

Biological Activities and Chemical Composition of Brazilian Bromeliaceae Species – A Systematic Review

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Abstract: Studies of Bromeliaceae species have demonstrated the presence of a large variety of chemical constituents that have important biological activities such as: antimicrobial, antihelmintic, antinociceptive, antitumor, antiulcer and gastroprotective. Thus, this systematic review reports the studies in the literature about the biological activities and chemical composition of Brazilian Bromeliaceae species. The terms “Bromeliaceae”, “phytochemistry” and “pharmacology” were used to search articles in the databases LILACS, PUBMED, SCIELO, SCIENCE DIRECT and SCOPUS published until January 2016. From a total of 652 studies found, 14 met the inclusion and exclusion criteria and were selected for the research. Moreover, the present review identified 10 chemically defined natural molecules reported in the literature obtained from Brazilian Bromeliaceae species, belonging to the classes of flavonoids, coumaric acid derivatives and sterols. The data reviewed here suggest that there is a large chemical and pharmacological potential in species of Bromeliaceae, which justifies the interest in studying these plants.

Keywords: Bromeliaceae, Phytochemistry, Biological Activities

1. Introduction

The Bromeliaceae family is predominantly neotropical and comprises 58 genera and approximately 3172 species divided into three subfamilies: Pitcairnioideae, Bromeliads Tillandsioideae [1, 2]. It is widely distributed on the American continent, from the states of Virginia and Texas in the southern United States, to central Argentina and Chile, except for a single species of west tropical Africa [3]. About 50% of the known species found in Brazil, that mainly occur in the Atlantic Coastal forest, but they can also be seen in the Amazon region, at Caatinga, Cerrado, Restinga, Campos Rupestres and semiarid regions [4].

Although with this large number of species, the Bromeliaceae family has not been well screened for its chemical constituents. However, there is a considerable amount of identified chemical compounds, which mostly

belong to the class of triterpenoids and flavonoids. Other classes of compounds such as sterols, diterpenoids, cinnamic acid derivatives, substituted glycerols, lignans and nitrogen-containing compounds, among others, have also been identified in this family but to a lesser extent [5, 6]. From a pharmacological point of view also there are few studies in the literature with species of Bromeliaceae. However, a number of studies have shown significant pharmacological properties, such as: antimicrobial [7], antihelmintic [8, 9, 10], antinociceptive [11, 12], antitumoral [13], antioxidant [14], antiulcer [15], and gastroprotective activities [16].

Despite their importance, there are no systematic reviews on the pharmacological activity of Bromeliaceae family. Accordingly, we conducted for the first time a systematic review of the literature to examine and synthesize the literature on chemical composition and pharmacological activity of Brazilian Bromeliaceae species, and then identify

those species that assess pharmacological activity.

2. Materials and Methods

This work was carried out according to the guidelines for Transparent Reporting of Systematic Reviews and Meta-Analyses (PRISMA statement) [17]. The search was conducted in five specialized databases (LILACS, PUBMED, SCIELO, SCIENCE DIRECT and SCOPUS), using different combinations of the following keywords: Bromeliaceae, phytochemistry and pharmacology. The databases were searched for studies conducted in the period up to and including January 2016. All electronic search titles, selected abstracts, and full-text articles were independently reviewed by a minimum of two reviewers (M.P.C. and M.G.S). To resolve disagreements on the inclusion/exclusion of certain studies was agreed consensus among the reviewers. In this systematic review were included studies that investigated the phytochemical and/or pharmacological activities of Brazilian Bromeliaceae species. Studies were excluded according to the following exclusion criteria: review articles, meta-analyses, abstracts, conference proceedings, editorials/letters

and case reports. One of the reviewers was responsible for extracting the data, which were checked by the second reviewer. The information derived from studies were related to the name of Bromeliaceae species investigated, the origin of the species investigated, part of the plant used, the type of preparation, the isolated chemical substance (if any), the tested biological activity and the model used.

3. Results and Discussion

A total of 652 studies were identified for preliminary electronic review. The primary search identified 01 from LILACS, 175 from PUBMED, 05 from SCIELO, 448 from SCIENCE DIRECT and 23 from SCOPUS. After the removal of duplicates and review articles, meta-analyses, abstracts, conference proceedings, editorials/letters and case reports a total of 298 articles was screening for relevant titles and abstracts. Eighty-eight articles were submitted for a full-text review. Fourteen articles met the inclusion and exclusion criteria established. A flow chart illustrating the progress of study selection and number of articles at each stage were performed (Figure 1).

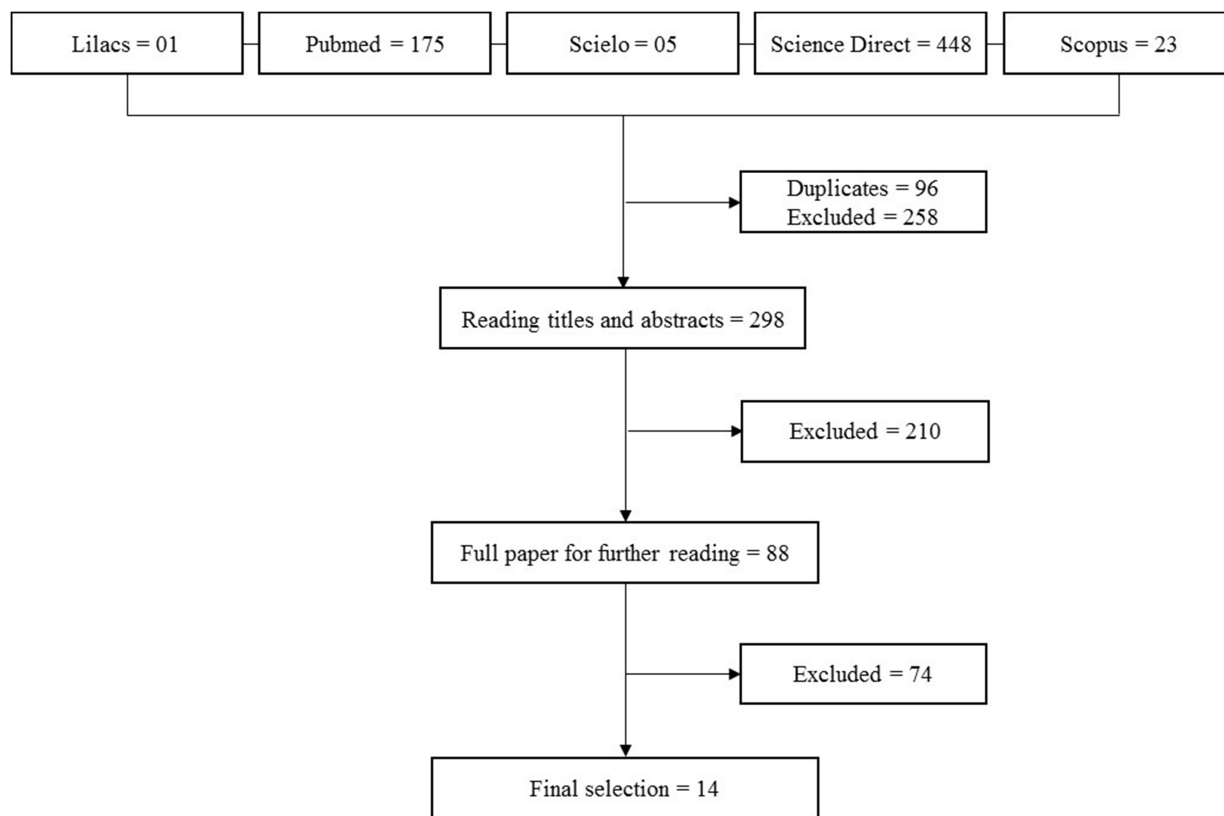


Figure 1. Flowchart of search and selection of studies.

3.1. Pharmacological Activity and Chemical Composition of Crude Plant Extracts and Fractions

In accordance with what can be observed in Table 1, a wide variety of species within the Bromeliaceae family present pharmacological potential, especially the species *Ananas comosus* and *Tillandsia* species genus. The first study found related to this genus was conducted by Costa et al.

[18]. In this study, the seventeen medicinal plants used popularly in Brazil for their reputed analgesic properties were collected in the state of São Paulo and their ethanolic extract was tested in mice by the writhing and tail flick methods. Among the *Tillandsia usneoides*, belonging to Bromeliaceae family, presented a very pronounced effect in the tail flick test.

In a study conducted by Delaporte et al. [19], the crude methanolic extract of the aerial parts of *Tillandsia streptocarpa* was investigated for their acute toxicity using an oral administration in mice and tested for antiedematogenic, antioxidant and antimicrobial activities, through the methods of *Croton* oil-induced ear edema test, 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging and microdilution method, respectively. The methanolic extract and the hexane fraction showed significant ($P < 0.05$) inhibition of ear edema, observed at 2 mg/ear in the *Croton* oil-induced mice ear edema test. In the DPPH free radical scavenging test was observed for the methanolic extract a strong antioxidant effect ($IC_{50} = 0.0056\%$, w/v). The antimicrobial activity assay showed that the crude methanolic extract was inactive against the strains analyzed. However, the methanolic extract of ripe fruits of *Bromelia balansae* was used through the resazurin microtiter assay to measure the biological activity *in vitro* against *Mycobacterium tuberculosis*. The results showed that the extract showed antibacterial activity with moderate effect, displaying a minimal inhibitory concentration of 128 mg/mL [19].

Domingues et al. [9] evaluated the antihelmintic activity of *Ananas comosus* against *Haemonchus contortus* in Santa Inês sheep. The aqueous extract of pineapple skin (AEPS), bromelain from pineapple stems (B4882) and residue from pineapple processing was evaluated *in vitro* and *in vivo* tests. The egg hatch test (EHT) and larval development test (LDT) were performed and the results obtained in the *in vitro* study showed that the aqueous extract was very effective with a dose-dependent inhibitory effect. In the egg hatch test, the LC_{50} and LC_{90} were, respectively, 31 and 81 mg/mL for the aqueous extract, and 0.50 and 2 mg/mL for bromelain. In the larval development test, the LC_{50} and LC_{90} were, respectively, 1.7 and 7.3 mg/mL for the aqueous extract, and 0.019 and 0.086 mg/mL for bromelain.

Six Brazilian Bromeliaceae species was screened for antioxidant activity by assessment of their capacity to scavenge the DPPH radical utilizing a total of twenty different extracts encompassing fruit leaves and rhizomes. According to what was observed in the study, it can be stated that polar rhizome extracts from Bromeliaceae representatives assayed here show better antioxidant results than those from leaves (ANOVA, $P < 0.05$). The best results

were found to rhizome methanolic extracts of the species *Vriesea procera* (EBMRVP) and *Neoregelia cruenta* (EBMRNC). Leaf extracts showed weak to moderate activities. The EBMRVP and EBMRNC are good DPPH radical-scavengers with about 90% of DPPH scavenged under the experimental conditions [20].

Ethanollic extract from the leaves from *Encholirium spectabile* was used for evaluate their antinociceptive effects. The evaluation was carried in mice using chemical and thermal models of nociception. The results showed that ethanollic extract has antinociceptive activity with reduction the number of writhings by 68.59, 79.33 and 65.28%, respectively. Additionally the extract decreased the paw licking time in the first phase, as well in the second phase of the formalin test [11].

In a study conducted by Silva et al. [16], the extracts (methanol [MeOH] and dichloromethane [DCM]) obtained from the leaves of *Ananas ananassoides* were evaluated for their ability to protect the gastric mucosa against injuries caused by necrotizing agents (0.3 M HCl/60% ethanol, absolute ethanol, non-steroidal anti-inflammatory drugs, and pylorus ligation) in mice and rats. The obtained results demonstrated the gastric anti-ulcer activity of the DCM extract. In contrast, the MeOH extract did not show any significant antiulcerogenic activity but presented mutagenic action. Similarly, a study conducted by Carvalho et al. [15] evaluated the antiulcer activity of an ethanollic extract of *Encholirium spectabile* (ES-EtOH) using four experimental models of induced acute gastric ulceration: absolute ethanol-induced gastric ulcer, HCl/ethanol-induced gastric ulcer, ibuprofen-induced gastric ulcer, ischemia and reperfusion-induced gastric ulcer. ES-EtOH (100 mg/kg p.o) protected the gastric mucosa against ulceration that was induced by absolute ethanol (53%), ethanol/HCl (75%), ibuprofen (52%) and ischemia/reperfusion (43%).

These results show the importance of the investigation Bromeliaceae plants with pharmacologic potential. A total of 14 articles in the literature were selected for the investigation of pharmacological activity of various plants of this family. The plants are listed in Table 1 in chronological order of publication years. The botanical name, origin, part used, preparation, biological activity, model and reference are also listed.

Table 1. Plant extracts summary showing pharmacological activity.

Botanical name	Origin	Part used	Preparation	Biological activity	Model	Reference
<i>Tillandsia usneoides</i>	Brazil	—	Ethanollic extract	Analgesic activity	Writhing test, tail flick test	Costa et al. [18]
<i>Tillandsia streptocarpa</i>	Brazil	Aerial parts	Crude methanolic extract	Acute toxicity and antiedematogenic, antioxidant and antimicrobial activities	<i>Croton</i> oil-induced ear edema, DPPH free radical scavenging, microdilution method	Delaporte et al. [19]
<i>Tillandsia streptocarpa</i>	Brazil	Aerial parts	Hexane fraction	Antiedematogenic activity	<i>Croton</i> oil-induced ear edema	Delaporte et al. [19]
<i>Nidularium procerum</i>	Brazil	Leaves	Aqueous extract	Anti-allergic activity	Allergic pleurisy in actively sensitized mice	Vieira-de-Abreu et al. [30]
<i>Nidularium</i>	Brazil	Leaves	Aqueous crude	Anti-inflammatory	Induced pleurisy in mice	Amendoeira et

Botanical name	Origin	Part used	Preparation	Biological activity	Model	Reference
<i>procerum</i>			extract	activity	Writhing test, hyperalgesia, hot plate assay, bradykinin-induced edema, pleurisy	al. [31]
<i>Nidularium procerum</i>	Brazil	Leaves and rhizomes/roots	Methanolic extract	Antinociceptive activity	induced by lipopolysaccharide, cyclooxygenase inhibition assay and toxicological assay	Amendoeira et al. [12]
<i>Ananas ananassoides</i>	Brazil	Leaves	Methanol and dichloromethane extracts	Gastroprotective	Gastric ulcer induced by ethanol	Silva et al. [16]
<i>Bromelia antiacantha</i>	Brazil	Fruits	Aqueous and methanol extracts	Antioxidant activity	Reduction in DPPH	Santos et al. [35]
<i>Ananas bracteatus</i>	Brazil	Leaves and fruits	Hexane extract, methanolic extract	Antiradical activity	DPPH UV spectrophotometric assay	Rocha et al. [20]
<i>Bromelia antiacantha</i>	Brazil	Leaves	Hexane extract, methanolic extract	Antiradical activity	DPPH UV spectrophotometric assay	Rocha et al. [20]
<i>Alcantarea brasiliiana</i>	Brazil	Leaves and rhizomes	Hexane extract, methanolic extract	Antiradical activity	DPPH UV spectrophotometric assay	Rocha et al. [20]
<i>Neoregelia cruenta</i>	Brazil	Leaves and rhizomes	Hexane extract, methanolic extract	Antiradical activity	DPPH UV spectrophotometric assay	Rocha et al. [20]
<i>Pitcairnia flammea</i>	Brazil	Leaves and rhizomes	Hexane extract, methanolic extract	Antiradical activity	DPPH UV spectrophotometric assay	Rocha et al. [20]
<i>Vriesea procera</i>	Brazil	Leaves and rhizomes	Hexane extract, methanolic extract	Antiradical activity	DPPH UV spectrophotometric assay	Rocha et al. [20]
<i>Encholirium spectabile</i>	Brazil	Aerial parts	Ethanolic extract	Antiulcer activity	Induced gastric ulcer in mice and rats	Carvalho et al. [15]
<i>Bromelia balansae</i>	Brazil	Roots, leaves and fruits	Methanolic extract	Antimycobacterial activity	Biological activity <i>in vitro</i> against <i>Mycobacterium tuberculosis</i> by resazurin microtiter assay	Coelho et al. [21]
<i>Bromelia antiacantha</i>	Brazil	Leaves and fruits	Alcoholic extract, hexane, chloroform and ethyl acetate extract	Antimicrobial, cytotoxic, molluscicidal and antioxidant activities	Minimum inhibitory concentrations (MIC), toxicity bioassay, molluscicidal activity assay	Manetti et al. [22]
<i>Encholirium spectabile</i>	Brazil	Leaves	Crude ethanol extract	Antinociceptive activity	Acute toxicity, acetic acid-induced writhing in mice, formalin test, hot plate test and motor coordination test	Lima-Saraiva et al. [11]
<i>Ananas comosus</i>	Brazil	Skins	Aqueous extract	Antihelminthic activity	Egg hatch test (EHT), Larval development test (LDT)	Domingues et al. [9]
<i>Neoglaziovia variegata</i>	Brazil	Leaves and aerial parts	Ethanolic extract	Acaricidal activity	Adult immersion test (AIT)	Dantas et al. [23]

3.2. Isolation and Pharmacological Activity of Chemically Defined Molecules

According to the data shown in the Table 2, it was observed that the Bromeliaceae family is promising for the presence of biomolecules with biological activities, considering the few studies in the literature that are related to Brazilian species. Only three articles were found in the

literature addressing Brazilian species of the Bromeliaceae. In this sense, it is necessary to invest more in research using Brazilian species, in order to know the chemical composition of these and isolate bioactive molecules, and investigate their biological and pharmacological potential. The studies with Brazilian Bromeliaceae species show important activities related to these molecules, such as antibacterial activity, antioxidant activity and acute toxicity activity.

Coelho et al. [21] evaluated the chemical composition of *Bromelia balansae* species, a medicinal plant commonly used in the central region of Brazil as a cough syrup and also eaten roasted. The authors developed a method based on comparative high performance liquid chromatography with diode array detection and ultraviolet analysis to check for the presence of flavonols in the crude methanol extract of fruits, leaves, and roots of *B. balansae*. The chromatography profiles of the methanolic extracts of fruits, leaves, and roots could be established by comparing the retention times and ultraviolet spectra of the peaks with those of isolated compounds from fruit extract. Four flavonols were isolated: kaempferol-3-*O*- α -*L*-rhamnopyranoside, kaempferol-3-*O*- α -*L*-rhamnopyranosyl-(1 \rightarrow 6)- β -*D*-glucopyranoside, quercetin-3-*O*- α -*L*-rhamnopyranosyl-(1 \rightarrow 6)- β -*D*-glucopyranoside and kaempferol 3,7-di-*O*- α -*L*-rhamnopyranoside. The identification of all compounds was achieved by the experimental data (infrared, nuclear magnetic resonance, and mass spectrometry). Their structures were also confirmed by comparing with literature data. The flavonoids, such as flavonols, are widely present in the plant kingdom, being found in almost all fruits and vegetables. However, according to the authors, the occurrence of glycoside flavonols in fruits from *B. balansae* is reported for the first time here in this species and in the genus *Bromelia*. For isolation and identification of *B. balansae* molecules, the authors developed a method based on comparative high performance liquid chromatography with diode array detection and ultraviolet analysis to check for the presence of flavonols in the crude methanol extract of fruits, leaves, and roots of *B. balansae*. The chromatography profiles of the methanolic extracts of fruits, leaves, and roots could be established by comparing the retention times and ultraviolet spectra of the peaks with those of isolated compounds from fruit extract.

Rocha et al. [20] evaluated the chemical composition of *Ananas bracteatus*. The crude methanolic extract of *A. bracteatus* (denominated EMFA) was suspended in H₂O:MeOH solution (6:4) and partitioned with hexane, CH₂Cl₂, EtOAc and BuOH, affording dichloromethane fraction (PDFA), ethyl acetate fraction (PAFA) and butanol

fraction (PBFA). The PAFA was concentrated under reduced pressure affording 3 g of a residue, which was re-dissolved in a CHCl₃:MeOH solution (6:1) and submitted to a liquid-liquid extraction procedure successively with 5% sodium bicarbonate. The purification of the crude methanol extract of the leaves of *A. bracteatus* afforded four metabolites: 2-*O*-feruloyl glyceride, 2-*O*-*p*-coumaroyl glyceride, 5,7,4'-trihydroxy-3,3',5'-trimethoxyflavone and 3-*O*- β -*D*-glucopyranosyl sitosterol. To confirm the identity of the substances, the ¹H and ¹³C NMR techniques and UV spectroscopy were used.

Delaporte et al. [19] investigated the antiedematogenic, antioxidant and antimicrobial activities of the crude methanolic extract of the aerial parts of *Tillandsia streptocarpa*. Also, the antiedematogenic activity of the hexane fraction resulting from the partition of the crude methanolic extract was evaluated. For the isolation of substances, the hexane fraction of the methanolic extract was submitted to a chromatographic column on silica gel, eluting with a mixture of hexane:dichloromethane and dichloromethane:ethyl acetate in increasing polarity, yielding 221 fractions of 7 mL each. After thin layer chromatography (TLC) comparison, fractions with a similar TLC pattern were grouped into 13 sub-fractions. The chemical investigation on the hexane fraction resulted in the isolation of cycloartenol 1,4',5-dihydroxy-3',7-dimethoxyflavanone and a mixture of stigmasterol, β -sitosterol and campesterol. To confirm the identity of the substances, the ¹H and ¹³C NMR techniques were used.

The present review encountered 10 chemically defined natural molecules reported in the literature obtained from Brazilian Bromeliaceae family plants. The active compounds, which have been isolated and identified, belong to the classes of flavonoids (6), coumaric acid derivatives (3) and sterols (1). The compounds are listed in Table 2 in chronological order of publication years. Each entry gives the following informations in sequence: botanical name, origin, part used, chemical substance, class, biological activity, model and reference.

Table 2. Chemically defined molecules and pharmacological activity.

Botanical name	Origin	Part used	Chemical substance	Class	Biological activity	Model	Reference
<i>Tillandsia streptocarpa</i>	Brazil	Aerial parts	Cycloartenol	Sterol	—	Acute toxicity test, antibacterial and antifungal assays and Croton oil-induced ear edema	Delaporte et al. [19]
<i>Tillandsia streptocarpa</i>	Brazil	Aerial parts	4',5-dihydroxy-3',7-	Flavonoid	—	Acute toxicity test, antibacterial and antifungal assays and Croton oil-induced ear edema	Delaporte et al. [19]
<i>Ananas bracteatus</i>	Brazil	Leaves and fruits	2- <i>O</i> -feruloyl glyceride	Ferulic acid derivative	—	Chromatography on Sephadex® LH-20 gel, silica gel 60 and	Rocha et al. [20]

Botanical name	Origin	Part used	Chemical substance	Class	Biological activity	Model	Reference
<i>Ananas bracteatus</i>	Brazil	Leaves and fruits	2- <i>O-p</i> -coumaroyl glyceride	Coumaric acid derivative	—	Amberlite XAD-2, RMN Chromatography on Sephadex® LH-20 gel, silica gel 60 and Amberlite XAD-2, RMN Chromatography on Sephadex® LH-20 gel, silica gel 60 and Amberlite XAD-2, RMN Chromatography on Sephadex® LH-20 gel, silica gel 60 and Amberlite XAD-2, RMN	Rocha et al. [20]
<i>Ananas bracteatus</i>	Brazil	Leaves and fruits	5,7,4'-trihydroxy-3,3',5'-trimethoxyflavone	Flavonoid	—	Amberlite XAD-2, RMN Chromatography on Sephadex® LH-20 gel, silica gel 60 and Amberlite XAD-2, RMN Chromatography on Sephadex® LH-20 gel, silica gel 60 and Amberlite XAD-2, RMN	Rocha et al. [20]
<i>Ananas bracteatus</i>	Brazil	Leaves and fruits	3- <i>O-β-D</i> -glucopyranosyl sitosterol.	Coumaric acid derivative	—	Amberlite XAD-2, RMN Chromatography on Sephadex® LH-20 gel, silica gel 60 and Amberlite XAD-2, RMN	Rocha et al. [20]
<i>Bromelia balansae</i>	Brazil	Roots, leaves and fruits	Kaempferol-3- <i>O-α-L</i> -rhamnopyranoside	Flavonoid	—	Column chromatography by Sephadex, infrared, nuclear magnetic resonance, and mass spectrometry, HPLC.	Coelho et al. [21]
<i>Bromelia balansae</i>	Brazil	Roots, leaves and fruits	Kaempferol-3- <i>O-α-L</i> -rhamnopyranosyl-(1→6)- <i>β-D</i> -glucopyranoside	Flavonoid	—	Column chromatography by Sephadex, infrared, nuclear magnetic resonance, and mass spectrometry, HPLC.	Coelho et al. [21]
<i>Bromelia balansae</i>	Brazil	Roots, leaves and fruits	Quercetin-3- <i>O-α-L</i> -rhamnopyranosyl-(1→6)- <i>β-D</i> -	Flavonoid	—	Column chromatography by Sephadex, infrared, nuclear magnetic resonance, and mass spectrometry, HPLC.	Coelho et al. [21]
<i>Bromelia balansae</i>	Brazil	Roots, leaves and fruits	Kaempferol-3,7-di- <i>O-α-L</i> -rhamnopyranoside	Flavonoid	—	Column chromatography by Sephadex, infrared, nuclear magnetic resonance, and mass spectrometry, HPLC.	Coelho et al. [21]

4. Conclusions

The present study shows the potential of Bromeliaceae family, where several species have been studied for decades with respect to its chemical components and pharmacological activity. As a result, many compounds have been isolated and

identified, representing an advance in the chemistry of natural products. In general, the diversity of biological activities and metabolites observed in Bromeliaceae justify the interest in the study of species of this family, since it has good prospects for research with interesting chemical and pharmacological potential yet to be discovered.

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