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PHYTOCHEMICAL PROSPECTION AND BIOLOGICAL ACTIVITIES OF THE AMAZONIAN SPECIES *CARYOCAR VILLOSUM*

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ABSTRACT

Due to the Amazonian diversity, several species are used by the population for medicinal purposes. Among these species, there is *Caryocar villosum*, known as “piquiá”, used as a natural anti-inflammatory to prevent bronchitis, fever, cough, colds and liver problems, in addition to alleviating muscle pain and rheumatism, among others. This literature review aimed to present studies related to phytochemical prospection and biological activities of this species. To prepare this study, the bibliographic research methodology was adopted, in which the Pubmed, SciELO and Google Scholar databases were consulted, from which 27 articles published in the period 1972-2021 were selected. According to the survey, it is known that this species has numerous chemical components responsible for the reported biological effects. Based on ethnopharmacological information about the “piquiá”, several studies have been carried out on its biological activity. However, as it is still a little explored species scientifically, the mechanisms by which *Caryocar villosum* presents its actions are still unclear and need to be elucidated, since the species is widely used by the Amazon population.
KEYWORDS: Phytochemicals; Pharmacologic actions; Biological products.

PROSPECÇÃO FITOQUÍMICA E ATIVIDADES BIOLÓGICAS DA ESPÉCIE AMAZÔNICA *CARYOCAR VILLOSUM*

RESUMO

Devido à diversidade amazônica, várias espécies são utilizadas pela população para fins medicinais. Dentre essas espécies, destaca-se a *Caryocar villosum*, conhecida como “piquiá”, utilizada como anti-inflamatório natural para prevenir bronquites, febre, tosse, constipações e problemas hepáticos, além de aliviar dores musculares e reumatismo, entre outros. Esta revisão de literatura teve como objetivo apresentar estudos relacionados à prospecção fitoquímica e às atividades biológicas dessa espécie. Para elaboração deste estudo foi adotada a metodologia de pesquisa bibliográfica, na qual foram consultadas as bases de dados Pubmed, SciELO e Google Scholar de onde foram selecionados 27 artigos publicados no período de

1972-2021. De acordo com o levantamento, sabe-se que essa espécie possui inúmeros componentes químicos responsáveis pelos efeitos biológicos relatados. Com base em informações etnofarmacológicas sobre o “piquiá”, diversos estudos têm sido realizados sobre sua atividade biológica. Porém, por ainda ser uma espécie pouco explorada cientificamente, os mecanismos pelos quais a *Caryocar villosum* apresenta suas ações ainda permanecem obscuros e precisam ser elucidados, uma vez que a espécie é amplamente utilizada pela população amazônica.
PALAVRAS-CHAVE: Fitoquímicos; Ações farmacológicas; Produtos biológicos.

INTRODUCTION

It is widely known that medicinal plants are used for the treatment, cure and prevention of diseases. About 80% of the world population depends on the folk medicine for its basic health needs and almost 85% of those who resort to this practice use medicinal plants, their vegetal extracts and actice compounds (WHO, 2011). The knowledge about medicinal plants many times represents the only therapeutic resource of communities and ethnic groups (VEIGA JUNIOR, 2008). The use of plants in illnesses treatment and cure is as ancient as the human species (MACIEL *et al*., 2002). Pereira *et al*. (2021) carried out an ethnobotanical survey on the knowledge and use of medicinal plants in the Amazon, demonstrating the importance of regional plants with pharmacological action for the population. Thus, the authors mentioned some plants native to the Amazon region with pharmacological action, among them *Carapa guianensis* (“andiroba”) with anti-inflammatory, antiseptic and healing properties; *Physalis angulata* (“camapu”) for the treatment of neurodegenerative diseases, lowering cholesterol and strengthening immunity; *Baccharis trimera* (“carqueja”), used to regulate blood pressure and blood sugar levels and help strengthen the immune system; *Copaifera langsdorffii* (“copaíba”) for the treatment of skin wounds, has anti-inflammatory, healing and antiseptic properties, among other species.

Among these amazonian species, we can highlight *Caryocar villosum*, popularly known as “piquiá”, a well used species by the local population, mainly in folk medicine, in which the peels and fruits are used for the treatment of tumors, filariasis and mycoses. In addition, “piquiá” oil is used against dermatophyte infections (MAGID *et al*., 2008; CHISTÉ *et al*., 2012). The oil is also widely used as a natural anti-inflammatory to prevent bronchitis, fever, cough, colds and hepatic problems, besides relieving muscular pain and rheumatism (XAVIER *et al*., 2011; MORAIS; GUTJAHR, 2012; ASCARI *et al*., 2013).

Despite of its widespread use in the popular medicine, *Caryocar villosum* specie has few scientific studies about its pharmacological activity. In a recent studies, Roxo *et al*. (2020) demonstrated the antioxidant and antiaging properties of *Caryocar villosum* in *Caenorhabditis elegans*. Yamaguchi and Souza (2021) demonstrated that the “piquiá” fruit can be used in its entirety as a cosmetic product. Therefore, this literature review aimed to present studies related to phytochemical prospection and biological activities of this species.

MATERIAL AND METHODS

Data survey

The aim of this study was to carry out a literature review on the chosen topic. The bibliographic search was conducted using as databases available for institutional access " Google Scholar", "SciELO", "Medline" and "PubMed", using the following keywords as descriptors: "Phytochemicals", "Pharmacologic actions", " Biological products" using the Boolean operators " AND " and " OR", from which 27 articles published in the period 1972-2021 were selected. The inclusion criteria were papers in Portuguese, Spanish and English. The exclusion criteria were studies that did not refer to at least one of the research themes, with articles from 1972 to 2021.

To select the manuscripts, the abstracts were read with the participation of all authors. Information was collected related to the main phytochemical compounds that were isolated and characterized in the identified species, in addition to the biological and pharmacological studies carried out for the species under study.

RESULTS AND DISCUSSION

To carry out the bibliographical research, twenty-seven articles published in the period 1972-2021 were selected.

CARYOCAR VILLOSUM

Caryocaraceae family comprises 26 species spread in tropical and neotropical regions of the american continent and is divided into two genera: *Caryocar* and *Anthodiscus*. In this family, with existing species from Costa Rica to the brazilian southeast, the trees are medium and large size, with trifoliolate, stipulated, opposite or alternating leaves, and actinomorphic flowers (MAGID *et al*., 2006a; MARTINS; GRIBEL, 2007; XAVIER *et al*., 2011).

Caryocar genus presents 16 species, of which 12 are present in Brazil (**TABLE 1**). Its distribution covers a expansive territory from Costa Rica to Paraguay. In Brazil, it is found in greater abundance in Amazon (XAVIER *et al*., 2011; LEAL *et al*., 2016). The wood of *Caryocar* genus trees is used for the construction of houses and boats, due to the quality of its raw material. The pulp of its fruits is also used especially by the local people for cooking along with rice. The oil produced by the fruit pulp can be used to prepare regional dishes, substitute for butter, and to prepare soaps among other cosmetic applications (ASCARI *et al*., 2013). For the oil extraction, hexane is used, and a yield of approximately 46% for the pulp and 42% for the almond can be obtained (MAGID *et al*., 2008; XAVIER *et al*., 2011; MORAIS; GUTJAHR, 2012; CHISTÉ *et al*., 2013).

TABLE 1 – Main *Caryocar* genus species studied and reported on the scientific literature and where they occur in Brazil.

Location	Species	References
Amazon Region	*Caryocar glabrum* subsp. *glabrum*	PRANCE and SILVA, 2006
	Caryocar glabrum subsp. *parvifolium*	PRANCE and SILVA, 2006
	Caryocar microcarpum	KAWANISHI and RAFFAUF, 1986
	Caryocar pallidum	NISGOSKI *et al*., 1998
	Caryocar villosum	MORAIS and GUTJAHR, 2012
Cerrado	*Caryocar brasiliense*	MAGID *et al*., 2008; CHISTÉ *et al*., 2012
	Caryocar coriaceum	BARRADAS, 1972
	Caryocar cuneatum	BARRADAS, 1972

SOURCE: The authors

Caryocar villosum (“piquiá”), belonging to the order Theales, is one of the biggest oil trees and can reach from 35 to 50 meters in height. Besides the popular brazilian name, it is also known as “pikia”, “pekea” or “pékéya” in French Guiana (MAGID *et al*., 2006b, XAVIER *et al*., 2011; MORAIS; GUTJAHR, 2012).

The “piquiá” can occur throughout the Amazon Basin, being more prevalent on the mainland of the estuary region, and on part of the northeastern region. It is not a species at risk of extinction, despite of the continuous exploitation that allows its scarcity in some regions (Magid *et al*., 2006b; MORAIS; GUTJAHR, 2011; ALMEIDA *et al*., 2012). One of the aspects that contribute to its extinction is the burning in the forest, which reduces the presence of the bat *Lonchophylla thomasi*, responsible for “piquiá” pollination. Other bats species such as *Phyllostomus discolor* and bats belonging to the subfamily Glossophaginae, in addition to other animals are also related to the pollination process (MARTINS; GRIBEL, 2007).

The interest in “piquiá” is notorious, and reflects in its economic importance for riverside families and populars in several areas, once many components of the tree have some use, which varies from cooking to construction. *Caryocar villosum* has great nutritional value and consists of substances that result in diverse biological activities, such as saponins, phenolic compounds, flavonoids, carotenoids and vitamins C and E (CHISTÉ *et al*., 2013; LEAL *et al*., 2016).

The flowering of “piquiá” tree occurs between the months of July and November. The species does not usually fruit every year, but when it does, its fruits ripen between February and May, with an average annual production of 350 fruits. The “piquiá” fruit weighs an average of 280 grams, measures from 7 to 9 cm in diameter and has an irregular oblong-globose round shape. Its interior presents a pulp that constitutes 23% of the fruit total, while the almond is equivalent to 6% of total (MARX *et al*., 1997; MAGID *et al*., 2006a; MORAIS; GUTJAHR, 2012).

The “piquiá” seeds are oily, white and edible, fresh or processed; and can be used as an aphrodisiac. They have a fleshy and aromatic mass, rich in nutrients such as carotene, phosphorus, copper, iron and riboflavin. It is difficult to remove this mass from the endocarp, due to the presence of thin spines (MARX *et al*., 1997; ASCARI *et al*., 2013).

In the cosmetic industry, “piquiá” is used in the production of lotions, skin creams, soaps, shampoos, hair conditioners, bath salts, post-depilatory creams and makeup. Due to having a melting point similar to the human skin temperature, the oil from the almond is very useful for dermatological formulations (MORAIS; GUTJAHR, 2012).

In the feeding, the fruit is consumed cooked in water and salt and can be used in the preparation of juices and liquors. Its peels are used in the production of a paint used as a dye for threads and nets. Its trunk is a raw material in shipbuilding and civil construction, for being a material very resistant to attacks by insects that feed on wood. Its peels, along with the fruit, are used by the populars as a poison for fish; a toxicity related to the presence of saponins (MAGID *et al*., 2006a; MAGID *et al*., 2006b; XAVIER *et al*., 2011; MORAIS; GUTJAHR, 2012).

Concerning the popular medicinal use of the species, the peels and fruit are used by the indigenous tribes of Brazil, Venezuela, French Guiana and Colombia to treat external tumors, filariasis and mycoses. Along with “pequi” oil (*Caryocar brasiliense*), “piquiá” oil is used against dermatophyte infections in Northeast Brazil (MAGID *et al*., 2006b; MAGID *et al*., 2008; CHISTÉ *et al*., 2012).

The oil is also widely used as a natural anti-inflammatory to prevent bronchitis, fever, cough, colds and liver problems, in addition to relieving muscle pain and rheumatism. Because it has a large amount of vitamin A, the fruit is consumed to combat and prevent vision disorders. The peels are used to treat fungal infections known as chilblains (XAVIER et al., 2011; MORAIS; GUTJAHR, 2012; ASCARI *et al*., 2013).

PHYTOCHEMICAL PROSPECTION AND ISOLATED SUBSTANCES FROM *C. VILLOSUM*

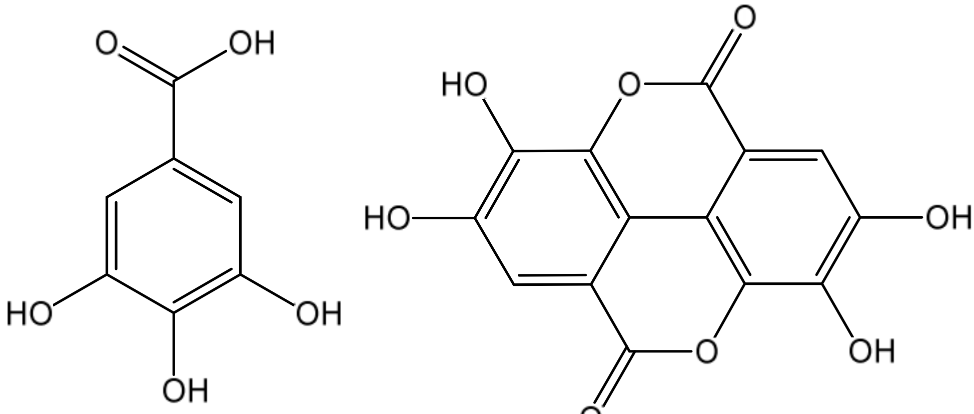
Chisté *et al*. (2013) quantified the amount of total tannins present in extracts obtained from the “piquiá” pulp by different solvents and, as a result, the hydroethanolic extract was shown to have the greatest presence of such compounds.

Among the substances present in the pulp of the “piquiá” fruit, there are the phenolic and carotenoid compounds. With regard to phenolic compounds, a study showed that *C. villosum* was the fruit with the highest amount of these substances among 18 different analyzed pulps (BARRETO *et al*., 2009). According to the study performed by Chisté *et a*l. (2012), the hydroethanolic extract obtained from the fruit pulp revealed the highest content of phenolic compounds; while the ethanolic extract presented the highest content of carotenoids.

Yamaguchi *et al*. (2017) verified that the alcoholic extract obtained from the “piquiá” pulp presented the highest amount of phenolic compounds, in comparision to the ones obtained from shells and seeds. After HPLC analysis, gallic and ellagic acids were defined as the major phenolic components of the extract. The content of total flavonoids was also higher in “piquiá” pulp extract. Still in the same study, the extracts obtained from the seeds resulted in the lowest values of phenolic compounds and flavonoids.

According to Almeida *et al*. (2012), several caratenoids were identified by HPLC-DAD-MS, which are: antheraxanthin, zeaxanthin, neoxanthin, violoxanthin, β-carotene and lutein. In addition, phenolic compounds were identified: gallic acid, ramnoside ellagic acid, ellagic acid, monogaloyl-glucose and hexahydroxydiphenyl-glucose. Chisté *et al*. (2012) also identified 17 phenolic compounds and 12 caratenoids through HPLC analysis of *C. villosum* lyophilized extracts. Therefore, according to Chisté *et al*. (2012), the major compounds found were gallic acid (**1**), ranoside ellagic acid, deoxyhexoside ellagic acid and ellagic acid (**2**) (**FIGURE 1**).

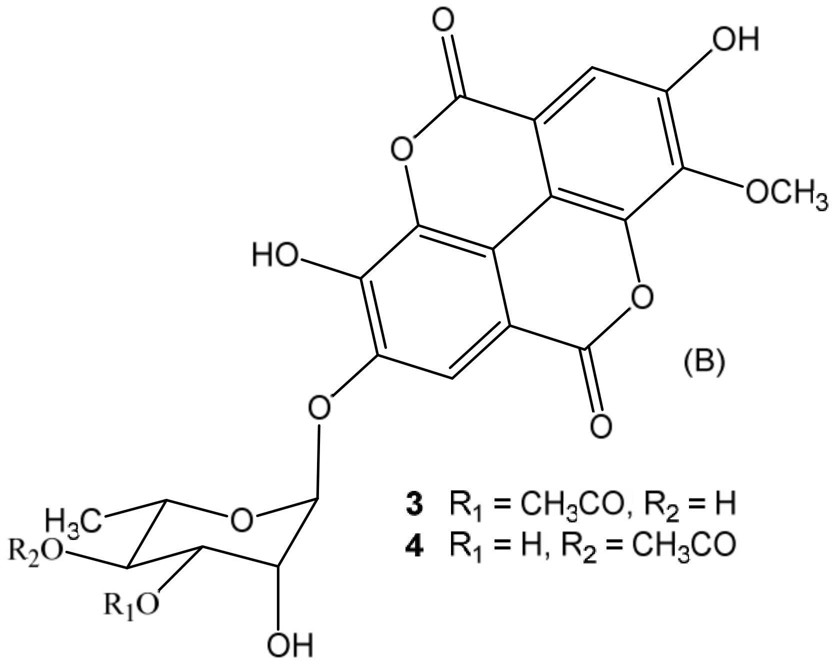
FIGURE 1: Main phenolic compounds isolated from *Caryocar villosum*: gallic acid (1) and ellagic acid (2).



(**1**) (**2**)

Magid *et al*. (2008) isolated and identified through nuclear magnetic resonance (NMR) spectroscopy fifteen phenolic compounds from extracts obtained from the barks of *Caryocar villosum* branches. The compounds 3-O-methyl-4′-(3″-O-acetyl)-a-L-ramnopyranosyl ellagic acid (3) and 3-O-methyl-4′-(4″-O-acetyl)-O-a-L-ramnopyranosil ellagic acid (4) were reported for the first time in the literature (**FIGURE 2**), the other isolated compounds were: 3-O-methyl-4′-(2″-O-acetyl)-O-a-L-ramnopyranosil ellagic acid; 3-O-methyl-4′-O-a-L-ramnopyrananosyl ellagic acid; ellagic acid; 5-O-galloyl-D-hamamelofuranose; 2’-O-galloyl-D-hamamelofuranose; 2’,5-di-O-galloyl-D-hamamelofuranose; 2’,3,5-tri-O-galloyl-D-hamamelofuranose; 1,2’,3,5-tetra-O-galloyl-b-D-hamamelofuranose; 1,2,3,4,6-penta-O-galloyl-b-D-glucose; chorilagine; tercatain; chebulagic acid and putranjivaine A.

FIGURE 2: Phenolic glycosides isolated from the barks of *Caryocar villosum* branches.



Caryocarosides, which are types of saponins, are also among the substances found in the phytochemical study of *Caryocar villosum*. In another work done by Magid *et al*. (2006a), the authors isolated and determined the structure of 24 caryocarosides obtained from the fruit peels and pulp, 14 of which were new compounds (**5**-**18**) (**TABLE 2**). Subsequently, Magid *et al*. (2006b) studied the barks of the species branches and managed to isolate 7 caryocarosides, 5 of them were new compounds (**19-23**) (**FIGURE 3**).

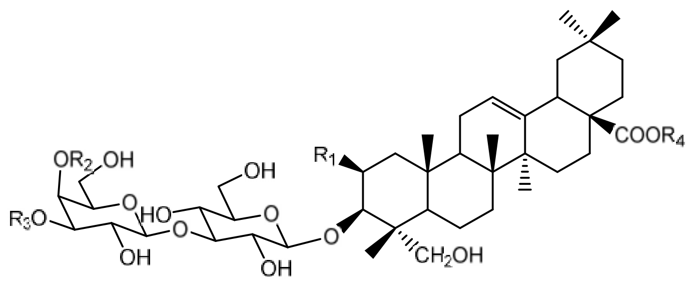
TABLE 2 – Caryocarosides obtained from the fruit peels (5-12) and pulp (13-18) (MAGID *et al*., 2006a).

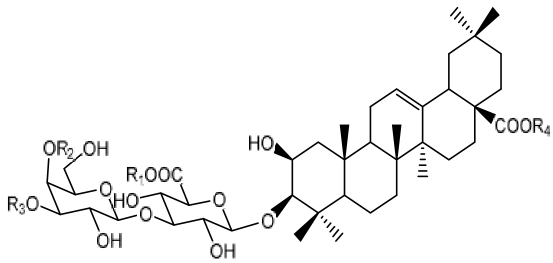
COMPOUNDS	R_1	R_2	R_3	R_4
5	**H**	**H**	**Xyl-**	**Glc’-**
6	**OH**	**H**	**Xyl-**	**Glc’-**
7	**H**	**H**	**Gal’-**	**Glc’-**
8	**OH**	**H**	**Gal’-**	**Glc’-**
9	**OH**	**H**	**Xyl-(1□3)- Gal’-**	**Glc’-**
10	**H**	**Xyl-(1□3)-Gal”-**	**H**	**H**

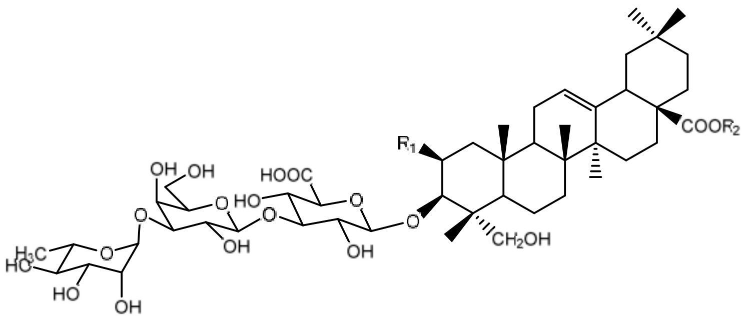
		(1□3)-Gal'-		
11	**OH**	**Xyl-(1□3)-Gal''-** **(1□3)-Gal'-**	**H**	**H**
12	**OH**	**Xyl-(1□3)-Gal''-** **(1□3)-Gal'-**	**H**	**H**
13	**-CH_3**	**H**	**H**	**Glc-**
14	**H**	**H**	**Xyl-**	**Glc-**
15	**-CH_3**	**H**	**Xyl-**	**Glc-**
16	**H**	**Xyl-(1□3)- Gal'-**	**H**	**H**
17	**H**	**Xyl-(1□3)-Gal''-** **(1□3)-Gal'-**	**H**	**H**
18	**H**	**Xyl-(1□3)-Gal''-** **(1□3)-Gal'-**	**H**	**Glc-**

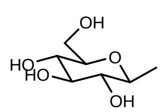
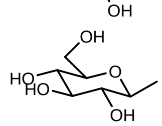
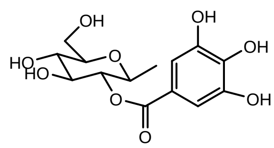
SOURCE: The authors

FIGURE 3: Caryocarosides isolated from branches bark of *Caryocar villosum* (**19**-**23**).



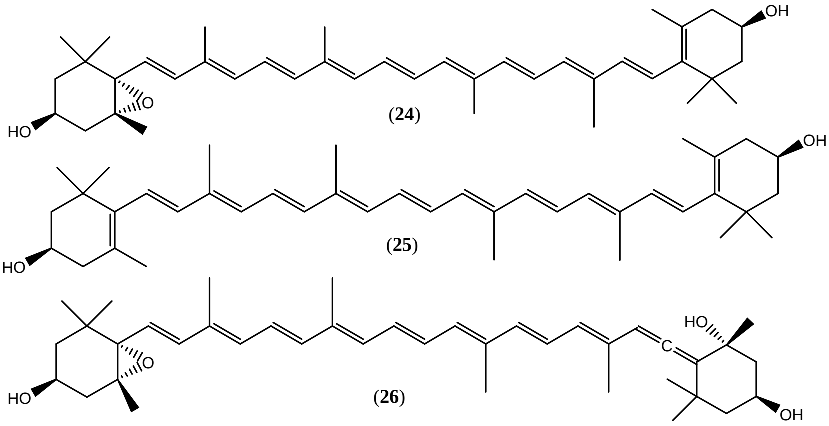




	R1	**R2**
19	**H**	**H**
20	**OH**	**H**
21	**H**	
22	**OH**	
23	**H**	

Among the carotenoids present in the pulp detected by Almeida *et al*. (2012), the main ones were anteraxanthin (**24**) and zeaxanthin (**25**); but neoxanthin (**26**), violaxanthin, β-carotene and lutein were also present (**FIGURE 4**). Similar results for carotenoids were presented by Chisté and Mercadante (2012) and by Chisté *et al*. (2012), in which the main substances were trans-antheraxanthin, trans-zeaxanthin, trans-neoxanthin and lutein.

FIGURE 4: Main carotenoids found in *Caryocar villosum*: anteraxanthin (**24**), zeaxanthin (**25**) e neoxanthin (**26**).



The only tocopherol detected in the pulp of the species was *α*-tocopherol. In the fruit, substances such as oleic acid, steroids and volatile substances such as *β*-bisabolene, 2-heptadone, (E) -nerolidol and furfural were all identified (MARX *et al*., 1997; ALMEIDA *et al*., 2012; CHISTÉ *et al*., 2013; LEAL *et al*., 2016).

Polonini *et al*. (2012) used gas chromatography to detect and quantify the fatty acids present in "piquiá" oil. Linoleic acid was the most abundant, followed by oleic and palmitic acid.

Marx *et al*. (1997) conducted a wide study about the chemical composition of the "piquiá" pulp. Palmitic and oleic acids were the main component fatty acids, responsible for more than 50% of the total found. Among the sterols, the most abundant found were 7,25-stigmastadienol, β-sitosterol and stigmasterol. Regarding the existing minerals, calcium, magnesium and phosphorus stood out, presenting, respectively, the values of 83, 52 and 41 mg / 100g. Still in the same study, γ-aminobutyric acid was the non-protein amino acid with the highest concentration, and taurine and o-phosphoethanolamine were the most abundant biogenic amines.

The oil extracted from the fruit has a large amount of fatty acids and vitamins A, C and B complex, as well as phytosterols, sitosterols, stigmasterol, lanosterol, steroids and triterpenoids (XAVIER *et al*., 2011 ; MORAIS; GUTJAHR, 2012). After the oil analysis through gas chromatography coupled with mass spectrometry, the main fatty acid esters were identified: methyl hexadecanoate, methyl octadecanoate and methyl (E) -octadecenoate (XAVIER *et al*., 2011).

TABLE 3: Main components present in the species *Caryocar villosum*.

COMPONENTS	PAPERS
Gallic and ellagic acids	YAMAGUCHI *et al*. (2017)
Antheraxanthin, zeaxanthin, neoxanthin, violoxanthin, β-carotene, lutein, gallic acid, ramnoside ellagic acid, ellagic acid, monogaloyl-glucose and hexahydroxydiphenyl-glucose	ALMEIDA *et al*. (2012)
Gallic acid, ranoside ellagic acid, deoxyhexoside ellagic acid and ellagic acid	CHISTÉ *et al*. (2012)
Trans-antheraxanthin, trans-zeaxanthin, trans-neoxanthin and lutein	CHISTÉ and MERCADANTE (2012); CHISTÉ *et al*. (2012)
Linoleic acid	POLONINI *et al*. (2012)
Methyl hexadecanoate, methyl octadecanoate and methyl (E) –octadecenoate	XAVIER *et al*. (2011)
3-O-methyl-4′-(3″-O-acetyl)-a-L-ramnopyranosyl ellagic acid, 3-O-methyl-4′-(4″-O-acetyl)-O-a-L-ramnopyranosil ellagic acid, 3-O-methyl-4′-(2″-O-acetyl)-O-a-L-ramnopyranosil ellagic acid; 3-O-methyl-4′-O-a-L-ramnopyrananosyl ellagic acid; ellagic acid; 5-O-galloyl-D-hamamelofuranose; 2’-O-galloyl-D-hamamelofuranose; 2’,5-di-O-galloyl-D-hamamelofuranose; 2’,3,5-tri-O-galloyl-D-hamamelofuranose; 1,2’,3,5-tetra-O-galloyl-b-D-hamamelofuranose; 1,2,3,4,6-penta-O-galloyl-b-D-glucose; chorilagine; tercatain; chebulagic acid and putranjivaine A	MAGID *et al*. (2008)
Caryocarosides	MAGID *et al*. (2006a) MAGID *et al*. (2006b)
Palmitic and oleic acids	MARX *et al*. (1997)

SOURCE: The authors

BIOLOGICAL ACTIVITIES OF *CARYOCAR VILLOSUM*

The “piquiá” fruit pulp has substances that capture free radicals, an effect related to the high content of phenolic compounds, including flavonoids. Among 18 fruit pulps analyzed for antioxidant activity, piquiá stood out with the highest amount of antioxidant capacity equivalent to the Trolox® for the capture of free radicals (BARRETO *et al*., 2009; ALMEIDA *et al*., 2012).

The ethanolic and hydroethanolic extracts obtained from “piquiá” pulp and shells managed to scavenge free radicals in the DPPH and ABTS assays, showing an efficient antioxidant activity similar to quercetin and Trolox®, the standards used during the tests. These results were consistent with a cell-based antioxidant assay, in which the hydroethanolic extract obtained from “piquiá” seeds and both hydroethanolic and ethanolic extracts obtained from pulp and shells presented significant values of oxidation inhibition rate, decreasing the production of reactive oxygen species (YAMAGUCHI *et al*. 2017).

Chisté *et al*. (2012) conducted a research in which different extracts obtainend from piquiá pulp were tested for the ability to capture reactive nitrogen species and reactive oxygen species. The aqueous and hydroethanolic extracts were those that obtained the lowest IC_{50} values against hypochlorous acid (HOCl), nitric oxide (.NO) and peroxynitrite (ONOO-). The hydroethanolic extract showed 37% of inhibition for the superoxide radical (O2.-), while for the aqueous extract the result was 15%. The ethanolic, ethanol / ethyl acetate and ethyl acetate extracts did not show any antioxidant effect, even in the highest concentrations tested.

Still with regard to antioxidant activity, Chisté *et al*. (2013) performed the peroxyl radical (ROO.) capture test, noting that the hydroethanolic extract, obtained from the “piquiá” pulp, was the most efficient in capturing these radicals, compared to other extracts. For the singlet oxygen ($^1O_2$) extinction test, it was expected that the ethanolic extract would obtain better performance due to its highest content of carotenoids, which are recognized as the best extinguishers of these radicals; however, aqueous and hydroethanolic extracts showed better results, as hydroethanolic extract being the most active.

The “piquiá” demonstrated larvicidal activity, which was verified in a toxicity test with *Artemia salina*, a species of crustacean. In the referred research, the executors evaluated both the methanolic extracts obtained from the peel of the fruit and the pulp and the crude fraction of saponins. As a result, the three extracts obtained an efficient larvicidal activity, being the methanolic extract of the pulp more active than the extract of the fruit peels. However, the fraction of saponins obtained the best performance. These results imply the potential use of “piquiá” as a pesticide and antitumor agent, and also support the use of parts of the plant as a poison for fish (MAGID *et al*., 2006a).

Magid *et al*. (2006b) verified the cytotoxic activity of two caryocarosides saponins isolated from “piquiá” peels extract in a test against human keratinocytes. These saponins were identified as 3-O-β-D-glucuronopyranosyl-hederagenin (caryocaridoside II-5) and 3- O-β-D-galactopyranosil- (1 → 3) -β-D-glucuronopyranosyl hederagenin (caryocaroside II-7) (MAGID *et al*., 2006a) and showed moderate activity. The “piquiá” fruit peels extract showed tyrosinase inhibition activity in an *in vitro* assay (MAGID *et al*., 2008).

C. villosum extracts were evaluated for their cytotoxicity through the use of tumoral and non-tumoral human cells in specific test, besides to a hemolytic assay. As results, the extracts obtained from “piquiá” pulp, seeds and shells demonstrated low cytotoxicity and exhibitted no capacity in causing damage or hemolysis to cell membranes, what suggests a safety in consuming this species (YAMAGUCHI *et al*. 2017).

The evaluation of the photoprotective activity carried out by Polonini *et al*. (2012) demonstrated that “piquiá” oil obtained a low sun protection factor. However, Yamaguchi *et al*. (2016) observed photoprotective activity for piquiá peels extract in a study that aimed to measure the absorption in the wavelengths referring to the ultraviolet regions A, B and C, components of UV radiation, responsible for problems resulting from much exposure to the sun. The ethanolic and hydroethanolic extracts of the “piquiá” showed the highest values of wavelength, 298 nm and 308 nm, respectively, which resulted in an excellent photoprotective action similar to the compounds used in sunscreens such as *p*-aminobenzoic acid, even when the extracts have been diluted. This property may be related to the presence of phenolic compounds, which are responsible for the protection of plants against ultraviolet radiation.

The “piquiá” fruit pulp showed antigenotoxic activity in a study by Almeida *et al*. (2012). In that study, all doses evaluated presented a protective effect on the micronucleus test, when bone marrow cells received prior treatment with the piquiá pulp before being treated with doxorubicin. The piquiá pulp also decreased the DNA damage induced by the genotoxic effect of doxorubicin, mainly in the heart and liver cells. The mechanism suggested for this activity may be related to the presence of antioxidant substances in the “piquiá” pulp, such as carotenoids and phenolic compounds, which were detected in the fruit (ALMEIDA *et al*., 2012).

Yamguchi *et al*. (2017) performed an anti-inflammatory *in vitro* assay, in which cells were previously exposed to lipopolysaccharide (LPS) before being treated with “piquiá” extracts in different concentrations in order to verify the nitric oxide production. The results showed that all the extracts obtaied from “piquiá” pulp, seeds and shells significantly inhibitted the nitric oxide production at low concentrations, demonstrating an anti-inflammatory activity.

The fixed oil extracted from “piquiá” was evaluated for topical anti-inflammatory activity in animal models. In the granuloma test, all doses administered significantly inhibited the formation of granulomatous tissue in a dose-dependent manner, when compared to the positive control group dexamethasone. For the paw edema test, the oil reversed the edema formation, having its greatest action after 4 hours of the administration of carrageenan. While in the vascular permeability test, the applied dose of the oil reversed the response to histamine by 40%, being significant if compared to the positive control. According to the authors, the observed effects are related to the fatty acid esters found in fixed piquiá oil, which have the ability to modulate the acute and chronic inflammatory response (XAVIER *et al*., 2011).

TABLE 4: Biological activities described in *Caryocar villosum* species.

BIOLOGICAL ACTIVITY	PAPERS
Antioxidant	BARRETO *et al*. (2009); ALMEIDA *et al*. (2012); CHISTÉ *et al*. (2012); CHISTÉ *et al*. (2013); YAMAGUCHI *et al*. (2017)

Larvicidal	MAGID *et al*. (2006a)
Cytotoxic	MAGID *et al*. (2006b); YAMAGUCHI *et al*. (2017)
Photoprotective	POLININI *et al*. (2012); YAMAGUCHI *et al*. (2016)
Antigenotoxic	ALMEIDA *et al*. (2012)
Anti-inflammatory	XAVIER *et al*. (2011); YAMAGUCHI *et al*. (2017)

SOURCE: The authors

FINAL CONSIDERATIONS

Considerating that *Caryocar villosum* is extremely important for the amazonian population, there was a need to accomplish this literature review about the studies related to phytochemical prospection and biological activities of this species, which can be consulted in the future as a parameter for the comprehension of the pharmacological activity as well as the mechanism of action of *Caryocar villosum*.

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