BOLETIN LATINOAMERICANO Y DEL CARIBE DE PLANTAS MEDICINALES Y AROMÁTICAS
© / ISSN 0717 7917 / www.blacpma.ms-editions.cl

Articulo Original / Original Article

Valorization of *Campomanesia xanthocarpa* leaves: Chemical composition and antioxidant activity of crude extract and fractions

[Valorización de hojas de *Campomanesia xanthocarpa*: composición química y actividad antioxidante de extracto crudo y fracciones]

Rosângela Rumi Sugauara[1], Wanessa de Campos Bortolucci[1], Carla Maria Mariano Fernandez[1], Márcia Regina Pereira Cabral[2], Regina Aparecida Correia Gonçalves[2], Maria Helena Sarragiotto[3], José Eduardo Gonçalves[4,5], Nelson Barros Colauto[6], Giani Andrea Linde[7], Maria Graciela Iecher Faria Nunes[1], Suelen Pereira Ruiz[1] & Zilda Cristiani Gazim[1]

[1]Programa de Pós-Graduação em Biotecnologia aplicada à Agricultura, Universidade Paranaense, Umuarama, Brazil
[2]Programa de Pós-Graduação em Ciências Farmacêuticas, Departamento de Farmácia, Universidade Estadual de Maringá, Maringá, Brazil
[3]Departamento de Química, Universidade Estadual de Maringá, Maringá, Brazil
[4]Mestrado em Tecnologia Limpas/ eInstituto Cesumar de Ciência, Tecnologia e Inovação – ICETI. Centro Universitário Cesumar, Maringá, Paraná, Brazil
[6]Programa de Pós-Graduação em Ciências de Alimento; Faculdade de Farmácia da Universidade Federal da Bahia; Ondina, Salvador, Bahia, Brazil
[7]Programa de Pós-Graduação em Alimentos, Nutrição e Saúde; Escola de Nutrição- Universidade Federal da Bahia, Salvador, Bahia, Brazil

Reviewed by:
Ignacio Agudelo
Universidad de Buenos Aires
Argentina

Akondi Butchi Raju
IBN-Sina National College for Medical Studies
Saudi Arabia

Correspondence:
Suelen Pereira **RUIZ:**
suelenruiz@prof.unipar.br

Section Biological activity

Received: 5 August 2021
Accepted: 22 February 2022
Accepted corrected: 1 April 2022
Published: 30 May 2023

Citation:
Sugauara RR, Bortolucci WC, Fernandez CMM, Cabral MRP, Gonçalves RAC, Sarragiotto MH, Gonçalves JE, Colauto NB, Linde GA, Nunes MGIF, Ruiz SP, Gazim ZC Valorization of Campomanesia xanthocarpa leaves: Chemical composition and antioxidant activity of crude extract and fractions
Bol Latinoam Caribe Plant Med Aromat
22 (3): 301 - 313 (2023).
https://doi.org/10.37360/blacpma.23.22.3.22

Abstract: *Campomanesia xanthocarpa* leaves are a byproduct of fruit production without studies on antioxidant activity. Thus, this study aimed to identify the antioxidant compounds of *C. xanthocarpa* leaves by ultra-high performance liquid chromatography coupled with electrospray ionization-quadrupole-time of flight-mass spectrometry (UHPLC-ESI/qTOF) and by different *in vitro* antioxidant methods. The crude extract of *C. xanthocarpa* leaves had a yield of 15.2% and only five out of 37 fractions of the crude extract had antioxidant activity. The crude extract presented greater antioxidant activity than the isolated fractions. The identified antioxidant compounds were phenolic acids (gallic acid and chlorogenic acid), flavonoids (quercetin and naringenin 7,4'-dimethoxy) and an organic acid (quinic acid). Leaves of *C. xanthocarpa* have high concentration of antioxidant compounds and it is a promising plant for the development of applications in the food, cosmetic, and pharmaceutical fields. The extraction of antioxidant compounds can add value to the productive chain of this plant.

Keywords: Guabiroba; Gallic acid; Quercetin; Chlorogenic acid; Quinic acid.

Resumen: Las hojas de *Campomanesia xanthocarpa* son un subproducto de la producción de frutos sin estudios sobre la actividad antioxidante. Así, este estudio tuvo como objetivo identificar los compuestos antioxidantes de las hojas de *C. xanthocarpa* mediante cromatografía líquida de ultra alta resolución acoplada con espectrometría de ionización-cuadrupolo-tiempo de vuelo-masa por electropulverización (UHPLC-ESI / qTOF) y mediante diferentes métodos antioxidantes *in vitro*. El extracto crudo de hojas de *C. xanthocarpa* tuvo un rendimiento del 15,2% y solo cinco de las 37 fracciones del extracto crudo tuvieron actividad antioxidante. El extracto crudo presentó mayor actividad antioxidante que las fracciones aisladas. Los compuestos antioxidantes identificados fueron ácidos fenólicos (ácido gálico y ácido clorogénico), flavonoides (quercetina y naringenina 7,4'-dimetoxi) y un ácido orgánico (ácido quínico). Las hojas de *C. xanthocarpa* tienen una alta concentración de compuestos antioxidantes y es una planta prometedora para el desarrollo de aplicaciones en los campos alimentario, cosmético y farmacéutico. La extracción de compuestos antioxidantes puede agregar valor a la cadena productiva de esta planta.

Palabras clave: Guabiroba; Ácido gálico; Quercetina; Ácido clorogénico; Ácido quínico.

INTRODUCTION

The utilization of synthetic antioxidants in foods has become a concern for consumers and industries and has motivated the search for sources of natural antioxidants to be applied in food, pharmaceutical, cosmetics, and chemical industries (Lourenço *et al*., 2019). Plants have complex non-enzymatic and enzymatic antioxidant defense systems efficient to avoid the toxic effects of free radicals. Chloroplasts and mitochondria are the main powerhouses and sites of reactive oxygen species (ROS) generation within plants, thus explaining why all plants have an antioxidant system (Kasote *et al*., 2015).

Brazil has great plant diversity and regularly uses a lot of these plants in diets or in therapies, according to the local ethnopharmacology (FAO, 2013). *Campomanesia xanthocarpa* (Mart.) Berg belongs to the family Myrtaceae, is found in the Central-Western, Southeastern, and Southern regions of Brazil, and has several synonymous scientific names such as *Campomanesia crenata* Berg, *Campomanesia dusenii* Kausel, *Campomanesia malifolia* Berg, *Campomanesia rhombea* var. *grandifolia* O.Berg, *Campomanesia rhombea* var. *kleinii* D.Legrand, *Campomanesia rhombea* var. *parvifolia* O.Berg, *Campomanesia xanthocarpa* var. *malifolia* (Berg) C.D.Legrand, *Eugenia xanthocarpa* Mart., *Psidium eugenioides* Miq., *Psidium malifolium* F.Müll., and *Psidium punctulatum* Miq (Hassler, 2018).

It is a medium-size fruit tree, popularly known as guabiroba or gabiroba and the wood is used in civil construction, lathes, curving works, musical instruments, and also as firewood and charcoal. The fruits are traditionally consumed *in natura* or jellies, ice creams, juices, and flavorings in distillates (Markman *et al*., 2004; Vallilo *et al*., 2006). The pulp and seed of *C. xanthocarpa* fruit have been reported to have antioxidant activity (Santos *et al*., 2012; Pereira *et al*., 2015; Salmazzo *et al*., 2019). However, the leaves of this perennial plant have not been studied regarding its antioxidant activity instead of the fruit which is harvested only once a year (Luz & Krupek, 2014). Leaves of *C. xanthocarpa* are used in popular medicine as teas for gastrointestinal disorders, fever, inflammation, and hypercholesterolemia (Lorenzi, 2000; Klafke *et al*., 2010). Antimicrobial (Markman *et al*., 2000), antiulcerogenic (Markman *et al*., 2004), anti-hypertensive (Sant'anna *et al*., 2017), and hypocholesterolemic (Klafke *et al*., 2010) properties have also been reported. Moreover, the leaves are considered safe for consumption without toxic effect up to 5 g/kg in rats (Markman *et al*., 2004).

The fruit farming of *C. xanthocarpa* is recommended for intercropping and agroforestry systems and this tree produces a great amount of leaves that is pruned in order to facilitate the harvest, eliminate not promising antlers, aerate the canopy, and form a plant architecture suitable for better management, however, in this system, the leaves are discarded (Coradin *et al*., 2011). Therefore, finding a practical use for the leaves of this plant can be a sustainable practice that may add value to the productive chain of the fruit cultivation.

There have been no reports found on the chemical compound identification or the antioxidant activity of *C. xanthocarpa* leaves, only the chemical compound classes have been described (Markman *et al*., 2004; Klafke *et al*., 2010; Sant'anna *et al*., 2017). Thus, this study aimed to identify the chemical compounds of *C. xanthocarpa* leaves by ultra-high performance liquid chromatography coupled with electrospray ionization-quadrupole-time of flight-mass spectrometry (UPLC-ESI-Q-TOF-MS) and to evaluate the antioxidant activity of the crude ethanolic extract and isolated fractions.

MATERIALS AND METHODS

Plant material

Leaves of *C. xanthocarpa* were collected in the morning from April 2016 to April 2018 at the Medicinal Herbarium of Paranaense University in Umuarama, at the coordinates S23º 46.225' and WO 53º 16.730' with altitude of 391 m. The plant is registered in the Medicinal Herbarium of Paranaense University under the registration number 276 and is registered in the National Management System of the Genetic Patrimony and Associated Traditional Knowledge (SisGen) under the registration number A80EA0F.

Leaf crude extract

The leaves (320 g) were dried on a mat at room temperature, ground in a knife mill until obtaining granulometry of 850 μm and submitted to the dynamic maceration process with solvent (70% ethyl alcohol) renewal (Miranda *et al*., 2009). The filtrate was concentrated under reduced pressure in a rotary evaporator (Tecnal, model TE-211) at 40°C until obtaining the crude extract of leaves.

Fractioning in chromatographic column of the crude extract of leaves

For the column chromatography, silica gel 60 (0.063-0.200 mm) was used as the stationary phase in the 1:25 ratio; it was previously activated by heating at 105°C for 45 min. The extract (6 g) was submitted to a glass column chromatography (DiogoLab, 30 × 3.5 cm) and eluted with hexane (100%), hexane:dichlorometane (9:1, 8:2, 7:3, 5:5, 3:7, 2:8, 1:9; volume/volume), dichlorometane (100%), dichloromethane:ethyl acetate (9:1, 8:2, 7:3, 5:5, 3:7, 2:8, 1:9; volume/volume), ethyl acetate (100%), ethyl acetate:methanol (9:1, 8:2, 7:3, 5:5, 3:7, 2:8, 1:9; volume/volume) and methanol (100%). Next, the obtained fractions were concentrated using a rotary evaporator (Tecnal TE-210). The obtained fractions with a similar chemical profile were regrouped by thin layer chromatography analysis, resulting in 37 fractions. Those fractions that had antioxidant activity were submitted to identification analysis by UHPLC-ESI/qTOF.

Antioxidant activity of crude extract and isolated fractions

Determination of total phenolic content

The determination of the total phenol content in the crude extract and fractions of leaves was done by spectroscopy in the visible region utilizing Folin-Ciocalteu method, following Swain *et al*. (1959), with modifications (Sousa de Sá *et al*., 2012). The samples of the extract and isolated fractions were diluted in methanol at 1.0 mg/mL. The reagent solution consisted of 155 µL Folin-Ciocalteu solution, 125 µL sodium carbonate solution followed by 20 µL diluted sample (1 mg/mL) in each well of the microplate. The mixture was kept at rest in the dark for 60 min and read in a Microplate Reader (SpectraMax Plus^{384}) at 760 nm in triplicate.

The calibration curve was obtained by seven dilutions of gallic acid (0-100 µg/mL). The equation of the calibration curve was obtained by linear regression according to equation 1:

$$\mathbf{A = 0.0196\ C - 0.031} \qquad \mathbf{(R^2 = 0.9997)} \qquad \mathbf{Eq.\ 1}$$

Where A represents the measured absorbance, C the concentration of gallic acid equivalents, and R^2 represents the coefficient of determination for multiple regression. The results were expressed as µg of gallic acid equivalent per mg of sample.

Free radical sequestration method by DPPH°

To determine the free radical sequestration capability by DPPH° (2,2-diphenyl-1-picrylhydrazyl), the methodology described by Rufino *et al*. (2007), was used. An aliquot of 0.1 mL of different concentrations of extract and fractions (1.00, 0.75, 0.50, and 0.25 mg/mL), with 3.9 mL of methanolic solution of DPPH° (60 µM), prepared in the moment of the activity. For the negative control, 0.1 mL of methanol in the DPPH° solution (60 µM) was used. The mixtures were kept in the dark at room temperature for 30 min. The absorbance reduction was measured at 515 nm in a UV/VIS spectrophotometer. The total antioxidant capacity of the extract and isolated fractions was calculated utilizing a standard quercetin solution (60 µM) as a reference of 100%. From the correlation between absorbance *versus* sample concentration, the concentration required to reduce 50% free radicals (IC_{50}) was determined.

Ferric ion reducing antioxidant power method

The ferric ion reducing antioxidant power (FRAP) method was evaluated as described by Rufino *et al*. (2006a), FRAP reagent was prepared with a mixture of 25 mL acetate buffer (0.3 M), 2.5 mL aqueous solution of 2,4,6-tris(2-pyridyl)-s-triazine (TPTZ, 10 mM), 2.5 mL ferric chloride aqueous solution (20 mM), and 3 mL ultrapure water. The reagent solution consisted of 10 µL samples (crude extract and isolated fractions) at different concentrations (1.00, 0.75, 0.50, and 0.25 mg/mL), 290 µL FRAP reagent in each well of the microplate. The mixture was placed in a microplate reader (SpectraMax Plus^{384}) and kept at 37°C for 30 min for absorbance reading at 595 nm. Using a standard curve of ferrous sulfate (0-2000 µM), the percentage of antioxidant activity was calculated. The antioxidant activity was expressed in µM ferrous sulfate/mg of sample.

β-carotene/linoleic acid co-oxidation system

The antioxidant capacity of the extract and isolated fractions was evaluated by the β-carotene/linoleic acid co-oxidation (BCLA) method, according to Mattos *et al*. (2009). This method evaluates the sample capacity to protect β-carotene from the attack of free radicals generated by the linoleic acid. The β-carotene solution (1 mL) was prepared by dissolution of 20 mg β-carotene in 1 mL chloroform, which was

placed in a round bottom flask, containing 40 µL linoleic acid and 530 µL Tween 40 emulsifier. After the chloroform removal, in a rotary evaporator at 50ºC, 450 mL ultrapure water (previously saturated with oxygen for 30 min) was added under vigorous agitation. Aliquots (5 mL) of this emulsion were transferred to a series of assay tubes containing 1 mL of crude extract and isolated fractions at the concentrations of 1.0, 0.75, 0.5, and 0.25 mg/mL. Next, the tubes were placed in water bath at 50ºC for 120 min, and the absorbance was measured at 470 nm, initially and in the time intervals of 0, 15, 30, 45, 60, 75, 90, 105, and 120 min. Trolox was used as standard reference. The antioxidant activity was expressed as an oxidation inhibition percentage.

Analysis by ultra-high performance liquid chromatography coupled with electrospray ionization-quadrupole-time of flight-mass spectrometry

The crude extract and the isolated fractions that presented antioxidant activity were analyzed by ultra-high performance liquid chromatography (UHPLC) (Shimadzu, Nexera X2) coupled to high-resolution mass spectrometer (QTOF Impact II, Bruker Daltonics Corporation, USA), equipped with source of ionization by electrospray. The capillary tension was operated in negative ionization mode, defined at 4500 V, and with a compensation potential of final plate of -500 V. The parameters of dry gas were adjusted for 8 L/min a 200°C with nebulization gas pressure of 4 bar. The fragmentation, collision induced dissociation (CID), was done using argon and collision energy of 15 at 30 eV. The data were collected at 50-1300 *m/z* with an acquisition rate of 5 spectra per second, and the ions of interest were selected by automatic fragmentation of scanning by tandem mass spectrometry (MS/MS). The chromatographic separation was carried out using a C18 column (75 × 2.0 mm i.d., 1.6 µm Shim-pack XR-ODS III). The gradient mixture of A (H_2O) and B (acetonitrile) solvents was: 5% B 0-1 min, 30% B 1-4 min, 95% B 4-8 min, kept at 95% B 8-17 min, at 40°C. The identification of these compounds was proposed in a review of the genus *Campomanesia* (Schmeda-Hirschmann, 1995; Sant'anna *et al*., 2017), besides the error value of the mass and the comparison to databases such as MassBank (**http://www.massbank.jp**) and Human Metabolome Database (**http://www.hmdb.ca**).

Statistical analysis

All the tests were done in triplicate. The results were submitted to analysis of variance (ANOVA) and the differences between the arithmetic averages were determined by Duncan's test ($p \leq 0.05$) by Statistica software, version 13.3 (StatSoft South America, Quest Software Inc, Ok, USA), serial number JPZ711I235230FA-T.

RESULTS

The yield of the crude ethanolic extract of leaves was 15.2%. The crude extract was divided into 37 fractions, and five of them had antioxidant activity (Table No. 1). By DPPH° method, the crude extract and ethyl acetate:methanol (7:3) fraction had the greatest values of antioxidant activity with IC_{50} of 0.067 and 0.450 mg/mL, respectively (Table No. 1). These samples also had the greatest total phenol contents ($p \leq 0.05$) of 175.680 and 150.850 µg of gallic acid equivalent per mg of sample, respectively (Table No. 1). This indicates that the group of chemical compounds and not a specific compound has the antioxidant activity and that it is probably found mostly in the ethyl acetate:methanol (7:3) fraction. By FRAP method, the crude extract and the fractions did not have considerable activity in iron reduction (Table No. 1). By BCLA system, the crude extract and the dichloromethane:ethyl acetate (8:2) apolar fraction had greater antioxidant activity with β-carotene protection in the reaction of 68.3 and 52.5%, respectively, representing an antioxidant activity equivalent to 86 and 66% of trolox positive control (Figure No. 1).

The chemical compounds of the crude extract were classified as phenolic acids (gallic acid and chlorogenic acid), flavonoids (quercetin and naringenin 7,4'-dimethoxy) and an organic acid (quinic acid) (Table No. 2). The chemical compounds of the fractions were classified as phenolic acid (gallic acid) for dichloromethane:ethyl acetate (9:1) and ethyl acetate:methanol (7:3) fractions, and the flavonoid (naringenin 7,4'-dimethoxy) for dichloromethane:ethyl acetate (8:2), dichloromethane:ethyl acetate (7:3), ethyl acetate:methanol (9:1), and ethyl acetate:methanol (7:3) fractions (Table 2). The chemical compounds were identified by ion *m/z* 169.0143 $[M-H]^-$ as gallic acid, ion *m/z* 191.0529 $[M-H]^-$ as quinic acid, ion *m/z* 353.0879 $[M-H]^-$ as chlorogenic acid, ion *m/z* 301.0350 $[M-H]^-$ as quercetin, and ion *m/z* 299.0874 $[M-H]^-$ as naringenin 7,4'-dimethoxy (Table No. 2).

Table No. 1
Antioxidant activity of the crude ethanolic extract and fractions of *Campomanesia xanthocarpa* leaves by the methods of free radical sequestration by DPPH° (2,2-diphenyl-1-picrylhydrazyl), FRAP (ferric ion reducing antioxidant power), and total phenolic content

Sample	DPPH° IC_{50} (mg/mL)	FRAP (µM ferrous sulfate/ mg of sample)	Total phenols (µg of gallic acid/ mg of sample)
Crude extract	0.067 ± 0.033^{b}	0.670 ± 0.111^{d}	175.680 ± 13.709^{a}
Dichloromethane:ethyl acetate (9:1)	5.515 ± 0.892^{f}	0.008 ± 0.006^{f}	83.503 ± 6.974^{d}
Dichloromethane:ethyl acetate (8:2)	1.298 ± 0.057^{e}	0.243 ± 0.042^{e}	123.214 ± 2.765^{c}
Dichloromethane:ethyl acetate (7:3)	5.013 ± 0.674^{f}	0.446 ± 0.020^{c}	51.956 ± 7.091^{e}
Ethyl acetate:methanol (9:1)	0.842 ± 0.024^{d}	0.693 ± 0.097^{d}	83.248 ± 1.082^{d}
Ethyl acetate:methanol (7:3)	0.450 ± 0.013^{c}	1.064 ± 0.134^{b}	150.850 ± 0.001^{b}
Quercetin	0.010 ± 0.001^{a}	-	-
Trolox	-	9.175 ± 0.001^{a}	-

The values are the arithmetic average ± standard deviation of the experiment in triplicate. IC_{50} = half maximal inhibitory concentration. Values in the same column with different letters are significantly different by Duncan's test ($p \leq 0.05$)

DISCUSSION

The phenolic compounds identified in the crude ethanolic extract constitute heterogeneous secondary metabolites produced by plants and that are important natural antioxidants able to neutralize free radicals by donating hydrogen or electrons, capturing metallic ions or inhibiting enzymes involved in the generation of free radicals (Pereira *et al*., 2009; San Miguel-Chávez, 2017; Gatto *et al*., 2021). The results of UHPLC-ESI/qTOF made evident phenolic compounds in the extract of *C. xanthocarpa* leaves such as gallic acid, quercetin, chlorogenic acid, naringenin 7,4'-dimethoxy, and the organic acid as quinic acid. These results are in accordance with the high content of total phenols of 175.68 µg of gallic acid equivalent per mg determined for the crude extract. For the ethanolic extract of *C. xanthocarpa* leaves, compounds such as gallic acid, chlorogenic acid, quercetin, and theobromine, and the presence of saponins, tannins, terpenes, and flavonoids (Table No. 3) are described in the literature. These studies corroborate the chemical identification found in our study.

There are few reports on phenols and flavonoids of *C. xanthocarpa* leaves (Sant'anna *et al*., 2017; Dalastra *et al*., 2019). Sant'Anna *et al*. (2017), demonstrated relevant content of phenolics and flavonoids compounds and the possible presence of chlorogenic acid, gallic acid, quercetin, and theobromine (Table No. 3) in the aqueous extract of *C. xanthocarpa* leaves, but without the chemical identification of the compounds. On the other hand, for *C. xanthocarpa* seeds, the total phenols were 1.7656 µg of gallic acid equivalent per mg (Santos *et al*., 2012). Our results of total phenols for the ethanolic extract of *C. xanthocarpa* leaves were approximately 10-fold higher than in the seeds (Santos *et al*., 2012), our result may be related to the high antioxidant activity found in the leaf extracts with IC_{50} of 0.067 mg/mL by DPPH° and protection of 70% by BCLA.

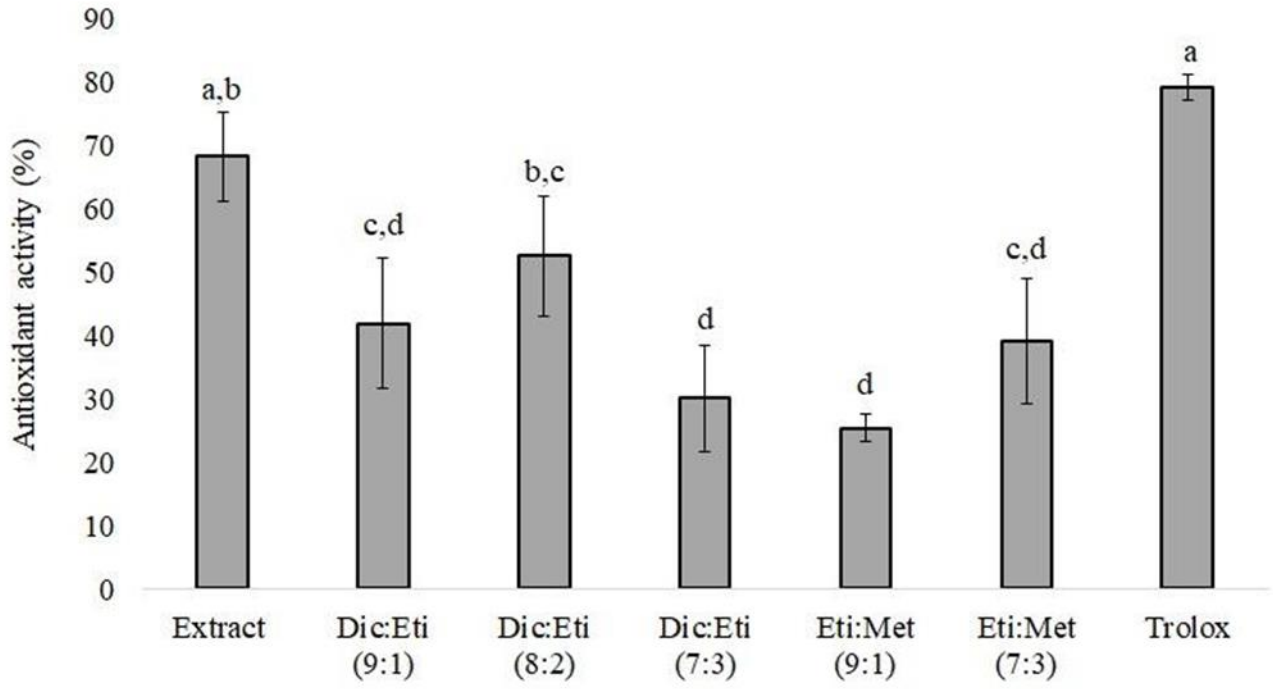

Figure No. 1
Antioxidant activity of the crude ethanolic extract and fractions of *Campomanesia xanthocarpa* leaves by β-carotene/linoleic co-oxidation (BCLA) method. Extract = crude extract obtained from the dried leaves, Dic:Eti (9:1) = fraction obtained with dichloromethane:ethyl acetate (9:1), Dic:Ace (8:2) = fraction obtained with dichloromethane:ethyl acetate (8:2), Dic:Eti (7:3) = fraction obtained with dichloromethane:ethyl acetate (7:3), Eti:Met (9:1) = fraction obtained with ethyl acetate:methanol (9:1), Eti:Met (7:3) = fraction obtained with ethyl acetate:methanol (7:3). Samples were tested at 0.25 mg/mL. Trolox = positive control at 0.2 mg/mL. Values with different letters are significantly different by Duncan's test ($p \leq 0.05$)

One of the identified compounds in the extract of *C. xanthocarpa* leaves was naringenin 7,4'-dimethoxy, a naringenin derivate. Brighente *et al*. (2007), reported high antioxidant activity for naringenin with IC_{50} of 0.018 mg/mL by DPPH°. In its structure, naringenin has two hydroxyl groups in the sites 5 and 7 of the A ring, and a carbonyl group in the site 4 of C ring that reduce iron ions and avoid oxidative reactions (Cook & Samman, 1996). Naringenin is abundant in foods such as citric fruits, honey, bee pollen (Zheng *et al*., 2019), besides having antioxidant activity (Cavia-Saiz *et al*., 2010), it has been reported to have immunomodulatory activity (Maatouk *et al*., 2016) as well as antitumoral (Lin *et al*., 2014), anti-inflammatory (Li *et al*., 2015), antiaterogenic (Lee *et al*., 2001), and UVB-radiation protector activities (El-Mahdy *et al*., 2008).

Quercetin, also identified in our study in *C. xanthocarpa* leaves, has capacity to sequester oxygen-reactive species such as O_2^{*-}, NO^- and $ONOO^-$ donating a proton and redistributing its charge by resonance (Mariani *et al*., 2008; Wang *et al*., 2016). In antioxidant assays, quercetin is utilized as an analytic standard with values of IC_{50} from 0.55 to 6.55 µg/mL by DPPH° (Takao *et al*., 2015; Rusmana *et al*., 2017; Singh *et al*., 2018). Quercetin is related to antitumor activity (Hashemzaei *et al*., 2017) as well as antiviral (Ganesan *et al*., 2012), antibacterial (Rattanachaikunsopon & Phumkhachorn, 2010), anti-proliferative, anti-arterosclerotic, and anti-inflammatory (Kleemann *et al*., 2011) activities.

Table No. 2
Chemical composition of the crude ethanolic extract and fractions of *Campomanesia xanthocarpa* leaves by UHPLC-ESI/qTOF

Compound	RT (min)	Molecular formula	*m/z* Theoretical $[M-H]^-$	*m/z* Experimental $[M-H]^-$	Error (ppm)	Fragments	Sample
Gallic acid	0.71	$C_7H_6O_5$	169.0131	169.0143	± 7.10	125	Extract, Dic:Eti(9:1), Eti:Met (7:3)
	0.73			169.0118	± 7.69		
	0.77			169.0108	± 13.61		
Quinic acid	1.31	$C_7H_{12}O_6$	191.0550	191.0529	± 10.98	173, 127, 85	Extract
Chlorogenic acid	1.45	$C_{16}H_{18}O_9$	353.0867	353.0879	± 3.39	191, 179, 161	Extract
Quercetin	1.70	$C_{15}H_{10}O_7$	301.0342	301.0350	± 2.66	273, 151, 107, 83	Extract
Naringenin 7,4'-dimethoxy	9.33	$C_{17}H_{16}O_5$	299.0914	299.0874	± 13.37	281, 271	Extract, Dic:Ac e (8:2), Dic:Eti (7:3), Eti:Met (9:1),
	9.34			299.0867	± 15.71		
	9.38			299.0885	± 9.69		
	9.36			299.0874	± 13.37		
	9.37			299.0870	± 14.71		Eti:Met (7:3)

RT = retention time (min). Extract = crude extract obtained from the dried leaves, Dic:Eti (9:1) = fraction obtained with dichloromethane:ethyl acetate (9:1), Dic:Ace (8:2) = fraction obtained with dichloromethane:ethyl acetate (8:2), Dic:Eti (7:3) = fraction obtained with dichloromethane:ethyl acetate (7:3), Eti:Met (9:1) = fraction obtained with ethyl acetate:methanol (9:1), Eti:Met (7:3) = fraction obtained with ethyl acetate:methanol (7:3)

Table No. 3
Major compounds, total phenols, flavonoids and antioxidant activity of *Campomanesia xanthocarpa* reported

Plant part	Extraction solvent	Major compounds	Total phenolic content	Total flavonoid content	Antioxidant activity (µg/mL)	Source
Leaf	Ethanol-Water	Flavonoids, saponins and tannins	-	-	-	Markman *et al*., 2004
Leaf	-	saponins, tannins, terpenes and flavonoids	-	-	-	Klafke *et al*., 2010
Leaf	Water	gallic acid chlorogenic acid quercetin theobromine	3.74 mg GAE/mL	2.51 rutin mg equivalents/g	-	Sant'Anna *et al*., 2017
Leaf	Ethanol-Water	-	-	52.64 µg de catechin/g	-	Dalastra *et al*., 2019
Fruit	Ethanol-Water	-		7.18 µg de catechin/g	-	
Fruit	Ethanol Hexane	2',4'-dihydroxy-5'-methyl-6'-methoxychalcone 2',4'-dihydroxy-3',5'-dimethyl-6'-methoxychalcone 2'-hydroxy-3'-methyl-4',6'-dimethoxychalcone 2',6'-dihydroxy-3'-methyl-4'-methoxychalcone 5-hydroxy-7 methoxy-8-methylflavanone 7-hydroxy-5-methoxy-6-methylflavanone	-	-	Ethanolic extract: 87.53 DPPH° Hexanic extract: 97.85 DPPH°	Salmazzo *et al*., 2019
Seed	Ethanol	-	1.76 µg GAE/ mg	-	75.52 DPPH°	Santos *et al*., 2012

The chlorogenic acid, also identified in the extract of *C. xanthocarpa* leaves, has IC_{50} of 6.41 µg/mL by DPPH° (Singh *et al*., 2018). The antioxidant activity is related to the presence of neighboring hydroxyl groups that can stabilize free radicals by positive charge approach (Rice-Evans *et al*., 1996; Lan, 2007; Sato *et al*., 2011). The chlorogenic acid is also related to the protective activity of intestinal membranes in rats (Sato *et al*., 2011), antibacterial, hepatoprotective, cardioprotective, anti-inflammatory, antipyretic, neuroprotective, anti-obesity, antiviral, antimicrobial, and antihypertensive activities, besides eliminating free radicals, and being a central stimulating agent of the nervous system (Naveed *et al*., 2018).

The gallic acid, identified in the crude extract and dichloromethane:ethyl acetate (9:1) and ethyl acetate:methanol (7:3) fractions, is a phenolic acid

utilized as food additive and analytical standard to determine the phenolic content of vegetal extracts by the total phenol test. Gallic acid is a natural antioxidant with IC_{50} of 0.0026 mg/mL by DPPH° (Brighente et al., 2007) and 3.52 µmol of Fe^{+2}/µg by FRAP (Pandey & Rizvi, 2012). The antioxidant activity is related to the presence of three hydroxyl groups that can react with free radicals and prevent oxidative damages (Pandey & Rizvi, 2012; Badhani *et al*., 2015). The gallic acid is reported as an apoptosis inducer with antitumor (Sun *et al*., 2016), antimicrobial (Rajamanickam *et al*., 2019), and anti-melanogenic (Kim, 2007) activities.

The quinic acid has been characterized as a inducer of antioxidants nicotinamide and tryptophan (Pero *et al*., 2009) thus, it has been related with anti-inflammatory activity through factor kappa B (NF-kappaB) (Zeng et al., 2009), a suppressive effect of hepatoma (AH109A cells) invasion *in vitro* (Yagasaki *et al*., 2000), protective effect on human lymphocytes from damage induced by X-ray (Cinkilic *et al*., 2013) and from cell death induced by tetrahydropapaveroline (Soh *et al*., 2003) and antimicrobial activity against *Staphylococcus aureus* (Bai *et al*., 2018). Chuda *et al*. (1996), isolated derivatives of quinic acid (dicaffeoylquinic acids) with antioxidant activity 10-fold smaller than BHA (3-*tert*-butyl-4-hydroxyanisole) by BCLA, indicating intermediate antioxidant activity.

In our study, the crude leaf extract had greater antioxidant activity than the separate fractions, probably due to the greater concentration of antioxidant compounds in the extract. However, the fraction with two antioxidants, such as gallic acid and naringenin 7,4'-dimethoxy, had greater antioxidant activity by DPPH°, FRAP, or total phenols. By BCLA, the fraction containing naringenin 7,4'-dimethoxy had greater antioxidant activity, but similar ($p \leq 0.05$) to the crude extract. The methods of DPPH°, FRAP and total phenols evaluate the capacity to sequester free radicals and to reduce metal ions. Thus, these methodologies have high correlation with the number of available hydroxyl groups and, consequently, with phenolic groups. However, the BCLA method evaluates the inhibitory power of free radicals generated during linoleic acid peroxidation, and are mainly related to lipophilic antioxidant compounds (Rufino *et al*., 2006b; Alves *et al*., 2010).

The crude extract of *C. xanthocarpa* leaves contains a mixture of antioxidant compounds such as gallic acid, quercetin, chlorogenic acid, naringenin 7,4'-dimethoxy, and quinic acid was the one that had greater antioxidant activity when compared to isolated fractions. These compounds found in *C. xanthocarpa* leaves are regularly found in human diet and, due to their pharmacological properties, which are beneficial to health, are also commercialized as nutraceuticals by the pharmaceutical and food industries (Boot *et al*., 2008; Wang *et al*., 2016). The mixture of antioxidant compounds can increase or reduce the antioxidant activity, depending on the type and amount of compounds in the mixture (Freeman *et al*., 2010; Hajimehdipoor *et al*., 2014), but in our study it increased the antioxidant activity. This makes evident the potential utilization of *C. xanthocarpa* leaves as natural antioxidants and that the crude extract is more effective than the isolated fractions.

CONCLUSIONS

The crude extract of *C. xanthocarpa* leaves has yield of 15.2% and only 5 out of 37 fractions of the crude extract has antioxidant activity. The crude extract of *C. xanthocarpa* leaves has high antioxidant activity by DPPH° and BCLA. All five fractions with antioxidant activity have low antioxidant activity by FRAP. The identified chemical compounds of the crude extract are phenolic acids (gallic acid and chlorogenic acid), flavonoids (quercetin and naringenin 7,4'-dimethoxy) and an organic acid (quinic acid). In the dichloromethane:ethyl acetate (9:1) and ethyl acetate:methanol (7:3) fractions, the identified chemical compound is the gallic acid (phenolic acid), and for dichloromethane:ethyl acetate (8:2), dichloromethane:ethyl acetate (7:3), ethyl acetate:methanol (9:1), and ethyl acetate:methanol (7:3) fractions, it is naringenin 7,4'-dimethoxy (flavonoid). Leaves of *C. xanthocarpa* have high concentration of antioxidant compounds and it is a promising plant to develop applications in the food, cosmetics, and pharmaceutical industries.

ACKNOWLEDGMENTS

The authors thank Paranaense Universidade, Maringá State Univeristy, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brazil CAPES -finance code 001- and Conselho Nacional de Desenvolvimento Científico e Tecnológico –CNPq- for the fellowship and financial support.

REFERENCES

Alves CQ, David JM, David JP, Bahia MV, Aguiar RM, Sobrinho JM. 2010. Métodos para determinação da atividade antioxidante *in vitro* em substratos orgânicos. **Quim Nova** 33: 2202 - 2210. **https://doi.org/10.1590/S0100-40422010001000033**

Bai J, Wu Y, Zhong K, Xiao K, Liu L, Huang Y, Wang Z, Gao HA. 2018. Comparative study on the effects of quinic acid and shikimic acid on cellular functions of *Staphylococcus aureus*. **J Food Prot** 81: 1187 - 1192. **https://doi.org/10.4315/0362-028X.JFP-18-014**

Badhani B, Sharma N, Kakkar R. 2015. Gallic acid: a versatile antioxidant with promising therapeutic and industrial applications**. RSC Adv** 5: 27540 - 27557. **https://doi.org/10.1039/C5RA01911G**

Boot AW, Haenen GRMM, Bast A. 2008. Health effects of quercetin: From antioxidant to nutraceutical. **Eur J Pharmacol** 585: 325 - 337. **https://doi.org/10.1016/j.ejphar.2008.03.008**

Brighente IMC, Dias M, Verdi LG, Pizzolatti MG. 2007. Antioxidant activity and total phenolic content of some Brazilian species. **Pharm Biol** 45: 156 - 161. **https://doi.org/10.1080/13880200601113131**

Cavia-Saiz M, Busto MD, Izquierdo MCP, Ortega N, Mateos MP, Muñiz P. 2010. Antioxidant properties, radical scavenging activity and biomolecule protection capacity of flavonoid naringenin and its glycoside naringin: a comparative study. **J Sci Food Agri** 90: 1238 - 1244. **https://doi.org/10.1002/jsfa.3959**

Chuda Y, Ono H, Kameyama MO, Nagata T, Tsushida T. 1996. Structural identification of two antioxidant quinic acid derivatives from garland (*Chrysanthemum coronarium* L.). **J Agric Food Chem** 44: 2037 - 2039. **https://doi.org/10.1021/jf960182**

Cinkilic N, Cetintas SK, Zorlu T, Vatan O, Yilmaz D, Cavas T, Tunc S, Ozkan L, Bilaloglu R. 2013. Radioprotection by two phenolic compounds: chlorogenic and quinic acid, on X-ray induced DNA damage in human blood lymphocytes *in vitro*. **Food Chem Toxicol** 53: 359 - 363. **https://doi.org/10.1016/j.fct.2012.12.008**

Cook NC, Samman S. 1996. Flavonoids: chemistry, metabolism, cardioprotective effects, and dietary sources. **J Nut Biochem 7**: 66 - 76. **https://doi.org/10.1016/S0955-2863(95)00168-9**

Coradin L, Siminski A, Reis A. 2011. **Espécies nativas da flora brasileira de valor econômico atual ou potencial: plantas para o futuro - Região Sul**. Brasília: Ministério do Meio Ambiente. **https://www.gov.br/mma/pt-br/assuntos/biodiversidade/fauna-e-flora/Regiao_Sul.pdf**

Dalastra V, Southier N, Anaissi FJ, Dalastra J, Yamazaky RK. 2019. Flavonoids present in extracts of *Campomanesia xanthocarpa* Berg. **Braz J Dev** 5: 8983 - 8991. **https://doi.org/10.34117/bjdv5n7-101**

El-Mahdy MA, Zhu Q, Wang QE, Wani G, Patnaik S, Zhao Q, Arafa El-S, Barakat B, Mir SN, Wani AA. 2008. Naringenin protects HaCaT human keratinocytes against UVB-induced apoptosis and enhances the removal of cyclobutane pyrimidine dimers from the genome. **Photochem Photobiol** 84: 307 - 316. **https://doi.org/10.1111/j.1751-1097.2007.00255.x**

FAO (Food and Agriculture Organization of the United Nations), 2013. SAFA: Sustainability Assessment of Food and Agriculture Systems Guidelines. Food and Agriculture organization of the United Nations: Roma, Italy.

Freeman BL, Eggett BL, Parker TL. 2010. Synergistic and antagonistic interactions of phenolic compounds found in navel oranges. **J Food Sci** 75: C570 - C576. **https://doi.org/10.1111/j.1750-3841.2010.01717.x**

Ganesan S, Faris AN, Comstock AT, Wang Q, Nanua S, Hershenson MB, Sajjan US. 2012. Quercetin inhibits rhinovirus replication *in vitro* and *in vivo*. **Antivir Res** 94: 258 - 271. **https://doi.org/10.1016/j.antiviral.2012.03.005**

Gatto LJ, de Oliveira GRB, Rech KS, Moura PF, Gribner C, Merino FJZ, Ávila S, Dias JFG, Miguel OG, Miguel MD. 2021. nhibition of α-glucosidase, pancreatic lipase, and antioxidant property of *Myrcia hatschbachii* D. Legrand containing gallic and ellagic acids. **Bol Latinoam Caribe Plant Med Aromat** 20: 226 - 243. **https://doi.org/10.37360/blacpma.21.20.3.18**

Hajimehdipoor H, Shahrestani R, Shekarchi M. 2014. Investigating the synergistic antioxidant effects of some flavonoid and phenolic compounds. **Res J Pharmacogn** 1: 35 - 40.

Hashemzaei M, Far AD, Yari A, Heravi RE, Tabrizian K, Taghdisi SM, Sadegh SE, Tsarouhas K, Kouretas D, Tzanakakis G, Nikitovic D, Anisimov NY, Spandidos DA, Tsatsakis AM, Rezaee R. 2017. Anticancer and apoptosis-inducing effects of quercetin *in vitro* and *in vivo*. **On Rep** 38: 819 - 828. **https://doi.org/10.3892/or.2017.5766**

Hassler M. 2018. **World plants: Synonymic checklists of the vascular plants of the world** (version Nov 2018).

In: Roskov Y, Ower G, Orrell T, Nicolson D, Bailly N, Kirk PM, Bourgoin T, DeWalt RE, Decock W, Nieukerken E, Penev L, Species 2000 & ITIS Catalogue of Life, 2020-02-24 (2020). Digital resource at **http://www.catalogueoflife.org/col** Species 2000: Naturalis, Leiden, the Netherlands.

Kasote DM, Katyare SS, Hegde MV, Bae H. 2015. Significance of antioxidant potential of plants and its relevance to therapeutic applications. **Int J Biol Sci** 11: 982 - 991. **https://doi.org/10.7150/ijbs.12096**

Kim YJ. 2007. Antimelanogenic and antioxidant properties of gallic acid. **Biol Pharm Bull** 30: 1052 - 1055. **https://doi.org/10.1248/bpb.30.1052**

Klafke JZ, Da Silva MA, Panigas TF, Belli KC, De Oliveira MF, Barichello MM, Rigo FK, Rossato MF, Soares Dos Santos AR, Pizzolatti MG, Ferreira J, Viecili PR. 2010. Effects of *Campomanesia xanthocarpa* on biochemical, hematological and oxidative stress parameters in hypercholesterolemic patients. **J Ethnopharmacol** 127: 299 - 305. **https://doi.org/10.1016/j.jep.2009.11.004**

Kleemann R, Verschuren L, Morrison M, Zadelaar S, Van Erk MJ, Wielinga PY, Kooistra T. 2011. Anti-inflammatory, anti-proliferative and anti-atherosclerotic effects of quercetin in human *in vitro* and *in vivo* models. **Atherosclerosis** 218: 44 - 52. **https://doi.org/10.1016/j.atherosclerosis.2011.04.023**

Lan WU. 2007. Effect of chlorogenic acid on antioxidant activity of *Flos lonicerae* extracts. **J Zhejiang Univ Sci B** 8: 673 - 679. **https://doi.org/10.1631/jzus.2007.B0673**

Lee CH, Jeong TS, Choi YK, Hyun BH, Oh GT, Kim EH, Kim JR, Han JI, Bok SH. 2001. Anti-atherogenic effect of citrus flavonoids, naringin and naringenin, associated with hepatic ACAT and aortic VCAM-1 and MCP-1 in high cholesterol-fed rabbits. **Biochem Biophys Res Commun** 284: 681 - 688. **https://doi.org/10.1006/bbrc.2001.5001**

Li YR, Chen DY, Chu CL, Li S, Chen YK, Wu CL, Lin CC. 2015. Naringenin inhibits dendritic cell maturation and has therapeutic effects in a murine model of collagen-induced arthritis. **J Nut Biochem** 26: 1467 - 1478. **https://doi.org/10.1016/j.jnutbio.2015.07.016**

Lin EJ, Zhang X, Wang DY, Hong SZ, Li LY. 2014. Naringenin modulates the metastasis of human prostate cancer cells by down regulating the matrix metalloproteinases-2/-9 via ROS/ERK1/2 pathways. **Bangladesh J Pharmacol** 9: 419 - 427. **https://doi.org/10.3329/bjp.v9i3.19730**

Lorenzi, H. 2000. **Árvores brasileiras: Manual de identificação e cultivo de plantas arbóreas nativas do Brasil**. Plantarum, Nova Odessa, São Paulo, Brasil.

Lourenço SC, Martins Mm, Alves VD. 2019. Antioxidants of natural plant origins: From sources to food industry applications. **Molecules** 24: 4132. **https://doi.org/10.3390/molecules24224132**

Luz IJ, Krupek RA. 2014. Reproductive phenology, fruit and seed biometry of *Campomanesia xanthocarpa* O. Berg. (Myrtaceae). **Estudos de Biologia, Ambiente e Diversidade** 36: 115 - 124. **https://doi.org/10.7213/estud.biol.36.086.AO12**

Maatouk M, Elgueder D, Mustapha N, Chaaban H, Bzéouich IM, Loannou I, Kilani S, Ghoul M, Ghedira K, Ghedira LC. 2016. Effect of heated naringenin on immunomodulatory properties and cellular antioxidant activity. **Cell Stress Chaperones** 21: 1101 - 1109. **https://doi.org/10.1007/s12192-016-0734-0**

Mariani C, Braca A, Vitalini S, Tommasi N, Visioli F, Fico G. 2008. Flavonoid characterization and *in vitro* antioxidant activity of *Aconitum anthora* L. (Ranunculaceae). **Phytochemistry** 69: 1220 - 1226. **https://doi.org/10.1016/j.phytochem.2007.12.009**

Markman BEO, Bugno A, Taba MO, Kato ETM. 2000. Atividade antimicrobiana do extrato hidroalcoólico de *Campomanesia xanthocarpa*. **Rev Bras Cienc Farm** 36: 55.

Markman BEO, Bacchi EM, Kato ETM. 2004. Antiulcerogenic effects of *Campomanesia xanthocarpa*. **J Ethnopharmacol** 94: 55 - 57. **https://doi.org/10.1016/j.jep.2004.04.025**

Mattos LM, Moretti CL, Muniz LB, Silva EYY. 2009. Protocolo de análises para determinação da atividade antioxidante total em hortaliças no sistema β-caroteno/ácido 40 component. **Comunicado Técnico Embrapa** 1: 1 - 5.

Miranda CG, Arantes MCB, Rezende MH, Oliveira LMG, Freitas MRF, Nogueira JCM, Paula JR, Bara MT. 2009. Pharmacognostic characterization of leaves and seeds of *Albizia lebbeck* (L.) Benth. (Fabaceae). **Rev Bras Farmacogn** 19: 537 - 544. **https://doi.org/10.1590/S0102-695X2009000400005**

Naveed M, Hejazi V, Abbas M, Kamboh AA, Khan GJ, Shumzaid M, Ahmad F, Babazadeh D, Fangfang X, Ghazani FM, Wenhua L, Xiaohui Z. 2018. Chlorogenic acid (CGA): A pharmacological review and call for further research. **Biomed Pharmacother** 97: 67 - 74. **https://doi.org/10.1016/j.biopha.2017.10.064**

Pandey KB, Rizvi SI. 2012. Ferric reducing and radical scavenging activities of selected important polyphenols present in foods. **Int J Food Prop** 15: 702 - 708. **https://doi.org/10.1080/10942912.2010.498547**

Pereira DM, Valentão P, Pereira JA, Andrade PB. 2009. Phenolics: from chemistry to biology. **Molecules** 14: 2202 - 2211. **https://doi.org/10.3390/molecules14062202**

Pereira MC, Hill LE, Zambiazi RC, Mertens-Talcott S, Talcott S, Gomes CL. 2015. Nanoencapsulation of hydrophobic phytochemicals using poly (dl-lactide-co-glycolide) (PLGA) for antioxidant and antimicrobial delivery applications: Guabiroba fruit (*Campomanesia xanthocarpa* O. Berg) study. **LWT – Food Sci Technol** 63: 100 - 107. **https://doi.org/10.1016/j.lwt.2015.03.062**

Pero RW, Lund H, Leanderson T. 2009. Antioxidant metabolism induced by quinic acid. Increased urinary excretion of tryptophan and nicotinamide. **Phytother Res** 23: 335 - 346. **https://doi.org/10.1002/ptr.2628**

Rajamanickam K, Yang J, Sakharkar MK. 2019. Gallic acid potentiates the antimicrobial activity of tulathromycin against two key bovine respiratory disease (brd) causing-pathogens. **Front Pharmacol** 9: 1 - 9. **https://doi.org/10.3389/fphar.2018.01486**

Rattanachaikunsopon P and Phumkhachorn P. 2010. Contents and antibacterial activity of flavonoids extracted from leaves of *Psidium guajava*. **J Med Plants Res** 4: 393 - 396. **https://doi.org/10.5897/JMPR09.485**

Rice-Evans CA, Miller NJ, Paganga G. 1996. Structure- antioxidant activity relations ships of flavonoids and phenolic acids. **Free Radic Biol Med** 20: 933 - 956. **https://doi.org/10.1016/0891-5849(95)02227-9**

Rufino MSM, Alves RE, Brito ES, Morais SM, Sampaio CG, Jiménez JP, Calixto FDS. 2006a. Metodologia científica: determinação da atividade antioxidante total em frutas pelo método de redução do ferro (FRAP). **Comunicado Técnico Embrapa** 125: 1 - 4.

Rufino MSM, Alves RE, Brito ES, Filho JM, Moreira AVB. 2006b. Metodologia Científica: determinação da atividade antioxidante total em frutas no sistema β-caroteno/ácido linoleico. **Comunicado Técnico Embrapa** 126: 1 - 4.

Rufino MSM, Alves RE, Brito ES, Morais SM, Sampaio CG, Jiménez JP, Calixto FDS. 2007. Metodologia científica: determinação da atividade antioxidante total em frutas pela captura do radical livre DPPH°. **Comunicado Técnico Embrapa** 127: 1 - 4.

Rusmana D, Wahyudianingsih R, Elisabeth M, Balqis B, Maesaroh M, Widowati W. 2017. Antioxidant activity of *Phyllanthus niruri* extract, rutin and quercetin. **Indonesia Biomed J** 9: 84 - 90. **https://doi.org/10.18585/inabj.v9i2.281**

Salmazzo GR, Verdan MH, Silva F, Cicarelli RM, Mota JDS, Salvador MJ, Carvalho JE, Cardoso CAL. 2019. Chemical composition and antiproliferative, antioxidant and trypanocidal activities of the fruits from *Campomanesia xanthocarpa* (Mart.) O. Berg (Myrtaceae). **Nat Prod Res** 15: 1 - 5. **https://doi.org/10.1080/14786419.2019.1607333**

San Miguel-Chávez R. 2017. Phenolic antioxidant capacity: A review of the state of the art. In Soto-Hernandez M, Palma-Tenango M, Garcia-Mateos MR. Phenolic compounds, biological activity. IntechOpen. **https://www.intechopen.com/chapters/53658**

Sant'anna LS, Merlugo L, Ehle CS, Limberger J, Fernandes MB, Santos MC, Mendez ASL, Paula FR, Moreira CM. 2017. Chemical composition and hypotensive effect of *Campomanesia xanthocarpa*. **Evid Based Compl Alt** 1: 1 - 11. **https://doi.org/10.1155/2017/1591762**

Santos MS, Miguel OG, Petkowicz CLO, Cândido LMB. 2012. Antioxidant and fatty acid profile of gabiroba seed (*Campomanesia xanthocarpa* Berg). **Ciênc Tecnol Aliment** 32: 234 - 238. **https://doi.org/10.1590/S0101-20612012005000045**

Sato Y, Itagaki S, Kurokawa T, Ogura J, Kobayashi M, Hirano T, Sugawara M, Iseki K. 2011. *In vitro* and *in vivo* antioxidant properties of chlorogenic acid and caffeic acid. **Int J Pharm** 403: 136 - 138. **https://doi.org/10.1016/j.ijpharm.2010.09.035**

Schmeda-Hirschmann G. 1995. Flavonoids from *Calycorectes, Campomanesia, Eugenia* and *Hexachlamys* species. **Fitoterapia** 66: 373 - 374.

Singh DP, Verma S, Prabha R. 2018. Investigations on antioxidant potential of phenolic acids and flavonoids: the common phytochemical ingredients in plants. **J Plant Biochem Physiol** 6: 1000219. **https://doi.org/10.4172/2329-9029.1000219**

Soh Y, Kim JA, Sohn NW, Lee KR, Kim SY. 2003. Protective effects of quinic acid derivatives on tetrahydropapaveroline-induced cell death in C6 glioma cells. **Biol Pharm Bull** 26: 803 - 807.

https://doi.org/10.1248/bpb.26.803

Sousa de Sá PG, Guimarães AL, Oliveira AP, Siqueira Filho JA, Fontana AP, Damasceno PKF, Branco CRC, Branco A, Almeida JRGS. 2012. Fenóis totais, flavonoides totais e atividade antioxidante de *Selaginella convoluta* (Arn.) Spring (Selaginellaceae). **Rev Ciênc Farm Básica Apl** 33: 561 - 566.

Sun G, Zhang S, Xie Y, Zhang Z, Zhao W. 2016. Gallic acid as a selective anticancer agent that induces apoptosis in SMMC-7721 human hepatocellular carcinoma cells. **Oncol Lett** 11: 150 - 158. **https://doi.org/10.3892/ol.2015.3845**

Swain T, Hills WE. 1959. The phenolic constituents of *Punnus domestica*. The quantitative analysis of phenolic constituents. **J Sci Food Agric** 19: 63 - 68. **https://doi.org/10.1002/jsfa.2740100110**

Takao LK, Imatomi M, Gualtieri SCJ. 2015. Antioxidant activity and phenolic content of leaf infusions of Myrtaceae species from Cerrado (Brazilian Savanna). **Braz J Biol** 75: 948 - 952. **https://doi.org/10.1590/1519-6984.03314**

Vallilo MI, Bustillos OV, Aguiar OT. 2006. Identificação de terpenos no óleo essencial dos frutos de *Campomanesia adamantium* (cambessedes) O. Berg. Myrtaceae. **Rev Inst Florest** 18: 15 - 22.

Wang W, Sun C, Mao L, Ma P, Liu F, Yang J, Gao Y. 2016. The biological activities, chemical stability, metabolism and delivery systems of quercetin: A review. **Trends Food Sci Technol** 56: 21 - 38. **https://doi.org/10.1016/j.tifs.2016.07.004**

Yagasaki K, Miura Y, Okauchi R, Furuse T. 2000. Inhibitory effects of chlorogenic acid and its related compounds on the invasion of hepatoma cells in culture. **Cytotechnology** 33: 229 - 235. **https://doi.org/10.1023/A:1008141918852**

Zeng K, Thompson KE, Yates CR, Miller DD. 2009. Synthesis and biological evaluation of quinic acid derivatives as anti-inflammatory ag ents. **Bioorg Med Chem Lett** 19: 5458 - 5460. **https://doi.org/10.1016/j.bmcl.2009.07.096**

Zheng YZ, Deng G, Guo R, Chen DF, Fu ZM, DFT. 2019. DFT Studies on the antioxidant activity of naringenin and its derivatives: effects of the substituents at C3. **Int J Mol Sci** 20: 1450. **https://doi.org/10.3390/ijms20061450**