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Original Article

Parkia from Cerrado: phytochemical bioprospection, toxicity and *in vitro* bioactivities of bark and flower extracts

Parkia do Cerrado: bioprospecção fitoquímica, toxicidade e bioatividade *in vitro* dos extratos da casca e da flor

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Abstract

Parkia platycephala is the only species of the genus *Parkia* that is endemic to the brazilian Cerrado and the tree symbol of the state of Tocantins, but there are still few studies regarding its bioprospecting. In this study, we aimed to investigate the phytochemical composition, toxicity and bioactivities of the bark and flower of *Parkia platycephala*. Hot sequential extractions (Soxhlet) were performed using methanol and hydroethanolic solution (70%), after degreasing the sample (hexane). The presence of flavonoids, tannins, steroids and alkaloids was detected in the preliminary screening. Trilinolein, (*Z*)-9-octadecenamide, 3-O-methyl-d-glucose were detected by Gas Chromatography coupled to Mass Spectrometry (GC-MS). In the Liquid Chromatography with Diode Array Detector (LC-PDA) analysis, it was detected exclusively ferulic acid (bark) and ellagic acid (flower). The ethanolic extract of the bark (IC_{50}=10.69 ± 0.35 μgmL^{-1}) has an antioxidant potential (DPPH• radical) higher than that of the rutin standard (IC_{50}=15.85 ± 0.08 μgmL^{-1}). All extracts showed excellent anticholinesterase potential (Ellman), with emphasis on the ethanol extract of the flower (IC_{50} =5.34 ± 0.12 μgmL^{-1}). Regarding toxicity (*Artemia salina*), the methanolic extract of the bark and the ethanolic extract of the flower presented high and moderate levels, respectively. Such results limit the concentrations of biological activities in this study, however, the antioxidant and anticholinesterase indices fall short of toxicity. The results demonstrated promising antioxidant and anticholinesterase activities of both the bark and the flower of *Parkia platycephala*.

Keywords: anticholinesterase, antioxidant, *Artemia salina*, chromatography, fava de bolota.

Resumo

A *Parkia platycephala* é a única espécie do gênero *Parkia,* endêmica do Cerrado brasileiro e a árvore símbolo do estado do Tocantins, porém ainda com pouco estudos com relação a sua bioprospecção. Neste estudo, objetivamos realizar a caracterização fitoquímica, avaliar a toxicidade e as atividades antioxidante e anticolinesterásica dos extratos da casca e da flor da *Parkia platycephala.* Foram realizadas extrações sequenciais a quente (Soxhlet), utilizando hexano, metanol e solução hidroetanólica (70%). A presença de flavonoides, taninos, esteroides e alcaloides foi detectada na triagem preliminar. A análise por Cromatografia Gasosa acoplada a Espectrometria de Massa (GC-MS) indicou a presença de variados compostos, tais como trilinoleina, (*Z*)-9-octadecenamida, 3-O-methyl-*d*-glucose e methylsulfinyl(methylthio)-methane. Na análise por Cromatografia Líquida com Detector de Arranjo de Diodo (LC-PDA), destacam-se o ácido elágico, presente apenas nos extratos da flor, e o ácido ferúlico, presente apenas nos extratos da casca. Os extratos da casca predominaram quanto ao potencial antioxidante (radical DPPH•), sendo que o extrato etanólico (IC_{50}=10,69 ± 0,35 μgmL^{-1}) superou o padrão rutina (IC_{50}=15,85 ± 0,08 μgmL^{-1}). Todos os extratos apresentaram excelentes potenciais anticolinesterásicos (teste de Ellman), com ênfase no extrato etanólico da flor (IC_{50}=5,34 ± 0,12 μgmL^{-1}). Em relação à toxicidade (*Artemia salina)*, o extrato metanólico da casca e o extrato etanólico da flor, apresentaram níveis elevado e moderado, respectivamente. Tais resultados limitam as concentrações das atividades biológicas deste estudo, entretanto, os índices antioxidante e anticolinesterásico ficam aquém da toxicidade. Os resultados mostraram as promissoras atividades antioxidante e anticolinesterásica da casca e flor da *Parkia platycephala.*

Palavras-chave: anticolinesterase, antioxidante, *Artemia salina*, cromatografia, fava de bolota.

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1. Introduction

The species *Parkia platycephala* (*P. platycephala*), popularly called *fava de bolota* or *faveira* belongs to the *Fabaceae* family. It is an endemic species of the Brazilian Cerrado, defined as *Parkia* do Cerrado (Hopkins, 1986). Its bark and flowers have the characteristics of plants that can withstand adversity, such as the Cerrado species. It has thick, suberous and fire-resistant bark, blooms in the middle of the dry season, and has inflorescences in purple spherical chapters that hang from long peduncles (Carvalho, 2014).

The *Parkia* genus has a collection of 35 species distributed throughout the Neotropics, Asia and Africa, of which 12 species have medicinal studies, including *P. platycephala* (Saleh et al., 2021). Studies have always referred to leaves and seeds in literature on the gastroprotective, anti-inflammatory, and antimicrobial effects of the *P. platycephala* species (Silva et al., 2019; Fernandes et al., 2010).

Although some studies had already emphasized the bioprospecting of the bark and flower of species in the *Parkia* genus (Fernandes et al., 2022; Ralte et al., 2022; Silva et al., 2010), none reported the potential antioxidant and anticholinesterase properties of the sequential extracts (methanolic and ethanolic) obtained after hexane degreasing.

In addition to certain parameters, such as the methodology and solvents used (Santos et al., 2021), soil-climate conditions, and the growth rate of the species (Marinho et al., 2022), can influence the characterization and quantification of metabolites present in a biological system. This brings new perspectives to studies related to the bioactivities of species (Pilon et al., 2020).

Currently, there is no analytical technique capable of measuring all metabolites in a single experiment (Pilon et al., 2020), so it is necessary to build libraries of extracts from biodiversity (Almeida et al., 2022; Lowell et al., 2015). Thus, according to Bajkacz and Adamek (2017), organic solvent extractions are still the best choice for extraction and detection of these metabolites due to their efficiency and compatibility with the main analytical platforms, such as chromatography.

According to Mushtaq et al. (2014), when conducting an indiscriminate search for metabolic profiles, the methanol solvent or methanol-water mixture is widely used due to its lower selectivity in extracting a variety of metabolites such as sugars, organic acids, alkaloids, and phenolic compounds, among others. Another possibility in terms of metabolite profile is the sequential use of solvents with increasing polarity, resulting in an increase in the concentration of different metabolic classes (Costa, unpublished 2021).

In addition to the variability of secondary metabolite extractions, both toxicity bioassays and *in vitro* tests evaluating different biological activities are required to understand the effects of plant extracts (Moura et al., 2012). Typically, the first evaluation of a plant extract is to check its antioxidant capacity, that is, its potential to inhibit reactive species. Although necessary, these species in excess attack other stable compounds, triggering oxidative reactions that are directly related to various diseases (Otaegui-Arrazola et al., 2014).

One of these diseases is Alzheimer's disease (AD), whose treatment is based on the inhibition of the enzyme acetylcholinesterase (AChE), a role that has been occupied by natural compounds (Vecchio et al., 2021). In addition, the antitumor activity of plant extracts can also be suggested based on their positive toxicity against *Artemia salina*, aiming at prospecting for antineoplastic drugs (Gatto et al., 2020).

Thus, the objective of this study was to perform phytochemical bioprospecting, to determine the antioxidant and anticholinesterase activities and to determine the toxicity of extracts from the bark and flower of the *Parkia platycephala* species.

2. Material and Methods

2.1. Collection and preparation

The bark and flower samples of *Parkia platycephala* were collected in the city of Palmas-TO, at the Federal University of Tocantins (UFT), Campus Palmas (10°10'55" S and 48°21'45" W). They were registered and incorporated into the UFT Herbarium under number HTO 12007 and the project is registered with the National Genetic Heritage Management System (SISGEN) under number A06B860. The samples underwent drying at 60 ºC for 48 hours, sprayed with a knife mill, and were stored in closed glass bottles in a light-free environment.

2.2. Extraction

The pulverized samples underwent a degreasing process followed by sequential hot extraction in a soxhlet apparatus. Initially, 10 g of each sample was decreased using the organic solvent hexane (400 mL), during 5 h of reflux. After 12 h of natural drying in an exhaust hood, each sample underwent a second extraction using the organic solvent methanol for 5 h of reflux, obtaining the bark methanolic extracts (BME) and the flower methanolic extracts (FME). Again, each sample was dried for 12 h, followed by the last extraction with hydroethanolic solution (70%), obtaining the bark ethanolic extracts (BEE) and the flower ethanolic extracts (FEE).

2.3. Phytochemical bioprospecting

2.3.1. Phytochemical screening

The qualitative identification of classes of secondary metabolites was performed through analyses based on precipitation and/or color reactions, with specific reagents for flavonoids, tannins, phytosterols/terpenoids, quinones, saponins and alkaloids (Saraiva et al., 2018; Simões et al., 2017; Matos, 2009).

2.3.2. Characterization by Liquid Chromatography with Diode Array Detection (LC-PDA)

The analysis followed the methodology described by Fernandes et al. (2022), in which the extracts were

solubilized in water:methanol (8:2, v:v) and evaluated in an analytical LC column (LC-6AD Shimadzu, Kyoto, Japan) with the aid of a photodiode detector system (PDA) that was monitored between wavelengths λ = 200-800 nm and a temperature of 25 ºC. Standards (Sigma, St. Louis, MO) of caffeic acid, ellagic acid, vanillic acid, sinapic acid, ferulic acid and gallic acid, rutin, luteolin, apigenin, naringin, kaempferol and quercetin were used prepared in methanol-water at the concentration of 1000 μgmL^{-1}. Both patterns were easily identified and quantified based on their absorption spectra in the UV region and retention time. The patterns found in the extracts were unambiguously identified by performing co-injection experiments in which aliquots of the extracts and standards were mixed and diluted to a known volume and analyzed by LC. Calibration curves were determined by linear regression (with 10 concentration ranges) using LC. The average standard errors for the peak areas of replicated injections (n = 5) were less than 2%, showing a good repeatability of the calibration curve, which obtained as coefficients of determination (r^2) 0.9994 for caffeic acid (Y= 0.004+ 2.23x10^{-5} X), ellagic acid (Y= 0.006 + 2.74x10^{-5} X), ferulic acid (Y= 0.006+ 1.67x10^{-5} X) and gallic acid (Y= 0.007 + 1.41x10^{-5} X) and r^2 = 0.9996 for naringin (Y= 0.008 + 2.11 10^{-3} X) and kaempferol (Y= 0.003 + 1.98x10^{-3} X).

2.3.3. Characterization by Gas Chromatography Coupled to Mass Spectrometry (GC-MS)

The extracts were analyzed by GC-MS using a Shimadzu® model QP2020 Ultra chromatograph equipped with a ZB-5HT column (30 m long x 0.25 mm internal diameter x 0.25 μm film thickness). The analyses were carried out under the following conditions: heating at 50 °C for 1 min, until reaching 320 °C in 35 min. Injection temperature: 320 °C; Interface temperature: 320 °C; Carrier gas (Helium): 1 mLmin^{-1}; The electron energy was 70 eV and the temperature of the ion source was 320 °C; scan mode. 1 μL of each extract was injected, in which the constituents were identified by comparison with the mass spectra of the NIST 14 library.

2.4. In vitro bioactivities

2.4.1. Antioxidant activity

The determination of antioxidant power followed the descriptions by Peixoto-Sobrinho et al. (2011) with some modifications. The antioxidant capacity was measured by the elimination of the stable free radical 2,2-diphenyl-1-picrylhydrazyl (DPPH• radical) using the rutin pattern as a positive control. In triplicate, 0.5 mL of different concentrations of extracts or standards (10; 30; 70; 130; 200 μgmL^{-1}, p.v^{-1}) were added to 3 mL to methanolic solution of DPPH• radical (40 μgmL^{-1}, p.v^{-1}). The blank was constructed by replacing DPPH• with methanol in the reaction medium. The reaction complex and the blank were shaken and kept for 30 minutes protected from light, and the absorbances were measured at 517 nm in a spectrophotometer calibrated with methanol. The absorbance of the DPPH• radical solution at 40 μgmL^{-1} was also measured and used as a negative control. The free radical scavenging activity or antioxidant activity (AA) was expressed as the percentage of inhibition determined by the Equation 1:

$$AA\ (\%) = \left[Ac - \left(Aa - Ab / Ac \right) \right] x\ 100 \quad (1)$$

where AA (%) is the percentage of antioxidant activity; Ac, the absorbance of the negative control; Aa, the absorbance of the sample; Ab, the absorbance of the blank. The IC_{50} (μgmL^{-1}) was obtained using the calibration curves obtained by plotting the different concentrations in relation to AA%, using the Graphpad Prism 9 program by non-linear regression (Graphpad Prism, 2020).

2.4.2. Anticholinesterase activity

The potential of acetylcholinesterase inhibition (iAChE) was determined using a 96-well plate assay, as described by Ellman et al. (1961). The following solutions were used per well: 25 μL of acetylthiocholine iodide (15 mM), 125 μL of 5.5'-dithiobis-[2-nitrobenzoic] in the Tris/HCl solution (50nM, pH = 8, with 0.1 M of NaCl and 0.02 M of $MgCl_2.6H_2O$. (3 mM, DTNB or Ellman's reagent)), 50 μL of the Tris/HCl solution (50 nM, pH = 8, with 0.1% bovine serum albumin (BSA)), 25 μL of the extract sample dissolved in DMSO (1%) and diluted 10 times in Tris/HCl solution (50 mM, pH = 8) to obtain a final concentration of 0.2 mg/mL (Rhee et al. 2001; Trevisan et al., 2003). The absorbance was measured at 405 nm for 30 seconds. Then, 25 μL of the enzyme acetylcholinesterase (0.25 U.mL^{-1}) was added and the absorbance was measured once per minute for a total of 25 minutes of incubation of the enzyme. As a negative standard, all solutions were used except for the sample. The dilutions of the samples and the positive standards used in the quantitative evaluations in microplate, starting from a stock solution with a concentration of 2 mgmL^{-1} were: 200; 100; 50; 25; 12.5; 6.25; 3.12; 1.56 and 0.78 μgmL^{-1}. All samples were analyzed in triplicate. The values referring to the natural colorins of the extracts were extinguished from the analysis. The percentage of inhibition of acetylcholinesterase was calculated by comparing the reaction rates (substrate hydrolysis) of the samples in relation to the blank (considered total AChE activity, 100%). The standard used as a positive control was physostigmine (eserine).

2.5. Toxicity with Artemia salina

Toxicity analysis was performed using the method with *A. Salina* according to the methodology of Meyer et al. (1982), with adaptations. Initially, the eggs of *A. Salina* were prepared for hatching of the nauplii after 24 hours of exposure to artificial light (60W incandescent lamp) by dissolving 0.1g of the eggs in 1 L of saline solution at 3%, with salt synthetic marine and pH adjusted between 8 to 9 (with 1 M sodium carbonate).

After the hatching of the nauplii, test tubes were prepared in triplicate with 5 mL of the extracts (BME, BEE, FME, FEE) diluted in DMSO (1%) saline solution. The tests were carried out with various concentrations (4; 200; 1,000; 4,000 μgmL^{-1}), and for the control group only DMSO (1%) solution diluted in saline (3%) was used. All samples were

adjusted to a pH of 8 to 9. After a period of 24 hours, the number of immobile nauplii was counted and the percentage of mortality was determined from which the IC_{50} of each extract was determined using the Graphpad Prism 9 program by non-linear regression. The classification of extracts followed the criteria established by Nguta et al. (2011), who defined extracts with IC_{50} values < 100 μgmL^{-1} as highly toxic, 100 < IC_{50} < 500 μgmL^{-1} as moderately toxic, 500 < IC_{50} < 1,000 μgmL^{-1} as low toxic and IC_{50} > 1,000 μgmL^{-1} as non-toxic. The IC_{50} was determined using the Graphpad Prism 9 program, by non-linear regression.

2.6. Statistical analysis

The content of chemical characterization (quintuplicate), toxicity (triplicate) and biological activities (triplicate) are presented as mean ± standard deviation (SD) of the determination. Analysis of variance (ANOVA) and Tukey's test were used to identify significant differences between means ($p < 0.05$).

3. Results

3.1. Phytochemical analysis

3.1.1. Phytochemical screening

The analysis of the metabolite classes of the bark and flower extracts of *P. platycephala* revealed the presence of flavonoids, tannins, phytosterols and/or triterpenoids in both extracts, however, alkaloids were detected only in the BME (Table 1).

3.1.2. Profile of active compounds using GC-MS

In the GC-MS analysis, the chromatograms of the extracts of the bark (Figure 1) and the flower (Figure 2) of *P. platycephala* obtained by sequential extraction indicated by similarity the presence of 20 compounds. The compounds that presented the highest percentage of area are shown in Table 2.

3.1.3. Profiling active compounds using LC-PDA

LC-PDA analysis of the bark and flower extracts of *P. platycephala* revealed the presence of four phenolic compounds (gallic acid, ellagic acid, caffeic acid and ferulic acid and two flavonoids (kaempferol and naringin) (Table 3).

Table 1. Chemical tests for class of phytochemical compounds of bark and flower extracts of *P. platycephala* obtained by sequential extraction (BME - bark methanolic extract; BEE - bark ethanolic extract; FME – flower methanolic extract; FEE - flower ethanolic extract).

Metabolite	BME	BEE	FME	FEE
Flavonoids	+	+	+	+
Tannins	+	+	+	+
Phytosterols / Triterpenoids	+	+	+	+
Quinones	-	-	-	-
Saponins	-	-	-	-
Alkaloids	+	-	-	-

+ presence: - absence.

3.2. Antioxidant and anticholinesterase activities

The determination of the *in vitro* antioxidant and anticholinesterase potential of the extracts of the bark and flower of *P. platycephala* are shown in Table 4. For the antioxidant analysis with the DPPH•, the IC_{50} values obtained were between 10.69 ± 0.35 and 38.67 ± 0.66 μgmL^{-1}, and for the anticholinesterase analysis, the values were between 5.34 ± 0.12 and 18.82 ± 0.01 μgmL^{-1}.

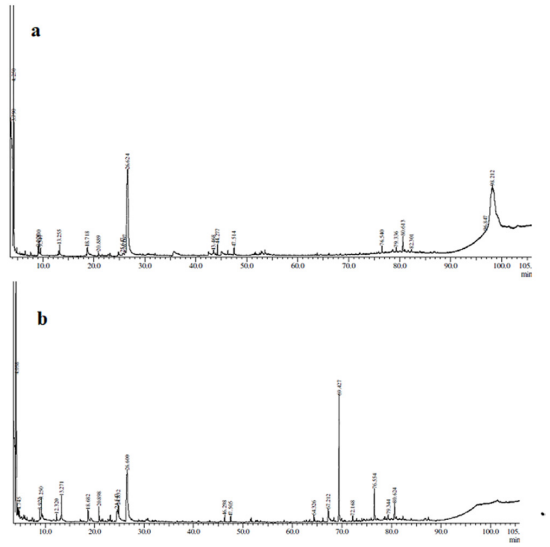

Figure 1. GC-MS analysis: chromatogram of extracts from the bark of *P. platycephala*: (a) BME - bark methanolic extract, (b) BEE - bark ethanolic extract.

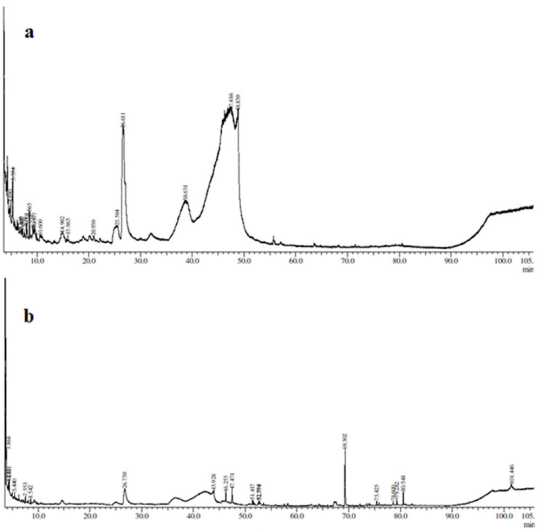

Figure 2. GC-MS analysis: chromatogram of extracts from the flower of *P. platycephala*: (a) FME – flower methanolic extract, (b) FEE – flower ethanolic extract.

Table 2. Main chemical constituents identified by GC-MS in *Parkia platycephala* extracts obtained by sequential extraction (BME - bark methanolic extract; BEE - bark ethanolic extract; FME - flower methanolic extract; FEE - flower ethanolic extract).

RT (min)	Compound	Peak area (%)			
		BME	BEE	FME	FEE
3.745 - 4.250	(methylsulfinyl)(methylthio)-methane	12.00	26.41	-	40.53
3.868	acetic acid	-	-	-	3.85
4.232	2-propenoic acid	-	-	-	1.21
4.401	n-Propyl acetate	-	-	-	2.74
5.440	furfural	-	-	0.77	0.86
18. 682 - 18.718	catechol	1.55	2.05	-	-
26.600 - 26.624	1,2,3-benzenetriol	27.07	22.56	10.05	18.01
38.631	ethyl alpha-d-glucopyranoside	-	-	5.24	-
43.928 - 47.486	3-O-methyl-d-glucose	-	-	63.78	1.70
47.471 - 47.514	n-hexadecanoic acid	0.65	0.68	-	3.09
69.427	(Z)-9-octadecenamide	-	20.02	-	12.02
76.554	octacosanol	-	4.50	-	-
79.282 - 79.336	stigmasterol	0.38	0.64	-	1.68
80.548 - 80.624	γ-sitosterol	1.65	2.71	-	3.60
82.301	lupeol	0.41	-	-	-
98.212	trilinolein	47.20	-	-	-
101.446	E,E,Z-1,3,12-nonadecatriene-5,14-diol	-	-	-	2.01

RT: retetion time.

Table 3. Active compounds identified by LC-PDA in bark and flower extracts of *P. platycephala* obtained by sequential extraction (BME - bark methanolic extract; BEE - bark ethanolic extract; FME - flower methanolic extract; FEE - flower ethanolic extract).

	Concentration (mgg^{-1})			
Compound	BME	BEE	FME	FEE
Gallic acid	132.4 ± 0.7^{Bb}	81.4 ± 0.3^{Db}	163.6 ± 1.2^{Aa}	90.1 ± 0.7^{Ca}
Ellagic acid	-	-	110.1 ± 0.8^{Ab}	73.4 ± 0.5^{Bb}
Cafeic acid	105.7 ± 0.8^{Ac}	78.7 ± 0.2^{Bc}	-	-
Ferulic acid	161.3 ± 0.7^{Aa}	88.8 ± 0.2^{Ba}	-	-
Kaempferol	74.9 ± 0.4^{Ae}	41.2 ± 0.1^{Ce}	64.4 ± 0.4^{Bd}	37.2 ± 0.1^{Dd}
Naringin	84.7 ± 0.4^{Ad}	44.9 ± 0.1^{Cd}	77.1 ± 0.5^{Bc}	41.9 ± 0.1^{Dc}

Values represent the mean followed by the standard deviation (mean ± SD). Different superscript lowercase letters between lines indicate no significant similarities, and different superscript capital letters between column indicate no significant similarities ($p < 0.05$, ANOVA followed by Tukey's test).

Table 4. Antioxidant potential (DPPH•) and acetylcholinesterase inhibitory (iAChE) activity of *P. platycephala* bark and flower extracts obtained by sequential extraction (BME - bark methanolic extract; BEE - bark ethanolic extract; FME - flower methanolic extract; FEE - flower ethanolic extract; RUT - rutin control and PHY- physostigmine control).

Extract	DPPH• *	iAChE **
	(IC_{50})	(IC_{50})
	μgmL^{-1}	μgmL^{-1}
BME	15.83 ± 0.45^{b}	18.82 ± 0.01^{e}
BEE	10.69 ± 0.35^{a}	12.86 ± 0.21^{d}
FME	24.98 ± 0.25^{c}	9.44 ± 0.40^{c}
FEE	38.67 ± 0.66^{e}	5.34 ± 0.12^{b}
RUT	15.85 ± 0.08^{b}	-
PHY	-	1.15 ± 0.05^{a}

*Concentrations of extracts or standards (10 – 200 μgmL^{-1}, p/v); **Concentrations of extracts or standards (0.78 – 200 μgmL^{-1}, p/v). Values represent the mean followed by the standard deviation (mean ± SD). Different superscript lowercase letters between lines indicate no significant similarities ($p < 0.05$, ANOVA followed by Tukey's test).

3.3. Toxicity Artemia salina

Table 5 shows the results of the bioassay with *A. salina* evaluating the extracts of the bark and flower of *P. platycephala* obtained by sequential extraction. The IC_{50} values obtained were between 31.31 ± 4.80 and 630.00 ± 0.01 μgmL^{-1}, indicating high and low levels of toxicity among the extracts.

4. Discussion

In the results found in the phytochemical screening, the influence of polarity on extraction of *P. platycephala* bark was observed. The detection of alkaloids was only positive using methanol solvent (BME).

Regarding methodology and collection area, Silva et al. (2010) analyzed ethanol extracts from the bark of *P. platycephala* obtained by hot extraction (water bath) collected in the state of Maranhão (Cerrado biome). They did not detect the presence of phytosterols, triterpenoids, or tannins in the analyzed extract, a divergent result of this research.

For the flower extracts, as well as the presence of flavonoids, tannins, saponins and terpenoids being detected in this study, there are also reports of these compounds in the methanolic extract of the Indian *Parkia timoriana* species, obtained by a single hot (Soxhlet) extraction (Ralte et al., 2022). However, the single extraction in this study also revealed the presence of alkaloids (Ralte et al., 2022).

Through these data, it was once again found that the geographical location of the plant influences the production of metabolites and can consequently generate cultural particularities about their use (Castro and Léda, 2021).

Analysis by GC-MS of extracts from the bark and flower of *P. platycephala* indicated the presence of stigmasterol, γ-stigmasterol, and lupeol, confirming the presence of phytosteroids and/or triterpenoids according to phytochemical screening.

In the FME extract (Table 2), a high percentage of the compound 3-O-methyl-d-glucose (60%) was observed. In addition, the ethyl alpha-d-glucopyranoside (5.4%) was identified exclusively in this extract. Regarding the flower extracts of *P. platycephala,* only in the FEE, the compounds: acetic acid, propenoic acid, propyl acetate and E,E,Z-1,3,12-nonadecatriene-5,14-diol were detected.

In the bark extracts, the compounds trilinolein (47.2%) and (Z)-9-octadecenamide (20%) stood out with high concentrations in BME and BEE, respectively. In addition, (methylsulfinyl)(methylthio)-methane and catechol compounds were detected in both extracts. The compound octacosanol was identified only in BEE. No other studies of chemical characterization by gas chromatography related to bark and flower extracts of the genus *Parkia* were detected.

In the analysis by LC-PDA, the compounds gallic acid, naringin, and kaempferol were detected in the four extracts of *P. platycephala*. Ellagic acid was detected only in flower extracts (FME and FEE), while caffeic and ferulic acids were detected only in bark extracts (BME and BEE). Such characteristics were also verified in the crude extracts (bark and flower) of *P. platycephala,* obtained by hot extraction with ethanol (70%), without the degreasing process (Fernandes et al., 2022).

Studies with the flower methanolic extract of another *Parkia* species, *Parkia roxburghii*, confirmed the presence of gallic and ellagic acids in this genus (Dubey et al., 2020). Characterization studies by liquid chromatography were not detected for extracts of the bark and flower of the genus *Parkia*.

The major contents of all compounds were detected in the methanolic extracts. In the FME, gallic acid (163.6 ± 1.2 mgg^{-1}) and ellagic acid (110.1 ± 0.8 mgg^{-1}) were observed. In the BME, other compounds were found, such as caffeic acid (105.7 ± 0.8 mgg^{-1}), ferulic acid (161.3 ± 0.7 mgg^{-1}), naringin (84.7 ± 0.4 mgg^{-1}) and kaempferol (74.9 ± 0.4 mgg^{-1}).

When comparing the results of this study with the crude extracts (70% ethanol extraction), without the degreasing process, of the flower and bark of *P. platycephala* published by Fernandes et al. (2022), we observed that the flower extract continues to present major levels of gallic acid and ellagic acid, as well as the bark extract has major levels of the other compounds. However, it is possible to observe that the methodology used had a direct influence on the results obtained, especially in relation to the concentrations of phenolic acids. There was a reduction of approximately 17% in the concentration of gallic acid (BME) when compared to the crude extract (Fernandes et al., 2022).

In the analysis of the antioxidant activity of extracts from *P. platycephala* flower, obtained by sequential extraction, the result was superior for the FME (IC_{50} = 24.98 ± 0.25 μgmL^{-1}) to that obtained for the crude extract, with 70% ethanolic solution (IC_{50} = 35.45 ± 1.36 μgmL^{-1}) (Fernandes et al., 2022).

Dubey et al. (2020) analyzed the antioxidant activity of the methanolic extract of the Indian *Parkia roxburghii* flower, and observed an IC_{50} value = 68,000 ± 0.004 μgmL^{-1}, while Ralte et al. (2022) obtained an approximate value for the methanolic extract of the Indian *Parkia timoriana* flower (IC_{50} = 70.05 ± 0.07 μgmL^{-1}).

Also analyzing the antioxidant activity of *P. platycephala*, excellent potential was observed in the bark extracts, with the BEE (IC_{50} = 10.69 ± 0.35 μgmL^{-1}) having a DPPH• radical inhibitory capacity superior to that of the rutin standard (IC_{50} = 15.85 ± 0.08 μgmL^{-1}) and the BME (IC_{50} =15.83 ± 0.45 μgmL^{-1}) having significantly similar capacity to the same standard.

Comparing the result of the BEE obtained in this study with the result presented by Fernandes et al. (2022), for extract obtained by 70% hydroethanolic extraction (raw

Table 5. Toxicity and 50% lethal concentration (IC_{50}) of *P. platycephala* bark and flower extracts by *Artemia salina* test.

Extract ***	IC_{50} (μgmL^{-1})	Toxicity #
BME	31.31 ± 4.80	high
BEE	630.00 ± 0.01	low
FME	597.60 ± 0.01	low
FEE	252.50 ± 0.01	moderate

*** Concentrations of extracts (4 - 4,000 μgmL^{-1}, p/v); # IC_{50} values < 100 μgmL^{-1} as highly toxic; 100 < IC_{50} < 500 μgmL^{-1} as moderately toxic; 500 < IC_{50} < 1,000 μgmL^{-1} as low toxic.

extract) (IC_{50} = 14.72 ± 0.13 μgmL^{-1}), it was observed that the methodology used in this study presented better DPPH• radical inhibition rate.

Tala et al. (2013) evaluated the antioxidant activity of Brazilian *Parkia biglobosa* bark through an extraction with dichloromethane-methanol (1:1, v:v) macerated at room temperature and its aqueous and ethyl acetate fractions. Of these three extracts, the aqueous fraction of the bark showed the best antioxidant activity, with an IC_{50} of 37.1 ± 0.1 μgmL^{-1}, significantly lower than the antioxidant results obtained in this study.

The expressive antioxidant capacity of the bark of *P. platycephala* can be attributed to some compounds such as: (Z)-9-octadecenamide and octacosanol, are present in BEE, trilinolein is present in BME, and ferulic acid, caffeic acid, and 1,2,3-benzenetriol are present in both extracts.

Anwer et al. (2022) asserted that (*Z*)-9-octadecenamide is one of the representatives of fatty acids with relevant antioxidant capacity. Recent studies corroborate this perception (Emre and Kursat, 2022) through the application of bioinformatics methods aimed at predicting the pharmacokinetics of (*Z*)-9-octadecenamide. Due to its modular capacity, it demonstrates a significant probability of binding to various targets, including enzymes, receptors, and transcription factors, with important effects in the treatment of oxidative stress (Fatoki et al., 2021).

Octacosanol is a natural compound with several biological effects including antioxidant, anti-inflammatory and antiparkinson properties (Zhou et al., 2022; Oliveira et al., 2012; Wang et al., 2010). Harrabi et al. (2018) reported the high relationship between the natural compound policosanol (75% octacosanol) and the antioxidant capacity of the DPPH• radical.

The compound 1,2,3-benzenetriol, among phenolic antioxidants, is one of the most effective in breaking chain reactions of free radicals (Saluja et al., 2016). Additionally, 1,2,3-benzenetriol acts as a pro-oxidant due to its ability to undergo auto-oxidation in aqueous or alkaline environments, forming superoxide radicals, hydrogen peroxide, and hydroxyl radicals (Omoruyi et al., 2020). It was through this mechanism of auto-oxidation of 1,2,3-benzenetriol that a superoxide scavenging assay was developed to analyze certain antioxidants with reliability and low cost (Zhang et al., 2016; Ramasarma et al., 2015; Li, 2012).

Trilinolein is commonly used in traditional Chinese medicine. Its antioxidant power neutralizes free radical damage associated with atherogenesis, and it is associated with benefits in the treatment of circulatory disorders (Chan et al., 2002).

According to Table 3, among the compounds detected by LC-PDA, ferulic acid was the major compound in the bark extracts. The relationship between the presence of ferulic acid and high potential antioxidants is common in the literature (Lima et al., 2024; Ayna et al., 2020; Paiva et al., 2013). In this context, there are also reports about the antioxidant capacity of caffeic acid, with an effect mainly on reactive nitrogen species (Combet et al., 2010; D'ischia, 2005), which contribute to the etiology of neurological disorders, including ischemic stroke and neurodegeneration (Lee et al., 2016).

Unlike the antioxidants, extracts from the bark of *P. platycephala* showed lower anticholinesterase potentials compared to extracts from the flower. Among the four extracts tested, FEE had the highest acetylcholinesterase inhibition power (IC_{50} = 5.34 ± 0.12 μgmL^{-1}), followed by FME (IC_{50} = 9.44 ± 0.40 μgmL^{-1}).

It was observed specifically in these two extracts the presence of ellagic acid, a compound that has been highlighted in the face of cholinergic neuronal degeneration, resulting from the systemic administration of lipopolysaccharide compounds (Dornelles et al., 2020). Other compounds, which also have an acetylcholinesterase inhibitory effect, are phytosterols, stigmasterol and γ-sitosterol (Sanchez-Martínez et al., 2022; Karimi et al., 2021; Gade et al., 2017), which are present in FEE and BEE and recurrent in species of the genus *Parkia* (Saleh et al., 2021).

The bark and flower of *P. platycephala* possess remarkable bioactive potential. However, among the various extracts, two extracts warrant particular attention in terms of toxicity: BME (IC_{50} = 31.31 ± 4.80 μgmL^{-1}) and FEE (IC_{50} = 252.50 ± 0.01 μgmL^{-1}), as classified by Nguta et al. (2011) as highly toxic and moderately toxic, respectively. This experiment suggests potential antitumor activity against solid tumors, since the IC_{50} in *A. salina* is ten times higher than the dose of antitumor cell inhibition (Rosa et al., 2016). Thus, in terms of toxicity, the sequential extraction is more effective for the bark extracts, as well as the 70% ethanol extraction is for the flower extracts (Fernandes et al., 2022).

Nounagnon et al. (2017) also observed high toxicity in the ethanol extracts of the bark of *Parkia biglobosa*, with a lethal concentration two times higher than the leaf extracts. There were no reports of toxicity tests with flower extracts from the *Parkia* genus.

The high toxicity exhibited by BME can be explained by the presence of alkaloids, which was detected in the phytochemical screening of the extracts. This class of metabolites, very common in plants, is responsible for phytotoxic effects, necessary in combating herbivorous pests and animals (Griffiths et al., 2021). It is also believed that the presence of trilinolein (47.20% area) is related to this effect, as its cytotoxicity has been demonstrated in human cancer cells (Abalos et al., 2021). Additionally, the compound 1,2,3-benzenetriol, used as a biocide (Gao et al., 2020), showed a high percentage of area in this extract (27.07%).

Finally, it is suggested that *P. platycephala* extracts continue to be used for further studies regarding these bioactivities.

5. Conclusion

Through the bioprospection of *Parkia* do Cerrado (*P. platycephala* Benth.), it was found that the bark extracts have high antioxidant activities, and the flowers have anticholinesterase activity. These activities may be linked to the presence of flavonoids, tannins, steroids, and alkaloids, particularly phenolic acids (gallic acid, ellagic acid, ferulic acid, and caffeic acid), flavonon (naringin),

flavonol (kaempferol), and phytosterols (stigmasterol and γ-sitosterol).

All extracts exhibited toxic potential, which may set limits for the continuation of studies on the assessed biological activities, as the potentials obtained are much lower than the extract toxicity data. It is recommended that *P. platycephala* extracts should be further studied to isolate the active ingredients and evaluate their effects to increase their potential use in therapeutic practices.

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References

ABALOS, N.N., EBAJO JUNIOR, V.D., CAMACHO, D.H. and JACINTO, S.D., 2021. Cytotoxic and apoptotic activity of aglaforbesin derivative isolated from *Aglaia loheri* Merr. on HCT116 human colorectal cancer cells. *Asian Pacific Journal of Cancer Prevention*, vol. 22, no. 1, pp. 53-60. http://dx.doi.org/10.31557/APJCP.2021.22.1.53. PMid:33507679.

ALMEIDA, A.A., LEITE, J.P.V., SIMÃO, M.V.R.C. and SILVA, H.R.V., 2022. Molecular bioprospecting of plant extracts: experience report of the BIOPROS/UFV group in the search for antitumor compounds. *Revista Fitos,* vol. 16, no. suppl. 2, pp. 238-246. https://doi.org/10.32712/2446-4775.2022.1285.

ANWER, S.S., SDIQ, K.H., MUHAMMADA, K.R. and ALADDIN, L.M., 2022. Phenolic compound and fatty acid properties of some microalgae species isolated from Erbil City. *Brazilian Journal of Biology = Revista Brasileira de Biologia*, vol. 82, pp. e256927. https://doi.org/10.1590/1519-6984.256927.

AYNA, A., ÖZBOLAT, S.N. and DARENDELIOGLU, E., 2020. Quercetin, chrysin, caffeic acid and ferulic acid ameliorate cyclophosphamide-induced toxicities in SH-SY5Y cells. *Molecular Biology Reports*, vol. 47, no. 11, pp. 8535-8543. http://dx.doi.org/10.1007/s11033-020-05896-4. PMid:33040267.

BAJKACZ, S. and ADAMEK, J., 2017. Evaluation of new natural deep eutectic solvents for the extraction of isoflavones from soy products. *Talanta*, vol. 168, no. 1, pp. 329-335. http://dx.doi.org/10.1016/j.talanta.2017.02.065. PMid:28391863.

CARVALHO, P.E.R., 2014. *Faveira (Parkia platycephala)*. Brasília: Embrapa Informação Tecnológica; Colombo: Embrapa Florestas. *Espécies Arbóreas Brasileiras*, pp. 265-271, vol. 5.

CASTRO, M.R. and LÉDA, P.H.O., 2021. Normativas sanitárias e a distribuição geográfica na fabricação de fitoterápicos no Brasil. *Revista Fitos*, vol. 15, no. 4, pp. 550-565. http://dx.doi.org/10.32712/2446-4775.2021.1123.

CHAN, P., THOMAS, G.N. and TOMLINSON, B., 2002. Protective effects of trilinolein extracted from *Panax notoginseng* against cardiovascular disease. *Acta Pharmacologica Sinica*, vol. 23, no. 12, pp. 1157-1162. PMid:12466054.

COMBET, E., MESMARI, A.E., PRESTO, N.T., CROZIER, A. and MCCOL, K.E.L., 2010. Dietary phenolic acids and ascorbic acid: influence on acid-catalyzed nitrosative chemistry in the presence and absence of lipids. *Free Radical Biology & Medicine*, vol. 48, no. 6, pp. 763-771. http://dx.doi.org/10.1016/j.freeradbiomed.2009.12.011. PMid:20026204.

D'ISCHIA, M., 2005. Nitrosation and nitration of bioactive molecules: toward the basis of disease and its prevention. *Comptes Rendus Chimie*, vol. 8, no. 5, pp. 797-806. http://dx.doi.org/10.1016/j.crci.2005.02.008.

DORNELLES, G.L., OLIVEIRA, J.S., ALMEIDA, E.J.R., MELLO, C.B.E., RODRIGUES, B.R., SILVA, C.B., PETRY, L.S., PILLAT, M.M., PALMA, T.V. and ANDRADE, C.M., 2020. Ellagic acid inhibits neuroinfammation and cognitive impairment induced by lipopolysaccharides. *Neurochemical Research*, vol. 45, no. 10, pp. 2456-2473. http://dx.doi.org/10.1007/s11064-020-03105-z. PMid:32779097.

DUBEY, R.K., UPADHYAY, G., SINGH, V. and PANDEY, S., 2020. Antioxidant potential and free radical scavenging activity *of Parkia roxburghii*, G. Don, a lesser known leguminous tree from North East India. *South African Journal of Botany*, vol. 131, pp. 454-461. http://dx.doi.org/10.1016/j.sajb.2020.03.013.

ELLMAN, G.L., COURTNEY, K.D., ANDRES JUNIOR, V. and FEATHERSTONE, R.M., 1961. A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochemical Pharmacology*, vol. 7, no. 2, pp. 88-95. http://dx.doi.org/10.1016/0006-2952(61)90145-9. PMid:13726518.

EMRE, I. and KURSAT, M., 2022. Biochemical parameters and antioxidant property of three Salvia L. taxa endemic in Turkey. *Brazilian Journal of Biology = Revista Brasileira de Biologia*, vol. 82, pp. e239539.

FATOKI, T.H., AKINTAYO, C.O. and IBRAHEEM, O., 2021. Bioinformatics exploration of olive oil: molecular targets and properties of major bioactive constituents. *Oilseeds & fats Crops and Lipids*, vol. 28, no. 36, pp. 1-8. https://doi.org/10.1051/ocl/2021024.

FERNANDES, H.B., SILVA, F.V., PASSOS, F.F., BEZERRA, R.D., CHAVES, M.H., OLIVEIRA, F.A. and MENESES-OLIVEIRA, R.C., 2010. Gastroprotective effect of the ethanolic extract of *Parkia platycephala* Benth. Leaves against acute gastric lesion models in rodents. *Biological Research*, vol. 43, no. 4, pp. 451-457. http://dx.doi.org/10.4067/S0716-97602010000400010. PMid:21526272.

FERNANDES, R.M.N., RODRIGUES, M.A.M., CARDOSO, C.A.L., PANONTIN, J.F., ALVES, D.R., MORAIS, S.M. and SCAPIN, E., 2022. Phytocomponents, evaluation of anticholinesterase activity and toxicity of hydroethanolic extracts of *Parkia platycephala* Benth. *Journal of the Brazilian Chemical Society*, vol. 33, no. 12, pp. 1414-1422. http://dx.doi.org/10.21577/0103-5053.20220077.

GADE, S., RAJAMANIKYAM, M., VADLAPUDI, V., NUKALA, K.M., ALUVALA, R., GIDDIGARI, C., KARANAM, N.J., BARUA, N., PANDEY, R., UPADHYAYULA, V.V.R., SRIPADI, P., AMANCHY, R. and UPADHYAYULA, S.M., 2017. Acetylcholinesterase inhibitory activity of stigmasterol & hexacosanol is responsible for larvicidal and repellent properties of *Chromolaena odorata*. *Biochimica et biophysica acta. General subjects*, vol. 1861, no. 3, pp. 541-550. http://dx.doi.org/10.1016/j.bbagen.2016.11.044.

GAO, Y., FU, Q., LU, J., YANG, H., ORR, P.T., ZHANG, F., DONG, J., ZHANG, M., GU, Q., ZHOU, C. and BURFORD, M.A., 2020. Enhanced pyrogallol toxicity to cyanobacterium *Microcystis aeruginosa* with increasing alkalinity. *Journal of Applied Phycology*, vol. 32, no. 3, pp. 1827-1835. http://dx.doi.org/10.1007/s10811-020-02096-2.

GATTO, L.J., FABRI, N.T., SOUZA, A.M., FONSECA, N.S.T., FURUSHO, A.S., MIGUEL, O.G., DIAS, J.F.G., ZANIN, S.M.W. and MIGUEL, M.D., 2020. Chemical composition, phytotoxic potential, biological activities and antioxidant properties of *Myrcia hatschbachii* D. Legrand essential oil. *Brazilian Journal of Pharmaceutical*

Sciences, vol. 56, pp. e18402. http://dx.doi.org/10.1590/s2175-97902019000318402.

GRAPHPAD PRISM, 2020. *Version 9.0.0 for Windows*. California: GraphPad Software Inc.

GRIFFITHS, M.R., STROBEL, B.W., HAMA, J.R. and CEDERGREEN, N., 2021. Toxicity and risk of plant-produced alkaloids to *Daphnia magna*. *Environmental Sciences Europe*, vol. 33, no. 10, pp. 1-12. http://dx.doi.org/10.1186/s12302-020-00452-0.

HARRABI, S., FERCHICH, A., BACHELI, A. and FELLAH, H., 2018. Policosanol composition, antioxidant and anti-arthritic activities of milk thistle (*Silybium marianum* L.) oil at different seed maturity stages. *Lipids in Health and Disease*, vol. 17, no. 1, pp. 82. http://dx.doi.org/10.1186/s12944-018-0682-z. PMid:29661192.

HOPKINS, H.C.F., 1986. *Parkia* (Leguminosae: mimosoidea). *Flora Neotropica*, vol. 43, pp. 1-123.

KARIMI, I., YOUSOFVAND, N. and HUSSEIN, B.A., 2021. *In vitro* cholinesterase inhibitory action of *Cannabis sativa* L. *Cannabaceae* and in silico study of its selected phytocompounds. *In Silico Pharmacology*, vol. 9, no. 1, pp. 13. http://dx.doi.org/10.1007/s40203-021-00075-0. PMid:33520592.

LEE, C.T., YU, L.E. and WANG, J.Y., 2016. Nitroxide antioxidant as a potential strategy to attenuate the oxidative/nitrosative stress induced by hydrogen peroxide plus nitric oxide in cultured neurons. *Nitric Oxide*, vol. 54, pp. 38-50. http://dx.doi.org/10.1016/j.niox.2016.02.001. PMid:26891889.

LI, X., 2012. Improved pyrogallol autoxidation method: a reliable and cheap superoxide-scavenging assay suitable for all antioxidants. *Journal of Agricultural and Food Chemistry*, vol. 60, no. 25, pp. 6418-6424. http://dx.doi.org/10.1021/jf204970r. PMid:22656066.

LIMA, Â.C.O., DIAS, E.R., REIS, I.M.A., CARNEIRO, K.O., PINHEIRO, A.M., NASCIMENTO, A.S., SILVA, S.M.P.C., CARVALHO, C.A.L., MENDONÇA, A.V.R., VIEIRA, I.J.C., BRAZ FILHO, R. and BRANCO, A., 2024. Ferulic acid asmajor antioxidant phenolic compound of the *Tetragonisca angustula* honey collected in Vera Cruz – Itaparica Island, Bahia, Brazil. *Brazilian Journal of Biology = Revista Brasileira de Biologia*, vol. 84, pp. e253599. https://doi.org/10.1590/1519-6984.253599.

LOWELL, A.N., SANTORO, N., SWANEY, S.M., MCQUADE, T.J., SCHULTZ, P.J., LARSEN, M.J. and SHERMAN, D.H., 2015. Microscale adaptation of *in vitro* transcription/translation for high throughput screening of natural product extract libraries. *Chemical Biology & Drug Design*, vol. 86, no. 6, pp. 1331-1338. http://dx.doi.org/10.1111/cbdd.12614. PMid:26147927.

MARINHO, T.A., OLIVEIRA, M.G., MENEZES-FILHO, A.C.P., CASTRO, C.F.S., OLIVEIRA, I.M.M., BORGES, L.L., MELO-REIS, P.R. and SILVA JUNIOR, N.J., 2022. Phytochemical characterization, and antioxidant and antibacterial activities of the hydroethanolic extract of *Anadenanthera peregrina* stem bark. *Brazilian Journal of Biology = Revista Brasileira de Biologia*, vol. 82, pp. e234476. https://doi.org/10.1590/1519-6984.234476.

MATOS, F.J.A., 2009. *Introdução à fitoquímica experimental*. 3. ed. Fortaleza: UFC, 150 p.

MEYER, B.N., FERRIGNI, R.N., PUTNAM, J.E., JACOBSEN, L.B., NICHOL, S.D.E. and MCLAUGHLIN, J.L., 1982. Brine shrimp: a convenient general bioassay for active plant constituents. *Planta Medica*, vol. 45, no. 31, pp. 31-34. http://dx.doi.org/10.1055/s-2007-971236.

MOURA, N.S., VASCONCELOS, A.C.M., BERNABÉ, B.M., TEIXEIRA, L.J.Q. and SARAIVA, S.H., 2012. Ensaios toxicológicos: um estudo sobre a utilização de testes *in vivo* e *in vitro*. *Enciclopédia Biosfera*, vol. 8, no. 15, pp. 1945-1959.

MUSHTAQ, M.Y., CHOI, Y.H., VERPOORTE, R. and WILSON, E.G., 2014. Extraction for Metabolomics: Access to The Metabolome. *Phytochemical Analysis*, vol. 25, no. 4, pp. 291-306. http://dx.doi.org/10.1002/pca.2505. PMid:24523261.

NGUTA, J.M., MBARIA, J.M., GAKUYA, D. and GATHUMBI, P.K., 2011. Biological screening of Kenya medicinal plants using *Artemia salina* L. (Artemiidae). *Pharmacologyonline*, vol. 2, pp. 458-478.

NOUNAGNON, M., DAH-NOUVLESSOUNON, D., N'TCHA, C., NANOUKON, C., ASSOGBA, F., LALÈYÈ, F.O.A., NOUMAVO, P., GBÉNOU, D.J. and BABA-MOUSSA, L., 2017. Phytochemical composition, antimicrobial and cytotoxicity activities *of Parkia biglobosa* (Jacq) benth extracts from Benin. *Journal of Pharmacognosy and Phytochemistry*, vol. 6, no. 2, pp. 35-42.

OLIVEIRA, A.M., CONSERVA, L.M., FERRO, J.N.S., BRITO, F.A., LEMOS, R.P.L. and BARRETO, E., 2012. Antinociceptive and anti-inflammatory effects of octacosanol from the leaves of *Sabicea grisea* var. grisea in mice. *International Journal of Molecular Sciences*, vol. 13, no. 2, pp. 1598-1611. http://dx.doi.org/10.3390/ijms13021598. PMid:22408410.

OMORUYI, F., SPARKS, J., STENNETT, D. and DILWORTH, L., 2020. Superoxide dismutase as a measure of antioxidant status and its application to diabetes. In: V. R. PREEDY, ed. *Diabetes: oxidative stress and dietary antioxidants*. London: Academic Press, pp. 409-417. http://dx.doi.org/10.1016/B978-0-12-815776-3.00041-3.

OTAEGUI-ARRAZOLA, A., AMIANO, P., ELBUSTO, A., URDANETA, E. and MARTÍNEZ-LAGE, P., 2014. Diet, cognition, and Alzheimer's disease: food for thought. *European Journal of Nutrition*, vol. 53, no. 1, pp. 1-23. http://dx.doi.org/10.1007/s00394-013-0561-3. PMid:23892520.

PAIVA, L.B., GOLDBECK, R., SANTOS, W.D. and SQUINA, F.M., 2013. Ferulic acid and derivatives: molecules with potential application in the pharmaceutical field. *Brazilian Journal of Pharmaceutical Sciences*, vol. 49, no. 3, pp. 395-411. http://dx.doi.org/10.1590/S1984-82502013000300002.

PEIXOTO SOBRINHO, T.J.S., CASTRO, V.T.N.A., SARAIVA, A.M., ALMEIDA, D.M., TAVARES, E.A., AMORIM, E.L. and PEIXOTO SOBRINHO, T.J.S., 2011. Phenolic content and antioxidant capacity of four Cnidoscolus species (Euphorbiaceae) used as ethnopharmacologicals in Caatinga, Brazil. *African Journal of Pharmacy and Pharmacology*, vol. 5, no. 20, pp. 2310-2316. http://dx.doi.org/10.5897/AJPP11.608.

PILON, A.C., SELEGATO, D.M., FERNANDES, R.P., BUENO, P.C.P., PINHO, D.R., CARNEVALE-NETO, F., FREIRE, R.T., CASTRO-GAMBOA, I., BOLZANI, V.S. and LOPES, N.P., 2020. Metabolômica de plantas: métodos e desafios. *Quimica Nova*, vol. 43, no. 3, pp. 329-354.

RALTE, L., KHIANGTE, L., THANGJAM, N.M., THANGJAM, N.M., KUMAR, A. and SINGH, Y.T., 2022. GC–MS and molecular docking analyses of phytochemicals from the underutilized plant, *Parkia timoriana* revealed candidate anti-cancerous and anti-inflammatory agents. *Scientific Reports*, vol. 12, no. 1, pp. 3395. http://dx.doi.org/10.1038/s41598-022-07320-2. PMid:35233058.

RAMASARMA, T., RAO, A.V., DEVI, M.M., OMKUMAR, R.V., BHAGYASHREE, K.S. and BHAT, S.V., 2015. New insights of superoxide dismutase inhibition of pyrogallol autoxidation. *Molecular and Cellular Biochemistry*, vol. 400, no. 1-2, pp. 277-285. http://dx.doi.org/10.1007/s11010-014-2284-z. PMid:25416864.

RHEE, I.K., VAN DE MEENT, M., INGKANINAN, K. and VERPOORTE, R., 2001. Screening for acetylcholinesterase inhibitors from amaryllidaceae using silica gel thin-layer chromatography in combination with bioactivity staining. *Journal of Chromatography. A*, vol. 915, no. 1-2, pp. 217-223. http://dx.doi.org/10.1016/S0021-9673(01)00624-0. PMid:11358251.

ROSA, C.S., VERAS, K.S., SILVA, P.R., LOPES-NETO, J.J., CARDOSO, H.L.M., ALVES, L.P.L., BRITO, M.C.A., AMARAL, F.M.M., MAIA,

J.G.S., MONTEIRO, O.S. and MORAES, D.F.C., 2016. Composição química e toxicidade frente *Aedes aegypti* L. e *Artemia salina* Leach do óleo essencial das folhas de *Myrcia sylvatica* (G. Mey.) DC. *Revista Brasileira de Plantas Medicinais*, vol. 18, no. 1, pp. 9-26. http://dx.doi.org/10.1590/1983-084X/15_006.

SALEH, M.S.M., JALIL, J., ZAINALABIDIN, S., ASMADI, A.Y., MUSTAFA, N.H. and KAMISAH, Y., 2021. Genus *Parkia*: phytochemical, medicinal uses, and pharmacological properties. *International Journal of Molecular Sciences*, vol. 22, no. 2, pp. 618. http://dx.doi.org/10.3390/ijms22020618. PMid:33435507.

SALUJA, R.K., KUMAR, V. and SHAM, R., 2016. Stability of biodiesel: a review. *Renewable & Sustainable Energy Reviews*, vol. 62, pp. 866-881. http://dx.doi.org/10.1016/j.rser.2016.05.001.

SANCHEZ-MARTÍNEZ, J.D., ALVAREZ-RIVERA, G., GALLEGO, R., FAGUNDES, M.B., VALDES, A., MENDIOLA, J.A., IBANEZ, E. and CIFUENTES, A., 2022. Neuroprotective potential of terpenoid-rich extracts from orange juice by-products obtained by pressurized liquid extraction. *Food Chemistry: X*, vol. 13, pp. 100242. http://dx.doi.org/10.1016/j.fochx.2022.100242. PMid:35498984.

SANTOS, M.A.C., VIANA, A.F.S., SILVA, B.A., SANTOS, A.S., ABREU, A.S. and MOREIRA, D.K.T., 2021. Avaliação de diferentes métodos de extração e atividade antioxidante de compostos bioativos do resíduo madeireiro de maçaranduba (*Manilkara huberi* (Ducke) Standl.). *Revista Fitos*, vol. 15, no. 1, pp. 32-39. http://dx.doi.org/10.32712/2446-4775.2021.948.

SARAIVA, L.C.F., MAIA, W.M.N., LEAL, F.R., MAIA-FILHO, A.L.M. and FEITOSA, C.M., 2018. Triagem fitoquímica das folhas de *Moringa oleífera. Boletim Informativo Geum*, vol. 9, no. 2, pp. 12-19.

SILVA, N.L.A., MIRANDA, F.A.A. and CONCEIÇÃO, G.M., 2010. Triagem Fitoquímica de plantas de cerrado, da área de proteção ambiental municipal do Inhamum, Caxias, Maranhão. *Scientia Plena*, vol. 6, no. 2, pp. 1-17.

SILVA, R.R.S., SILVA, C.R., SANTOS, V.F., BARBOSA, C.R.S., MUNIZ, D.F., SANTOS, A.L.E., SANTOS, M.H.C., ROCHA, B.A.M., BATISTA, K.L.R., COSTA-JÚNIOR, L.M., COUTINHO, H.D.M. and TEIXEIRA, C.S., 2019. *Parkia platycephala* lectin enhances the antibiotic activity against multi-resistant bacterial strains and inhibits the development of Haemonchus contortus. *Microbial Pathogenesis*, vol. 135, pp. 103629. http://dx.doi.org/10.1016/j.micpath.2019.103629. PMid:31325571.

SIMÕES, C.M.O., SCHENKEL, E.P., MELLO, J.C.P., MENTZ, L.A. and PETROVICK, P.R., 2017. *Farmacognosia: do produto natural ao medicamento*. Porto Alegre: Artmed, 502 p.

TALA, V.R.S., SILVA, V.C., RODRIGUES, C.M., NKENGFACK, A.E., CAMPANER-SANTOS, L. and VILEGAS, W., 2013. Characterization of proanthocyanidins from *Parkia biglobosa* (Jacq.) G. Don. (Fabaceae) by flow injection analysis: electrospray ionization ion trap tandem mass spectrometry and liquid chromatography/electrospray ionization mass spectrometry. *Molecules (Basel, Switzerland)*, vol. 18, no. 3, pp. 2803-2820. http://dx.doi.org/10.3390/molecules18032803. PMid:23455671.

TREVISAN, M.T.S., MACEDO, F.V.V., MEENT, M., RHEE, I.K. and VERPOORTE, R., 2003. Seleção de plantas com atividade anticolinesterase para tratamento da doença de Alzheimer. *Quimica Nova*, vol. 26, no. 3, pp. 301-304. http://dx.doi.org/10.1590/S0100-40422003000300002.

VECCHIO, I., SORRENTINO, L., PAOLETTI, A., MARRA, R. and ARBITRIO, M., 2021. The state of the art on acetylcholinesterase inhibitors in the treatment of Alzheimer's disease. *Journal of Central Nervous System Disease*, vol. 13, pp. 1-13. http://dx.doi.org/10.1177/11795735211029113. PMid:34285627.

WANG, T., LIU, Y.Y., WANG, X., YANG, N., ZHU, H.B. and ZUO, P.P., 2010. Protective effects of octacosanol on 6-hydroxydopamine-induced Parkinsonism in rats via regulation of ProNGF and NGF signaling. *Acta Pharmacologica Sinica*, vol. 31, no. 7, pp. 65-774. http://dx.doi.org/10.1038/aps.2010.69. PMid:20581854.

ZHANG, Q., WANG, X., SONG, Y., FAN, X. and MARTÍN, J.F.G., 2016. Optimization of pyrogallol autoxidation conditions and its application in evaluation of superoxide anion radical scavenging capacity for four antioxidants. *Journal of AOAC International*, vol. 99, no. 2, pp. 504-551. http://dx.doi.org/10.5740/jaoacint.15-0223. PMid:26997318.

ZHOU, Y., CAO, F., LUO, F. and LIN, Q., 2022. Octacosanol and health benefits: biological functions and mechanisms of action. *Food Bioscience*, vol. 47, pp. 101632. http://dx.doi.org/10.1016/j.fbio.2022.101632.