Revista ARACÊ
ISSN: 2358-2472

USAGE OF LUEHEA DIVARICATA MART. BY AN AMAZONIC TRADITIONAL COMMUNITY AND ITS ANTIDIABETIC POTENTIAL

https://doi.org/10.56238/arev6n4-486

Date of submission: 31/11/2024 **Date of publication:** 31/12/2024

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ABSTRACT

Luehea divaricata Mart. is a medicinal plant traditionally used by the Amazonian quilombola community of Macapazinho, Pará, Brazil, for the treatment of diabetes mellitus. The species contains bioactive compounds with hypoglycemic properties, with dietary polyphenols, especially kaempferol, responsible for reducing blood glucose and improving insulin resistance. This study aims to document the ethnomedicinal usage of Luehea divaricata Mart. for diabetes treatment in the Macapazinho community and evaluate its phytotherapeutic potential through literature review. Field research was conducted between 2021 and 2022 using the Snowball Sampling method, involving 40 families (20% of the community). Participants reported using a decoction of the dried stem, administered orally

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Revista ARACÊ
ISSN: 2358-2472

under the guidance of local healthcare workers. A bibliographic review was additionally undertaken to identify bioactive compounds, assess their efficacy, and evaluate the plant's toxicity. The study found promising antidiabetic effects following a 10-day treatment regimen, attributed to the plant's bioactive compounds that reduce glycemia, protect pancreatic β cells, and improve insulin sensitivity. Additionally, toxicity studies conducted in animal models revealed no adverse effects at tested dosages. Luehea divaricata Mart. demonstrates significant antidiabetic potential with no observed toxicity, supporting its traditional use in the treatment of diabetes mellitus. These findings offer promising prospects for future pharmacological research and the development of new diabetes therapies.

Keywords: Medicinal Plant. L.Divaricata Mart. Diabetes Mellitus.

Revista ARACÊ
ISSN: 2358-2472

INTRODUCTION

The use of traditional therapeutic systems has been a fundamental component in the history of civilization, contributing to the resolution of health issues over many centuries. This practice is often the result of human observation of natural phenomena and the consequent search for solutions to alleviate illnesses. This interaction with the environment not only influences collective health practices, but also shapes vital aspects of social and cultural life in traditional communities (Marques et al., 2021; Pagani et al., 2017). In this context, indigenous peoples develop a deep understanding of the environment in which they live, which is enriched by symbolic values, beliefs and myths transmitted through accumulated experience and oral tradition (Adhikari et al., 2018; Olajuyigbe and Afolayan, 2012).

Traditional herbal medicine uses plants and their extracts for the treatment, prevention or relief of disease symptoms. It is based on knowledge passed down through generations, often forming part of specific traditional and cultural medical practices of different peoples around the world. Each culture has its own herbal medicine practices, which are influenced by their traditions, beliefs and historical experiences. This may include Ayurvedic medicine in India, traditional Chinese medicine, African herbal medicine, traditional Amazonian medicine, among others (Berlowitz et al., 2023; Elahee et al., 2019; Mahomoodall, 2013; Pandey et al., 2013). There are a number of ways medicinal plants can be used, such as teas, extracts, capsules, ointments and even directly in raw form. The choice of how to prepare and use a plant is often determined by specific traditions and local knowledge. This knowledge about the properties of plants and their uses is generally transmitted orally from generation to generation, although in many cultures there may also be rare written records (Vieira and Milward-de-Azevedo, 2023). Many traditional herbal medicine practices are being studied scientifically to better understand their mechanisms of action, efficacy and safety. This helps to integrate traditional knowledge with modern medicine, ensuring that treatments are safe and effective. This is a field of interest for both local communities and researchers seeking to understand and conserve this rich cultural heritage.

In South America there resides the greatest tropical forest in the World, the Amazon Rainforest, home to over 30 million people (Coura and Junqueira, 2012). The amazonian woodland represents one of the largest reserves of biological and pharmacological biodiversity on the planet, extending across nine countries in South America. This extensive

Revista ARACÊ
ISSN: 2358-2472

area hosts thousands of plant species used both in the traditional medicine of local communities and in contemporary science in the search for new treatments and medicines (Shanley and Luz, 2003). Tropical forests such as the Amazon are essential for maintaining plant biodiversity, especially medicinal plants, whose diversity is unique in these regions. These rich and complex ecosystems are home to more than half of the world's medicinal plant species, many of whose therapeutic potential has not yet been discovered. Moreover, since the 1990s, scientific studies have highlighted the richness of Amazonian ethnopharmacology and the importance of conserving this heritage for human health and environmental sustainability (Elisabetsky, 1991; Schultes and Raffauf, 1990). The loss of these species could result in the loss of traditional knowledge used by native Amazonian peoples and the extinction of medicinal potentials not yet discovered by science.

For instance, let us consider diabetes mellitus (DM). DM is currently a global pandemic, affecting approximately 536.6 million people, with projections of an increase to 578 million in 2030 and 783.2 million by 2045 (Saeedi et al., 2019; Sun et al., 2022). The global economic impact due to DM is significant and is likely to grow substantially. Currently, in Brazil, 15.7 million individuals live with diabetes, with predictions that this number will reach 40 million in 2030 and 49 million in 2045 (Sun et al., 2022). Meanwhile, plant species considered antidiabetic represent important sources for scientific research, mainly because they contain potentially hypoglycemic phytochemicals, which can act in the treatment of DM, alleviating symptoms and possible sequelae, and promoting economic advantages with low-cost treatments.

Diabetes mellitus is an endocrine disease, of multifactorial origin, resulting from insufficient production of insulin, lack thereof or the inability of insulin to properly exert its effects, leading to high blood sugar levels (hyperglycemia). This condition can cause serious damage to the heart, eyes, nerves, kidneys, and peripheral vascular system (Smetlzer & Bare, 2002). Historically, treatment with medicinal plants emerged as one of the first known therapeutic approaches in response to health problems such as these. Despite research in various areas on medicinal plants, adequate integration that relates traditional methods of use to the results of phytochemical studies is often lacking.

In the scientific literature there are many reports on medicinal plants that indicate the presence of phytochemicals with hypoglycemic potential, which may be useful in the treatment of Diabetes mellitus, helping to alleviate symptoms and prevent complications of the disease (Arya et al, 2012, Marmitt, et al, 2015; Oboh et al, 2014). Studies continue to

Revista ARACÊ
ISSN: 2358-2472

expand knowledge about the effects of these plants, based on empirical references (Cecílio et al, 2008). Among these plants, *Luehea divaricata* Mart. stands out.

L. divaricata is a large tree from the Malvaceae family. It has a natural geographic distribution that covers countries in South America, including Argentina, Paraguay, Uruguay and Bolivia (Carvalho, 2008; Tirloni, 2018). In Brazil, the species is found in riparian forest areas, both in waterlogged and/or well-drained soils and in deep and/or stony soils (de Oliveira et al., 2021).

In view of the above, this study addresses the use of *Luehea divaricata* Mart., known as "horse whip", in an Amazonian community in Brazil for the treatment of DM, correlating its benefits to the potential of the species through a bibliographical review of scientific articles considering the following aspects:

(i) Analysis of Bioactive Compounds of the species, such as alkaloids, flavonoids, and terpenoids, which may have hypoglycemic effects.

(ii) laboratory studies (in vitro) that analyzed the effect of the plant on pancreatic or liver cells, evaluating its ability to sensitivity to insulin or protection of pancreatic beta cells;

(iii) animal studies (in vivo) that demonstrate the plant's effectiveness in diabetes models. These studies generally involve administering the plant to diabetic animals and measuring parameters such as blood glucose and insulin levels.

(iv) and assessment of toxicity in animal studies (in vivo), verifying whether there is a need for caution in the use of the species.

We organize this paper as follows. In section 2, we characterize the community where the study took place and how we collected our data. In section 3, we report our results, both from our empirical data and from bibliographic review and in section 4 we conclude with our final remarks.

MATERIALS AND METHOD

STUDY AREA

The Macapazinho community is located in the Amazon region in the rural area of the city of Castanhal, in the state of Pará, Brazil, approximately 17 km away from the municipality's headquarters, located between the geographic coordinates 1°23'17.5"S latitude and 47°58'58.1"W longitude. The climate of the Amazon region is humid tropical, characterized by two well-defined seasons: the dry season, from July to December, with

Revista ARACÊ
ISSN: 2358-2472

rainfall of around 200 mm and maximum temperatures of up to 33°C; and the rainy season, from January to June, with total rainfall of 1500 mm and minimum temperatures of 20°C (Da Silva et al., 2019).

The Amazon region, characterized by its exuberant biodiversity and varied climate, has an immense wealth of plants that have been traditionally used by local populations to treat various illnesses. The choice of this community was motivated by the vast variety of plant species in the Amazon, combined with the traditional knowledge maintained by traditional communities, it constitutes a valuable source of data that can lead to the discovery of little-known medicinal plants and the development of herbal medicines. The abundant Amazonian flora, combined with the deep knowledge of traditional populations, encourage scientific research in this field of study for advances in natural medicine.

Macapazinho is a community formed by remnants of quilombos, made up of approximately 200 families who practice subsistence farming and artisanal fishing. In agricultural cultivation, the community mainly produces cassava (*Manihot esculenta*) and açaí (*Euterpe oleracea*), which are sold at markets in Castanhal. However, a significant portion of residents face economic challenges, with many families living in extreme poverty.

To survive, most residents depend on income transfer programs, such as the Bolsa Família Program and *Seguro Defeso*, which offer financial support to fishermen during critical periods for fishing (Soares et al., 2018). In addition to economic difficulties, the health of residents is a central concern, as they are affected by chronic diseases such as hypertension and diabetes. Limited access to specialized health services and poor infrastructure exacerbates these problems, making dependence on public health programs and the use of traditional knowledge as an alternative treatment essential.

DATA COLLECTION

The study was developed in two stages. The first stage was field research, assessing the usage of *L. divaricata* by a traditional community and the second was a comprehensive bibliographic review. We provide details below.

community access

To conduct the initial data collection in the quilombola community, the "Snowball Sampling" methodology was used (Goodman, 1961), suitable for research with groups that are difficult to access or small in size. The process began with the oldest resident, aged 90,

Revista ARACÊ
ISSN: 2358-2472

who nominated key informants, the community's health care providers. Based on these references, the information network was expanded, covering 40 families (20% of the community). These families confirmed the use of the medicinal plant “horse whip” (*L. divaricata*) in the treatment of diabetes.

free list application

Health caregivers who had extensive knowledge about medicinal plant treatments used in the community were found in the reference network. At this time, the "Free List" technique was applied, which consists of the free listing of plant species used by caregivers, an effective technique in ethnobotanical studies to collect data on local knowledge of medicinal plants (Quinlan, 2005). Among the main species identified, the “horse whip” (*Luehea divaricata*) stood out as a key species in the treatment of diabetes.

survey of methods of preparation and administration of *I. divaricata*

To collect information about the use of the species, a questionnaire was applied to the main local health care providers who used this medicinal plant in the ongoing treatment of diabetes, considering the following aspects: disease it treats, part of the plant used, therapeutic indication, preparation method, dosage, state of usage of the plant, conservation, among others.

The study had technological support through audio recording, on-site observations, in addition to use equipment, such as precision scales (weighing quantity of material), beaker (measuring quantity of water in tea), according to recommendations and techniques from scientific areas related to the project. To collect the data, the general objective of the research was explained, its benefits for science, society and the community, and a free and informed consent form (FICF, in Portuguese “Termo de Consentimento Livre e Esclarecido” (TCLE)) was presented to people who could accept and participate as informants. The project was submitted for consideration by the Ethics Committee of the Institute of Health Sciences of the Federal University of Pará so that it could obtain the decision of approval to carry out the work, being approved according to the ethics committee by CAAE 31443920600000019.

Revista ARACÊ
ISSN: 2358-2472

plant sample collection and taxonomy

A sample of the species was collected containing vegetative structures for later identification of the species. The sample was sent to a microcontrolled drying oven for around 50 minutes in the laboratory and after drying it was identified and deposited in the Medicinal Plant Database (DATAPLAME) confirming that it was indeed *Luehea divaricata*. The plant name was verified with World Flora Online.

review of scientific papers

A bibliographic survey was carried out, with the aim of extracting detailed scientific information about the effects of the plant *Luehea divaricata* on pancreatic cells, its influence on insulin sensitivity, protection of pancreatic beta cells, efficacy in diabetes models, bioactive compounds present and evaluation of toxicity. To ensure the relevance of the data collected, the international databases Scielo, PubMed and Google Scholar were used, chosen for their scope and scientific rigor in indexing relevant and updated articles in the research area.

RESULTS AND DISCUSSION

PREPARATION AND ADMINISTRATION OF NATURAL TREATMENT FOR DIABETES

In Macapazinho, *Luehea divaricata*, popularly known as “horse whip”, is traditionally used to treat diabetes. The part of the plant used is the stem, which is used in dried form. The treatment is administered orally, being prepared by decoction of 2 spoonfuls of stem bark in 1 liter of water. The dosage recommended by all healthcare providers is half a glass daily (Table 1).

Table 1: Preparation data in the Macapazinho quilombola community.

SCIENTIFIC NOMENCLATURE		VERNACULAR
Family	Malvaceae	No mention
Species	*Luehea divaricata* Mart.	Horse whips (Açoita cavalo)
Growth Habit	Tree	The same
Usage Indication	Diabetes	The same
Part Used	Stem bark	Bark
State of Use	Dried	The same
Preparation Method	Decoction	Boiled
Administration Route	Oral	Take as medicine
Daily Administration	Every day before	The same

Revista ARACÊ
ISSN: 2358-2472

SCIENTIFIC NOMENCLATURE		VERNACULAR
Family	Malvaceae	No mention
Species	*Luehea divaricata* Mart.	Horse whips (Açoita cavalo)
	lunch	
Quantity of Stem Bark	Tablespoons of bark	A small handful
Quantity of Water	1 liter	A pot of water
Dosage	½ cup per day (80 mL)	Half a cup
Treatment Duration	10 days for blood glucose normalization	The same
Conservation	One week in the refrigerator	The same

The treatment should be administered daily before lunch, with the expectation of normalization of blood glucose levels after a period of 10 days. The preparation must be kept for a week, during which time users report being able to eat normally without showing symptoms or worsening of the disease.

Understanding the methods of preparation, administration and cultural contexts that involve the use of this vegetable is fundamental to the effectiveness and safety of these therapeutic practices. Therefore, exploring and documenting this knowledge are essential steps to integrate traditional practices with contemporary medicine, thus promoting the health and well-being of traditional communities. These plant resources not only reflect the ancestral and cultural wisdom of these communities, but also offer promising alternatives to conventional treatments.

The presence of health caregivers in the Macapazinho community demonstrates the deep-rooted practice of their cultural traditions, highlighting an intimate connection between human beings and the environment. These women play a crucial role in promoting local health, employing ancestral practices to prevent and treat illnesses. Its techniques include the use of medicinal plants, natural therapies and cultural rituals, fundamental to the identity and sustainability of communities. Furthermore, they serve as mediators between the conventional healthcare system and the local community. Integrating this traditional knowledge can result in more holistic and culturally appropriate health practices, better meeting the needs of local populations (Ghaedi et al, 2017).

Revista ARACÊ
ISSN: 2358-2472

NOMECLATURE OR VERNACULAR NAMES

In Brazil, the names of *L. divaricata* vary according to the species' region of occurrence: Estriveira and Ivitinga (Bahia); horse whip (Goiás); Açoita-cavalo and Ivatingui (Minas Gerais); Açoita-cavalo, Açoite-cavalo, Salta-cavalo and Soita-cavalo (Paraná); Horse whip, Red horse whip (Rio Grande do Sul); Horse whip and Possum bag (State of Rio de Janeiro); Açoita-cavalo, Açoita-cavalos and Pau-de-canga (Santa Catarina); Açoita-horse, Açoita-horse-do-mído, Açoita-cavalos, Açoita-cavalos-blanco, Açoite-cavalo, Estriveira, Ibitinga, Ivantingui, Salta-cavalo and Vatinga (State of São Paulo) (Silva et al., 2021; Tanaka et al., 2005). In other regions of Brazil, it is known as Ibatingui, Pau-de-canga and Caiboti (Batista et al., 2016; Lorenzi, 2002). In the quilombola community of Macapazinho, state of Pará, this plant is also known as "horse whip".

These names, loaded with cultural and practical meanings, play a crucial role in the environmental and cultural conservation of these communities. Each community immersed in its historical, geographic and social context develops its own nomenclature for the plants they use in medicinal practices. The attribution of such names is often permeated by myths and collective health experiences, contributing to the uniqueness of local terminology.

ANALYSIS OF BIOACTIVE COMPOUNDS OF THE SPECIES AND HYPOGLYCEMIC EFFECTS

Studies show bioactive compounds in *L. divaricata* that have anti-inflammatory, analgesic and immunostimulating effects. Rosa et al., (2014) found chemical compounds in the hydroalcoholic extract of the bark of *L. divaricata*, including epicatechin, stigmasterol, lupeol and α, β-amyrin. In the leaves and bark of the plant, tannins, flavonoids and saponins were identified (Vargas et al., 1991), as well as vitexin, maslinic acid and epicatechin (Tanaka et al., 2005). In a phytochemical screening of the leaves, flavonoids, tannins, saponins and mucilage were also found, in addition to smaller amounts of alkaloids, fixed oils, anthocyanidins, carotenoids and polysaccharides (Calixto-Júnior et al., 2016).

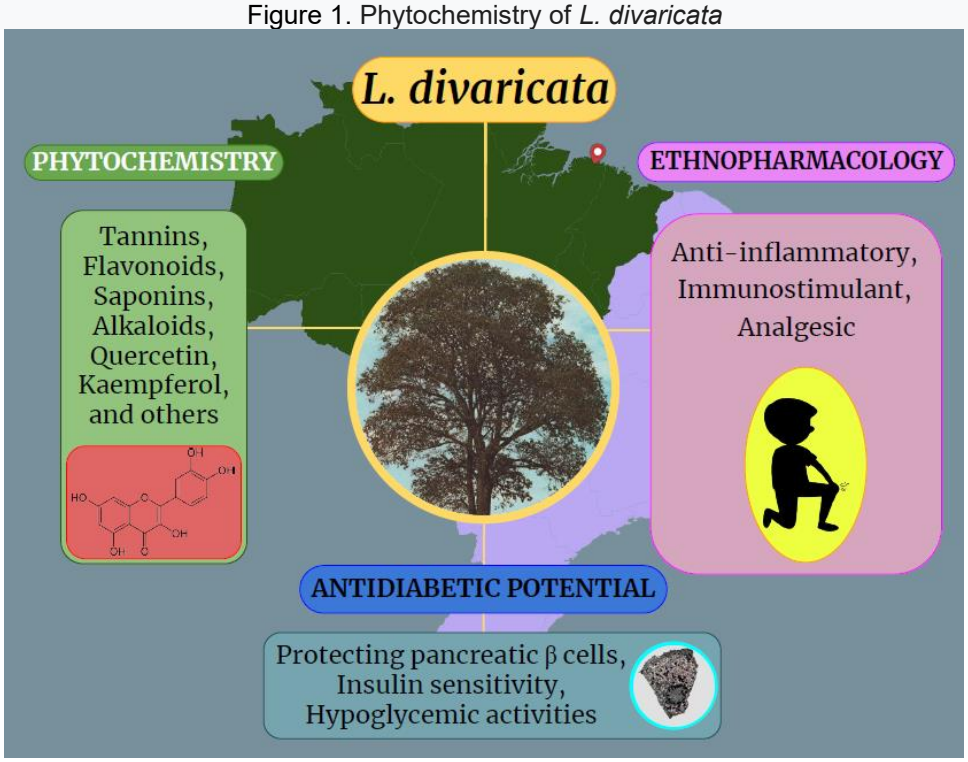
Other studies reveal that samples of *L. divaricata*, collected in the region of Belém do Pará, Brazil, present reducing sugars, proteins, amino acids, tannins, catechins, flavonoids, carotenoids, steroids, triterpenoids and saponins in their leaves (Portal et al., 2013). Furthermore, the alcoholic extract of the leaves contains tannins, saponins and flavonoids, such as quercetin (Figure 1), rutin and vitexin (Lopes, 1990). The study by Arantes et al., (2014), shows that the ethanolic extract of the leaves contains gallic acids, chlorogenic and

Revista ARACÊ
ISSN: 2358-2472

caffeic acids, quercetin, rutin and kaempferol.

Among the active ingredients found in *Luehea divaricata*, quercetin is highlighted as a compound with antidiabetic potential, which consequently makes this molecule a suitable target for future scientific studies. The compound is characterized as an important member of the flavonoid class, and is found in fruits, grains and vegetables that elucidate its functional mechanisms (Chen et al., 2010; Shi et al., 2019).

Figure 1. Phytochemistry of *L. divaricata*



EFFECT OF THE SPECIES ON PANCREATIC CELLS AND THEIR INSULIN SENSITIVITY CAPACITY

Other biologically active compounds such as alkaloids, flavonoids, terpenes, and phenolics demonstrate promising hypoglycemic activities (Bahmani et al., 2014). Studies indicate the potential and control of type 2 DM through certain dietary polyphenols (Kim et al., 2016). These polyphenols include flavonoids, stilbenes, lignans and phenolic acids, with the flavonoids subdivided into flavonols, isoflavones, flavones, anthocyanins, flavonoids and flavanones (Manach et al., 2004).

Another active compound that helps control DM is kaempferol, which when administered orally, demonstrates a reduction in fasting blood glucose and an improvement in insulin resistance (Vinayagam and Xu, 2015). The compound kaempferol has a

Revista ARACÊ
ISSN: 2358-2472

protective effect on pancreatic β cells, its protective action is related to an improvement in cAMP signaling, with inhibition of cell apoptosis (Zhang and Liu, 2011). This is significant as many patients with diabetes manifest loss of β-cell mass and apoptosis, contributing to disease progression (Butler et al., 2003).

ANIMAL STUDIES (IN VIVO) THAT DEMONSTRATE THE PLANT'S EFFECTIVENESS IN DIABETES MODELS

In animal models, research also indicates beneficial effects of quercetin in diabetes. A study carried out with diabetic mice showed hyperglycemic control after consuming a diet containing 0.08% quercetin (Kim et al., 2011). According to Martins and collaborators (2020), the effect of quercetin, considering the blood glucose levels and body weight of Wistar rats, was significant, as the active compound reduced blood glucose levels, and can act to prevent problems cardiovascular and diabetic patients. These findings corroborate the results of the study by Alam et al., (2014), who demonstrated quercetin's ability to reduce insulin resistance and glucose levels in diabetic rats, highlighting its potential as a promising antidiabetic compound.

ASSESSMENT OF TOXICITY IN ANIMAL STUDIES (IN VIVO)

Studies by Bighetti et al., (2004) and Felicio et al., (2011) show some data that point to the low genotoxic and mutagenic potential of the species, as well as the absence of toxicity in mice. Research conducted by Nunes et al., (2015) showed that the crude extract of *L. divaricata* bark did not cause significant toxicity when administered in acute doses, resulting in no mortality or behavioral changes in Wistar rats. However, when administered for a period of 28 days in doses of 200 and 400 mg/kg of crude plant extract, biochemical, histological effects and oxidative processes were observed, indicating the need for caution regarding prolonged use of the plant for therapeutic purposes.

On the other hand, in Argentina, *L. divaricata* is used to treat DM, with "Francisco Alvarez" as its common name in the region (Degen et al., 2005). The vegetable is also used to treat type 2 DM in people affected by the disease, who consult the National Health Center for Diabetes program n° 9 in the municipality of Asunción in Paraguay (Acosta et al., 2018). To date, there are few studies available on the toxicity of *L. divaricata.*

Revista ARACÊ
ISSN: 2358-2472

FINAL REMARKS

When recording the use of *L. divaricata* by the Amazonian community, empirical validation was observed through traditional health practices employed by local caregivers. This convergence between knowledge highlights the need for a holistic approach to treating diabetes, considering both ancestral methods and scientific discoveries.

Based on the bibliographical survey of available studies, the results suggest that *Luehea divaricata* has promising potential in the treatment of DM, mainly due to its bioactive compounds, such as alkaloids, flavonoids, terpenes and phenolics. These components have demonstrated significant hypoglycemic activities, with some studies highlighting the specific role of kaempferol in protecting pancreatic β cells and improving insulin sensitivity.

Furthermore, research in animal models corroborates the therapeutic benefits of the plant, showing beneficial effects in reducing blood glucose and improving metabolic parameters associated with diabetes. The lack of significant toxicity in acute studies suggests a favorable initial safety profile, although further investigation is needed to understand the potential effects of prolonged use of the plant.

Despite the encouraging evidence, it is crucial to conduct additional studies to further evaluate the long-term toxicity and clinical efficacy of *Luehea divaricata* in humans. These efforts are essential to validate its traditional use and explore its potential as a complementary therapy in the management of DM, thus contributing to the development of new therapeutic options based on robust scientific evidence. Furthermore, this plant species represents a significant resource that can contribute to the objectives of the National Program of Medicinal Plants and Phytotherapeutics (PNMPF) in Brazil.

ACKNOWLEDGEDMENTS

G. N. F. Silva gratefully acknowledge Capes (grant number 88887.653217/2021-00) for full financial support. M. E. Pereira gratefully acknowledge CNPq (grant number 140471/2022-7) for full financial support.

Revista ARACÊ
ISSN: 2358-2472

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