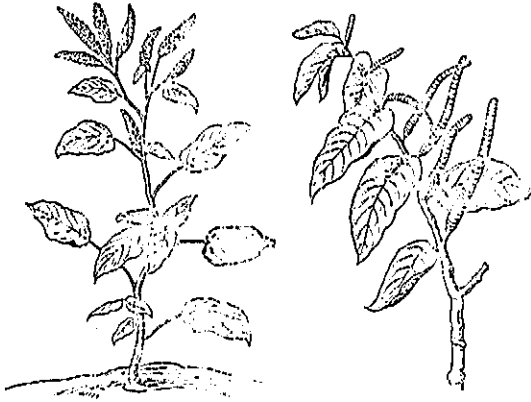


Fig. 3. *Jaborandi* illustration on page 108 of Piso's work (1948). The plant pictured on the left appears to represent a species of *Pilocarpus*, the one on the right, a species of *Piper*.

with fresh, crushed *laborandi* roots. This cure took place in the presence of the Count of Nassau. A translation of Piso's "Of *Jaborandi*, its properties and use" (Piso, 1648) follows (botanical names in Latin have been inserted).

"This plant is still called *Jaborandi* by the old inhabitants and by us. There are two kinds, and both are famous and medicinal. The first grows to the height of a shrub and only in firm and fertile soils; the leaves and flowers resemble those of the bay [*Laurus nobilis* L.]. Its main stem is as thick as one's small finger and is knotty with long internodes; it is round and dark green, giving off similarly knotty branches at the nodes. These branches bear at the nodes opposite or alternate leaves that are six to ten inches long, dark green, glossy and mucronate. The seed is borne within buds and are very hot and caustic. The root is fine and mucilaginous, a condition to which is due the value of this plant. It is hot in the third degree and dry, and its underground parts are caustic, for which reason it can be used as a substitute for "piretro" [*Anacyclus Pytherum* (L.) Link].

"The second has the same name, because it possesses the same properties, although they are not so strong. It is bushy, not much unlike mangiericao [*Cacalia* sp.]; it prefers dry and arid soils, and, as in the first plant, its virtues reside in the roots.

"The Indians praise the properties of both plants, as they revealed both to the Portuguese and to me, and they are accepted today as panaceas. They do have good medicinal applications, oftentimes serving as an antidote. A handful at least of the root, ground up and added to a generous serving of wine, counteracts the effects of poison through sweating and urination. I saw an Indian prove this, in the presence of His Excellency, the Count of Nassau.

"Finally, their sharp acidity produces beneficial effects as a sternutatory. Furthermore, this special attractive property enables them to be used as a substitute for a strong masticatory to remove phlegm from the head by way of the mouth, thus relieving the eyes from the effects of chronic colds."

Piso repeatedly mentioned *jaborandi* as a treatment for a form of ophthalmitis, for curing spasms, certain catarrhal diseases, dropsy and poisoning. His scientific companion, Marcgrave, spoke in more general terms of *jaborandi* roots soaked in water as a cure for gonorrhoea, poisons, deficiency of urine and (urinary) calculus. The drug was said to be used also to relieve toothache. In no cases, however, did it appear that he was referring to his own observations.

Taunay has supposed that *jaborandi* was used mainly "como grande eliminador", that is, as an agent "to purge away, drive out" (Taunay, 1948).

One of the few observations of anthropologists or scientific travellers is that of Ehrenreich who mentioned *jaborandi* as a diaphoretic among the Botocudo (Ehrenreich, 1887). This late 19th century information is interesting, since we have so many other statements of authors concerning the sudorific effects of plants called *jaborandi*.

Coutinho reported that he had found the sudorific agent *par excellence*; he evidently had had opportunities to see the plant in use in his native Pernambuco (Coutinho, 1874).

Maia informed Edwall that the natives considered species of *Piper* to be cures for wounds and scurvy (Edwall, 1901). In Paris, Gubler, whose source of information apparently was Coutinho, wrote that *Piper nodosum* Mart. was employed for the cure of infected wounds and serious ulcers (Gubler, 1874). This use of *Piper* is common in the ethnopharmacology of Indians of tropical America (Schultes, personal communication).

Levi-Strauss mentioned pounded and parched leaves of *Piper Jaborandi* and *Pilocarpus pennatifolius* Lem. for healing wounds, and he referred to *uribarataya* or *ibirarta-iba* (*Pilocarpus pennatifolius*) as a sedative used in Brazil (Levi-Strauss, 1950). There is no indication that these observations are based on identified botanical voucher specimens.

A specific use of roots of *javyrandi* (called "*Piper ordium*")* has been reported by Cadogan from the Mbya-Guaraní (Cadogan, 1955). These Indians are said to use the drug in treating cases of intestinal worms in cattle.

Von Martius, who had long and detailed contact with several Indian tribes during his scientific explorations in Brazil in the early 19th century, reported, in 1844, that a medicine man, when sucking wounds caused by poisonous animals or weapons, could protect himself with tobacco (*petum*) or sialagogic roots of a species of *Piper* (*jaborandi*) kept in the mouth (von Martius, 1844).

Langgaard detailed a specific effect from chewing *jaborandy* roots (Langgaard, 1948). The drug induces the sensation of a rapid tremor of the tongue, and, when air is drawn in, the lips feel cold, whereas they feel warm when air is expelled. At the same time, excessive salivation is induced. Hoehne has reported numbness of the tongue (Hoehne, 1939). This effect is not uncommon with piperaceous plants and, in fact, Schultes and García-Barriga have recently described a new species — *Piper erythroxyloides*

*A binomial which apparently has not been validly published.

R. E. Schult. et García-Barriga — the leaves of which are chewed, much like those of the coca plant (*Erythroxylon Coca* Lam), for this effect by the Motilones of northeastern Colombia (Schultes, 1975).

Soares de Souza, whose "Tratado" of 1587 is basic to our understanding of the Guaraní, seems to be the first to have mentioned *jaborandi* in the colonial literature of Brazil (Soares de Souza, 1851). He reported that it was valuable for curing ulcers of the mouth. He mentioned *jaborandiba*, apparently a kind of *Piper*, as a remedy against toothache. His observation that "water boiled with *jaborandi* and laurel leaves is good for washing the face after a shave" seems to be based on personal experience.

Writing about the medicine of the Tupinamba, Métraux (1948) made an observation of great importance when he remarked that "a great many medicinal herbs are enumerated in early descriptions of the Brazilian coast, but it is stated only rarely whether the plants actually were used by the Indians for medicinal purposes or whether they had been adopted by early European colonists, who were extremely eager to discover miraculous virtues in the Brazilian flora".

According to many reports, profuse sweating and salivation seem to have been the most commonly observed effects from taking *jaborandi* drugs. One may, therefore, ask: Did the Guaraní take the drug to perspire? If so, it was most probably for therapeutic purposes, since many Indians employed sweating to cure certain diseases. In this connection, it is interesting that von Martius agreed with modern explorers in stating that an Indian does not sweat profusely: "He is subject to a uniform, insensible transpiration, but he perspires much less than the negro or the white man". Not even during dances does the Brazilian Indian seem "to produce the immense quantity of perspiration, which, in hot countries, runs from the forehead of other races of men" (von Martius, 1845).

Lowie, writing on disease and shamanism in eastern Brazil, stated that "eastern Brazilians have a number of profane therapeutic devices, such as scarification, to prevent fatigue (Tapuya); massaging, flogging, and sweating the patient with the aid of hot rocks (Botocudo); and bleeding with a blocked arrow shot at the forehead (Cayapo, Botocudo)" (Lowie, 1946). According to Métraux (1946a), "the Purí exposed sick people to a steam bath — the patient crouched on all fours over a large glowing hot stone, which women sprinkled with water from their mouths".

Therapeutic sweating for sick people has certainly been much more widely used than noted in the literature. In Central America, with so many South American Indian traits, we know that the Lenca used sweating for treating fevers and "the patient is wrapped in as much cloth as possible to produce sweating" (Stone, 1948). From the Sumo and Mosquito (Caribbean lowland tribes), Kirchoff reported that "infections, snake bites and diseases such as malaria are cured by both shamans and laymen, the latter using infusions of herbs and a large number of native medicines. Steam baths followed by a cold plunge are also employed. Baths in hot springs and partial burial in hot sand are common practices, especially among Sumo" (Kirchoff, 1948).

To return to South America, we find that Crevaux published a drawing of a Roucoyenne woman who, after parturition, rests in her hammock, seemingly enjoying a steam bath which her husband prepared by pouring water over a hot stone under the hammock (Crevaux, 1883). The Tupí-Guaraní do not seem to have used steam baths. Would it not be plausible to assume that perhaps they had found adequate sweating agents in such plants as *jaborandi*?

Introduction of *jaborandi* to western medicine

The introduction of *jaborandi* leaves to western medicine goes back a century to Symphronio Olympio Cezar Coutinho (1832 - 1887) (Fig. 4). Information about his life is scant (Caminhoá, 1887; Almeida Costa, 1948, 1968; do Valle, 1966, 1974). We know that he was born in the state of Pernambuco and that his parents came from distinguished families of north-eastern Brazil. He entered the Faculty of Medicine of Bahía at 16 and graduated in 1853.

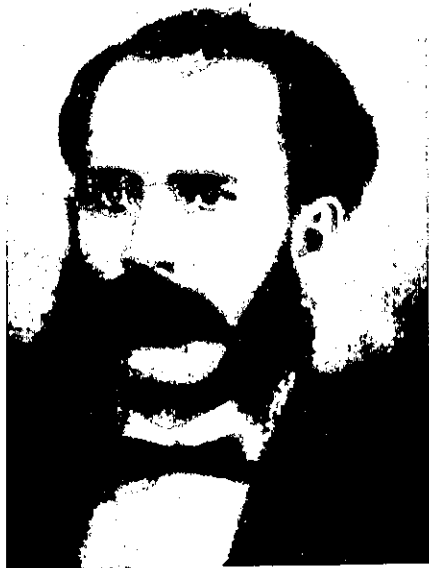


Fig. 4. Symphronio Olympio Cezar Coutinho (1832 - 1887).

According to Almeida Costa, Coutinho travelled in the interior of Pernambuco and learned about the *jaborandi* plant to which many properties, including high toxicity, were attributed.

Caminhoá states that Coutinho went to Europe about 1873, taking samples of *jaborandi* leaves, which he routinely employed in his practice as an active diaphoretic and sialagogue. We do not know how long Coutinho remained in Europe, but we do know that he received his doctoral degree

from the Faculty of Medicine of Paris. His thesis was titled: "De l'évacuation des fragments calculeux après la lithotricie" (Coutinho, 1880). After his return to Brazil, he practiced urology in Rio de Janeiro, where he died in 1887.

Coutinho's findings were demonstrated in the presence of Professor Adolph Gubler (1930). Gubler had a multifaceted career, one part of which was the study of drugs such as aconitine, potassium bromide, the Calabar bean, chloral, curare, and quinine. Gubler was struck by the action of the leaves brought back from South America by Coutinho, particularly since he had an interest in the excretion of drugs. The copious perspiration and salivation — sometimes liters — induced by *jaborandi* leaves especially attracted his attention.

Soon *jaborandi* leaves and pharmaceutical preparations thereof were being employed in the treatment of many diseases (Nicolini, 1876). At a time when few active drugs existed, one does not wonder that advantage was taken of the striking action of *jaborandi* infusions. They were used in fever, stomatitis, enterocolitis, laryngitis and bronchitis, bronchiectasis, influenza, pneumonia, hydropericarditis, hydropsy, psoriasis, intoxications, neurosis, and renal disease — to mention only a few of the conditions for which they were valued.

Jaborandi may have done some good in laryngitis, and its use is understandable in dehydration in hydropsy, an application already mentioned by Piso. The plant, which in fact had already been taken to Europe in 1847, was soon being cultivated in England, Belgium and Germany.

Identification of *jaborandi* and official *folia jaborandi*

While the medically important *jaborandis* are species of *Pilocarpus*, it is true that the vernacular name is commonly applied to other rutaceous and the numerous piperaceous plants. Ethnobotanically, the term is much broader than it is in the pharmacological sciences, but even in the latter field there is still confusion. It is clear that the term refers primarily and officially to *Pilocarpus pinnatifolius*, *P. Jaborandi* and *P. microphyllus* — the present sources of commercial pilocarpine, but a survey of the botanical and pharmacological literature will serve to point out the confusion that surrounds the application of this vernacular designation.

In his *Flora do Brasil*, Corrêa (1909) indicated that *jaborandi* was *Pilocarpus pinnatifolius*. In his *Dicionario Brasileira de Plantas Mediciniais*, Penna (1946) enumerated eleven presumed current vernacular names referable to *jaborandi*, giving botanical identifications for each one. *Jaborandi*, *jaborandi verdadeiro*, *jaborandi do norte* and *jaborandi do Dr. Coutinho*, he maintains, are all names for *Ottonia Anisum* Spring. (= *Piper Jaborandi* Vell.) of the Piperaceae, but the unreliability of this dictionary is at once evident when the author places the piperaceous genus *Ottonia* in the Rutaceae! His *jaborandi manso* he identifies as the same *Ottonia Anisum* and as

Artanthe mollicoma (Kunth) Miq. (= *Piper mollicomum* Kunth). *Jaborandi capoty* he refers to *Artanthe cernua* (Vell.) Presl. (= *Piper cernuum* Vell.). *Jaborandi da mata virgen* again is *Ottonia Anisum* in his list. He designates *jaborandi de fruto grande* as *Pilocarpus macrocarpus* Engl. and *jaborandi de tres folhas* as the rutaceous *Monnieria trifolia* Loefl. *Jaborandi do Rio* he identifies as *Artanthe geniculata* (Sw.) Miq. (= *Piper geniculatum* Sw.), while he calls *Piper aduncum* L. and *Piper reticulatum* L. both *jaborandis falsos*. One cannot help wondering how many of these presumed vernacular names are actually current among the people, or ever have been: especially such names as *jaborandi do Dr. Coutinho*!

In an extensive summary of the history and anatomical studies of *jaborandi*, Imbesi (1944) identified the source plant as *Pilocarpus pinnatifolius*. Hoehne (1939) figured *Pilocarpus pinnatifolius* as the "true *jaborandi*", although he pointed out that, according to Kunkel, pilocarpine occurs also in the leaves of *Piper reticulatum* and that *sertanejos* ("country folk") utilize both *Pilocarpus* and several species of *Piper* as *jaborandis* for their properties as sialagogues and against toothache and stomach cramps.

A recent botanical summary of the Brazilian *jaborandis* has been published by Corrêa in his *Dicionario das Plantas Uteis do Brasil* (Corrêa, 1969), who states that the name is applied to "numerous plants, all medicinal, of the Rutaceae and Piperaceae". As a general epithet, *jaborandi* refers to the following: *Pilocarpus giganteus* Engl. (Rio de Janeiro), *Pilocarpus Jaborandi* Holmes (also known as *arruda do mato*) which is official in the *Farmacopeia Brasileira*, *Pilocarpus pauciflorus* St. Hil. (Santa Catarina, Rio de Janeiro), *Pilocarpus Selloanus* Engl. (southern Brazil), *Pilocarpus spicatus* St. Hil. (Guanabara, Rio de Janeiro, São Paulo), *Pilocarpus subcoriaceus* Engl. (Rio de Janeiro), and *Zanthoxylum elegans* Engl. of the Rutaceae; and *Piper Gardneri* DC., *Piper laetum* DC., *Piper maculatum* DC. and *Piper sebastianopolitense* DC. He identifies *jaborandi da mata virgen* or *jaborandi do mato* as *Otteria Jaborandi* (Vell.) Kunth (= *Piper Jaborandi* Vell.) and *Piper leptostachya* Hook. et Arn., the latter an introduced Australian species. As *jaborandi do norte*, Corrêa cites *Pilocarpus pinnatifolius* (from Pernambuco to Santa Catarina and the Matto Grosso). *Jaborandi falso* he states is the name for *Piper caenothifolium* HBK., *Piper reticulatum* L. and *Piper tuberculatum* Jacq. Under *jaborandi manso*, he lists *Piper colubrina* Link, *Piper corcovadense* DC., *Piper Hookeri* Miq., *Piper mollicomum* Kunth and *Piper unguiculatum* R. et P. And finally, Corrêa indicates that *jaborandi legitimo* is referrible to *Pilocarpus microphyllus*.

A review of a few randomly selected pharmacologically oriented sources provides convincing evidence that official *jaborandi* or *folia jaborandi* unquestionably represent a species of *Pilocarpus*, but it likewise supplies ample evidence that there is still uncertainty concerning several of the species.

Jaborandi was listed as *Pilocarpus* in the *United States Pharmacopoeia (USP)* from 1882 to 1936; in the *National Formulary* from 1936 to 1950; and again in the USP from 1950 to the present. Several major American

textbooks and manuals have enumerated one or more of the following species: *Pilocarpus Jaborandi* (*Pernambuco jaborandi*), *Pilocarpus microphyllus* (*Maranham jaborandi*, an erroneous rendering of *Maranhão jaborandi*) and *Pilocarpus pinnatifolius* (*Paraguay jaborandi*) (Carr *et al.*, 1929; Claus, 1961; Drill, 1958; Goodman and Gilman, 1970; Goth, 1964; Henry, 1949; Morton, 1977; Tschirch, 1923; Wood *et al.*, 1940; Youngken, 1943).

The *Dispensatory of the United States* clearly points out that the term *jaborandi* or *jamguarandi*, while commercially and officially applied to leaves of several species of *Pilocarpus*, designates in South America "various pungent, sudorific plants, some of which have no botanical relation at all with *Pilocarpus*".

In addition to these three major species of *Pilocarpus*, other species have in the past entered commerce as *jaborandis* (Wood *et al.*, 1940): *P. spicatus* St. Hil. appeared in England in 1895 as *Arcati jaborandi* (Carr *et al.*, 1929); *P. racemosus* Vahl was introduced in 1903 as a new kind of *jaborandi* from the West Indies, under the name *Guadaloupe jaborandi* (Rocher, 1898; Sprague, 1909; Holmes, 1903, 1904). Other species, though never official, have entered commerce: for example, the Brazilian *Pilocarpus trachylophus* Holmes (Wood *et al.*, 1940) and *P. pauciflorus* St. Hil. (Tschirch, 1923). In 1923, a chemical analysis of a Venezuelan *jaborandi* — *Pilocarpus heterophylla* A. Gray, locally called *borrachera* ("intoxicant") with reference to the poisoning of cattle eating the leaves — showed that this species did not compare favourably with the official species (Black *et al.*, 1923).

At an early date, the botanical confusion as to the species of *Pilocarpus* involved in supplying *jaborandi* led several specialists (Rusby, 1903; Lloyd *et al.*, 1904) to suggest dropping the use of the vernacular term *jaborandi* altogether. It was Rusby, for example, who pointed out that at least one of the *jaborandis* listed in the *United States Pharmacopoeia* — *Pilocarpus Sellowianus* — was "nearly worthless" (Rusby, 1903).

In the Amazon regions of Brazil, *jaborandi* refers to the rutaceous *Monnieria trifolia* Loefl. and has the vernacular names of *jaborandi do Pará*, *jaborandi de tres folhas*, *alfavaca de cobra* (Le Cointe, 1934), *pimenta de lagarta* and *alfavaca brava* (Albuquerque, 1976). This species is reputedly bitter, tonic, sudorific and diuretic (Le Cointe, 1934) — undoubtedly the reason for its being called *jaborandi*.

Even more confusion has been introduced into the picture of *jaborandi* by the statement that occasionally in Brazil the following rutaceous species are so called: *Esenbeckia febrifuga* A. Juss., *Zanthoxylum elegans* Engl., *Z. Naranjillo* Griseb. and *Z. Peckholtianum* Engl.; as well as the scrophulariaceous *Herpestes chamaedryoides* HBK., *H. gratioloides* Benth. and *H. Monnieria* HBK. (Duval, 1903). It has even been reported that in India, Ceylon and Java the rutaceous *Toddalia aculeata* Pers. and *T. inermis* Pers. are known by the same vernacular name (Duval, 1903).

The Brazilian State of Maranhão leads in the production of *jaborandi*, although other states in northeastern Brazil are likewise producers. *Pilocarpine* is no longer prepared in Brazil, but there is still a demand for the

leaves for export (Mors and Rizzini, 1966). In the vicinity of Rio de Janeiro, the term *jaborandi*, according to these authors, is still locally applied to several species of *Piper* (*P. corcovadense* and *P. Jaborandi*), the leaves and twigs of which have a numbing action on the mucous membrane of the mouth and are, consequently, employed to deaden toothache. They consider the species of *Piper* as "false *jaborandis*".

Pharmacology of pilocarpine

In 1875, Hardy and Gerrard independently discovered an alkaloid which was called pilocarpine (Hardy, 1875; Gerrard, 1875). The chemical structure of pilocarpine was described by Jowett a quarter of a century later (Jowett, 1900a, b, 1901a, b) and by Pinner and co-workers (Pinner and Kohlhammer, 1900a, b, 1901; Pinner and Schwarz, 1902a, b). The complete synthesis was achieved by Preobrashenskij and co-workers thirty years later (Preobrashenskij *et al.*, 1933, 1935a, b).

In 1876, Langley investigated the action of pilocarpine upon the secretion of saliva (Langley, 1876). He discovered that it was due not to stimulation of the ganglia but to action on end organs, since it could be counteracted by atropine but not by nicotine. Before the discovery of acetylcholine, pilocarpine was a readily available compound to mimic stimulation of the parasympathetic (Holmstedt, 1975). The pharmacology of the drug was studied in detail by Harnack (1886) and Marshall (1904). The effects in man, both child and adult, were elucidated in uninhibited experiments carried out not only by Gubler (1885) but also by Ringer and Gould (1875). The latter discovered the antagonistic effect that belladonna has on the symptoms provoked by *jaborandi*.

All these therapeutic applications of pilocarpine fell into disuse and were discontinued. What remained was its use in ophthalmology, where it had been introduced as a miotic by Weber (1876). Its action in lowering the intraocular pressure was observed later. Schlegel pointed out this ophthalmic effect of pilocarpine. He also thought that pilocarpine, like physostigmine, had an initial increasing effect on intraocular pressure (Schlegel, 1885). He did not recommend pilocarpine alone, because, according to his results, its action was weaker than that of physostigmine. However, the mixture of the two remains to this day one of the mainstays in ophthalmology. In addition, pilocarpine remains an important tool in experimental pharmacology and physiology (Lamble and Lamble, 1975).

Acknowledgements

This work was supported by grants from the Swedish Medical Research Council (Nos. 25X-04041-04A, 04X-00199-12B and 70E-3743-04A), the

Tricentennial Fund of the Bank of Sweden (68/53:1), the Wallenberg Foundation, the National Institute of Mental Health MH 12007, the Karolinska Institute (B.H.), and Anna Ahrenberg's Scientific Foundation of Gothenburg, Sweden (H.W.).

Our thanks are extended to Dr. Afranio do Amaral, São Paulo; Dr. Wolmar Bondeson, Stockholm; Dr. Vera P. Coelho, Indianapolis and São Paulo; Professors Åke Fridh and Gunnar Harling, Gothenburg University; Mrs. Melanie Janér, Rio de Janeiro; Dr. Bo Peterson, Botanical Museum, Gothenburg University; Professors Egon Schaden and José Ribeiro do Valle, São Paulo.

References

- de Albuquerque, B. W. P., Revisão taxonômica das Rutaceae do Estado do Amazonas. *Acta Amazônica*, 6 (1976) 34.
- de Almeida Costa, O., A introdução do jaborandi em terapêutica pelo Dr. Symphronio Coutinho. *Rev. Fl. Med.*, 15 (1948) 459 - 478.
- de Almeida Costa, O., The introduction of jaborandi into therapeutics by Dr. Symphronio Coutinho. *Rev. Bras. Farm.*, 49 (1968) 323 - 330.
- Anonymous, *Kew Bull.*, (1891) 179.
- Bailey, J. F., *Queensl. Agric. J.*, 2 (1898) 387.
- Bertoni, M. S., *La Civilización Guaraní. III. Etnografía*, Alta Paraná, Paraguay, 1927, Conocimientos: La Higiene Guaraní. La Medicina Guaraní. Puerto Bertoni.
- Black, O. F., Kelley, J. W. and Stickberger, W. W., A chemical examination of a Venezuelan jaborandi. *Am. J. Pharm.*, 95 (1923) 4 - 7.
- Cadogan, L., *Breve Contribución al Estudio de la Nomenclatura Guaraní en Botánica*, Bol. 196, Serv. Tecn. Interamericano Coop. Agric., Asunción, Paraguay, 1955.
- Caminhoá, J. M., *Compendio de Botanica Geral e Médica* (1879 - 1884), Typographia da Estatística, Rio de Janeiro, 1887.
- Carr, F. H. et al., *Allen's Commercial Organic Analysis*, Vol. 7, 5th edn., Blackiston, Philadelphia, 1929, p. 120 ff.
- Claus, E. P., *Pharmacognosy*, 4th edn., Lea and Febiger, Philadelphia, 1961, p. 359.
- Corrêa, M. P., *Flora do Brazil*, Typographia da Estatística, Rio de Janeiro, 1909, p. 98.
- Dicionario das Plantas Uteis do Brasil*, Vol. 4, Ministerio da Agricultura, Rio de Janeiro, 1969, pp. 360 - 369.
- Coutinho, S., Note sur un nouveau médicament diaphorétique et sialagogue: le jaborandi du Brésil. *J. Therap.*, 1 (1874) 161 - 165.
- Coutinho, S., De l'évacuation des fragments calculeux après la lithotricie. *Thesis, Faculty of Medicine, Paris*, 1880.
- Crevaux, J., *Voyages dans l'Amérique du Sud*, Paris, 1883.
- Drill, V. A., *Pharmacology in Medicine*, 2nd edn., McGraw-Hill, New York, 1958, p. 366.
- Duval, A., Les jaborandis. *Bull. Sci. Pharm.*, 5 (1903) 41 - 109; *Trav. Lab. Mat. Méd. Ecole Super. Pharm.*, 1 (4) (1903) 1 - 31.
- Duval, A., Recherches sur les jaborandis et leurs succédanés. *Trav. Lab. Mat. Méd. Ecole Super. Pharm.*, 3 (1) (1905) 1 - 130.
- Edwall, G., O jaborandi no Estado de São Paulo. *Bol. Agric.*, Ser. 2, (1) (1901) 508 - 519.
- Ehrenreich, P., Ueber die Botocudos der brasilianischen Provinzen Espiritu Santo und Minas Geraes. *Z. Ethnol.*, 19 (1887) 1 - 46, 49 - 82.
- da Fonseca Filho, O., O Brasil e as ciências naturais nos séculos XVI a XVIII. *Ciênc. Cult.* (São Paulo), 25 (1973) 10 - 11, 946 - 957, 1015 - 1029.
- Gerrard, A. W., Alkaloid and active principle of jaborandi. *Pharm. J.*, 5 (1875) 865.

- Goodman, L. S. and Gilman, A., *The Pharmacological Basis of Therapeutics*, 4th edn., MacMillan, London, 1970, p. 473.
- Goth, A., *Medical Pharmacology: Principles and Concepts*, Mosby, St. Louis, 1964, p. 61.
- Gubler, A., *Commentaires Thérapeutiques du Codex Médicamentarius*, Libr. Bailliere, Paris, 1885.
- Gubler, A., Remarques sur la note précédente. *J. Thérap.*, 1 (1874) 165 - 167.
In Hirsch, A. (ed.), *Biograph. Lexikon der hervorragenden Ärzte aller Zeiten und Völker*, 2nd edn., Urban and Schwarzenberg, Berlin, 1930, pp. 879 - 880.
- Gudger, E. W., George Marcgrave, the first student of American natural history. *Pop. Sci. Monthly*, (Sept) (1912) 250 - 274.
- Hardy, M. E., Sur le jaborandi (*Polycarpus pinnatus*). *Bull. Soc. Chim. Paris*, 24 (1875) 497 - 500.
- Harnack, E., Ueber die Alkaloide der Jaborandiblätter. *Arch. Path. Pharmacol.*, 20 (1886) 439 - 445.
- Henry, T. A., *The Plant Alkaloids*, 4th edn., Blakiston, Philadelphia, 1949, p. 621.
- Hoehne, F. C., *Plantas e Substancias Vegetais, Toxicas e Medicinai*s, Graficars, São Paulo, 1939.
- Holmes, E. M., *Pharm. J.*, Ser. 4, 17 (1903) 713; 18 (1904) 54.
New drugs introduced during the last fifty years. *J. Am. Pharm. Assoc.*, 12 (1923) 715 - 717.
- Holmstedt, B., Pages from the history of research on cholinergic mechanisms. In P. G. Waser (ed.), *Cholinergic Mechanisms*, Raven Press, New York, 1975, p. 1 - 21.
- Imbesi, A., Contribuição ao estudo das plantas medicinais. O *Pilocarpus pennatifolius* Lem. da Silicia. *Rev. Fl. Med.*, 11 (1944) 87 - 106, 123 - 140, 155 - 169.
- Jowett, H. A. D., Pilocarpine and the alkaloids of jaborandi leaves. *J. Chem. Soc.*, 77 (1900a) 473 - 498.
- Jowett, H. A. D., The constitution of pilocarpine. Part I. *J. Chem. Soc.*, 78 (1900b) 851 - 860.
- Jowett, H. A. D., The constitution of pilocarpine. Part II. *J. Chem. Soc.*, 79 (1901a) 580 - 602.
- Jowett, H. A. D., The constitution of pilocarpine. Part III. *J. Chem. Soc.*, 79 (1901b) 1331 - 1346.
- Kirchhoff, P., The Caribbean lowland tribes: The Mosquito, Sumo, Paya, and Jicaque. *Handbook of South American Indians*, Vol. 4, Bur. Am. Ethnol., Bull. 143, Washington, DC, 1948, pp. 219 - 229.
- Lamble, A. P. and Lamble, J. W., Some effects of pilocarpine and acetylcholine on the responses of the guinea-pig *vas deferens* to hypogastric nerve stimulation and transmural stimulation and applied (-)-noradrenaline. *J. Pharm. Pharmacol.*, 27 (1975) 85 - 87.
- Langgaard, Th. J. H., *Diccionario de Medicina Doméstica e Popular*, Vol. 2, E.-L., Rio de Janeiro, 1948.
- Langley, J. N., The action of pilocarpine on the sub-maxillary gland of the dog. *J. Anat. Physiol.*, 11 (1876) 173 - 180.
- Le Cointe, P., *A Amazônia Brasileira*, Vol. 3, Livraria Classica, Belém do Pará, 1934, p. 211.
- Levi-Strauss, C., The use of wild plants in tropical South America. *Handbook of South American Indians*, Vol. 6, Bur. Am. Ethnol., Bull. 143, Washington, DC, 1950, pp. 465 - 486.
- Lloyd, J. U. et al., *Drug Treatise*, No. 3, Lloyd, Cincinnati, 1904.
- Lowie, R. H., Eastern Brazil: An introduction. *Handbook of South American Indians*, Vol. 1, Bur. Am. Ethnol., Bull. 143, Washington, DC, 1946, pp. 381 - 398.
- Marcgravi (Marcgraf) de Liebstad, G., *Historiae Rerum Naturalium Brasiliae*. *Historia Naturalis Brasiliae*, Leyden and Amsterdam, 1648.
- Marcgrave, J., *Historia Natural do Brasil*, Companhia Editora Nacional, São Paulo, 1942.
- Marshall, C. R., Alkaloids of jaborandi. *J. Physiol.*, 31 (1904) 127 - 156.

- von Martius, C. Fr. Ph., *The Natural History, the Diseases, the Medical Practice and the Materia Medica of the Aborigines of Brazil* (transl. John MacPherson), Calcutta, 1845.
- von Martius, K. Fr. Ph. Das Naturell, die Krankheiten, das Artzthum und die Heilmittel der Urbewohner Brasiliens. *Repert. Pharm.*, 34 (1844) 1 - 46, 145 - 181, 289 - 356.
- Métraux, A., The Purí-Coroado linguistic family. *Handbook of South American Indians*, Vol. 1, Bur. Am. Ethnol., Bull. 143, Washington, DC, 1946a, pp. 523 - 530.
- Métraux, A., The Botocudo. *Handbook of South American Indians*, Vol. 1, Bur. Am. Ethnol., Bull. 143, Washington, DC, 1946b, pp. 531 - 540.
- Métraux, A., The Tupinamba. *Handbook of South American Indians*, Vol. 3, Bur. Am. Ethnol., Bull. 143, Washington, DC, 1948, 95 - 133.
- Mors, W. B. and Rizzini, C. T., *Useful Plants of Brazil*, Holden-Day, San Francisco, 1966.
- Morton, J. F., *Major Medicinal Plants — Botany, Culture and Uses*, Charles C. Thomas, Springfield, IL, 1977.
- Nicolini, H., Historique des Pilocarpus. Etude Botanique, Pharmacologique et Chimique, Physiologique et Thérapeutique du *Pilocarpus pennatifolius*. Thesis, Montpellier, 1876.
- Nordenskiöld, E., Modifications in Indian culture through inventions and loans. *Comp. Ethnogr. Studies*, 8 (1930). Gothenburg, Sweden.
- Pardal, R., Medicina aborigen americana. *Humanior, Bibl. del Americanista moderno*, Secc. C, Vol. 3. Buenos Aires, 1937.
- Penna, M., *Dicionario Brasileiro de Plantas Mediciniais*, 3rd edn., Livraria Kosmos Editora, Rio de Janeiro, 1946.
- Pinner, A. and Kohlhammer, E., Ueber Pilocarpin. I. Mitteilung. *Ber. Dtsch. Chem. Ges.*, 33 (1900a) 1424 - 1431.
- Pinner, A. and Kohlhammer, E., Ueber Pilocarpin. II. Mitteilung. *Ber. Dtsch. Chem. Ges.*, 33 (1900b) 2357 - 2363.
- Pinner, A. and Kohlhammer, E., Ueber Pilocarpin. III. Mitteilung. *Ber. Dtsch. Chem. Ges.*, 34 (1901) 727 - 736.
- Pinner, A. and Schwarz, R., Ueber Pilocarpin. *Ber. Dtsch. Chem. Ges.*, 35 (1902a) 192 - 210. Ueber Pilocarpin. Constitution des alkaloids. *Ber. Dtsch. Chem. Ges.*, 35 (1902b) 2441 - 2459.
- Piraja da Silva, M. A., Introdução, notas e comentarios a obra de Gabriel Soares. *Brasilienia Documenta* (Moderatore et auctore Edgard de Cerqueira Falcão), Vol. 7, 1974, São Paulo.
- Piso (Pisonis), William (Guilielmi, Guilherme), *De Medicina Brasiliensi*, Historia Naturalis Brasiliae, Leyden and Amsterdam, 1648.
- Piso, Guilherme, Da Medicina Brasileira (transl. A. Correia). *Historia Natural do Brasil Ilustrada*, Companhia Editora Nacional, São Paulo, 1948, pp. 1 - 137.
- Preobrashenskij, N. A. and Preobrashenskij, W. A., Über die Alkaloide der Jaborandi-Blätter. VII. Mitteilung: Die Spaltung der unbeständigen Anthyl-paraconsäure (racem. Pilopsäure) in die optischen Antipoden. *Ber. Dtsch. Chem. Ges.*, 68 (1935a) 847 - 849.
- Preobrashenskij, N. A., Poljakowa, A. M. and Preobrashenskij, W. A., Über die Alkaloide der Jaborandi-Blätter. VIII. Mitteilung: Die Synthese der D-Homo-pilopsäure. *Ber. Dtsch. Chem. Ges.*, 68 (1935b) 850 - 852.
- Preobrashenskij, N. A., Wompe, A. F., Preobrashenskij, W. A. and Schtschukina, M. N., Über Alkaloide der Jaborandiblätter. III. Mitteilung: Synthese des Pilocarpins und des Pilocarpidins. *Ber. Dtsch. Chem. Ges.*, 66 (1933) 1536 - 1541.
- Ringer, S. and Gould, A. P., On jaborandi. *Lancet*, (Jan. 30) (1875) 157 - 159.
- Rocher, G., Un nouveau jaborandi des Antilles Françaises. *Ann. Inst. Colon. Marseille*, 5 (2) (1898) 165 - 166.
- Rusby, H. H., The Pilocarpus leaves of commerce. *Pharm. Rev.*, 21 (1903) 374.
- Sampaio, T., *Tupí na Geografia Nacional*, 1918.
- Schlegel, J., Manometrische Untersuchungen über die Beeinflussung des intraocularen Druckes durch Pilocarpin. *Naunyn-Schmiedebergs Arch. Pathol. Pharmacol.*, 20 (1885) 271 - 290.

- Schultes, R. E., De plantis toxicariis è Mundo Novo tropicale commentationes XII. Notes on biodynamic piperaceous plants. *Rhodora*, 77 (1975) 165 - 170.
- Soares de Souza, G., Tratado descritivo do Brazil em 1587. *Rev. Inst. Hist. Geogr. Brasil*, 14 (1851) 14 - 423.
- Soares de Souza, G., Notícia do Brasil. *Brasiliensia Documenta*, Vol. 7, São Paulo, 1974.
- Sprague, J. T. A., *Pilocarpus racemosus*. *Kew Bull.*, (1909) 76.
- Stone, D., The Northern Highland Tribes: The Lenca. *Handbook of South American Indians*, Vol. 4, Bur. Am. Ethnol., Bull. 143, Washington, DC, 1948, pp. 205 - 217.
- Stradelli, E., Vocabulários da língua geral português-nheêngatú e nheêngatú-português. *Rev. Inst. Hist. Geogr. Brasil*, 104, 158 (1929) 5 - 768.
- Taunay, A. de E., Jorge Marcgrave de Liebstad (1610 - 1644). Escorço biografico. In J. Marcgrave, *Historia Natural do Brasil*, Companhia Editora Nacional, São Paulo, 1942, Comentários, pp. I - XXXVI.
- Taunay, A. de E., Guilherme Piso (1611 - 1678). Escorço biografico. In G. Piso, *Historia Natural do Brasil Ilustrada*, Companhia Editora Nacional, São Paulo, 1948, pp. 213 - 228.
- Tschirch, A., *Handbuch der Pharmakognosie*, Vol. 3, Part 1, Tauchnitz, Leipzig, 1923.
- do Valle, J. R., Primordia pharmacologiae. *III Congressus Mundialis Pharmacologiae. Sancti Pauli - MCMLXVI*, Rev. Tribunais, São Paulo, 1966.
- do Valle, J. R., O 1.º centenário da introdução do jaborandi em terapêutica por Sinfônio Coutinho (1874 - 1974). *Ciênc. Cult.* (São Paulo), 26 (3) (March) (1974) 298 - 309.
- de Varnhagen, F. A., Breves commentarios a precendente obra de Gabriel Soares. *Rev. Inst. Hist. Geogr. Brasil*, 14 (1851) 367 - 415.
- Weber, A., Ueber die Wirkung des Pilocarpium muriaticum. *Centralbl. Med. Wiss.*, (44) (1876) 769 - 772.
- Whitehead, P. J. P., The original drawings for the *Historia naturalis Brasiliae* of Piso and Marcgrave (1648). *Soc. Bibliogr. Nat. Hist.*, 7 (4) (1976) 409 - 422.
- Wood, H. C. et al., *Dispensatory of the United States*, 22nd edn., 1940.
- Youngken, H. W., *Textbook of Pharmacognosy*, 5th edn., Blakiston, Philadelphia, 1943, pp. 499 - 501.