Review

**Libidibia ferrea** (Mart. ex Tul.) L. P. Queiroz: A review of the biological activities and phytochemical composition

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**Libidibia ferrea** (Mart. ex Tul.) L. P. Queiroz is a medicinal plant widely known in Brazil as “jucá” or “paufferro” that belongs to the Fabaceae family. The species is native to Brazil and is mainly found in the North and Northeastern regions. It has been studied for its biological activities and chemical composition. Scientific literature has reported that this species contains different extracts and/or isolated compounds which have antimicrobial, anti-inflammatory, analgesic, antioxidant and hypoglycemic properties, as well as others that are in popular use. The phytochemical literature reports on the presence of fatty acids, terpenoids, phenolic compounds and polysaccharides. However, further studies are necessary to find new bioactive molecules with biological relevance based on traditional medicine. The purpose of this review is to provide a broad and updated overview about the relevance of **Libidibia ferrea** species in regard to general aspects, traditional medicines, biological activities and chemical composition data.

**Key words:** **Libidibia ferrea**, medicinal properties, phytochemistry.

**INTRODUCTION**

The Genus Libidibia (Fabaceae family) includes 500 species of trees distributed worldwide. It is characterized by its content of polyphenols, terpenes and steroids, as well as polysaccharide substances, which are principally responsible for its biological properties (Zanin et al., 2012). The main species of this genus are native to Brazil, and are distributed in different regions all over the country (Flora do Brasil, 2014).

Several uses in traditional medicine are described for different parts (barks, fruits, leaves, seeds and stems). This species is one of 71 species of medicinal plants included in the national list of medicinal plants of interest to the Brazilian Public Health System (Relação Nacional de Plantas Medicinais de Interesse ao Sistema Único de Saúde — RENISUS), due to its importance in public health and potential medicinal applications in Brazil (Brasil, 2009). In regard to the species **Libidibia ferrea** (Mart. ex Tul.) L. P. Queiroz var. ferrea, the present work consists of a survey of the literature from several databases included original articles, books, sites and theses (Periodicos CAPES, PubMed, Science Direct, SciELO, SciFinder, Scopus and Web of Science).
Some key words used were Caesalpinia, Caesalpinia ferrea, Libidibia ferrea, Juca and Pau ferro, chosen because of the scientific name, synonyms, and main popular names of the species in accordance with the sites “Embrapa” (http://www.cnpf.embrapa.br) “Flora do Brasil” (http://floradobrasil.jbrj.gov.br), Tropicos (http://www.tropicos.org) and the plant list (http://www.theplantlist.org). The software MDL/Isis Draw Freeware Version 2.5 was used to draw the chemical structures.

GENERAL ASPECTS

Libidibia ferrea (Mart. ex Tul.) L. P. Queiroz var. ferrea belongs to the Fabaceae family, it is also called Caesalpinia ferrea and is popularly known as “jucá” or “pau ferro” (Lorenci, 2002; Matos, 2007). With regard to its etymology, “Caesalpinia” was named after Andrea Caesalpinio (an Italian botanist); and “ferrea”, which means iron, is due to the high density of this wood (Embrapa, 2014). This species is considered a native tree to Brazil and is endemic to the North and Northeastern regions (Alagoas, Bahia, Ceará, Paraíba and Pernambuco), mainly in the geographic area dominated by the Caatinga (Brazilian savanna). Moreover, the species is cultivated in other countries for its use in the forestation of streets and parks and goes by the name of Brazilian ironwood (Matos, 2007). Therefore, the species plays an important role in environmental preservation and it can also have significant economic impact on the country (Embrapa, 2014). The L. ferrea tree is between 10 to 15 m in height and has a thin trunk with a diameter of 40 to 60 cm. The leaves are a bipinnate composite type measuring 15 to 19 cm in length, with opposite pinnae 5 to 11 and the leaflets have 8 to 24 pinnae. The fruits are indehiscent and have a hard pod and are dark brown in color (Figure 1) (Lorenci, 2002).

BIOLOGICAL ACTIVITIES

Since 1960, the species has been studied for biological activities and most of these studies were based on popular information about the indications, usage mode, and parts of the plant used in the preparation.

Traditional medicine

Previous ethnopharmacological studies show that L. ferrea is used in many parts of Brazil for the treatment of a number of diseases and its resources are part of a traditional knowledge about this species (Albuquerque et al., 2007). In this context, Barros (1982) related that the seeds and bark of L. ferrea have been used in traditional medicine in the form of tea and potions to lose weight and to clean injuries. The fruits are mainly used against anemia, lung disease (cough followed by bleeding) and diabetes. Some of its therapeutic activities have been described in scientific literature. Balbach (1972) described in his book that the infusion of stem bark of L. ferrea had been used for treating enterocolitis and diarrhea. Braga (1976), in the third edition of the book “Plantas do Nordeste, Especialmente do Ceará”; reports several therapeutic properties, including the treatment and alleviation of asthma, bruises, chronic cough and wounds, and the roots are antipyretic and anti-diabetic. According to Lewis (1988), the roots of L. ferrea are used as an antipyretic and antiarrheal and the decoction of the wood showed a healing and antisecretory effect. Thomas et al. (1998), gave the first description that the aqueous extract had anti-inflammatory and analgesic properties.

Some experiments in animals have shown the analgesic, anti-inflammatory and anti-ulcer activity of the fruit and bark extract of this species (Bacchi and Sertié, 1994; Bacchi et al., 1995; Carvalho et al., 1996). Also during the 90s, activities were described for treating respiratory tract diseases, dysentery and diabetes (Bragança, 1996). According to Maia (2004) the fruits are anti-diarrheal and have healing effects and it was also noted that the roots are antipyretic.

Allelopathic activity

The study of Oliveira et al. (2012) was to evaluate the allelopathic potential of leaves, stem bark and mature pods of L. ferrea on seed germination and seedling development of lettuce (Lactuca sativa). The extracts of leaves and pods obtained, reduced the germination percentage of L. sativa and the authors concluded that the different extracts showed allelopathic activity.

Anti-inflammatory, analgesic and antinoceptive effects

Carvalho et al. (1996), conducted a preliminary study about the anti-inflammatory and analgesic activities of crude aqueous extract from the fruits of L. ferrea obtained by maceration. The crude extract (CE) showed inhibition in the formation of edema. In the intraperitoneal assay injection of acetic acid when treated with 10 mg/kg and 20mg/kg of the CE, the number of writhes was reduced. In addition, the carrageena test induced rat hind paw edema showed inhibition when given a 300 mg/kg oral dose of the CE.

More recently, hydroalcoholic extract (95%) of pods (peels and seeds) obtained by agitation was assessed for anti-inflammatory and analgesic activities. The extract at
a dose of 50 mg/kg (body weight) showed inhibition of ear edema and of vascular permeability. The extract was also able to reduce cell migration to the peritoneal cavity. In addition, the induction test for acetic acid at doses of 12.5, 25 and 50 mg/kg reduced the number of contortions. Furthermore, the study reports that in the formalin test, the effects presented from the extract appeared only in the second phase (Lima et al., 2012). The pods were used for total polysaccharide (TP) assay and this gave three polysaccharide rich fractions (FI, FII, FIII). The TP (1 mg/kg), inhibited the paw edema induced by carrageenan and FIII inhibited the inflammatory parameters in the paw edema induced by the following stimuli: bradykinin, carrageenan, compound 48/80, dextran, histamine, nitric oxide, serotonin and prostaglandin E2. Furthermore, FIII inhibited the carrageenan-induced edema in animals. Themodel of peritonitis inhibited cell migration and protein leakage by carrageenan and N-formyl-methionyl-leucyl-phenylalanine (fMLP).

Finally, biochemical and hematological parameters were also observed during treatment with FIII (1 mg/kg) and according to the results, body weight loss, damage to heart, spleen or liver were not observed. However, hepatic markers were not affected and the level of urea showed high values (Pereira et al., 2012). The fruits were subjected to supercritical fluid extraction (SFE) using CO2 and used in the development of wound dressings. Subsequently, tests of cytocompatibility and anti-inflammatory capacity were evaluated (Dias et al., 2013). The aqueous extract and lipid portion from L. ferrea seed were obtained and both presented anti-inflammatory and central analgesic properties. The authors indicated that lipids are responsible for the dose related antinociceptive action in models of noiception. In addition, they inhibited opioid, cholinergic receptors and COX-2 (Sawada et al., 2014).

The crude extracts of barks (acetone-water or aqueous turbo-extracts) were evaluated in relation to analgesic and anti-inflammatory activities. In the anti-inflammatory activity, the leukocyte migration model was used, and the carrageenan peritonitis showed a reduced amount of leukocyte migration. However, analgesic activity by the hot plate test and acetic-acid induction showed no positive results (Araújo et al., 2014).

Antimicrobial and antifungal activity

The antimicrobial activity of the methanol extract (80%, maceration) of the fruit was assessed by Minimal Inhibitory Concentration (MIC). The MIC values obtained were 25.0 to 100.00 µg/mL using American Type Culture Collection (ATCC) strains of Candida albicans, Streptococcus mutans, Streptococcus salivarius, Streptococcus oralis and Lactobacillus casei. Furthermore, the authors indicated the activity of the extracts in biofilm formation, however, when compared with the control, low activity was reported (Sampaio et al., 2009). For crude aqueous extract obtained from the seeds after treatment with NaCl and phosphate buffer, antibacterial activities were observed across Staphylococcus aureus, Bacillus subtilis, Enterobacter aerogenes, Salmonella choleraeinsis, Klebsiella pneumoniae and Pseudomonas aeruginosa strains; and antifungal activity was observed with Aspergillus niger, Colletotrichum lindemuthianum, Colletotrichum truncatum, Fusarium oxysporum, Fusarium solani, Fusarium palidoroseum, Mucor sp., Neurospora sp., Penicillium hergueli, Phomopsis sp., Phytophthora gandrum, Rhizoctonia solani and Thricoderma viridae. In this same study, the extract showed cellulase and amylase activities, and important larvicide porpetie against Aedes aegypti (Cavalheiro et al., 2009).

In the screening performed by Ferreira et al. (2013) the crude extracts from bark showed antifungal property, inhibiting the growth of ATCC yeast of Candida spp. The MIC obtained for C. albicans and Candida krusei was more effective in CEIs obtained with ethanol: water or acetone:water; and was similar to Cronobacter dublinensis and Candida glabrata. The authors suggest the effectiveness of this plant against Candida non-albicans species. The Minimal Fungicidal Concentration (MFC) revealed that the ethanolic extract obtained reached an important value for the C. dublinensis.

Studies showed that the combined action of erythromycin with hydroalcoholic extract (70%) from fruits presented synergistic potential against S. aureus, and the structural damage of staphylococcal DNA was reported (Silva et al., 2013). Ethanol extract of fruits was analyzed for the existence of microorganisms and this was verified by the absence of S. aureus, P. aeruginosa and Eschenichia coli. The antimicrobial assay for S. mutans and S. oralis was evaluated at 20 days and 140 days after preparation of extract, and also revealed effective results (Marreiro et al., 2014).

Antifungal effects of ethanolic extract showed activity of several levels against Aspergillus parasiticus and the extracts were effective in controlling the growth and production of aflatoxins by A. parasiticus (Martins et al., 2014). Araújo et al. (2014), also evaluated the antibacterial activity of the extracts from bark against Gram-positive strains (S. aureus, Staphylococcus epidermidis, Enterococcus faecalis and a clinical isolate of methicillin-resistant S. aureus) and Gram-negative strains (E. coli, Salmonella enteritidis, Shigella flexneri and K. pneumoniae). The CE of acetone: water (7:3) showed greater inhibition against most of the bacteria, whereas the CE aqueous showed greater activity against the S. epidermidis, E. faecalis and Shigella flexinerei.

Regarding the MIC, the results indicated that acetone: water CE yielded better results compared to the aqueous, in addition, most Gram-negative bacteria were resistant
Antidiabetic

The hydroalcoholic extract (80%) of fruits was partitioned, giving 1-BuOH extract, the residue and the fraction 7 showed better inhibitory activity against aldose redutase (Ueda et al., 2002). Ueda et al. (2004), tested the aldose redutase in vitro of ellagic acid and 2-(2,3,6-trihydroxy-4-carboxyphenyl)ellagic acid, from fruits of L. ferrea, and it was verified that both compounds dose-dependently inhibited sorbitol accumulation in erythrocytes, lens and sciatic nerve under in vitro incubation with glucose. On the other hand, studies by Carvalho et al. (2010) indicated that the aqueous extracts, when used in chronic treatment on the vascular reactivity of alloxan-induced diabetic rats, were not able to modify the contractions or relaxations. Vasconcelos et al. (2011), obtained the aqueous CE from the barks and evaluated the hypoglycaemic properties and the mechanisms of reduction of glucose level in blood of diabetic rats via protein kinase B (PKB/Akt), AMP-activated protein kinase (AMPK) and acetyl-CoA carboxylase (ACC). The authors verified that the CE reduced blood glucose levels and improved the metabolic state of the animals. P-Akt was increased and P-ACC was reduced in the liver and skeletal muscle of the treated animals, P-AMPK was reduced only in the skeletal muscle. The biochemical parameters at a dose of 450 mg/kg/day presented reductions in levels of urea, uric acid, AST and ALT.

Antioxidant

In studies carried out by Silva et al. (2011), the ethanolic extract of fruits, exhibited strong antioxidant activity in the in vitro test and demonstrated a significant and linear correlation between the phenolic content and the antioxidant activity by phosphomolibdenium assay as well as the superoxide radical scavenging activity. On the other hand, the DNA nicking assay presented the ability to extract, especially E. coli.
to inhibit the DNA degradation. A study on the antioxidant capacity by scavenging the application of free radical diphenylpicrylhydrazyl (DPPH) radical was performed by Port’s et al. (2013), presented moderate activity, and when analyzed with the β-Carotene/linoleic acid system, the results showed high values.

**Antitumor**

Gallic acid and methyl gallate, isolated from fruits, were tested by the in vitro Epstein–Barr virus early antigen and were observed to decrease significantly the average number of papillomas, thus promoting the effects of 12-O-tetra-decanoylphorbol-13-acetate on skin tumor formation in mice (Nakamura et al., 2002; 2002). In 2003, the cancer chemopreventive activity of 2-(2,3,6-trihydroxy-4-carboxyphenyl)ellagic acid from fruits was evaluated and the two-stages of mouse skin papillomas induced were inhibited by this compound (Inada et al., 2003).

**Others activities**

The replication of herpes simplex virus (HSV) and poliovirus (PV) were evaluated by sulfated polysaccharide (seeds) and the authors proved the inhibition of virus absorption in the stages after penetration and the synthesis of viral protein (Lopes et al., 2013). The cardiovascular effect of aqueous CE (stem bark) demonstrates that it induces hypotension associated with tachycardia in normotensive rats. At a dose of 40 mg/kg, it induces transient bradycardhyriasms. The occurrence of vasodilatation in rat mesenteric artery mediated by ATP-sensitive K⁺ channel openings was also reported (Lopes et al., 2013). The induction of apoptosis in human leukemia HL 60 cells and quantified by HPLC (Silva et al., 2014). Chalcones and other compounds Pauferrol A, B and C showed inhibitory activities against human topoisomerase II and cell proliferation via the induction of apoptosis in human leukemia HL 60 cells (Nozaki et al., 2007). Bariani et al. (2012), have reported the use of trypsin inhibitors in seeds against the pathogenic fungi *Colletotrichum guanericola*, *Corynespora cassicola*, *Fusarium oxysporum* and *Sclerotium rolfsii*. The protein extracts were analyzed by SDS-PAGE and the effect in reducing sporulation and mycelial of these fungi was verified.

**CHEMICAL COMPOSITION**

**Fatty acids and terpenoids**

In the studies of Dias et al. (2013), the presence of fatty acids was reported in fruits after supercritical fluid extraction (SFE) using CO₂. The analysis by gas chromatography revealed that the fruits are composed of unsaturated and saturated fatty acids as well as terpenoids; there is also linoleic acid, palmitic acid, elaidic acid, gamma-sitosterol, stearic acid and lupenone. Moreover, 3,4-dimethylbenzadehyde and di-2-ethylhexylphthalat were also identified. Sawada et al. (2014), also identified the presence of fatty acids in the lipid portion of seeds, being linoleic, palmitic, oleic, estearic, palmitolenic and capric acids (Table 1).

**Phenolic compounds**

Among the phenolic compounds related to the different parts of *L. ferrea*, the condensed and hydrolysable tannins, and chalcones deserve special attention. Phytochemical studies by Thin Layer Chromatography (TLC) revealed the presence of coumarins, flavonoids, saponins, steroids (Gonzalez et al., 2004) and tannins (Gonzalez et al., 2004; Vasconcelos et al., 2011; Araújo et al., 2014). Ueda et al. (2002), isolated the ellagic acid and 2-(2,3,6-trihydroxy-4-carboxyphenyl) ellagic acid from fruits. According to Nakamura et al. (2002) gallic acid and methyl gallate were isolated from fruits. Also in fruits, the phenolic content was calculated from an obtained hydroalcoholic extract and values of 460 mg/g of gallic acid were found (Silva et al., 2011).

Sampaio et al. (2009), also calculated the content of polyphenols in methanolic extract, by the Prussian Blue Method and this was estimated at 7.3%. In addition, spectral analysis revealed hydroxy phenols and methoxilated compounds. Using High-performance liquid chromatography (HPLC) analysis, revealed the presence of in aqueous crude extracts. The analysis of aqueous crude extract by HPLC revealed the presence of gallic acid, catechin, epicatechin and ellagic acid (Vasconcelos et al., 2011; Araújo et al., 2014).

In the methanolic extract of the fruits, described by Silva et al. (2013), gallic acid and methylated gallate derivative compounds were found. Port’s et al. (2013), reported the presence of gallic acid and quercetin in methanolic extract of leaves. In the extractive solution of leaves, the polyphenolic content was calculated by Folin-Ciocalletu and the presence of gallic acid was identified and quantified by HPLC (Silva et al., 2014). Chalcones are also a substance that is present in this specie, the literature reports the presence of these compounds isolated from the stems of *L. ferrea*. The CE obtained with acetone when partitioned revealed the presence of Pauferrol A (Nozaki et al., 2007), Pauferrol B and C (Ohira et al., 2013).

**Polysaccharides**

The hydrocolloid extract purified from seeds contained 75% total carbohydrate and 9% protein. The 1D/2D NMR
Table 1. Main constituents from some parts of *Libidibia ferrea* (B: B; F: F; L: L; Se: Se; St: St).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>Plant part</th>
<th>Reference</th>
</tr>
</thead>
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<tr>
<td>Linoleic acid</td>
<td><img src="image" alt="Linoleic acid structure" /></td>
<td>F, Se</td>
<td>Dias et al., 2013; Sawada et al., 2014</td>
</tr>
<tr>
<td>Palmitic acid</td>
<td><img src="image" alt="Palmitic acid structure" /></td>
<td>F, Se</td>
<td>Dias et al., 2013; Sawada et al., 2014</td>
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<tr>
<td>Lupenone</td>
<td><img src="image" alt="Lupenone structure" /></td>
<td>F</td>
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<tr>
<td>Gamma-sitosterol</td>
<td><img src="image" alt="Gamma-sitosterol structure" /></td>
<td>F</td>
<td>Dias et al., 2013</td>
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<tr>
<td>3,4-dimethylbenzaldehyde</td>
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<td>F</td>
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<tr>
<td>di-2-ethylhexylphthalate</td>
<td><img src="image" alt="di-2-ethylhexylphthalate structure" /></td>
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<td>Dias et al., 2013</td>
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Table 1. Contd.

<table>
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<tr>
<th>Compound</th>
<th>Structure</th>
<th>Reference</th>
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<tr>
<td>Gallic acid</td>
<td><img src="image" alt="Gallic Acid" /></td>
<td>F, L, Stand B Nakamura et al., 2002a,b; Vasconcelos et al., 2011; Silva et al., 2013; Silva et al., 2014; Port’s et al., 2013; Araújo et al., 2014</td>
</tr>
<tr>
<td>Methyl gallate</td>
<td><img src="image" alt="Methyl Gallate" /></td>
<td>F Nakamura et al., 2002a,b; Silva et al., 2013</td>
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<tr>
<td>2-(2,3,6-trihydroxy-4-carboxyphenyl)ellagic acid</td>
<td><img src="image" alt="Ellagic Acid" /></td>
<td>F Ueda et al., 2002; 2004</td>
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<td>Ellagic acid</td>
<td><img src="image" alt="Ellagic acid" /></td>
<td>F, Stand B Ueda et al., 2002; 2004; Vasconcelos et al., 2011</td>
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<tr>
<td>Galactomannan</td>
<td><img src="image" alt="Galactomannan" /></td>
<td>F Souza et al., 2010</td>
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<tr>
<td>Quercetin</td>
<td><img src="image" alt="Quercetin" /></td>
<td>L Port’s et al., 2013</td>
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Table 1. Contd.

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<th>Substance</th>
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</tr>
<tr>
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<td>St and B Nozaki et al., 2007</td>
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<tr>
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<td><img src="structure7" alt="Pauferrol B" /></td>
<td>St and B Ohira et al., 2013</td>
</tr>
<tr>
<td>Pauferrol C</td>
<td><img src="structure8" alt="Pauferrol C" /></td>
<td>St and B Ohira et al., 2013</td>
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R<sub>1</sub> = OH, R<sub>2</sub> = H

R<sub>1</sub> = H, R<sub>2</sub> = OH
Table 1. Contd.

<table>
<thead>
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<th>St and B</th>
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<tr>
<td>Catechin</td>
<td></td>
<td>Vasconcelos et al., 2011; Araújo et al., 2014</td>
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<tr>
<td>Epicatechin</td>
<td></td>
<td>Vasconcelos et al., 2011</td>
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spectra indicated the presence of galactomannan with a (1→4)-linked-β-D-mannopyranose, partially substituted at O-6 with single-unit α-D-galactopyranose side-chains. The splitting of three $^{13}$C signals in the region of the 4-O-Manpyranose units revealed the α-D-Galpyranose units (Souza et al., 2010). Another study showed the presence of polysaccharides in aqueous extract from the seeds following sulfation. The analysis by $^{13}$C, $^1$H NMR and FT-IR revealed the presence of d-Galactose and d-Mannose monosaccharides (Lopes et al., 2013). The presence of galactomannan in the seeds was also proved by Gallão et al. (2013), and they also indicated that galactomannan is located at the endosperm.

**DISCUSSION**

This paper presents a review of the biological and phytochemical aspects of the species *L. ferrea*, whose importance and relevance to traditional medicine stands out due to its biological properties against anemia, lung disease and diabetes. Antipyretic activity is also reported in this species. Several studies confirmed such activities as antidiabetic, anti-inflammatory and antimicrobial; and this can be attributed to the presence of the compounds (chalcones, flavonoids, polysaccharides, tannins and terpenes) obtained from several extracts from different herbal parts (leaves, fruits or stem barks). However, further studies are still necessary to demonstrate the potential of *L. ferrea* as a source of bioactive molecules or its use with standardized extracts with biological and pharmacological relevance. Despite the promising pharmacological and biological data on the species related in the literature, there are few toxicological studies. The investigation of the extract's safety plays an important role in the establishment of its bioguided chemical profile with improved biological properties and low toxicology or side effects.

**Conclusion**

In conclusion, the data presented in this review about *L. ferrea* Mart. ex Tul. L. P. Queiroz, is a compilation of knowledge regarding its biological and phytochemical aspects, that may contribute as a basis to the development of research about its biological properties and chemical compounds, and further studies are needed to correlate the presence of such properties.

**ACKNOWLEDGEMENT**

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**Conflicts of interest**

The authors declare that they have no conflicts of interest.

**REFERENCES**


