Research, Society and Development, v. 9, n. 7, e14973784, 2020
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v9i7.3784

Características botânicas, agronômicas, fitoquímicas e biológicas de *Aspidosperma pyrifolium* Mart.: Uma revisão

Botanical, agronomic, phytochemical and biological characteristics of *Aspidosperma pyrifolium Mart.*: A review

Características botánicas, agronómicas, fitoquímicas y biológicas de *Aspidosperma pyrifolium* Mart.: Una revisión

Recebido: 19/04/2020 | Revisado: 22/04/2020 | Aceito: 23/04/2020 | Publicado: 26/04/2020

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Resumo

Conhecida popularmente como pereiro, *Aspidosperma pyrifolium* apresenta importância econômica devido a utilização de sua madeira. Contudo, não existem estudos que tragam informações relevantes relacionadas a características botânicas, agronômicas, fitoquímicas e biológicas envolvendo essa espécie vegetal. Diante disso, este trabalho teve como objetivo desenvolver um estudo sobre diferentes características de *A. pyrifolium*. O presente estudo tratou-se de uma revisão bibliográfica do tipo narrativa. Foram incluídos artigos, monografias, dissertações e teses recuperados a partir das bases de dados: Lilacs, Scielo, PubMed, *ScienceDirect* e Bancos de Teses e Dissertações de Universidades Públicas. Os estudos ressaltam o uso da *A. pyrifolium* por diversas populações, sobretudo, na região Nordeste do Brasil, mais precisamente no bioma Caatinga, onde apresenta importância econômica e ecológica. Em relação a metabólitos, observa-se a presença, principalmente, de flavonoides e alcaloides. Além disso, estudos também relatam que essa planta apresenta à ação analgésica, anti-inflamatória, contra ectoparasitos, infecções, disfunção erétil e atividade hipotensora, entretanto tem sido demonstrando toxicidade em diferentes modelos animais. Assim, observa-se que pereiro apresenta potencial para tornar-se um possível fármaco, fitofármaco e/ou fitoterápico.

Palavras-chave: *Aspidosperma pyrifolium*; Fitoquímica; Farmacologia.

Abstract

Known in popular medicine as “pereiro”, *Aspidosperma pyrifolium* has economic importance due to the use of its wood. However, there are no studies that provide relevant information related to botanical, agronomic, phytochemical and biological characteristics involving this plant species. Given the above, this study aimed to develop a study on different characteristics of *A. pyrifolium*. The present study is a narrative bibliographic review. Articles, monographs,

dissertations and theses retrieved from the following databases were included: Lilacs, Scielo, PubMed, ScienceDirect and Banks of Theses and Dissertations from Public Universities. The studies highlight the use of *A. pyrifolium* by several populations, especially in the Northeast region of Brazil, more precisely in the Caatinga biome, where it has economic and ecological importance. Regarding metabolites, the presence of flavonoids and alkaloids is mainly observed. In addition, studies also report that this plant has analgesic, anti-inflammatory action, combats ectoparasites and infections, improves erectile dysfunction and has hypotensive activity. On the other hand, toxicity has been reported in different animal models. Thus, it is observed that "pereiro" has the potential to become a possible drug, phytodrug and/or phytotherapic.

Keywords: *Aspidosperma pyrifoliu;* Phytochemical; Pharmacology.

Resumen

Conocido popularmente como pereiro, *Aspidosperma pyrifolium* tiene importancia económica debido al uso de su madera. Sin embargo, no hay estudios que brinden información relevante relacionada con las características botánicas, agronómicas, fitoquímicas y biológicas que involucran a esta especie de planta. Por lo tanto, este trabajo tuvo como objetivo desarrollar un estudio sobre diferentes características de *A. pyrifolium*. El presente estudio fue una revisión bibliográfica del tipo narrativo. Se incluyeron artículos, monografías, disertaciones y tesis recuperadas de las bases de datos: Lilacs, Scielo, PubMed, ScienceDirect y bancos de tesis y disertaciones de universidades públicas. Los estudios destacan el uso de *A. pyrifolium* por varias poblaciones, especialmente en la región noreste de Brasil, más precisamente en el bioma de Caatinga, donde tiene importancia económica y ecológica. En cuanto a los metabolitos, se observa la presencia, principalmente, de flavonoides y alcaloides. Además, los estudios también informan que esta planta tiene acción analgésica, antiinflamatoria contra ectoparásitos, infecciones, disfunción eréctil y actividad hipotensora, sin embargo, ha mostrado toxicidad en diferentes modelos animales. Por lo tanto, se observa que pereiro tiene el potencial de convertirse en un posible fármaco, fitofarmacéutico y / o fitoterapeuta.

Palabras clave: *Aspidosperma pyrifolium*; Fitoquímica; Farmacología.

1. Introduction

About ten thousand years ago, it was observed that the development of agriculture promoted by *Homo sapiens* had allowed the planting and development of vegetables that

served as a source of food and an energy base for their subsistence. Over time, plants are no longer seen as a source of food and are also used in religious rituals and as a way to promote health, either through eating or treating hunting injuries (Vale, 2002).

In Brazil, during the colonial period, the use of plants was mainly carried out by indigenous people and shamans for the treatment of various conditions. This practice became popular some time later among Europeans, however the mechanism responsible for promoting a cure was not yet known (Bruning, Mosegui & Vianna, 2012).

Over time and technological development, it was possible to establish that the biological activity promoted by vegetables was given from the presence of secondary metabolites, produced in times of injuries or as a form of defense (Andrade Júnior et al. 2018).

Thus, the knowledge of the presence of molecules with biological activity has aroused the interest of several researchers in order to develop drugs, phytodrugs or phytotherapics and enable the resolution of several problems observed today, such as the treatment of chronic, infectious and parasitic diseases and cancers.

It is estimated that there are about 120 thousand different plant species in Brazil and their toxic or pharmacological effects are still poorly known, especially in the Northeast region of Brazil, where, despite the diverse flora, there are few studies reporting the biological and technological potentials of their vegetation (França et al. 2008; Bruning, Mosegui & Vianna, 2012; Zeni et al. 2017), like *Aspidosperma pyrifolium*.

A. pyrifolium is popularly known as Pereiro and many studies highlight its use by several populations, especially in the Northeast region of Brazil, however there is no current research that brings relevant information related to botanical, agronomic, biological and technological characteristics involving this plant.

Thus, this study aimed to develop a literature review that brings together the botanical, agronomic, phytochemical and biological characteristics of *A. pyrifolium*.

2 Metodology

2.1 Study design

The present study was a narrative bibliographic review (Pereira et al. 2018), since it aims to bring extensive information regarding *Aspidosperma pyrifolium*. To search for materials, the following descriptors and keywords were used, isolated and associated in

various combinations: 1) *Aspidosperma pyrifolium*; 2) Pereiro; 3) agronomy; 4) botany; 5) pharmacology; 6) biological activity; 7) toxicology; 8) toxicological potential.

2.2 Inclusion and exclusion criteria

Studies that presented information related to *Aspidosperma pyrifolium* were included. Articles, monographs, dissertations and theses published in Portuguese, Spanish and English were used. The year of publication was not considered as a criterion for the adoption or exclusion of studies. However, works that dealt with other plants were excluded from the research.

2.3 Information sources

The articles were retrieved from the databases: Lilacs (Center Latin America and the Caribbean in Health Sciences), Scielo (Scientific Electronic Library Online), PubMed, ScienceDirect and Banks of Theses and Dissertations from Public Universities.

3 Literature review

3.1 Botany

Traditionally, morphological characters are the basis for delimiting species, due to their practicality of use, easy to obtain and low cost (Souza et al. 2014). It is known that despite the economic importance, both in the production of wood and in popular medicine, studies with an anatomical focus on the genus *Aspidosperma* are still scarce.

The morphological analysis of plant structures is the starting point for further analysis involving microscopy.

Anatomy can facilitate the understanding of its structures, mainly secretory, helping taxonomic, chemical and pharmacological botanical studies. In addition, it is extremely important and necessary to know the botanical aspects of a given species (Müeller 1860; Markgraf, 1968; Ezcurra 1981; Allorge & Poupat, 1991). Thus, over the years, the genus has been the target of several taxonomic and botanical studies

According to Tigre (1968) and Braga (1976), the *Aspidosperma pyrifolium* Mart is a regular tree (Figure 1b), which, on average, can reach about five meters in height. Its trunk is well developed, erect, but not very thick, with a diameter that varies between 15 to 20 centimeters. The canopy is normal. The bark is smooth and grayish, with white lenticels,

when the plant is young, and rough, when older. The pereiro's wood is light in color, moderately heavy, soft and easy to work, resistant and very durable, with a fine and uniform texture (Maia, 2004).

Below, in Figure 1, it is possible to observe some morphological characteristics of *A. pyrifolium*.

Figure 1. Visual aspects of *Aspidosperma pyrifolium* Mart, photographed in the Seridó microregion of Rio Grande do Norte/Brazil**.**

Source: Personal archive (SOUZA, JPB)

Its leaves (Figure 1a) are oval, simple, bitter, glabrous or hairy and their flowers are small, clear and, due to the essential oils present, they have a very pleasant scent that exudes in the environment at night. Flowering usually occurs in the beginning of the rains, between September and January, with the foliage not yet developed or in the beginning of development (Tigre, 1968; Braga, 1976; Lima, 1989).

It presents dry, dehiscent fruit (Figures 1c and 1d), in turn, it has the shape of a flattened drop (it is popularly known as “chicken”), light brown in color, with small gray warts, which holds about five seeds (Maia, 2004). Its seeds (Figure 1c), are winged, flat and

of marginal placentation. Its dispersion is made through the wind, and the fruiting occurs between the months of January to March (Lima, 1989).

3.2 Agronomic Characteristics

According to the Flora Species List in Brazil, *A. pyrifolium* is native, but not endemic to Brazil, with confirmed occurrences in the North (Pará), Northeast (Alagoas, Bahia, Ceará, Paraíba, Pernambuco, Piauí, Rio Grande do Norte, Sergipe), Midwest (Federal District, Goiás, Mato Grosso do Sul, Mato Grosso) and Southeast (Minas Gerais), encompassing the phytogeographic domains of the Amazon, Caatinga and Cerrado, although it is mostly observed in regions higher altitude (Lorenzi, 2008; Koch et al. 2015; Castello et al. 2019).

A. pyrifolium it has the ability to adapt to high temperatures, the average temperature that favors growth is around 26°C, and it also adapts to the low rainfall (below 800 mm/year) (Queiroz, 2011). In addition, intermittent drought has been shown to act as a promoter of growth and development in the early stages of this species. While the daily supply of water, it seems to hinder the growth of these vegetables (Freitas & Silva, 2018).

It was also observed that this plant has tolerance to salinity, which in turn, due to its deep root systems, contributes to the process of leaching of salts, lowering the water table and accelerating the process of soil recovery through greater nitrogen and organic matter fixation (Freitas et al. 2010; Sousa et al. 2012; Medeiros et al. 2017). This characteristic is important, since the excess of salts can cause a decrease in the photosynthetic rate, sweating and also cause leaf damage and nutritional changes (Munns, 2002).

3.3 Phytochemistry

The use of plants as a therapeutic alternative dates back to the beginning of human history and although there is a wide knowledge about medicinal plants today, the complexity of their constitution and biological activities makes research in this area always more and more necessary (Lins, 2016).

Some research on *Aspidosperma pyrifolium* has been contributing to scientific knowledge in the chemical, biological and pharmaceutical fields. Phytochemical research, more specifically, aims to know the chemical constituents of plant species or evaluate their presence (Messiades, 2014).

Plants produce a wide and diverse array of organic components divided into primary and secondary metabolites. Secondary metabolites have important ecological functions in

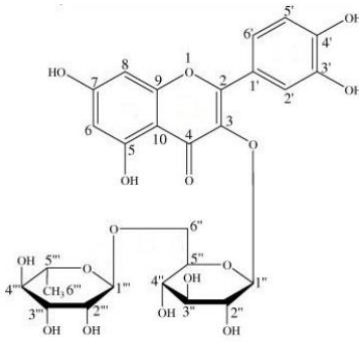
plants, such as: protecting plants against herbivores and pathogens, serve as attractions (smell, color, taste) for pollinators and function as agents of competition between plants and symbiosis between plants and microorganisms (Vizzotto, Krolow & Weber, 2010).

Secondary metabolites can be chemically divided into three main groups: phenolic compounds, terpenes and nitrogen-containing components (Pereira & Cardoso, 2012). Phenolic compounds constitute the most abundant class of secondary metabolites in plants, being subdivided into classes, according to their chemical structure.

The identification of secondary metabolites in plant species can be a source of information of therapeutic interest, with great potential for application in studies involving human health (Aires & Lima, 2014).

Among the phenolic compounds, the flavonoids are highlighted, which have the chemical structure described as C6-C3-C6, usually present in leaves, flowers, roots and fruits of plants and have several biological activities, among which we can mention: antibacterial, antiviral, anti-inflammatory, antioxidant and antitumor (Flambó, 2015). In relation to these compounds present in *A. pyrifolium*, rutin is found, a flavonoid very relevant for industrial pharmaceutical purposes (Figure 2) (Lima, 2015).

Figure 2. Chemical structure of rutin.



Source: Authors, 2020.

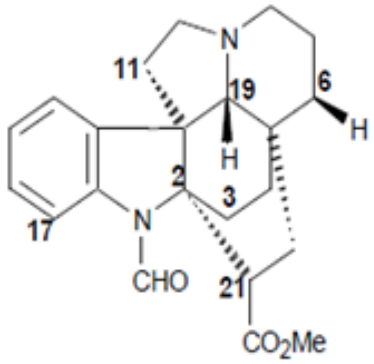
Lima et al. (2017), found rutin as the main chemical component, in addition to phenolic compounds in aqueous extract of *A. pyrifolium* leaves.

Alkaloids, in turn, are cyclic organic compounds that have at least one nitrogen atom in their ring and are classified according to the ring that contains one or more nitrogen atoms (Vizzotto, Krolow & Weber, 2010).

A striking feature of the *Aspidosperma* genus is the presence of indole alkaloids, which confer a wide spectrum of biological activities recognized in species of this genus

(Henrique, Nunomura & Pohlit, 2010). Several alkaloids have already been isolated from the bark, roots, leaves and branches of *A. pyrifolium*, as indole alkaloids of the aspidosfractin type skeleton (Figure 3) (Leite, 2016).

Figure 3. Indolic alkaloids Aspidofractin**.**



Source: Authors, 2020.

Nogueira et al., (2014) from the ethanolic extract of the seeds of *A. pyrifolium*, isolated a new alkaloid with rearranged Plumeran skeleton, the (–)-(3S,7S,21R)-rel-(3αH)-15(14→3)-abeo-2,16,17,20,6,7-hexahydro-15H,8aH,16a,20a-ethane-1H-indolizine[3,1-cd]carbazole, in addition to six known plumeran alkaloids, a tetrahydro-β-carbolinic alkaloid, and the heterosides of two iridoides and salicylic acid, which are being described for the first time for the species.

In extract from the bark of the stem of *A. pyrifolium*, Ceravolo et al. (2018), identified two main components compatible with the bisindole alkaloid Leucoridin B and a new compound, probably responsible for the activity against malaria parasites demonstrated in *in vitro* tests.

3.4 Biological Activities

Species of the genus *Aspidosperma* are widely used for the treatment of cardiovascular diseases, fever, malaria, diabetes and rheumatism, the decoction of the bark being the most commonly used form by the population. In addition, depending on the type of species, the purpose of use can be differentiated (Almeida et al. 2018).

In the northeast of Brazil, it is observed that the population makes use of *A. pyrifolium* peels for the treatment of inflammation, dermatitis, urinary tract infection, gastritis,

ectoparasites, epigastric and calming pain (Almeida et al. 2005; Albuquerque et al. 2007; Agra et al. 2007a; Agra et al. 2007b; Santos et al. 2015).

Popular reports from the rural area of the state of Rio Grande do Norte, Brazil, state that the elderly used the species to treat dizziness, urinary disorders, wound healing, inflammation and antioxidant (Lima et al. 2017; Fernandes & Bizerra, 2020).

In vitro studies have attested that this plant has photoprotective activity due to the presence of alkaloids and flavonoids (Nunes et al. 2018). This plant has also shown activity against ectoparasites such as ticks and ovicidal activity against lice eggs, also showing insecticidal and antibacterial activity (Oliveira et al. 2005; Trindade et al. 2008; Silva et al. 2014).

The aqueous extract obtained from the stem bark had a toxic effect against *Plutella xylostella* L. It can, therefore, act as a possible insecticide and assist in pest control (Torres et al. 2006). While in a study by Trindade et al. (2008) larvicidal activity was observed against this same insect, through extracts of stem bark, fruits and roots (Trindade et al. 2008).

In the study developed by Ceravolo et al. (2018), the crude extract of the stem bark and the fractions rich in alkaloids and ethyl acetate showed *in vitro* activity against malaria parasites. Two extracts and two fractions tested *in vivo* caused a significant reduction in *Plasmodium berghei* parasitemia in experimentally infected mice. These findings make the species a candidate for further investigation in order to produce a new antimalarial, mainly considering that the active extract did not present toxicity with respect to mutagenic effects in genototoxicity tests.

A. pyrifolium contains substances such as aspidospermine and quebrachamine, which has shown adrenergic blocking activity in urogenital tissues, and is therefore used in folk medicine to treat erectile dysfunction and symptoms of benign prostatic hyperplasia (Deutsch et al. 1994).

Regarding erectile dysfunction, the decrease in the release of adrenaline caused by this plant is interesting, since this substance would cause the constriction of the penile arteries, through the α-$_1$ adrenergic receptors, coupled to G_q/G_{11} protein, making it impossible therefore, the influx of blood and thus the penile erection (Alves & Veloso, 2004; Golan et al. 2009).

Prostatic hyperplasia, in turn, is a disease commonly seen in individuals over 50 years of age. This disease causes an increase in the size of the prostate causing difficulties at the moment of urination, in which the patient generally presents bladder tenesmus, polycyturia and noctiuria (UFRGS, 2015). The decrease in adrenaline concentrations made possible by

the use of pear can prevent this catecholamine from being present in α-$_1$ adrenergic receptors, with relaxation of the urogenital musculature, reduction of tension in the muscles of the prostate and urethra, allowing urination.

According to Nogueira et al. (2014), the aqueous fraction resulting from the liquid-liquid partition of the ethanolic extract of *Aspidosperma pyrifolium* seeds showed antinociceptive and anti-inflammatory activities in the formalin tests, abdominal contortion induced by acetic acid and paw edema by carrageenan.

Lima et al. (2017), investigated the ability of the aqueous extract of *A. pyrifolium* leaves to reduce inflammation induced by carrageenan and by poisoning through the scorpion *Tityus serrulatus* in mice, as well as the cytotoxic effects of this extract, and the results revealed that the extract is safe. Both the extract and the rutin showed a reduction in cell migration in the peritoneal cavity and, similarly, the poisoned animals also showed a reduction in edema, inflammatory cell infiltration and vasodilation in the lungs, revealing the action of *A. pyrifolium* against inflammation caused by poison of *Tityus serrulatus* and carrageenan, with a potential anti-inflammatory application.

Another biological activity observed was the hypotensive effect in dogs, however, due to the high cytotoxicity evidenced in these animals, its ingestion in oral medicinal preparations is not recommended. In rats, this ability was also observed (Craveiro, Matos & Surur, 1983). Although the mechanism of action for this species has not yet been elucidated for this activity, it was observed that other species of this genus seem to act by causing a relaxing effect by inhibiting voltage-gated calcium channels (Cav) present in the smooth muscles of the blood vessels (Furtado et al. 2017). The absence of calcium ions in the cytoplasm prevents the calcium-calmodulin complex formation, which, in turn, will not activate the myosin light chain kinase, which will not phosphorylate the myosin light chain, preventing muscle contraction and causing the reduction of the vascular peripheral resistance, with vasodilation and decreased blood pressure.

However, medicinal plants do not only present attractive biological activities, they may contain toxic characteristics that may lead to discouraging their use. The consumption of pereiro by animals is related to the reduction of reproductive rates, the development of diseases and the consequent decrease in animal production. Thus, the losses, mainly of an economic nature, should be highlighted, as it is estimated that about one million cattle die from poisoning due to the consumption of toxic plants. In the case of the pereiro, more specifically, intoxications are generally reported in the dry season, because in this period the leaves are still green and are the last to fall (Sousa et al. 2014).

The malformations evidenced in goats and cattle are mainly flexion of the pelvic limbs, brachignathy, microphthalmia, prognathism, ocular dermoid and anal atresia (Sousa et al. 2014). In addition, *A. pyrifolium* leaf extract was verified that promoted hemolysis and was lethal to the *Artemia salina* organism (Lima & Soto-Blanco, 2010). While in Swiss albino mice, methanolic extract was administered in the intraperitoneal region, leading these animals to show decreased reflexes, spasms and irritation of the conjunctiva (Nóbrega, 2008).

A. pyrifolium has demonstrated toxic effects in animals during pregnancy, in which rats and goats have slowed fetal development. In addition, in small ruminants and rats, abortions were observed (Panter & Stegelmeier, 2011; Coppock & Dziwenka, 2017). In goats it was also observed intoxication and abortion due to the consumption of this plant and, in pregnant rats, fetal weight loss and maternal intoxication were evidenced (Lima & Soto-Blanco, 2010).

Finally, hydroalcoholic extracts from this plant demonstrated cytotoxic activity, presenting a half maximal inhibitory concentration (IC_{50}) of 62 µg/mL (Pessoa et al. 2006). It is suggested that the probable toxic activity may be related to monoterpenoid indole alkaloids that are isolated in this type of species such as N-formyl-aspidofractin, aspidofractinin and 15-dimethoxypyrifoline (Araújo et al. 2007).

However, further studies are needed to elucidate, in fact, which metabolites and at what concentrations they can cause toxic effects in animals and humans.

4. Final Considerations

The pereiro presents itself as a plant of social and economic importance, especially in the Northeast region of Brazil due to its anatomical characteristics that provide wood of interesting quality, in addition to being relevant for ecological purposes.

Regarding its metabolites, the presence of nitrogen-rich compounds, especially alkaloids, stands out. The use of *A. pyrifolium* has already been consolidated by the population for the treatment of inflammation, dermatitis and urinary infection, also presenting hypotensive activity and acting against erectile dysfunction in animal models. However, its toxicological potential is still poorly understood, being reported mainly in animals.

Thus, it is noted that the pereiro has potential for the possible development of drugs, phytodrug and / or phytotherapic. However, more phytochemical and pharmacological studies

are required, in addition to *in vitro* and *in vivo* tests, including animal and human models, in order to expand knowledge about the species and enable possible clinical use.

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