Acta Botanica Brasilica - 33(2): 183-190. April-June 2019.
doi: 10.1590/0102-33062019abb0030

Review

Mururé (*Brosimum acutifolium* Huber) in the treatment of syphilis in colonial Amazonia: historical data to the actual contribution to treatment

Erika Fernanda de Matos Vieira[1], Flávia Cristina Araújo Lucas[2*], Maria da Graça Ribeiro Campos[3, 4] and Carolina Mesquita Germano[5]

Received: January 27, 2019
Accepted: May 13, 2019

ABSTRACT

Historical ethnobotanical studies of medicinal plants reveal important information about traditional practices of human groups and influence current understanding of the use of plants. The present article describes the ethnopharmacology of mururé (*Brosimum acutifolium*) since the XVIII century for the treatment of syphilis and correlates past and present therapeutic use. This information contributes to the appreciation of historical records in the contemporary use of natural products. The analysis of documental records is important for comparing information available overtime about the medicinal use and application of specific species. The present research was based on the analysis of a Jesuit work and other complementary documents. The medicinal effect of mururé is attributed to its latex, and dosage and adverse reactions are described. Historical documents stand out as valuable assets for pharmaceutical technology because they allow comparisons to be made between past and present uses of species as curative agents.

Keywords: alkaloid, bufotenine, ethnopharmacology, historical ethnobotany, natural products, saponin

Introduction

The historical study of medicinal plants is a research approach of ethnobotany by which information about plants and peoples is sought from historical records, including botanical, anthropological, ecological, and historical documents, that is still used and relevant today (Prance 2000; Medeiros & Hanazaki 2009). The knowledge that ethnic groups possess about nature has helped scientists learn about the chemical arsenal provided by this source, thereby fostering research into natural products and the relationship between the chemical structures of compounds and their biological properties (Viegas Júnior *et al*. 2006).

Medicines of natural origin, which are often used by native groups, began to spread throughout Brazil

1 Programa de Pós-Gradução em Ciências e Meio Ambiente, Universidade Federal do Pará, 66075-110, Belém, PA, Brazil
2 Herbário Prof Drª Marlene Freitas da Silva, Centro de Ciências Sociais e Educação, Universidade do Estado do Pará, 66050-540, Belém, PA, Brazil
3 Centro de Química de Coimbra, Universidade de Coimbra, 3000-548, Coimbra, Portugal
4 Observatório de Interação Planta-Medicamento, Faculdade de Farmácia, Universidade de Coimbra, 3000-548, Coimbra, Portugal
5 Programa de Pós-Graduação em Plantas Medicinais, Aromáticas e Condimentares, Universidade Federal de Lavras, 37200-000, Lavras, MG, Brazil

* Corresponding author: copaldoc@yahoo.com.br

during the colonial period (1500-1822). Knowledge and practices involving these medicines were disseminated by missionaries, naturalists, and travelers who experimented with new plants as methods to cure diseases based on plant chemistry (Costa 2007; Veríssimo & Pereira 2014). This period was marked by the use of natural resources to synthesize toxic and medicinal substances and to identify biologically active molecules (Viegas Júnior *et al*. 2006).

In this historical context, the Jesuit João Daniel (Daniel 2004), who lived in the Amazon for 16 years (1741 – 1757), experimented with a vast repertoire of herbal recipes. His main work, "The Treasure Discovered on the Great Amazon River" (original title: "O Tesouro Descoberto no Máximo rio Amazonas"), is impressive for its precise description of flora and its forms of use, considering that it was published almost 200 years ago (Pinto 2005; Val 2014). Daniel's writings are technical descriptions of healing techniques for the most common diseases of the time, which often became plagues or pests and were treated with medicinal plants (Sousa 2013).

Daniel (2004) commented on the seriousness of venereal diseases among natives and settlers in the Amazon, particularly syphilis. Veloso (2001) mentioned the numerous cases of syphilis that severely affected a large number of people in Europe, possibly after Columbus' expeditions to the Western Hemisphere, eventually leading to epidemics and innumerable social impacts (Veloso 2001). Daniel's description of the treatment of syphilis includes the frequent use of a plant popularly known as mururé (*Brosimum acutifolium* Huber; Moraceae), which was considered an effective remedy.

Until the discovery of penicillin, other treatments based on plants or chemical elements, such as mercury, bismuth, and arsenic salts, were used to treat syphilis; however, these treatments were ineffective and caused undesirable side effects (Carrara 1996; Veloso 2001). Syphilis is a contagious, systemic, chronic disease caused by the bacterium *Treponema pallidum*. It can be sexually (acquired syphilis) or vertically transmitted, the latter when a pregnant woman infects a fetus (congenital syphilis) (Neves & Araújo 2013).

References to major syphilis epidemics in Europe date as far back as the 15th century, although with unknown origins (Geraldes Neto *et al*. 2009). In 2006, the World Health Organization (WHO 2016) estimated there to be approximately 18 million cases of syphilis in the world with around 5.6 million new cases being detected every year. WHO also warned of the increasing resistance of the disease to penicillin due to its overuse. This, according to the Brazilian Health Regulatory Agency on Sanitary Surveillance (ANVISA 2016), is a serious concern because penicillin is also effective at treating other bacterial diseases.

Validating the use of plants to treat diseases is recommended by the Brazilian Ministry of Health (Brasil 2012). The strong curative efficacy of numerous plants has been known since ancient times, while the investigation of traditional knowledge and modern technologies to produce medicines continue to advance. WHO (2011) indicated that approximately 25 % of modern medicines directly or indirectly come from medicinal plants.

The aim of the present research is to share a case report that serves as an example of the tools and various steps to be followed in ethnobotanical research. The ethnopharmacology of mururé for the treatment of syphilis since the 18th century is described based on the analysis of documents containing information about its traditional uses over time. A correlation between its past and present therapeutic uses and the contribution of historical records to the use of natural products are also discussed.

Materials and methods

Documentary research

The main method adopted by this work involved collecting and analyzing documents (Godoy 1995). The data obtained were used in a comparative analysis of past and present uses of mururé (Medeiros & Hanazaki 2009).

Documentary research and the consultation of bibliographic works were both undertaken in this study. Despite their similarity, these approaches differ mainly in their sources; the former comprises records that were not analytically treated (primary sources) or which were insufficiently analyzed, whereas the latter includes material contributed by various authors about a theme (secondary sources) (Sá-Silva *et al*. 2009).

Research sources: consultation of works, databases and files

The following databases were searched to study the original works of João Daniel: Portuguese-Brazilian Digital Library (http://bdlb.bn.gov.br/acervo/handle/20.500.12156.3/17); Library Catalogue of the University of Coimbra (http://webopac.sib.uc.pt/search~S); digital collection of the National Library of Rio de Janeiro (https://www.bn.gov.br); and virtual collection from the Central Library of the Federal University of Pará (http://bc.ufpa.br), which has a free PDF version of the "O Tesouro Descoberto no Máximo Rio Amazonas" (The Treasure Discovered on the Great Amazon River). The key words "jesuítas" (Jesuits), "Amazônia colonial" (colonial Amazonia), "plantas medicinais" (medicinal plants) and, "João Daniel" were used in all searches.

Other works and catalogs in libraries were also examined. Material from the 16th, 17th, and 18th centuries related to medicinal plants, the Amazon, and people (missionaries, travelers, and naturalists) who wrote about the colonial Amazon was surveyed. The consulted libraries were: Emílio Goeldi Museum of Pará, Belém (http://obrasraras.museu-goeldi.br), where the Rare Works Section and "Catálogo

Biblioteca Universitatis" (Universitatis Library Catalogue) were searched; digital library of rare and special works and historical documentation of the University of São Paulo (http://www.obrasraras.usp.br); and the collections "História da Companhia de Jesus no Brasil" (History of the Company of Jesus in Brazil) (Leite 2005) and "Ensaios de história das ciências no Brasil: das luzes à razão independente" (Essays on the history of science in Brazil: from light to independent reason) (Kury & Gesteira 2012). The use of several bibliographic sources focused on the Jesuits, medicinal botany, the Amazon, and the way of life in the sociocultural context of the 18th century allowed the combination of the different narratives and interpretations of João Daniel's writings.

The general library and the Faculty of Arts and Humanities at the University of Coimbra in Portugal were also visited. The most notable original documents and facsimiles consulted were: "Florae Lusitanicae et Brasiliensis Specimen Plantae exoticae Brasilienses" (Vandelli 1788); annual report of the feats of the Society of Jesus in parts of East India during the years of 604 and 605, by Father Fernam Guerreiro; and "História da Província Santa Cruz, A Que Vulgarmente Chamamos Brasil" (History of the Province of Santa Cruz, What We Vulgarly Call Brazil) (Gândavo 1576).

Species definition

The studied species — mururé or *Brosimum acutifolium* Huber (Moraceae) — was identified using taxonomic clues based on " Identificação de termos oitocentistas relacionados às plantas medicinais usadas no Mosteiro de São Bento do Rio de Janeiro, Brasil" (Identification of 19th century terms for medicinal plants used in the São Bento Monastery of Rio de Janeiro, Brazil) by Medeiros *et al*. (2010). The following criteria were used to properly confirm scientific nomenclature: (1) text search for the common names "moruré" and "mururé"; (2) detailed examination of morphological descriptions and life form of mururé by Daniel and other authors; and (3) confirmation of botanical identification using scientific articles and specimens listed in the Tropicos virtual herbarium (http://www.tropicos.org/Name/21300027), the "List of Species of Flora of Brazil" in the "Flora of Brazil 2020 Project" (Flora do Brasil 2020) and the International Plant Names Index (http://www.ipni.org/ipni/plantnamesearchpage.do). The search and confirmation of botanical names is necessary to avoid erroneous information about the studied species.

The spelling and punctuation of text in older works were modified based on current Portuguese norms. Transcription into Portuguese and the identification of linguistic terms that were typical of the time when the texts were written were based on "Strategy and Tactics of Transcription" (Castro & Ramos 1986). The vocabulary used in the quotes of some authors was absolutely respected.

Past-present comparative study

Past-present comparisons aimed to investigate how the use of plant resources in the past was related to local ethnoknowledge (Medeiros & Hanazaki 2009). Indicated therapeutic history was analyzed using directories of published scientific papers that provide information about compounds, isolated substances, and pharmacology. The directories used to search for such publications were: The Plant List (National Center for Biotechnology Information - http://www.theplantlist.org`), PubMed NCBI (https://www.ncbi.nlm.nih.gov/pubmed/), Scopus (https://www.scopus.com), Jstor (https://www.jstor.org), Virtual Health Library (Bireme - https://bvsalud.org), Phytotherapy Research (https://onlinelibrary.wiley.com/journal/10991573), and Pubchem Compound (https://pubchem.ncbi.nlm.nih.gov).

Results and discussion

The book "Tesouro Descoberto no Máximo rio Amazonas", written between 1757 and 1776 by Jesuit Father João Daniel (1722-1776), a missionary in the state of Maranhão and Grão-Pará, was selected as the main literature source of the present study. João Daniel was a naturalist and wrote this work while in prison in Lisbon (due to Pombaline orders resulting from conflicts between the Company of Jesus and the Marquês de Pombal government). His writings became a massive codex and is considered by many historians as a significant document about the Amazon during the colonial period (Salles 2004). It is the most comprehensive record and most complete source of knowledge about the Amazon during the 18th century because the information it contains is the result of extensive fieldwork and vast cataloging of data, especially about the flora of the region (Siewierski 2014). According to Tocantins (1976), although other publications of the same nature exist, this work is the "Ecological Bible of the Amazon".

Medical-pharmaceutical concepts during colonization

The advancement of religious and exploratory missions into the Amazon favored greater rapprochement and contact among different peoples and ethnicities. There are significant documentary data about diseases of various natures that proliferated during these encounters during the 18th century (Veríssimo & Pereira 2014). Sexually transmitted diseases such as syphilis became worrying and led to major social consequences, including behavioral changes in the population, such as the use of condoms made of sheep intestines, for example (Veloso 2001). In the work "Natural History of Brazil Illustrated" (1948), Guilherme Piso highlighted venereal disease ("mal venéreo") in African, Indian, Dutch and Portuguese peoples caused

by contagion during sexual intercourse. He considered this disease to be endemic to Brazil and noted efficient treatments with indigenous remedies ("[...] the cure is fast, only with indigenous remedies").

Increased incidences of diseases prompted a search for treatments using tests and formulas with therapeutic plants, which took place in houses built by the Jesuits near forests. According to João Daniel, the traditional pharmacies of the Jesuits were supplied with precious woods, miraculous barks, large forests of copaiba, *umeri* balsams, and leaves and bark of cinnamon and quina, among other plants. This allowed the Jesuits to take advantage of these natural resources and, with the help of the Amazon indigenous — which João Daniel referred to as "natural", such as the Aimorés, Mamainases, and Baré people who were deeply knowledgeable about the forest and extremely skilled at extracting its resources — use medicines in missions and give them to white settlers so that they could be sent to Europe where they were needed (Daniel 2004).

João Daniel frequently valued the commercial potential of Amazonian natural products. According to Pinto (2005), Daniel had a very peculiar intellectual and scientific vision for training missionaries who were part of the religious order, due to the importance of this knowledge as a mechanism of exploitation and power. His observations about the most notable ("notáveis") herbs of the Amazon, and the many medicinal plants he saw there, soon led him to think about the possibility of multiplying the herbs ("multiplicados herbulados") for commercialization, as they were rare products from America and could boost the economy of the 18th century.

The mururé plant

The plant cited in "O Tesouro descoberto..." (Daniel 2004) with the common name mururé is *Brosimum acutifolium* Huber (Moraceae). It is a terrestrial tree native to Brazil that occurs in the Amazon and Pantanal phytogeographic domains. It is known to occur in the North (states of Acre, Amazonas, Pará, Rondônia, and Roraima), Northeast (Maranhão) and Central-West (Mato Grosso) regions of the country, and possibly in the Southeast (São Paulo) (Flora do Brasil 2020). The Flora of Brazil lists three subspecies for this taxon, including *Brosimum acutifolium* subsp. *interjectum* C.C. Berg, which is endemic to Brazil and known to occur in the states of Amazonas, Pará and Maranhão in the Amazon region (Romaniuc Neto *et al*. 2015).

The species is described as a large tree that can reach 35-m in height with abundant white sap and elongate, lanceolate leaves (Berg & DeWolf 1975; Rodrigues 1989). It occurs in tropical and subtropical climates, where the average temperature is between 22 °C and 30 °C, and prefers sandy and clayey-sandy soils with a moderate amount of organic matter (Pinagé 2011).

Historical reports of syphilis, ethnopharmacology, and reactions in the body

João Daniel defined syphilis as the Gallic disease. "Gallic evil" was one of the common terms used to refer to the disease (Geraldes Neto *et al*. 2009), as well as "morbus gallicus" or French evil, due to a famous internal European conflict where the French army was defeated by the disease (not by weapons) (Sousa 1996).

The proven therapeutic efficacy of mururé was associated with the use of its exudate, called morure milk ("leite do morure"), which was extracted by cutting the bark of the tree. The action of this liquid in combatting syphilis was also reported by Pinagé (2011). Because of the abundance of the exudate produced Daniel called the tree King of the Milks ("Rei dos Leites"). The following transcription mentions the rapid curative effect of the exudate for syphilis after ingestion:

> "Morure milk: it is the King of the Milks because its effective virtue is superior to all. It is distilled from the tree known by the same name, which we have already described. It serves to cure the Gallic disease in a marvelous way, because no matter how severely affected by the disease, the sick person heals, and it takes in 24 hours, or less, to cure the disease without need for further preparation" (Daniel 2004, p. 556).

The administration of morure milk to patients affected by the disease was very simple. The product was directly ingested after being collected from a tree, within the shortest possible time after exposure to air, as indicated here: "[...] two full spoons or three moderate spoons". Daniel wrote that a few additional daily doses were necessary after the first dose, and that the treatment was effective within 24 hours or less. He also highlighted the reactions of the patient's body after ingestion.

One of the reactions observed after ingesting the milk was very concentrated urine with the presence of sediment, which resulted from an overload to the kidneys by the medicine and reflected curative action. This was interpreted as an indicator of the effect of the medicinal plant. A similar reaction of the urinary tract with the presence of concentrated sediments also occurs when syphilis patients use current medicines for this pathology (Neves & Araújo 2013; ANVISA 2016). Other observed effects were neurological disorders, described by Daniel as chills, tremors and seizures that started immediately after ingestion, and were treated by placing a warm cloth on the stomach.

Daniel also observed the action of the plant in cases of neurosyphilis, which could appear 12 to 18 months after infection and could be asymptomatic. His notes state "[...] and a small amount for the bones and nerves is enough to eliminate every disease in one night, and for bad mood".

Vargas *et al.* (2000) mentioned the strong psychological effect neurosyphilis had on the patient, while Barros *et al.* (2005) characterized it as an infection that affects the nervous system and can cause lesions to the brain and spinal cord. These clinical observations were similar to what Daniel reported. Neurosyphilis had great repercussions before the use of penicillin, and experienced a resurgence in the late 20th century, mainly in HIV patients who were more susceptible to the disease (Neves & Araújo 2013; Caixeta *et al.* 2014).

Mururé was also indicated for other illnesses, such as scrofula ("alporcas"), and all Gallic diseases: "[...] In the same way, it heals scrofula, and all diseases with gallic sin" (Daniel 2004). Scrofula is a swelling in the lymph nodes and is associated with tuberculosis (Sayahi & Thomas 2005; Capone 2006; Almeida 2012). Carrara (1996) reported that, in the past, syphilis was considered by the medical community as an aggravating factor of tuberculosis. Evidence of this was reported after Daniel started administering the milk when there were clinical symptoms of tuberculosis, which was considered a very effective treatment.

The experience and effectiveness of using mururé in the missions, both with Indians and Europeans, impressed João Daniel who soon saw potential for the exportation of the species for medicinal use in Europe. The subsequent introduction of the plant to Europe began its wide dissemination throughout the world. The articulation of knowledge, healing practices, and market views of the Jesuits was discussed by Pinto (2005), who analyzed the transfer of natural resources and traditional knowledge to other parts of the world, which promoted advances in the sciences (Calainho 2005; Medeiros & Hanazaki 2009; Laws 2013).

In this context, Daniel was a visionary because he promoted the value and use of vegetal riches in the region. Mururé and other plants were not simply studied as a result of the search for knowledge about specific plant species, but instead their study was driven by the fact that they were useful plants to the colony and cities abroad (Costa 2007; Santos 2013; São Bento & Santos 2015).

According to information published in Revista Careta (1918a; b, numbers 501 and 502), there was about six million reported cases of people affected by syphilis throughout Brazil in the 20th century. Due to this health crisis, drugstores popularized therapeutic treatments using mururé, as seen in the advertisements of the magazine (Fig. 1A, B).

In addition to the historical indications of this plant, the species has contemporary uses. The sap of *B. acutifolium* is still used by Amazonian communities on the Maruepaua River for the treatment of rheumatism, dislocations, and swelling of body parts (Baptista 2007). Moreover, in 2017

Figure 1. A. Advertisement for syphilis treatment using mururé in a magazine published in 1918. **B.** Advertisement for syphilis treatment using mururé in a magazine published in 1918. Source: Revista Careta, 1918, edition 502 and 501.

Figure 2. Mururé bark for sale by herbalists at the Ver-o-Peso Fair in 2017.

mururé bark could be found for sale as a medicinal product in the Ver-o-Peso Fair in Belém, Pará, the largest open fair in Latin America (IPHAN 2017). Contemporary indications are similar to those found in historical records from the 18th century and in the 1918 advertisements (Fig. 2). Herbalists of the Ver-o-Peso fair, who are considered holders and transmitters of traditional knowledge in an urban environment (Dantas & Ferreira 2013), continue to promote mururé as a curative and therapeutic product for syphilis.

Contemporary phytochemical studies and therapeutic applications

The presence of secondary metabolites in plants (compounds often produced after growth) can be influenced by various environmental, climatic or temporal factors, and can be associated with collection and storage methods (Gobbo-Neto & Lopes 2007). Discovering useable therapeutic plant species is still an extremely complex process, especially because of the diversity of plants. In this context, present traditional and popular knowledge, as well as information from communities that produced this type of knowledge in the past, remain valuable resources for identifying medicinally useful plants (Medeiros & Hanazaki 2009; Pereira & Cardoso 2012). In line with this, WHO (2011) reported that the amount of modern medicines derived from plants is significant and may reach 60 % of antitumor and antibacterial drugs.

Despite being used for other purposes (e.g., cosmetics and food), mururé is mainly employed for medicinal purposes because its latex and bark have efficient action against many diseases and its sap has antiarthritic and antisyphilitic properties (Rodrigues 1989; Pinagé 2011). A daily dose of the sap should be used for treating syphilis, but the dose must not exceed 8 g because excess of the product produces side effects such as joint pain, polyuria (increased amount of urine), nausea and dizziness. However, whereas Daniel only indicated the use of the sap, the literature also mentions using tea made from mururé bark (Matta 2003 *apud* Pinagé 2011).

Uses of this species by Amazonian communities have been reported by several studies. According to Coelho-Ferreira & Silva (2005), *B. acutifolium* is one of the 228 species that comprise the phytopharmacopoeia of the Marudá fishing community in the countryside of Pará. Monteles & Pinheiro (2007) documented the use of the species as a blood purifier (by preparing traditional "garrafadas" with its bark) by a Quilombola community in the municipality of Presidente Juscelino, Maranhão, which is located within the Amazon Biome, according to the Brazilian Institute of Geography and Statistics (IBGE 2016).

Pharmacological studies have isolated the flavonoid BAS1 [4'-hydroxy, 7, 8 - (2'', 2'' - *dimethyl*-pyran)-flavan] from the bark of *B. acutifolium* (Moraes 2011) and characterized the mechanism of its anti-inflammatory action in stimulated murine macrophages. The results demonstrated that high concentrations of BAS1 have a cytotoxic effect, with a reduction in factors causing inflammation, thus confirming its anti-inflammatory activity.

Maués (2013) investigated the antiproliferative and antineoplastic activities of four flavonoids from *B. acutifolium*, and isolated two flavans — 4'-hydroxy-7,8-(2",2"-dimethylpyran)-flavan (BAS-1) and 7,4'-dihydroxy-8,(3,3-dimethylalil)-flavan (BAS-4) — and two chalcones — 4,2'-dihydroxy-3',4'-(2",2"-dimethylpyran)-chalcone (BAS-6) and 4,2',4'-trihydroxy-3'-(3,3-dimetelalil)-chalcone (BAS-7) — from the bark, and tested their effects on rat glioblastomas in vitro. The study concluded that BAS-1, BAS-4, and BAS-7 had antineoplastic potential as agents in therapy, with BAS-4 being the most promising because its action on tumor cells was the most efficient and its cytotoxic activity was the least harmful to healthy cells.

Other studies also indicated the presence of various flavonoids in the bark of mururé (Torres *et al*. 2000; Takashima & Ohsaki 2002; Takashima *et al*. 2005). Takashima *et al*. (2005) evaluated the activity of four flavonoids against leukemia cells, and found them to have a cytotoxic effect on cells resistant to vincristine (the drug used to treat the disease). Some chemical compounds isolated from the sap of mururé extracted from bark, such as flavans (BAS-1 and BAS-4) and chalcone (BAS-7), were also observed in this study.

After conducting ethnobotanical studies in the interior of the Amazon, Baptista (2007) selected the concentrated sap of *B. acutifolium* for phytochemical experiments to test its antinociceptive (analgesic) and antiedematogenic actions in mice. The results revealed that, at certain doses, the concentrated sap prevented the development of edema in mice. The study also investigated the phytochemical constituents of the latex of *B. acutifolium* and found the presence of saponins, proteins, amino acids, phenols, and alkaloids. The results demonstrated that analgesia promoted by the concentrated sap was due to the presence of one or more secondary metabolites, such as saponin, which has anti-inflammatory activity. Anti-oedematous activity was observed and explained by the action of the sap on chemical mediators that promote an inflammatory state. According to Cruvinel *et al*. (2010), edema is a clinical sign of inflammation.

Baptista (2007) also studied acute and sub-acute toxicity and the metabolites present in mururé bark. The work identified saponins that damage cells by altering the permeability of membranes, thus leading to cell destruction. This type of effect can be explained by the amphiphilic behavior of saponins. Saponins can form complexes with steroids, proteins and membrane phospholipids that have a variable number of biological properties, including cell membrane functionality (Athayde *et al*. 2017).

In a study of takini, a hallucinogen prepared from the sap of *B. acutifolium* and used by shamans of the communities of Palikur, Wayãpi and, Kali'na, Moretti *et al*. (2006) identified the presence of the alkaloid bufotenine

(5-hydroxy-dimethyltryptamine), which is a compound with psychotrophic properties. This alkaloid is present in other species of *Brosimum*, such as *B. utile* (Kunth) Pittier, and has been studied for its antifungal and antibacterial activities due to its toxic effect on the DNA of microorganisms (Haro 2015; Manotoa 2015).

Overall, saponins are important because they not only act on cell membranes, but also help in the absorption of other compounds, thereby increasing immune response (Athayde *et al*. 2017). Moreover, the alkaloid bufotenine promotes bactericidal activity.

Conclusions

Current methods for the treatment of syphilis mostly involve the use of penicillin. Despite historical medical records testifying to the effectiveness of mururé, there is no contemporary reference of the indication of *B. acutifolium* for the treatment of this disease. The search for new medicines and the significant writings of João Daniel reinforce the natural value of plants, which, in the case of mururé due to its remarkable medicinal effects, gave it recognition as a potential drug in "The Treasure Discovered on the Great Amazon River". Countries with the most syphilis cases in the world, and that have elementary social problems that make the production and distribution of medicines difficult, should be aware of the potential value of natural drugs.

References

Almeida MAP. 2012. O Porto e as epidemias: saúde e higiene na imprensa diária em períodos de crise sanitária, 1854-56, 1899 e 1918. Revista de História da Sociedade e da Cultura 12: 371-391.

Anvisa - Agência Nacional de Vigilância Sanitária. 2016. Antimicrobianos - base teóricas e uso clínico http://www.anvisa.gov.br/servicosaude/controle/rede_rm/cursos/rm_controle/opas_web/modulo1/conceitos.htm 24 Jan. 2019.

Athayde ML, Taketa ATC, Gosmann G, Schenkel EP. 2017. Saponinas. In: Simões CMO, Schenkel EP, Mello JCP, Mentz LA, Petrovick PR. (eds.) Farmacognosia: do produto ao medicamento. Porto Alegre, Artmed. p. 285-304.

Baptista ER. 2007. Conhecimentos e práticas de cura em comunidades rurais amazônicas: recursos terapêuticos vegetais. PhD Thesis, Universidade Federal do Pará, Belém.

Barros AM, Cunha AP, Lisboa C, Sá MJ, Resende C. 2005. Neurossífilis: revisão clínica e laboratorial. Arquivos de Medicina 19: 121-129.

Berg CC, DeWolf GP. 1975. Moraceae. In: Lanjouw J, Stoffers AL. (eds.) Flora of Suriname. Vol. 5. Part 1. Leiden,E.J. Brill. p. 173-299.

Brasil. 2012. Ministério da Saúde. Práticas integrativas e complementares: plantas medicinais e fitoterapia na atenção básica. Brasília, Ministério da Saúde.

Caixeta L, Soares VLD, Reis GD, Costa JNL, Vilela ACM. 2014. Neurossífilis: uma breve revisão. Revista de Patologia Tropical 43: 121-129.

Calainho DB. 2005. Jesuítas e Medicina no Brasil Colonial. Tempo 19: 61-75.

Capone D. *et al*. 2006. Tuberculose Extrapulmonar. Revista Hospital Universitário Pedro Ernesto 5: 54-67.

Carrara S. 1996. Tributo a vênus: a luta contra a sífilis no Brasil, da passagem do século aos anos 40. Rio de Janeiro, Editora Fiocruz.

Castro I, Ramos MA. 1986. Estratégia e táctica da transcrição. In: Asensio JVPME. (ed.) Critique textuelle portugaise, actes du colloque. Paris, Fondation Calouste Gulbenkian. p. 99-122.

Coelho-Ferreira MRC, Silva MFF. 2005. A Fitofarmacopéia da Comunidade Pesqueira de Marudá, Litoral Paraense. Bo1etim do Museu Paraense Emilío Goeldi - Ciências Naturais 1: 31-43.

Costa KS. 2007. Natureza, colonização e utopia na obra de João Daniel. História, Ciências, Saúde – Manguinhos 14: 95-112.

Cruvinel WM, Mesquita Júnior D, Araújo JAP, *et al*. 2010. Sistema imunitário - Parte I. Fundamentos da imunidade inata com ênfase nos mecanismos moleculares e celulares da resposta inflamatória. Revista Brasileira de Reumatologia 50: 434-61.

Daniel J. 2004. Tesouro Descoberto no Máximo Rio Amazonas. Vol. 1-2. 1st. edn. Rio de Janeiro, Contraponto.

Dantas CFN, Ferreira RS. 2013. Os conhecimentos tradicionais dos (as) erveiros (as) da Feira do Ver-o-Peso (Belém, Pará, Brasil): um olhar sob a ótica da Ciência da Informação. Perspectivas em Ciência da Informação 18: 105-125.

Flora do Brasil 2020 em construção. 2019. *Brosimum*. Jardim Botânico do Rio de Janeiro. http://www.floradobrasil.jbrj.gov.br/reflora/floradobrasil/FB19770. 25 Abr. 2019.

Gândavo PM. 1576. História da província Santa Cruz, a que vulgarmente chamamos Brasil. Lisboa, Officina de Antonio Gonsaluez.

Geraldes Neto B, Soler ZASG, Braile DM, Daher W. 2009. A sífilis no século XVI: o impacto de uma nova doença. Arquivos de Ciências da Saúde 3: 127-129.

Gobbo-Neto L, Lopes NP. 2007. Plantas medicinais: fatores de influência no conteúdo de metabólitos secundários. Química Nova 30: 374-371.

Godoy AS. 1995. Pesquisa qualitativa: tipos fundamentais. Revista de Administração de Empresas 35: 20-29.

Haro ALJ. 2015. Estudio fitoquímico y evaluación de la actividad antidermatófica *in vitro* del látex de *Brosimum utile* (Kunth c.s.) (Leche de Sandi). Monograph, Escuela Superior Politécnica de Chimborazo, Chimborazo.

IBGE - Instituto Brasileiro de Geografia Estatística. 2016. Presidente Juscelino. https://cidades.ibge.gov.br/brasil/ma/presidente-juscelino/panorama. 25 Abr. 2019.

IPHAN – Instituto do Patrimônio Histórico e Artístico Nacional. 2017. Ver-o-Peso (PA). http://portal.iphan.gov.br/pagina/detalhes/828. 26 Mar. 2017.

Kury L, Gesteira H. 2012. Ensaios de história das ciências no Brasil: das Luzes à nação independente. Rio de Janeiro, EDUERJ.

Laws B. 2013. 50 plantas que mudaram o rumo da História. Rio de Janeiro, Sextante.

Leite S. 2005. História da Companhia de Jesus no Brasil. 1st. edn. São Paulo, Edições Loyola.

Manotoa AAM. 2015. Evaluación de la Actividad Antifúngica em *Moniliophthora roreri* de frutos de cacao (*Theobroma cacao* L.) de Extractos de Látex de sande de *Brosimum utile* Kunth. Monograph, Escuela Superior Politécnica de Chimborazo, Chimborazo.

Maués AL. 2013. Avaliação da atividade antiproliferativa e antineoplásica de flavonoides da espécie *Brosimum acutifolium* em modelos de glioblastoma in vitro. PhD Thesis, Universidade Federal do Pará, Belém.

Medeiros MFT, Andreata RHP, Valle LS. 2010. Identificação de termos oitocentistas relacionados às plantas medicinais usadas no Mosteiro de São Bento do Rio de Janeiro, Brasil. Acta Botanica Brasilica 24: 780-789.

Medeiros MFT, Hanazaki N. 2009. Etnobotânica histórica: princípios e procedimentos. 1st. Edn. Recife, NUPEEA.

Monteles R, Pinheiro CUB. 2007. Plantas medicinais em um quilombo maranhense: uma perspectiva etnobotânica. Revista de Biologia e Ciências da Terra 7: 38-48.

Moraes WP. 2011. Caracterização do mecanismo de ação antiinflamatória do flavonóide BAS1 isolado da planta *Brosimum acutifolium*. PhD Thesis, Universidade Federal do Pará, Belém.

Moretti C, Gaillard Y, Grenand P, Bévalot F, Prévosto JM. 2006. Identification of 5-hydroxytryptamine (bufotenine) in *takini* (*Brosimum acutifolium* Huber subsp. *acutifolium* C.C. Berg, Moraceae), a shamanic potion used in the Guiana Plateau. Journal of Ethnopharmacology 106: 198-202.

Neves CD, Araújo EC. 2013. Sífilis. In: Leão RNQ, Bichara CNC, Fahira Neto H, Vasconcelos PFC. (eds.) Medicina tropical e infectologia na Amazônia. Vol. 2. Belém, Samauma Editorial. p. 1075-1083.

Pereira RJ, Cardoso MG. 2012. Metabólitos secundários vegetais e benefícios antioxidantes. Journal of Biotechnology and Biodiversity 3: 146-152.

Pinagé GR. 2011. Moraceae. In: Rios MNS, Pastore Jr F. (orgs.) Plantas da Amazônia: 450 espécies de uso geral. Brasília, Universidade de Brasília. p. 2391-2453.

Pinto RF. 2005. A viagem das ideias. Estudos Avançados 19: 97-114.

Piso G. 1948. História Natural do Brasil- edição brasileira: (trad. Prof. Alexandre Correia, seguido do texto original, da biografia do autor e de comentários) História Natural do Brasil Ilustrada edição comemorativa do primeiro cinqüentenário do Museu Paulista ed. [S.l.], Companhia Editora Nacional.

Prance GT. 2000. Ethnobotany and the future of conservation. Biologist 47: 65-68.

Revista Careta. 1918a. Acervo digital da Biblioteca Nacional. Número 501, Ano XI. http://objdigital.bn.br/acervo_digital/div_periodicos/careta/careta_1918/careta_1918.htm 08 Abr. 2019.

Revista Careta. 1918b. Acervo digital da Biblioteca Nacional. Número 502, Ano XI. http://objdigital.bn.br/acervo_digital/div_periodicos/careta/careta_1918/careta_1918.htm 08 Abr. 2019.

Rodrigues RM. 1989. A Flora da Amazônia. Belém, Cejup.

Romaniuc Neto S, Carauta JPP, Vianna Filho MDM, *et al*. 2015. Moraceae. In: Lista de Espécies da Flora do Brasil. Jardim Botânico do Rio de Janeiro. http://floradobrasil.jbrj.gov.br/jabot/floradobrasil/FB19770. 24 Jan. 2019.

Salles V. 2004. Apresentação: Rapsódia Amazônica de João Daniel. In: Daniel J. (ed.) Tesouro descoberto no máximo rio Amazonas. Vol. 1. Rio de Janeiro, Contraponto. p. 11-35.

Santos FS. 2013. Indígenas, jesuítas e a farmacopeia verde das terras brasileiras: os segredos da Triaga Brasilica. Prometeica: Revista de Filosofía y Ciencias 8: 5-22.

São Bento VMC, Santos NP. 2015. Jesuítas e ciência: a produção de medicamentos através da Colecção de Varias Receitas de 1766. Revista Maracanan 13: 146-157.

Sá-Silva JR, Almeida CD, Guindane JF. 2009. Pesquisa documental: Pistas teóricas e metodológicas. Revista Brasileira de História & Ciências Sociais 1: 1-15.

Sayahi L, Thomas JA. 2005. Morphophonological and semantic adaptation of Arabisms in Galician. Cahiers Linguistiques d'Ottawa 33: 23-42.

Siewierski H. 2014. O Tesouro da Alteridade Amazônica na Obra do Padre João Daniel. Revista Sentidos da Cultura 1: 81-92.

Sousa CR. 2013. As práticas curativas na Amazônia colonial: Da cura da alma à cura do corpo (1707-1750). Amazônica: Revista de Antropologia 5: 362-384.

Sousa JG. 1996. Impacto social da sífilis: alguns aspectos históricos. Medicina Interna 3: 184-192.

Takashima J, Komiyama K, Ishiyama H, Kobayashi J, Ohsaki A. 2005. Brosimacutins J-M, four new flavonoids from *Brosimum acutifolium* and their cytotoxic activity. Planta Medica 71: 654-658.

Takashima J, Ohsaki A. 2002. Brosimacutins A-I, nine new flavonoids from *Brosimum acutifolium*. Journal Of Natural Products 65: 1843-1847.

Tocantins L. 1976. A Bíblia Ecológica do Padre João Daniel. In: Daniel J. (ed.) Tesouro descoberto no máximo rio Amazonas. Rio de Janeiro, Biblioteca Nacional. p. 7-24.

Torres SL, Arruda MS, Arruda AC, Müller AH, Silva SC. 2000. Flavonoids from *Brosimum acutifolium*. Phytochemistry 53: 1047-1050.

Val AL. 2014. Amazônia um bioma multinacional. Ciência e Cultura 66: 20-24.

Vandelli D. 1788. Florae Lusitanicae et brasiliensis specimen plantae exoticae B. Brasilienses. et epistolae ab eruditis viris Carolo A Linné Antonio De Haen ad Dominicum Vandelli Scriptae. Conimbricae: Ex Typografia Academico-Regia. Cum facultate Regiae Curiae Commissionis Generalis pro Examine, & Censura Librorum. Apud Bibliopolam Antonium Barneoud.

Vargas AP, Carod-Artal FJ, Del Negro MC, Rodrigues MPC. 2000. Demência por Neurossífilis: Evolução clínica e neuropsicológica de um paciente. Arquivos Neuro-psiquiatria 58: 578-582.

Veloso AJB. 2001. Da sífilis à sida. Medicina Interna 8: 56-61.

Veríssimo TC, Pereira J. 2014. Floresta Habitada: História da ocupação humana na Amazônia. Belém, Imazon.

Viegas Júnior C, Bolzani VS, Barreiro EJ. 2006. Os produtos naturais e a química medicinal moderna. Química Nova 29: 326-337.

WHO – World Health Organization. 2011. The world medicines situation 2011: traditional medicines: global situation issues and challenges. Geneva, WHO.

WHO – World Health Organization. 2016. Who guidelines for the treatment of *Treponema pallidum* (syphilis). Geneva, WHO.