Pharmacognosy
Ethnobotany, ecology, pharmacology, and chemistry of *Anredera cordifolia* (Basellaceae): a review

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**Abstract**
The potential of a plant with medicinal and nutritional properties, *Anredera cordifolia*, is reviewed. Its common names include “Bertalha” and “folha gorda” and it is popularly used for wound healing and against fungal infections and other types of infection. Its pharmacological properties have been widely investigated and acknowledged, especially with regard to its antibacterial activity, which improves the healing of wounds infected by *Staphylococcus aureus*, and to its antifungal activity against *Candida albicans*. It is an unconventional food plant, with leaves and aerial tubers used as food prepared in varied ways. It is also considered an invasive plant in several countries and thus classified as a weed. Its characteristics of a Brazilian native plant, with proven medicinal properties and unconventional use as food, underlie our study on its ecology and botanical classification, as well as the pharmacological assays and screening of chemical constituents.

**Key words**: antimicrobial activity, invasive plants, medicinal plants, phytochemistry, unconventional food plant.

**Introduction**
The traditional medicine approaches to the prevention and diagnosis of diseases, improvement of physical and mental functions, and maintenance of health also include medicinal plants (OMS 2013). These plants are used in different formulations (infusions, ointments, syrups, among others) for the treatment and cure of diseases, and they are considered to be an age-old tradition in healthcare (Veiga Junior *et al.* 2005; Oliveira *et al.* 2007).

In Brazil, a country rife with biodiversity, species regarded as medicinal tend to be highly estimated. For example, 89 new monographs on plants and the review of another 58 (Brasil 2017) were included in the second supplement of Brazilian Pharmacopoeia 5. Even though plants...
are broadly investigated in Brazil, it is widely known that many gaps still exist, especially in the case of angiosperms (Stehmann & Sobral 2017). Many plant species continue to be used in popular medicine without proven medicinal effects and despite the lack of knowledge of their possible undesirable effects (Heinzmann & Barros 2007).

With irrefutable medicinal properties, Anredera cordifolia (Ten.) Steenis stands out in the treatment of wounds, fungal infections, and other types of infections (Heisler et al. 2012). Anredera cordifolia, which belongs to the family Basellaceae, is of great interest, not only because of its pharmacological properties, but also because of its high nutritional value.

The family Basellaceae includes genera without fleshy to succulent tendrils, herbaceous plants, or occasionally woody plants and erect plants. These perennial plants have subterranean and aerial tubers, with simple leaves without stipules, and with succulent, herbaceous, or lignified stems (Erikson 2007; Pellegrini & Imig 2019).

Basellaceae has a pantropical distribution of the genera Anredera Juss., Basella L., Tournonia Moq., and Ullucus Caldas. In Brazil, Anredera cordifolia and Anredera tucumarensis (Lillo & Hauman) Sperling are native species (Pellegrini & Sakuragui 2017), and the genus Basella was introduced in Brazil (Souza & Lorenzi 2012).

Anredera is the largest genus of this family with approximately 12 species, with broader diversity in the Andean region. It differs from the genus Basella because of its inflorescences with thin rachises (vs. fleshy ones in Basella), connate sepalas (free ones in Basella), stalked and fragrant flowers (odorless and sessile in Basella), and spheroidal and echinate pollen (cuboidal and reticulate in Basella) (Erikson 2007; Pellegrini & Sakuragui 2017).

Native but not endemic to Brazil, Anredera cordifolia is popularly known as “bertalha, basela, folha-gorda, or trepadeira-mimos” (Pellegrini & Imig 2019; Souza & Lorenzi 2012). In Indonesia and neighboring regions, it is known as “binahong” (Sumartiningsih 2011), whereas in Australia it is called “madeira vine” (Vivian-Smith et al. 2007). In Argentina, it is known as “zarza-parilla” (Scarpa 2004) and “papa santa” (Hilgert 2001).

It is considered an unconventional food plant, as its leaves and aerial tubers are eaten in varied forms (Kelen et al. 2015), serving as an excellent source of proteins and fibers (Martinevski et al. 2013). The leaves are used for making breads (Martinevski et al. 2013) and the tubers can be eaten either cooked or fried (Kinupp & Lorenzi 2014). It is also grown as an ornamental plant (Souza & Lorenzi 2012) e.g., as hedge (Mogale et al. 2019). This species has a wide tropical distribution in America, Australia, China, Malaysia, Southern Pacific Islands, and Africa (Rasingam & Lakshminarasimhan 2012). In Brazil, it is found in the northeast (Bahia, Ceará, and Pernambuco); midwest (Mato Grosso do Sul); southeast (Espírito Santo, Minas Gerais, Rio de Janeiro, and São Paulo); and south (Paraná, Rio Grande do Sul, and Santa Catarina) (Pellegrini & Imig 2019).

In Brazil, this species has fallen into disuse (Kinupp et al. 2004), and it has been underinvestigated in pharmacological studies. In other countries such as Indonesia, many studies have been conducted, corroborating its pharmacological potential. A literature review was performed, demonstrating the medicinal and nutritional properties of this species, as well as its potential for the development of pharmaceuticals.

Materials and Methods

A literature search was conducted in Scielo, Scopus, Web of Science, Medline, and BioOne databases, in addition to books and other sources such as botanical gardens around the world. The scientific names (Anredera cordifolia and Bossingaultia gracilis) were used as descriptor, with no restriction imposed on year of publication. The species Anredera cordifolia was photographed in the city of Sarandi-RS (27°58′11″,9064″S - 52°54′29″,7864″W) and was identified by the curator Prof. Cristiano Roberto Buzatto. The exsiccates are stored under the number: RSPF 14413, at the Herbarium RSPF which is linked to the Zoobotanic Museum Augusto Ruschi (MUZAR), from the Institute of Biological Sciences of the University of Passo Fundo (UPF).

Results and Discussion

Botany, ecology, and chemical and biological control

Anredera cordifolia is a climbing plant, found in forest borders, on fences along roads, and in plots of land at 1,000 m to 2,000 m (Rasingam & Lakshminarasimhan 2012). It is also seen in anthropized regions, such as in vacant lots in urban areas (Fig. 1a) (Imig et al. 2015), as it is considered to be ruderal (Pellegrini & Sakuragui 2017).
Brazil, more specifically in the state of Rio Grande do Sul, it is found on the borders of rainforests and in the Pampa region (Souza & Lorenzi 2012; Pellegrini & Sakuragui 2017).

This species grows in well-lit environments and has fleshy tubers that may be seen in the nodes of aerial petioles (Fig. 1b) (Vivian-Smith et al. 2007). Its leaves are cordate to ovate (Boyne et al. 2013) very fleshy, dark green, shiny, and rarely elliptical (Imig et al. 2015; Pellegrini & Sakuragui 2017). It is characterized by white, pendent, and fragrant inflorescences (Souza & Lorenzi 2012) such as racemes or panicles, either axillary or terminal (Fig. 1c). The flowers are perfect with triangular to broadly ovate bracteoles, the sepals are broadly ovate to broadly elliptical, the petals are uniform, patent, elliptical to obovate, white or greenish white, with trifid style and capitate stigma. The fruit is a patent brown achene (Pellegrini & Sakuragui 2017).

*Anredera cordifolia* differs from *Anredera tucumarensis* because of the presence of aerial tubers, membranous leaves with no involute margins *in sicco*, poorly apparent secondary veins, connate bracteoles, uniform petals larger than the sepals, and trifid style (Erikson 2007; Pellegrini & Sakuragui 2017). In terms of leaf anatomy, the epidermis of *A. cordifolia* lacks trichomes and the stomata have two to three subsidiary cells on both leaf surfaces. The mesophyll has mucilage cells, calcium oxalate, narrow vascular bundles, and no sclerenchyma (Boyne et al. 2013). Chromosome analysis revealed that *A. cordifolia* subspecies *gracilis* has sexual reproduction, bearing viable fruits, with 2n = 24 chromosomes. *Anredera cordifolia* subspecies *cordifolia* only reproduces vegetatively, with 2n = 36 chromosomes (Xifreda et al. 2000).

Widely known in Portugal, this species was introduced there in 1961, when it was regarded as a species that would be problematic in the future (Silva et al. 2015). *Anredera cordifolia* includes highly invasive lianas, as a result of phenotypic plasticity (Pintó-Marijuan & Munné-Bosch 2013) and it is therefore classified as an “invasive plant” (Kinupp et al. 2004) or “weed” (Palmer et al. 2010). It is known as an “*alien plant*” in Australia, China, and Africa (Jian et al. 2008; Baard & Kraaij 2014; Byrne et al. 2017; Gao et al. 2018; Shen et al. 2018), where sustained effort has been put in for its control (Van Driesche et al. 2010).

In China, it is found in vacant lots, orchards, forests, roads, and conservation units, and it has been reported to invade crops such as banana, lemon, and orange (Shen et al. 2017; Zhu et al. 2018). In abandoned lands with yellow soil, there are a large number of vines as compared to other species, and these vines eventually reduce the number of seedlings, inhibiting restoration and ecological succession (Haitan et al. 2011). In New South Wales, Australia, it has been a threat to the local biodiversity, requiring control measures (Downey et al. 2010). A study undertaken in Argentina revealed that a beetle belonging to the family Chrysomelidae, *Plectonycha correntina* Lacordaire, may be used as a biocontrol agent against *A. cordifolia* (Cagnotti et al. 2007; Westhuizen 2011). This species is host to Dichotomophthora, they are used for the biological control of *A. cordifolia*, as they cause leaf abscesses, spots, and seed rot (Marin-Felix et al. 2019). Regarding chemical control, *Anredera cordifolia* is tolerant of glyphosate and fluroxypyr-mephtyl treatments in some cases (Waryszak et al. 2018).

![Figure 1](image1.jpg)

**Figure 1** – a-c. *Anredera cordifolia* – a. aerial parts; b. tubers; c. flowers. Scale bars: a. 21 mm; b. 10 mm; c. 4 mm.

*Pharmacobotany and chemistry of A. cordifolia*
Ethnobotany
In several regions around the world, *A. cordifolia* has been described and used as a medicinal plant. Studies carried out in Asia, especially in Indonesia and neighboring regions, used ointments and gels made from extracts of the plant, which demonstrated antibacterial activity (Zulfa *et al*. 2017), and efficacy in wound healing (Istyastono & Yuliani 2016; Shrivastav *et al*. 2018) including wounds infected by *Staphylococcus aureus* (Paju *et al*. 2013). The gel aided in the healing of burns (Istyastono & Yuliani 2016; Prasetyo & Heri Hadi 2013) and in the reduction of diabetic ulcers in rats (Kintoko & Desmayanti 2016). In Malaysia, *A. cordifolia* is used to treat diabetes, liver diseases, hypertension, hypercholesterolemia, blood clots, and mental and physical stress (Astuti *et al*. 2011). Moreover, in Thailand, its leaves and stalks are used by parturients as postpartum tonic (Panyaphu *et al*. 2011; Fitriana *et al*. 2015; Pitaloka & Sukandar 2018). Aqueous and chloroform extracts obtained from the roots inhibited the growth of several bacteria, including *Staphylococcus* and *Pseudomonas*, in a screening in Africa in which six medicinal species were tested (Tshikalange *et al*. 2005). The growth of *Streptococcus mutans* was inhibited by ethanolic extract of leaves (Rimporok *et al*. 2015). *Bacillus cereus*, *Salmonella enteritidis* (Rahmawati & Bintari 2014), *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus subtilis* (Paz *et al*. 1995), also had their growth inhibited by aqueous leaf extracts of the plant. On the other hand, the methanolic extract prepared from *A. cordifolia* leaves did not inhibit the growth of *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, and *Pseudomonas aeruginosa* (Amertha *et al*. 2012). A phytotherapeutic product with *A. cordifolia* seeds and other plants was efficient in inhibiting the growth of *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Neisseria gonorhoeae*, and also in inhibiting HIV-1 reverse transcriptase, without causing mutagenic effects (Mulaudi *et al*. 2015). Besides the antimicrobial activity of *A. cordifolia*, the literature describes a considerable number of pharmacological studies on this species. Promising effects of leaf extracts have been described against cervical cancer (Yuliani *et al*. 2015), and reduction of a tumor necrosis factor and other inflammatory mediators in macrophage lines (Laksmitawati *et al*. 2017). Ethanolic leaf extract of *A. cordifolia* and *Centella asiatica* L. exhibited anti-inflammatory activity in human red blood cells in a membrane stabilization assay (Sutrisno *et al*. 2016). Leaf extract microemulsion at 0.5 % also demonstrated antiaging effects (Nazliniwaty *et al*. 2018).

**Pharmacological assays**

**In vitro**
Several studies have shown promising results against microorganisms (Tshikalange *et al*. 2005; Yan *et al*. 2011; Garmana *et al*. 2014; Souza *et al*. 2014). The ethanolic extract obtained from the stem demonstrated antifungal activity against *Candida albicans* (Kumalasari & Sulistyani 2011). The infusion of *A. cordifolia* leaves at high concentrations inhibited the growth of *Porphyromonas gingivalis* and *Prevotella intermedia* (Maharani *et al*. 2018). The n-hexane, ethyl acetate and ethanolic extracts of *A. cordifolia* leaves showed activity against *Mycobacterium tuberculosis* strains, and the hexane extract showed better activity (Pitaloka & Sukandar 2018).

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In vivo assays

The literature describes a wide variety of in vivo pharmacological assays with raw extracts and fractions obtained from Anredera cordifolia. The oral administration, in Guinea pig (Cavia cobaya), of 50 mg leaf extract improved immunity and resistance during and after childbirth, also improving the blood parameters and quality of postpartum care (Wijayanti et al. 2016, 2017). Its leaf extract was also efficient in the wound healing of guinea pigs (Miladiyah & Prabowo 2012) and demonstrated vasodilatory properties in rabbits and toads (Sukandar et al. 2016a).

Tests with Wistar rats revealed that the ethanolic leaf extract of A. cordifolia works as an antiobesity medication (Sukandar et al. 2016b), has diuretic effects, and lowers blood pressure (Garmana et al. 2016), total cholesterol, and triglyceride levels (Lestari et al. 2015). Moreover, the ethanolic extract may be used to treat gout, as it reduces serum urate levels (Widyarini et al. 2015; Hendriani & Sukandar 2016).

Other assays indicated that the ethanolic extract was efficient in the treatment of kidney failure in Wistar rats (Sukandar et al. 2011, 2013), protected against the effects of ethanol on the renal proximal tubular epithelial cells of Sprague-Dawley albino rats (Asmariati et al. 2014). Also, the ethanolic extract exhibited analgesic activity in the “plantar test method” (Yuziani et al. 2014). The administration of ethanolic extract of A. cordifolia combined with that of black mulberry (Morus nigra L.) enhanced the lipid profile of rats (Sukandar et al. 2016c), and combined with the extract of Areca catechu L., it reduced the incidence of Ascaridia galli in Gallus gallus domesticus (Prastowo et al. 2017). The administration of A. cordifolia to Wistar rats for 3 days reduced cellular inflammation by 5% and increased fibroblast growth in bruises (Sumartiningsih 2011). A. cordifolia rhizomes contain ancordin, a protein that can inhibit trypsin and stimulate the cellular production of nitric oxide (Chuang et al. 2007).

Toxicity

Regarding toxic effects, Anredera cordifolia is not toxic to Wistar rats (Salasanti et al. 2014), and it does not have teratogenic effects on them (Sukandar et al. 2014). The cytotoxic, genotoxic, and antimutagenic effects of Boussingaultia gracilis Miers var. pseudobaselloides Bailey were investigated in Salmonella typhimurium (Ames test) and in human lymphocytes (comet assay), and was found to be non-toxic (Yen et al. 2001).

Phytochemistry

Even though the pharmacological properties of Anredera cordifolia have been widely investigated, reports on the chemical compounds present in its extracts are limited to phytochemical screening, to a study on its volatile constituents, and to some compounds in particular, such as saponins and flavonoids.


Other compounds isolated from A. cordifolia leaf extracts include 3,5,3',4'-tetrahydroxyflavone (Rahmawati et al. 2013) and the flavonoid 8-glucopyranosyl-4',5,7-trihydroxyflavone (vitexin) (Djamil 2012). Vitexin exhibited antioxidant activity when tested with the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method (Djamil 2012), and demonstrated in vitro α-glucosidase inhibitory activity and antidiabetic activity in alloxan-induced mice (Djamil 2012; Djamil et al. 2017). A new method for the extraction of this compound from A. cordifolia leaves, with a non-toxic and environmentally friendly solvent, was proposed (Mulia et al. 2017). Myricetin and morin were detected by high-performance liquid chromatography (HPLC), whereas kaempferol and quercetin were not found in A. cordifolia leaves extracts. The concentrations of polyphenols, flavonoids, and flavonols were determined by spectrophotometric methods, but anthocyanidins were not detected (Chao et al. 2014). On the other hand, Yang et al. (2008), in a work with 91 edible species, related the presence of quercetin in shoots of A. cordifolia.

The volatile constituents of the aerial parts were analyzed and the major compounds were phytol (15.33 %), alpha-pinene (9.0 %), and 6,10,14-trimethyl pentadecanone (6.12 %). In this work vitexin and isovitexin were also isolated (Abou-Zeid et al. 2007). The essential oil was analyzed by GC and GC-MS and 19 compounds were identified. Hydrocarbons were the main constituents (67.7 %) (Souza et al. 2014).
Lupeol and β-sitosterol (Basyuni et al. 2017), and ursolic acid (Yuliani & Istyastono 2013) were detected by thin-layer chromatography (TLC). Using TLC as a support, UV-VIS, and FTIR spectrophotometry, Ekaviantiwi et al. (2013) concluded that ethanolic extracts of leaves might contain p-coumaric acid. The presence of saponins was verified by general detection tests (foam formation), using TLC, and also by the analytical method (Astuti et al. 2011). The tests were positive for saponins in all plant parts.

Phytochemical screening was positive for flavonoids, saponins, steroids/terpenoids, and alkaloids (Ekaviantiwi et al. 2013; Rahmawati et al. 2013; Elya et al. 2015; Lestari et al. 2015, 2016; Sukandar et al. 2016c; Pitaloka & Sukandar 2018). Screening of alkaloids showed also negative results (Kumalasari & Sulistyani 2011; Garmana et al. 2014; Sukandar et al. 2016b; Kaunang & Semuel 2017) or positive ones only for Dragendorff’s reagent, with negative results for Bouchardat’s, Wagner’s, and Mayer’s reagents (Basyuni et al. 2017). Some authors found negative results in the screening test for tannins (Kumalasari & Sulistyani 2011; Elya et al. 2015; Lestari et al. 2015, 2016; Sukandar et al. 2016b) whereas some obtained positive results (Ekaviantiwi et al. 2013; Rahmawati et al. 2013; Garmana et al. 2016; Sukandar et al. 2016c; Kaunang & Semuel 2017; Pitaloka & Sukandar 2018). Polyphenols (Kumalasari & Sulistyani 2011; Sukandar et al. 2016b, c; Basyuni et al. 2017; Pitaloka & Sukandar 2018) and glucoside (Astuti et al. 2011; Elya et al. 2015) were also detected in screening tests. Some studies checked for the presence of quinones but all tests were negative (Garmana et al. 2014; Elya et

Table 1 – Phytochemical screening test results for A. cordifolia described in the literature.

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<tr>
<th>Reference</th>
<th>Saponins</th>
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<th>Flavonoids</th>
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(+)= positive tests; (-)= negative tests; *(+)= with Dragendorff’s reagent; **(-)= with Mayer, Bouchardat and Wagner’s reagents.
al. 2015; Lestari et al. 2015, 2016; Sukandar et al. 2016b, c). However, Pitaloka & Sukandar (2018) found positive results for quinones. Table 1 lists the articles and results obtained from phytochemical screening tests with A. cordifolia extracts.

Therefore, vitexin, isovitexin, myricetin, morin, 3,5,3’,4’-tetrahydroxyflavon and ursolic acid; larreagenin A, 3β-hydroxy-30-norolea12,19-dien-28-oic acid and its ethyl ester, 28-ethyl hydrogen 3β-hydroxylean-12-ene-28,29-dioate, and ethyl 3β-hydroxy-30-noroleana12,18-dien-29-oate were isolated from A. cordifolia extracts. The probable presence of p-coumaric acid, lupeol, and β-sitosterol was verified by TLC using a reference standard.

The present review demonstrates the main uses, as well as the medicinal and nutritional properties, of A. cordifolia. This plant is an invasive species in several countries, and the problems caused by it and its management should be addressed. A. cordifolia is a promising medicinal plant, as several pharmacological assays corroborate its efficacy, especially its antimicrobial activity. Some flavonoids, such as vitexin, isovitexin, morin, and myricetin, in addition to sapogenins such as ursolic acid were isolated from its extracts. Phytochemical screening evidenced the presence of metabolites such as alkaloids, flavonoids, saponins, steroids, and terpenoids. The isolation and identification of other chemical compounds and the characterization of a marker for this species are essential for the development of a phytotherapeutic agent from A. cordifolia extracts.

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Westhuizen LV (2011) Initiation of a biological control programme against madeira vine, Anredera
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cordifolia (Ten.) Steenis (Basellaceae), in South


