Ethnobotanical and Pharmacological Study of *Aspidosperma nitidum* Benth (Apocynaceae) – a Review

Inês Ribeiro Machado[1], Keila Rêgo Mendes[2], Maria Kellen da Silva Moço Tavares[1], Anália Arêdes[1] & Homero de Giorge Cerqueira[3]

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[1] Universidade Estadual do Norte Fluminense Darcy Ribeiro/UENF. Avenida Alberto Lamego, 2000, Parque Califórnia, Campos dos Goytacazes/RJ, Brasil. CEP: 28.013-600. <inesuenf@yahoo.com.br, mariakellen@hotmail.com, naliamg@hotmail.com>.

[2] Instituto Chico Mendes de Conservação da Biodiversidade/ICMBio, EQSW 103/104, Bloco "B", Complexo Administrativo, Setor Sudoeste, Brasília/DF, Brasil. CEP: 70.670-350. <keilastm@hotmailcom>.

[3] Academia de Polícia Militar do Barro Branco. Avenida Água Fria, 1923, Água Fria, São Paulo/SP, Brasil. CEP: 02.333-001.<homero.cerqueira@gmail.com>.

ABSTRACT – Carapanaúba (*Aspidosperma nitidum*) is a tree up to 25 meters high and 40 to 60cm in diameter, straight and with a striated trunk. It is a very resistant and easy to use plant mainly for making cables and tools. In addition to the use of this species in the timber industry, this plant has many medicinal properties. Among the pharmacological properties are antinociceptive, anti-inflammatory, antimicrobial, antioxidant, acetylcholinesterase inhibitory, gastroprotective, antitumor and antimalarial activities. The metabolites responsible for antinociceptive activity were not found in the investigated literature. For anti-inflammatory activity, possible activities of the compounds lupeol, sistoterol and stigmasterol were found. For antimicrobial activity, alkaloids, steroids, triterpenes and pentacyclics may be involved in the process. Alkaloids may be related to antioxidant activity. Regarding the inhibitory activity of acetylcholinesterase, the carbonyl ester may be responsible for such activity. For gastroprotective and antitumor activity, alkaloids were also found in the literature as possible involved in the process. Regarding antimalarial activity, the substances responsible for the mentioned activity were not found. The present work reviewed the ethnobotanical and pharmacological properties of *Aspidosperma nitidum*.

Keywords: Pharmacological activity of *Aspidosperma nitidum*; ethnobotanical property of *Aspidosperma nitidum*; properties of Apocynaceae.

Estudo Etnobotânico e Farmacológico de *Aspidosperma nitidum* Benth (Apocynaceae) – uma Revisão

RESUMO – Carapanaúba (*Aspidosperma nitidum*) é uma árvore com até 25m de altura e 40 a 60cm de diâmetro, reta e com tronco estriado. É uma planta muito resistente, bastante fácil de se trabalhar, utilizada principalmente para fabricar cabos e ferramentas. Além do uso dessa espécie na indústria madeireira, essa planta possui muitas propriedades medicinais. Entre as propriedades farmacológicas estão as atividades antinociceptivas, anti-inflamatórias, antimicrobianas, antioxidantes, atividade inibitória da acetilcolinesterase, gastroprotetiva, antitumoral e antimalárica. Os metabólitos responsáveis pela atividade antinociceptiva não foram encontrados na literatura investigada. Para atividade anti-inflamatória foram encontradas possíveis atividades dos compostos lupeol, sistoterol e estigmasterol. Para atividade antimicrobiana, os alcalóides, esteróides, triterpenos e pentacíclicos podem estar envolvidos no processo. Os alcalóides podem estar relacionados à atividade antioxidante. Em relação à atividade inibitória da acetilcolinesterase, o éster carbonílico talvez possa ser responsável por tal atividade. Para atividade gastroprotetora e antitumoral, os alcalóides também foram encontrados na literatura como possível envolvidos no processo. Quanto à atividade antimalárica, não foram encontradas as substâncias responsáveis pela atividade citada. O presente trabalho revisou as propriedades etnobotânicas e farmacológicas de *Aspidosperma nitidum*.

Palavras-chave: Atividade farmacológica de *Aspidosperma nitidum*; propriedade etnobotânica de *Aspidosperma nitidum*; propriedades da Apocynaceae.

Estudio Etnobotánico y Farmacológico de *Aspidosperma nitidum* Benth Apocynaceae – una Revisión

RESUMEN – Carapanaúba (*Aspidosperma nitidum*) es un árbol de hasta 25 metros de altura y 40 a 60cm de diámetro, recto y con un tronco estriado. Es una planta muy resistente, muy fácil de trabajar, utilizada principalmente para fabricar cables y herramientas. Además del uso de esta especie en la industria maderera, esta planta tiene muchas propiedades medicinales. Entre las propiedades farmacológicas se encuentran las actividades antinociceptivas, antiinflamatorias, antimicrobianas, antioxidantes, inhibidoras de la acetilcolinesterasa, gastroprotectoras, antitumorales y antipalúdicas. Los metabolitos responsables de la actividad antinociceptiva no se encontraron en la literatura investigada. Para la actividad antiinflamatoria, se encontraron posibles actividades de los compuestos lupeol, sistoterol y estigmasterol. Para la actividad antimicrobiana, pueden estar involucrados en el proceso alcaloides, esteroides, triterpenos y pentacíclicos. Los alcaloides pueden estar relacionados con la actividad antioxidante. Con respecto a la actividad inhibidora de la acetilcolinesterasa, el éster de carbonilo puede ser responsable de dicha actividad. Para la actividad gastroprotectora y antitumoral, también se encontraron en la literatura alcaloides como posibles implicados en el proceso. En cuanto a la actividad antipalúdica, no se encontraron las sustancias responsables de dicha actividad. El presente trabajo revisó las propiedades etnobotánicas y farmacológicas de *Aspidosperma nitidum*.

Palabras clave: Actividad farmacológica de *Aspidosperma nitidum*; propiedad etnobotánica de *Aspidosperma nitidum*; propiedades de Apocynaceae.

Introdution

As an ancient tradition in Asian and African countries, the use of plants as medicines has also become common in the Western world (Krettli *et al*., 2009; Oliveira *et al*., 2015). About a third of adults use herbs as an alternative therapy in their primary forms or as plant mixtures declared to be non-toxic, even after long-term use (Zhou *et al*., 2004). For the control of various diseases, herbal remedies continue to be important against malaria, for example, in poor and endemic areas (Willcox & Bodeker, 2004; Lima *et al*., 2015).

Carapanaúba (*Aspidosperma nitidum*) is a tree up to 25 meters high and 40 to 60cm in diameter, straight and with a grooved trunk and with many medicinal properties. Because of the holes in its trunk, the name Carapanaúba means Carapanã wood (mosquito). Although the Carapanaúba wood is heavy and hard, it is very resistant, but it is easy to work with, mainly used for making cables and tools (Bezerra *et al*., 2011).

A. nitidum is part of the subgroup Nitida, which are trees found in South and Central America, are commonly known in northern Brazil as "carapanaúba", which means "mosquito's nest" (carapanã = mosquito and ubá = tree) (Oliveira *et al*., 2008). The plant has its trunk divided longitudinally into thin lamellae and is also known as oarwood and sapupema, (Cointe, 1947). Still according to the same author, the habitat of this large tree is in the humid upland forests. The wood of this plant has a brownish yellow color, resistant, elastic, not attacked by termites. It is suitable for carpentry, tool handles, oars and other uses.

According to Ribeiro *et al*. (2002) the plant has numerous properties being used in the treatment of inflammation of the uterus and ovary, in diabetes, stomach problems, against cancer, as contraceptive and against fever and rheumatism (Weniger *et al*., 2001). In addition, the plant also used as a contraceptive, in the treatment of inflammation of the uterus and ovary, in diabetes, in stomach problems, against cancer, fever and rheumatism (Pereira *et al*., 2006). The plant has a bitter, febrifugal bark, useful in bronchitis (Cointe, 1945).

Thus, the objective of this review was to report the ethnobotanical and pharmacological properties of *Aspidosperma nitidum*. For this review, databases of *A. nitidum* were consulted, such as Google, Scielo, Periódicos Capes and CAPES in the period from 15 to 30 July 2020, based on the ethnobotanical and pharmaceutical attributions of the plant.

Ethnobotanical properties

It is through the ethnopharmacological approach that it is possible to investigate medicinal plants precisely because they combine information acquired from local communities that make use of medicinal flora with phytochemical and pharmacological studies carried out in specialized laboratories. This strategy is the one that allows

the selection of plant species and constitutes a valuable shortcut for the discovery of new drugs (Koehn *et al*., 2005; Braz-Filho, 2010).

Species of the genus *Aspidosperma* are generally used in the Amazon by indigenous and caboclo populations (Milliken, 1997) for medicinal purposes such as the treatment of inflammation of the uterus and ovary, diabetes, cancer, as contraceptives and treatment of malaria. The most used species are *A. nitidum*, *A. marcgravianum*, *A. carapanauba* and *A. desmantun* (Brandão *et al*., 1992; Milliken, 1997).

According to Añez (2009), among the carapanaubas of the *Aspidosperma* genus, people in the communities know and indicate only one of the species, *Aspidosperma nitidum*. The plant is used for prevention against malaria and also for its symptomatic treatment. It also has contraceptive properties and was rarely indicated as an abortion. Among the parts of the plant most used by the community there is stem bark that is used in the form of tea with few cooking or directly in water without boiling (Table 1).

A. nitidum latex is used to cure leprosy by Indians in the International Amazon, Colombia, Makuna and Taiwan (Ribeiro *et al*., 1999; Amazonica-TCA Cooperation Treaty, 1995) (Table 1). According to Bezerra *et al*. (2011), the plant oil is used by caboclos against malaria and as a contraceptive (Table 1). Used by more than 8,000 natives, the stem bark of the *A. nitidum* (carapanaúba) is used in various parts of Brazil to cure malaria (Brandão *et al*., 1992). The species *A. nitidum* in the state of Amapá is used to treat bronchitis and diabetes and in Manaus it is used as an anti-inflammatory, healing and contraceptive (TCA, 1995) (Table 1).

According to Milliken & Albert (1996), the bitter bark of *Aspidosperma nitidum* has been used to treat malaria and associated liver disorders. This practice is very widespread in the Amazon, although its effectiveness has not yet been proven. This species was consistently cited by indigenous groups in the state of Roraima, as effective against malaria during a survey of a group of antimalarial plants in the region (Table 1).

There are other reports of the use of *A. nitidum*, the Yanomarni Indians who lived in the most isolated regions, such as Xitei, where there was minimal external contact until the arrival of gold miners in 1988, collected antimalarial plants for internal use and among them was *A. nitidum* (Milliken & Albert, 1997).

In the ethnobotanical studies of Añez, (2009) in the Nossa Senhora Aparecida community in Silves, Amazonas, the most indicated use of *A. nitidum* was for the treatment of the digestive system such as stomach and liver disorders. However, in the community, the use of the plant has varied forms such as for the treatment of infection, diabetes, contraception, among other forms and uses. According to the author and according to the report of the resident of the community, the preparation made frequently was the use of the bark for diseases. These *A. nitidum* barks were placed directly in the water and after a few minutes it would become yellow, bitter and fit for consumption (Table 1).

Also according to Añez (2009), the use of *Aspidospema nitidum* with alcoholic beverages was little reported by the community, with only two reports. The men said they used the plant soaked in cachaça as a sexual stimulant (Table 1). The report of "garrafadas" with *A. nitidum* was not frequent, because the bitter taste did not allow the consortium with other plants. Regarding the doses used, the indication of the residents was to take the preparation of *A.nitidum* at room temperature until it is cured. The use of the preparation of the plant was made by men, women and children of all age groups, but the only restriction of use was in the case of pregnancy. There were no reports of adverse effects, despite the reported abortion properties of the plant. As malaria affects many residents of this community, the report was unanimous on the most frequent use of *A. nitidum* for the treatment of this disease with the use of its barks (Table 1). Añez (2009) concluded in his studies that the culture of using plant species from the Amazon is very present in the community and that this culture passes from generation to generation through oral transmission.

In each region it is possible to verify the use of *A. nitidum* in different ways and for different purposes, in the state of Pará, for example, a plant is used in the treatment of inflammation of the uterus and ovary, against diabetes, cancer, contraception and against fever and rheumatism (Weniger *et al*., 2001) (Table 1). Natives from different regions in the Amazon, on the other hand, use this plant as bark for the cure of malaria (Bourdy *et al*., 2004; Brandão *et al*., 1992) (Table 1).

Ferreira *et al.* (2015) examined wild plants grown and used to treat malaria and associated symptoms by communities in the municipalities of Pauini and Xapuri, in the states of Amazonas and Acre, respectively. During 2013, 86 people were interviewed in 9 rural communities in Pauini and Xapuri who were known to have the knowledge and use of medicinal plants. After each interview, walks (walking in the woods) were made, with a family informant to identify plants and collect samples of the species that were indicated. A total of 86 species of plants were indicated by rubber tappers and riverside dwellers for the treatment of malaria and associated symptoms. Of the 86 plants, 26 species were indicated only for the treatment of malaria, of which 2 had no indication of use for this purpose. Among the plants mentioned in the survey, the 10 most cited and used by the interviewees living in the 2 regions were highlighted. Among the 10 most mentioned plants was *A. nitidim*.

Table 1 – Ethnobotanical propreties of *Aspidosperma nitidum*.

ETHNOBOTANICAL PROPERTIES				
Activity	**Used form**	**Part of the plant used**	**Who use**	**References**
Against malaria, contraceptive	Bark tea or directly into the water	Stem	Local community in Silves, Amazonas	Añez (2009)
Leprosy	Látex	Stem	Indians in the International Amazon Colombia	Ribeiro *et al.* (1999); TCA (1995)
Malaria, contraceptive	Oil	Whole plant	Caboclos	Bezerra *et al.* (2001)
To treat bronchitis and diabetes	Barks	Stem	Community in the Amapá	TCA (1995)
Anti-inflammatory, healing and contraceptive	Barks	Stem	Community in Manaus	TCA (1995)
Malaria	Barks	Stem	Indigenous group of Roraima	Milliken & Albert (1996)
To treat digestive system, diabetes, contraceptive and malaria	Bark directly into the water	Stem	Community in Silves, Amazonas	Añez (2009)
Stimulant sexual	Barks in cachaça	Stem	Community in Silves, Amazonas	Añez (2009)
Inflammations of the uterus, ovary. To treat diabetes, cancer, contraception, against fever and rheumatism	Bark	Stem	Community in state of Pará	Weniger *et al.* (2001)
Malaria	Bark	Stem	Natives from different regions in the Amazon	Bourdy *et al.* (2004); Brandão *et al.* (1992)

Pharmacological properties

Antinociceptive activity

Antinociceptive activity is considered to have the capacity to cancel or transmit the stimuli that cause pain. According to Pereira *et al.* (2006), the ethanolic extract from the heartwood of *A. nitidum* was subjected to the formalin-induced nociception test. The studies showed that there was antinociceptive activity of the ethanolic extract (EE) of *A. nitidum* in relation to the results obtained using morphine (M) and diclofenac (D), used as controls of the first and second phases, respectively (Table 2). It was also observed that in both phases, morphine caused a reduction in licking time (Hunskaar *et al.*, 1985; Shibata *et al.*, 1989). Diclofenac and extract (EE) at doses of 100.0 and 300.0mg, showed activity only in the second phase of the test, indicating the existence of antinociceptive activity without the participation of the opioidergic system.

Anti-inflammatory activity

For studies to verify the anti-inflammatory activity, the intra-plantar injection of carrageenan to induce an acute and progressive increase in the volume of the animals' injected paw. This edema is proportional to the intensity of the inflammatory response and constitutes a useful parameter in the evaluation of anti-inflammatory activity (Castro, 2000). According to Pereira *et al*. (2006) the results indicate that the ethanolic extract from the heartwood of *A. nitidum* caused a reduction in edema induced by carrageenan in relation to the control of the test. According to the literature described in some studies, there is significant anti-inflammatory activity of the compounds lupeol (Geetha & Varalakshmi, 2001), sitosterol and stigmasterol (Gomez *et al*., 1999; Senatore *et al*., 1989) (Table 2).

In the work of Medeiros (2010), the doses of 30 and 100mg/kg of the ethanol fraction of *A. nitidum* tested showed significant anti-inflammatory activity in situations in which the inflammatory process is chronic and administration of doses is frequent. In the model used by the author, the animals were treated daily for 7 days. Thus, the author concluded that the ethanolic fraction of *A. nitidum* barks had anti-inflammatory activity in chronic processes and that the study of the effective dose may indicate that low concentrations are the most effective for this purpose.

Antimicrobian activity

Siminski *et al*. (2015) evaluated the antibacterial potential of *Aspidosperma nitidum* bark extracts against strains of *Staphylococus aureus* ATCC® 25923, *Escherichia coli* ATCC® 25922 and *Pseudomonas aeroginosa* ATCC®27853. *A. nitidum* extract was diluted in concentrations of 1: 2, 1:4, 1:8, 1:16 and 1:32. As a result of the experiment, there were two concentrations and showed greater inhibitory potential, with dilutions 1:8 and 1:32, followed by 1:2, 1:4 and 1:16 that did not vary statistically between them (Table 2). In the joint analysis between the three extracts tested for the organism *S. aureus* it was possible to verify that the extracts of *Aspidosperma nitidum* and of another plant tested by the authors were those that presented greater inhibitory values.

Several compounds are highlighted in *A. nitidum*, such as alkaloids, steroids, triterpenes and pentacyclics, which may be related to anti-inflammatory activity and thus explaining the frequency of the medicinal use of this plant by the population and also the inhibitory capacity against the tested microorganisms (Simpson, 2013) (Table 2).

Antioxidant activity

Phytochemical investigation has demonstrated an abundant presence of alkaloids in the bark of the species *A. nitidum*, however, the literature does not bring any study regarding the antioxidant activity of the species, which made Sales's work (2019) important from therapeutic view. Thus, tests were carried out to determine phenolic compounds that are acting as a potential protective agent against free radicals. Therefore, tests were carried out to evaluate the antioxidant capacity of the crude extract and fractions, using the methods of capturing DPPH radicals and reducing power. The antioxidant capacity of crude extract *Aspidosperma nitidum* bark fractions. was evaluated by the percentage of initial reduction of the 2,2-diphenyl-1-picryl-hydrazila (DPPH) stable radical by the samples in different concentrations.

The fractions obtained from the partition of the methanolic extract of *A. nitidum* from the chloroform, ethyl acetate and hydroalcoholic phases presented satisfactory results, since, for a compound to be considered active, it must have EC50 (concentration of the sample necessary to decrease 50% of free radicals) in a concentration below 50ppm. According to Sales (2019), the alkaloids may have exhibited DPPH free radical scavenging activity because they have phenolic hydroxyls capable of donating protons and neutralizing radicals (Table 2).

In other studies, Martins *et al*. (2016) *A. nitidum* extract exhibited good antioxidant activity despite the average. According to Prasad *et al*. (2012), the content of phenolic compounds that can vary from moderate to low in the extracts can influence this result.

Inhibitory activity of acetylcholinesterase

According to Sales (2019) for the prophylactic and therapeutic treatment of Alzheimer's disease and the hypothesis of using acetylcholinesterase inhibitor (AChE) has been

successful, with a great improvement in the quality of life of patients. The author also states that the search for substances with a low level of toxicity is increasingly intensified with the intensification of the investigation of plants used in traditional medicine, as a source of use of AChE inhibitors.

The role of these plant-based inhibitors is quite relevant because they bind to the enzyme in a reversible way by weak intermolecular bonds, thus allowing the recovery of the enzyme's active center (Sales, 2019).

In the work carried out by Sales (2019), among the isolated and tested substances, two can be highlighted, the PCAN_50.3 (partition of the methanolic extract from the bark of the chloroform phase with an unidentified isolated substance) and PCAN_8.2.2 (partition of the methanolic extract from the bark of the chloroform phase).

According to studies carried out by Horst (2012), it was expected that obtaining a moderate to potent acetylcholinesterase activity in the first substance, however, probably due to the little remaining mass for the test used by Sales (2019), the result obtained was below expectations, which would need to further isolate the substance to repeat the test. The second tested molecule showed a percentage of inhibition very close to the standard. Sales (2019) stated that this can be justified by the presence of carbonyl ester groups that act fundamentally at the active site of the enzyme, providing a reduction in their action in promoting the hydrolysis of acetylcholine (Table 2).

Sales (2019) recommended that for samples with inhibition percentage above 50%, the IC50 inhibition concentration values were calculated, in which the methanol extract, the aqueous extract, the chloroform phase and hydroalcohol phase partition in addition to the substance PCAN_8.2.2 (carapanaubina) showed satisfactory results.

Gastroprotective activity

The gastroprotective properties prevent damage to the gastric mucosa by the acidic content of the stomach, either by reducing the injury, or by increasing the protective effectiveness. One factor is the addition of the protective mucus layer, secreted bicarbonate, local blood microcirculation, mucosal vitality (and its cellular repair process) and the production of prostaglandins (Guyton *et al.*, 2004; Wallace, 2001).

In his studies with *A. nitidum*, Lima (2019) used four classic models: ethanol-induced ulcer, acidified ethanol, NSAIDs (non-steroidal anti-inflammatory) and pyloric ligation. The author realized that the different concentrations of the ethanolic fraction of *A. nitidum* did not alter pH and gastric secretion volume. However, in all ulcerogenic models (including NSAIDs) the ethanolic fraction of *A. nitidum* significantly reduced ulceration levels. Thus, Lima (2011) concluded that the ethanolic fractions of *A. nitidum* have a gastroprotective effect and, possibly, this effect is due to the action on the prostaglandin production pathway. However, other mechanisms of action cannot be ruled out precisely because of the high presence of indole alkaloids with pharmacological properties in the genus *Aspidosperma* (Table 2).

Antitumor activity

What underlies the in-depth study of *A. nitidum* in this respect is the presence of alkaloids from *Aspidosperma* species in the treatment of cancers (Kansal & Potier, 1986; Oliveira & Alencar-Filho, 1994).

Sales, (2019) evaluated the anticancer activity of substances isolated from *Aspidosperma* species, emphasizing the work with ellipticin and its synthetic derivatives, of which elipticinium (2-methyl-9 hydroxyielipticinium acetate) is marketed under the name of Celiptium® (Elipticinium), in France, for the treatment of breast cancer (Cragg & Newmann, 2005).

Among the samples tested by Sales (2019) the PCAN (partition of the methanolic extract from the bark of the chloroform phase) stood out, which was able to inhibit at least 90% of the proliferation, thus being considered active and, therefore, presented low IC50 value <30μg/mL. The substance PCAN_8.2.2 (partition of the methanolic extract from the bark of the chloroform phase), its light yellow color, suggesting the presence of an alkaloid, also showed a percentage of inhibition of about 74% and, consequently, for inhibitory percentages above 50%. It demonstrated the feasibility for checking *in vitro* cytoxicity in tumor cell lines.

According to the results of Sales (2019), the cytotoxic evaluation of extracts and fractions against tumor cell lines indicated that both PCAN and PCAN_8.2.2 proved to be active for the tumor

cell HCT116 (human colon carcinoma), HepG2 (human hepatocellular carcinoma) and MRC-5 (human lung fibroblast). These results can be justified by the presence of alkaloids in the sample, since, in species of the genus *Aspidosperma*, this class is responsible for its pharmacological activity (Table 2).

Antimalarial activity

Malaria affects millions of climatic and subtropical regions in the world. The disease is caused by infection with Plasmodium falciparum, generating an economic burden in several areas (Sachs & Malaney, 2002) because it causes death among unused individuals, especially children, non-immune travelers and pregnant women (WHO, 2011).

Data from the Ministério da Saúde (2019), pointed that between 2007 and 2016, malaria cases in Brazil showed a reduction. However, after almost 10 years, malaria had a significant increase in cases in 2017 (53% compared to 2016). In 2018, the country recorded 194. 513 reported cases of malaria, a reduction of 1% over the previous year.

In populations exposed to endemic transmission in sub-Saharan African countries and in certain regions of Latin America, medicinal plants offer an alternative in the treatment of malaria (Bourdy *et al*., 2004; Willcox & Bodeker, 2004; Adebayo & Krettli, 2011; Adebayo *et al*., 2012). Although there are synthetic combinations of drugs that are the basis for the treatment of malaria in Brazil, the plants are still used as medicines in the Amazon. In addition, elsewhere and represent a potential source of compounds in the development of new antimalarial drugs (Krettli, 2009).

According to the studies by Coutinho *et al*. (2013), extracts from the wood bark, leaves and branches of *A. nitidum*, popularly known as caraparnaúba, were prepared for tests against malaria parasites and cytotoxicity tests against cancer cells originating in the liver and normal monkey kidney cells. As a result, the bark extracts of *A. nitidum* were active against *Plasmodium falciparum* and showed low cytotoxicity *in vitro*. The data of the aforementioned authors confirm the antimalarial utility of the wood bark of *A. nitidum*, as an alternative that can help to control malaria. However, the molecules responsible for this antimalarial activity have not yet been identified by the authors (Table 2). The authors further state that considering their high selectivity index, fractions rich in alkaloids from the bark of the caraparnaúba can be useful in the development of new drugs antimalarials.

In addition to the work by Coutinho *et al*. (2013) affirming the *A. nitidum* properties against malaria, several species of *Aspidosperma* have anti-*P. falciparum* activity. (Oliveira *et al*., 2009; Andrade-Neto *et al*., 2007; Dolabela *et al*., 2012; Dolabela *et al*., 2015; Mitaine *et al*., 1996). According to Coutinho *et al*. (2013), *Aspidosperma pyrifolium* was the second best species tested in the *in vitro* activity against malaria parasites, preceded only by *A. nitidum*, a species highly used in antimalarial treatment in endemic areas in Brazil.

Table 2 – Pharmacological properties of *Aspidosperma nitidum*.

PHARMACOLOGICAL PROPERTIES			
Activity	**Related metabolite**	**Part of the plant used**	**References**
Antinociceptive activity	Unknown metabolite	Ethanolic extract from the heartwood	Pereira *et al*. (2006)
Anti-inflammatory activity	Lupeol, sistoterol and stigmasterol	Ethanolic extract from the heartwood	Geetha & Varalakshmi (2001); Gomez *et al*. (1999); Senatore *et al*. (1989)
Antimicrobian activity	Alkaloids, steroids, triterpenes and pentacyclics	Bark extract	Siminski *et al*. (2015); Simpson (2013)
Antioxidant activity	Alkaloids	Fractions obtained from the methanolic extract	Sales (2019)
Inhibitory activity of acetylcholinesterase	Carbonyl ester	PCAN_50.3 and PCAN_8.2.2	Sales (2019)
Gastroprotective activity	Alkaloids	Ethanolic fraction	Lima (2011)
Antitumor activity	Alkaloids	PCAN and PCAN_8.2.2	Sales (2019)
Antimalarial activity	Unknown metabolite	Wood bark extract	Coutinho *et al*. (2013)

Conclusion

Although scientific studies are demonstrating antinociceptive, anti-inflammatory, antimicrobial, antioxidant, inhibiting acetylcholinesterase activities, as well as antitumor and antimalarial activities of *Aspidosperma nitidum*, clinical studies in humans are necessary. It is also important that these studies are accurate to confirm all plant properties and to avoid possible human effects. In addition, it is essential to use protocols for the use of the plant in relation to variations and changes in formulations.

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