

ORIGINAL ARTICLE

Cardanols detected in non-polar propolis extracts from *Scaptotrigona aff. postica* (Hymenoptera, Apidae, Meliponini)

Cardanols detectados nos extratos apolares da própolis de *Scaptotrigona aff. postica* (Hymenoptera, Apidae, Meliponini)

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Abstract

The propolis produced by stingless bees of the tribe Meliponini is a viscous product that contains the resin collected from buds, leaves and plant exudates, mixed with salivary secretions, wax and soil. The species *Scaptotrigona aff. postica* (Latreille, 1807), (Hymenoptera, Apidae, Meliponinae) popularly known as “tubi” in Maranhão State, Brazil, does not mix soil to produce its propolis. The propolis from *S. postica* harvested in Barra do Corda, Maranhão State, is popularly used in the treatment of wounds and respiratory illnesses. The hydroalcoholic extract of this propolis, rich in flavone-6,8-di-C-glycosides (vicenin-2 and schaftoside), pyrrolizidine alkaloids derived from retronecine, catechin and caffeoylquinic acid derivatives exhibited antiviral activity against the herpes simplex and rubella viruses. The aim of this study was to increase knowledge about the chemical composition of the *S. postica* propolis by analyzing non-polar extracts obtained using hexane and chloroform as the solvents, by GC-EI-MS. A total of 15 constituents were identified comparing their respective mass spectral data with those available in the NIST data bases and those reported in the literature. The main constituents detected were the phenolic lipids, known as cardanols, 3-(4,7-heptadecadienyl) phenol (**5**), 3-(10-heptadecenyl) phenol (**7**), 3-heptadecylphenol (**9**) and 3-pentadecyl phenol or hydrocardanol (**13**), which predominated in the hexane extract, while the predominant constituents in the chloroform extract were 3-pentadecyl phenol or hydrocardanol (**13**) and 3-(8-pentadecenyl) phenol (**12**). The antioxidant, antitumoral, antifeedant, cytotoxic, anticarcinogenic, antiproliferative, antimicrobial, antileishmanial and larvicidal activities of the cardanols have been demonstrated in many studies.

Keywords: Chemical analyses; Stingless bee propolis; GC-EI-MS; 3-pentadecylphenol; 3-(10-heptadecenyl) phenol; Pharmacological activity.

Resumo

A própolis elaborada pelas abelhas sem ferrão (Apidae, Meliponini) é um material resinoso extraído de brotos, folhas e



exsudatos de plantas, que são misturados com secreções salivares, cera e solo. A espécie *Scaptotrigona aff. postica* (Latreille, 1807), (Hymenoptera, Apidae, Meliponini), popularmente conhecida como “tubi”, no estado do Maranhão, não mistura solo na produção da própolis. A própolis de *S. postica* coletada no município de Barra do Corda, estado do Maranhão, é usada popularmente no tratamento de feridas e doenças respiratórias. O extrato hidroalcoólico desta própolis é rico em flavonas-6,8- C -glicosídeos (vicenina e schaftosídeo), alcaloides pirrolizidínicos, catequinas e ácidos cafeoilquínicos, e mostrou atividade antiviral contra os vírus do herpes e da rubéola. O objetivo deste estudo foi ampliar o conhecimento sobre a composição química da própolis de *S. postica*, analisando os extratos apolares obtidos usando hexano e clorofórmio como solventes, por cromatografia gasosa acoplada a espectrometria de massas. Os 15 constituintes detectados foram identificados comparando os seus respectivos espectros de massas com espectros de massas compilados nas bases de dados NIST e reportados na literatura. Os principais constituintes encontrados foram os lípidios fenólicos, conhecidos como cardanóis, 3-(4,7-heptadecadienil) fenol (**5**), 3-(10-heptadecenil) fenol (**7**), 3-heptadecilfenol (**9**) e 3-pentadecilfenol ou hidrocarbônico (**13**), que predominaram no extrato hexânico, enquanto que, no extrato clorofórmico, os constituintes predominantes foram 3-pentadecilfenol ou hidrocarbônico (**13**) e 3-(8-pentadecenil) fenol (**12**). As atividades antioxidante, antitumoral, citotóxica, antiproliferativa e larvívora dos cardanóis foram demonstradas através de vários estudos.

Palavras-chave: Análise química; Própolis de abelhas sem ferrão; CG-EM; 3-pentadecilfenol; 3-(10-heptadecenil) fenol; Atividade farmacológica.

1 Introduction

Propolis is produced by the Africanized bee *Apis mellifera* (Huang et al., 2014) and by stingless bees of the tribe Meliponini (Batista et al., 2016) from resinous material collected from the buds, flowers and exudates of different plants, which is mixed with their mandibular secretions and wax. Some species of stingless bees add soil in the elaboration of their geopropolis (Dutra et al., 2014; Liberio et al., 2011), but the stingless bees *Scaptotrigona aff. postica* (Latreille, 1807), (Hymenoptera, Apidae, Meliponini), popularly known as “tubi”, in Maranhão State, Brazil, produce their propolis without the addition of soil (Souza et al., 2015; Sawaya et al., 2009). Stingless bees or meliponines play an important role in pollination and agriculture and are present in tropical and neotropical regions throughout the world (Batista et al., 2016; Pedro, 2014). Although the meliponines comprising the tribe Meliponini, possess stingers, they cannot be used in their defense. Stingless bees are less harmful to humans and domestic animals and are more resistant to the diseases and parasites than *Apis mellifera* (Sawaya et al., 2009; Araújo et al., 2015). In Brazil, 244 stingless bee species have been identified, mainly in the northern and northeastern regions, corresponding to about 20% of all neotropical species of stingless bees (Pedro, 2014).

The chemical composition of propolis varies according to the flora visited by the bees, the region, and the time of collection (Huang et al., 2014; Pasupuleti et al., 2017). Consequently, their quality and biological activities vary according to their botanical origin (Araújo et al., 2015; Ribeiro-Junior et al., 2015). The chemical composition of propolis from *Apis mellifera* is qualitatively the same in the geographic region where it was produced. For example, the Brazilian green propolis harvested in the southeast region of Brazil, is elaborated using *Baccharis dracunculifolia* as the resin source and possesses prenylated phenylpropanoids, caffeoylquinic acids and diterpenes as the main constituents (Oliveira et al., 2014; Righi et al., 2013; Fernandes-Silva et al., 2013).

On the other hand, in general, propolis from stingless bees exhibits a wide variation even among samples from the same region, since they collect material from plants near their hives (Araújo et al., 2015; Ribeiro-Junior et al., 2015). Thus, for example, cycloartane, ursane and oleanane derivatives and phenolic acids (protocatechuic acid and gallic acid) were detected in the geopropolis from *Melipona fasciculata* harvested in Palmeirândia, while gallic and ellagic acids were the main constituents detected in the geopropolis harvested in Fernando Falcão, both municipalities located in Maranhão State, northeastern Brazil (Batista et al., 2016). In addition, hydrolyzable tannins (gallotannins and ellagitannins) and phenolic

acids were detected in the geopropolis from *Melipona fasciculata* Smith harvested in Baixada Maranhense, Brazil (Dutra et al., 2014). However, the geopropolis samples from *Tetragonisca angustula*, independent of their geographic origin, presented a chemical composition similar to extracts from the flowers of *Schinus terebinthifolius* Raddi (Anacardiaceae), which was probably their resin source (Carneiro et al., 2016). Therefore, knowledge of the composition of propolis and of the plants visited as resin sources is very important (Sawaya et al., 2007).

Phenylpropanoids (Souza et al., 2013), di- and trigalloyl and phenylpropanyl heteroside derivatives (Santos et al., 2017a), hydrolysable tannins (Dutra et al., 2014), terpenes (monoterpenes, sesquiterpenes, diterpenes and triterpenes) (Torres et al., 2018; Santos et al., 2017a), fatty acids (Bankova et al., 1998), saponins (Araújo et al., 2015; Dutra et al., 2008), anacardic acid derivatives (Silva et al., 2008; Araújo et al., 2015) and alkaloids (Coelho et al., 2015) have been detected in the propolis from stingless bees. Flavonoids were detected in the geopropolis from the stingless Amazonian bees *Melipona interrupta* (Silva et al., 2013). Flavonoids, derivatives of glycosylated phenolic acids and terpenoids were detected in the geopropolis from the stingless bee *Melipona orbignyi* (Santos et al., 2017b). Prenylated benzophenone and cinnamic acid esters were detected in the geopropolis from *Melipona scutellaris* Latreille, indicating that a genus of the Clusiaceae family, especially *Kielmeyera* and *Clusia*, could be the resin sources of this geopropolis (Cunha et al., 2016). The phenylpropanoids, 6-O-p-coumaroyl-D-galactopyranose and 6-O-cinnamoyl-1-O-p-coumaroyl- β -D-glucopyranose, and flavonoids were detected in the geopropolis from *Melipona subnitida* Ducke (jandaíra), a stingless bee native to northeastern Brazil (Souza et al., 2013, 2018).

The isolation of the cycloartane triterpene magniferolic acid and 3 β -hydroxy-24-methylenecycloartan-26-oic acid, besides the flavonoids 3'-methyl quercetin, sakuranetin and kaempferol 7-methyl ether, indicated the exudates from *Eucalyptus citriodora* specimens as the resin source for the production of geopropolis from *Trigona spinipes* Fabricius, native to the Northeast of Brazil (Freitas et al., 2008). Di- and trigalloyl and phenylpropanyl heteroside derivatives, flavanones, diterpenes and triterpenes were detected in the geopropolis from *Melipona quadrifasciata anthidioides*, which exhibited activity in the prevention and treatment of various diseases related to oxidative stress, mutagenesis, inflammatory processes and microbial infections (Santos et al., 2017a). Triterpenoids are the chemical markers for the standardization of geopropolis from the Malaysian stingless bees, *Heterotrigona itama* (Zhao et al., 2017).

Qualitative and quantitative differences in the chemical composition of propolis can influence its biological activity (Santos et al., 2017b; Franchin et al., 2012). However, the propolis produced by different species of stingless bees in different regions of the world, exhibit antimicrobial (Cunha et al., 2013a), anticancer, antioxidant (Ferreira et al., 2017), anti-inflammatory (Araújo et al., 2015; Santos et al., 2017a, 2017b, 2017c), gastroprotective (Ribeiro-Junior et al., 2015), and antiviral (Coelho et al., 2015) activities. The geopropolis produced by *Melipona fasciculata* Smith exhibited antimicrobial activity against *Streptococcus mutans* and *Candida albicans* (Liberio et al., 2011). The geopropolis from *Melipona scutellaris* Latreille exhibited antimicrobial, antioxidant, anti-inflammatory, antinociceptive (Franchin et al., 2012; Silva et al., 2014) and antiproliferative activities (Cunha et al., 2013b, 2016). The geopropolis from *Melipona orbignyi* exhibited antioxidant, anti-inflammatory, antimutagenic and antimicrobial activities (Santos et al., 2017b), while the geopropolis from *Melipona mondury* exhibited therapeutic potential against inflammatory and oxidative infectious and neoplastic diseases (Santos et al., 2017c).

Large amounts of flavone-6,8-di-C-glycosides (vicenin-2 and schaftoside), pyrrolizidine alkaloids derived from retronecine, catechin derivatives and caffeoylquinic acid derivatives (Coelho et al., 2015), and lesser amounts of the hydroxycinnamic acid amide derivatives (Coelho et al., 2018) were detected in the hydroalcoholic extract of propolis from *Scaptotrigona aff. Postica*, harvested in Barra do Corda, Maranhão State. This extract exhibited antiviral activity against the herpes simplex (Coelho et al., 2015; Silva-Carvalho et al., 2015) and rubella (Coelho et al., 2018) viruses. Since the propolis from *S. postica* is a potential source of new bioactive compounds, more studies, including the chemical composition and biological activity of non-polar extracts, are needed to add

value to this bee product. Thus, the objective of this study was to carry out chemical analyses of the non-polar hexane and chloroform extracts obtained from the propolis of *S. postica*, using GC-EI-MS.

2 Material and methods

2.1 Non-polar extracts

The samples of propolis from *S. postica* were collected from beehives located in the municipality of Barra do Corda, in the central region of Maranhão State, northeastern Brazil (5° 30'S, 45° 14'O), in November 2011. The ecosystems of this region include mangrove swamps, floodplains, lakes and babassu palm forests. The apiary is located 100 m from the right side of the Mearim River.

The extractions were carried out in a Soxhlet apparatus using 5 g of propolis and 30 mL of either hexane or chloroform separately as the solvent, extracting for 6 hours (Luque de Castro & García-Ayuso, 1998; Fernandes-Silva et al., 2013). After extraction, the extracts were maintained in a refrigerator for two days and the precipitated wax then filtered off. The presence of soil was not observed. The filtrate was then concentrated in a rotary evaporator under reduced pressure, and finally concentrated to dryness on a water bath at a temperature of 50 °C to obtain dry hexane and chloroform extracts, which were weighed and analyzed by GC-EI-MS.

2.2 Analyses of the hexane and chloroform extracts by GC-EI-MS

1 µL aliquots of 1 mg mL⁻¹ hexane or chloroform solutions of the extracts were injected into the equipment in the split mode, using a Shimadzu GCMS-QP505A gas chromatograph equipped with a ZB-5ms fused silica capillary column BPX5 (non-polar, 5% phenyl arylene – 95% dimethylpolysiloxane) (30 m × 0.25 mm internal diameter × 0.25 µm film thickness) coupled to an ion-trap mass detector. Mass spectra were acquired in the electron-impact (EI) mode with an ionization voltage of 70 eV. The GC conditions were set as follows: the oven was programmed with an initial temperature of 100 °C, which was maintained for 5 min and then increased to 320 °C at a rate of 6 °C/min. The final temperature was maintained for 10 min. The air and hydrogen flow rates were 400 mL/min and 29.5 mL/min, respectively. Helium was used as the carrier gas at a flow rate of 2.1 mL/min, linear velocity of 53.8 cm/sec, column pressure of 150.0 KPa and total flow of 29.5 mL/min. The MS conditions were set as follows: filament current, 0.3 mA; detector voltage, -0.7 kV, ion source temperature, 300 °C; interface temperature, 300 °C; split ratio of 11 and scan speed of 2 scans s⁻¹. The mass range was 120-700 Da over 52 min (full scan mode). Identification of the non-polar constituents was carried out by comparison of the mass spectral data with those available in the NIST 08 (National Institute Standards Technology), Wiley-275 (Hewlett Packard) and Wiley/NBS libraries, and data available in the literature. The relative amounts of constituents were assumed to be proportional to the areas under the corresponding chromatogram peaks.

3 Results and discussion

This work evaluated the chemical compositions of hexane and chloroform extracts obtained from the propolis of *S. postica*. The yield of the hexane extract was 15.0%, based on the initial weight of the propolis (5 g), while the yield of the chloroform extract was 28.0%. Table 1 shows the identification of the constituents by comparison of their mass spectral data with those available in the NIST 08 (NIST Match Factor of 850), Wiley-275 (Hewlett Packard) and Wiley/NBS libraries and in the literature. The identification of the hydrocarbons, 1-pentadecene (**1**) and 1-heptadecene (**3**) was based on the NIST MS spectral database and data reported by Siddiquee et al. (2015) and by McNeil et al. (2018). The compound 2,4-di-tert-butylphenol (**2**) exhibited molecular ions M⁺ at *m/z* 206 and a base peak at *m/z* 191, indicating the loss of a methyl group, and was identified based on data reported by Kusch et al. (2011) and by

Irawan et al. (2018). The fatty acids *n*-hexadecanoic acid (**4**) and *n*-octadecanoic acid (**8**) were identified based on NIST MS spectral database and data reported by Bankova et al. (1998) and by Hernández-García et al. (2019). The diterpene, (-)-Kaur-16-ene (**6**) exhibited molecular ions M^{+} at m/z 272 and a base peak at m/z 257, and was identified based on NIST MS spectral database and data reported by Xie et al. (2011).

Cardanols or 3-alkylphenols with saturated and unsaturated chains, were the main constituents detected in the hexane and chloroform extracts, as can be seen in Table 1. The cardanols: 3-(4,7-heptadecadienyl) phenol (**5**) (17%), 3-(10-heptadecenyl) phenol (**7**) (21%) (mass spectrum shown in Figure 1), 3-heptadecyl phenol (**9**) (31%) (mass spectrum shown in Figure 2), and 3-pentadecylphenol or hydrocardanol (**13**) (11%) predominated in the hexane extracts. The predominant cardanols detected in the chloroform extract were 3-(8-pentadecenyl) phenol (**12**) (10%) (mass spectrum shown in Figure 3) and 3-pentadecylphenol or hydrocardanol (**13**) (48%) (mass spectrum shown in Figure 4). 5-Alkylresorcinols or cardols were detected in small amounts.

The cardanols exhibited characteristic electron impact mass spectra, with a base peak fragment at m/z 108 and a minor fragment at m/z 107, as shown in Table 1 and Figures 1-4, which were produced by simple benzylic cleavage (Wheeler et al., 1997; Ross et al., 2004; Gómez-Caravaca et al., 2010). Very little additional fragmentation was observed. The cardols exhibited a base peak fragment at m/z 124, due to the McLafferty rearrangement of the phenolic ring, and another minor fragment at m/z 123 (Table 1, Figure 5), due to the dihydroxytropylium ion formed by simple benzylic cleavage (Ross et al., 2004; Saitta et al., 2009; Geerkens et al., 2015).

Table 1. Constituents detected by GC-EI-MS in the non-polar extracts from the geopropolis of *Scaptotrigona aff. postica* (hymenoptera, apidae, meliponini).

	RT	EIMS	EIMS - Fragments	Identification	Reference	A* (%)	B* (%)
	min.	[M] ⁺	m/z** (%)				
1	9.19	210 (10)	111 (60), 85 (70), 71 (50), 69 (100)	1-pentadecene	NIST MS number** - 34721; Siddiquee et al. (2015); McNeil et al. (2018)	2	-
2	12.01	206 (20)	191 (100)	2,4-di-tert-butylphenol	Kusch et al. (2011); Irawan et al. (2018)	3	5
3	15.00	238 (10)	153 (35), 125 (35), 111 (50), 97 (50), 83 (50), 71 (70), 69 (100)	1-heptadecene	NIST MS number** - 11434, Siddiquee et al. (2015); McNeil et al. (2018)	-	7
4	17.30	256 (30)	213 (30), 185 (30), 157 (30), 129 (50), 83 (22), 73 (100)	<i>n</i> -hexadecanoic acid or palmitic acid	NIST MS Number** 151973, Bankova et al. (1998); Hernández- García et al. (2019)	-	5
5	17.95	328 (20)	147 (50), 133 (40), 120 (60), 108 (100), 107 (84)	3-(4,7-heptadecadienyl) phenol or Phenol, 3-(4Z,7Z)-4,7- heptadecadien-1-yl	Wheeler et al. (1997); Ross et al. (2004); Gómez-Caravaca et al. (2010)	17	3
6	18.33	272 (75)	257 (100), 229 (70), 213 (18), 147 (21), 125 (30), 105 (35), 91 (44), 69 (50)	(-)-Kaur-16-ene	NIST MS Number** 42566; Xie et al. (2011)	-	2

Table 1. Continued...

	RT	EIMS	EIMS - Fragments	Identification	Reference	A* (%)	B* (%)
	min.	[M] ⁺	m/z** (%)				
7	18.75	330 (10)	120 (30), 108 (100), 107 (40)	3-(10-Heptadecenyl) phenol	Wheeler et al. (1997); Ross et al. (2004); Gómez-Caravaca et al. (2010)	21	5
8	19.26	284 (10)	241 (30), 185 (40), 129 (50), 111 (17), 108 (29), 97 (31)	<i>n</i> -octadecanoic acid or stearic acid	NIST MS Number** 290961, Bankova et al. (1998); Hernández- García et al. (2019)	-	2
9	19.43	332 (10)	109 (10), 108 (100), 107 (40)	3-heptadecylphenol	Wheeler et al. (1997); Ross et al. (2004); Gómez-Caravaca et al. (2010); Geerkens et al. (2015)	31	1
10	22.02	344 (10)	163 (30), 124 (100), 123 (50)	5-(8,11-heptadecadienyl) resorcinol	Ross et al. (2004); Saitta et al. (2009); Geerkens et al. (2015)	5	1
11	22.25	320 (10)	125 (10), 124 (100), 123 (30)	5-pentadecyl resorcinol or cardol	Ross et al. (2004); Saitta et al. (2009); Geerkens et al. (2015)	5	1
12	22.89	302 (20)	120 (30), 108 (100), 107 (50)	3-(8-pentadecenyl) phenol	Ross et al. (2004); Saitta et al. (2009); Geerkens et al. (2015)	3	10
13	23.14	304 (20)	109 (12), 108 (100), 107 (40)	3-pentadecylphenol or hydrocardanol	Ross et al. (2004); Saitta et al. (2009); Geerkens et al. (2015)	11	48
14	23.49	346 (10)	125 (14), 124 (100), 123 (35)	5-(8-heptadecenyl) resorcinol	Ross et al. (2004); Saitta et al. (2009); Geerkens et al. (2015)	-	5
15	24.16	348 (10)	125 (10), 124 (100), 123 (40)	5-heptadecyl resorcinol or 1,3-Benzenediol, 5- heptadecyl	Ross et al. (2004); Saitta et al. (2009); Geerkens et al. (2015)	-	5

Contents in percentage (%) A = hexane extract; and B = chloroform extract. *mass-to-charge ratio - m/z. **NIST Match Factor - 850. RT = retention time; EIMS = electron impact mass spectra.

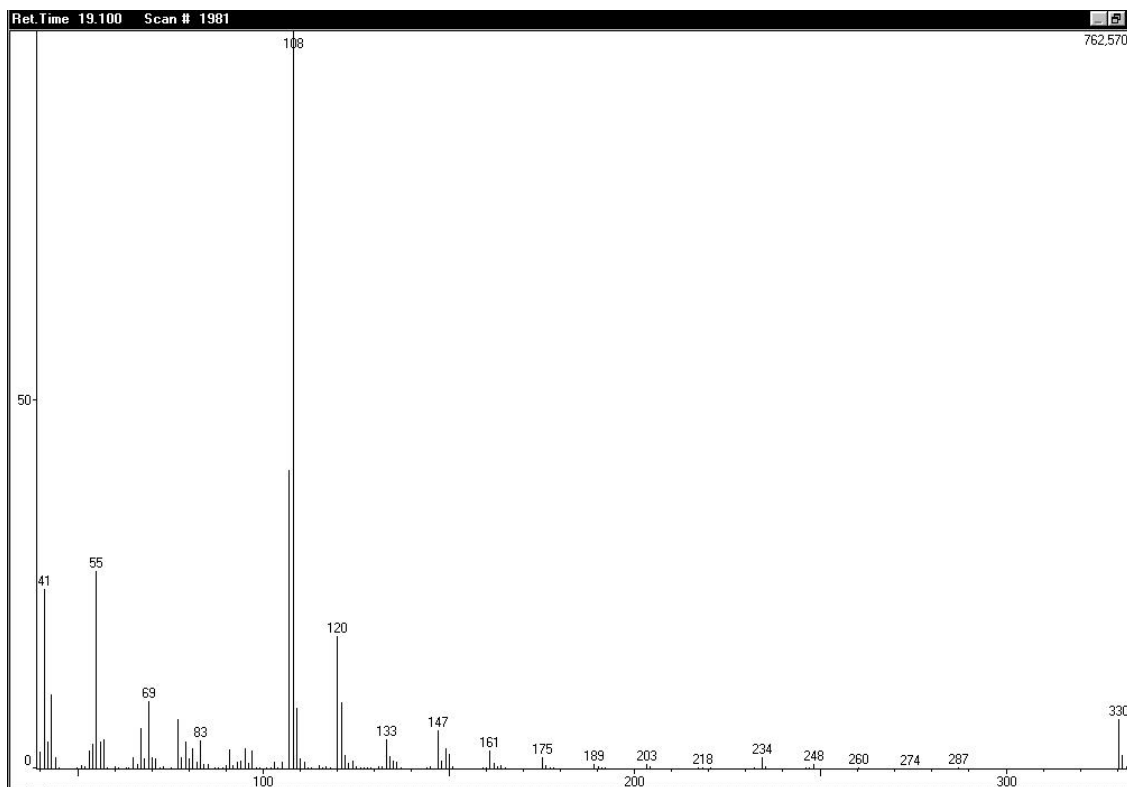


Figure 1. GC-EI-MS of the mass spectrum of 3-(10-heptadecenyl) phenol (7).

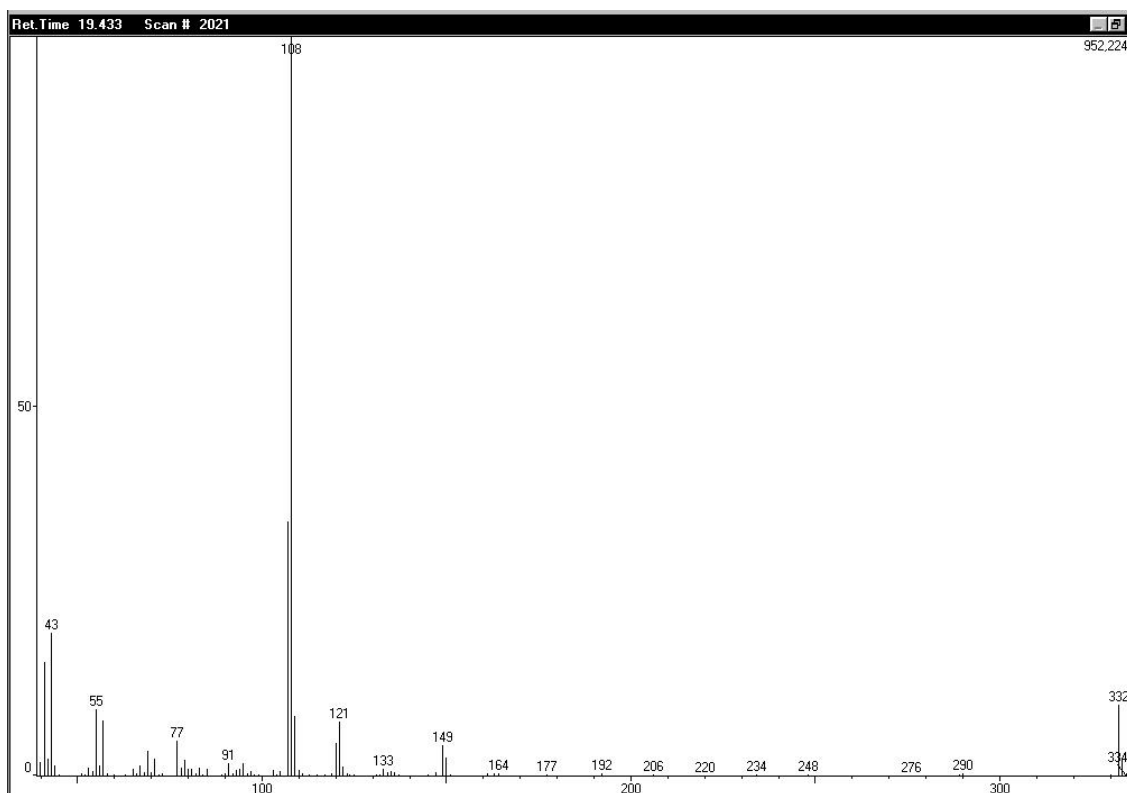


Figure 2. GC-EI-MS of the mass spectrum of 3-heptadecyl phenol (9).

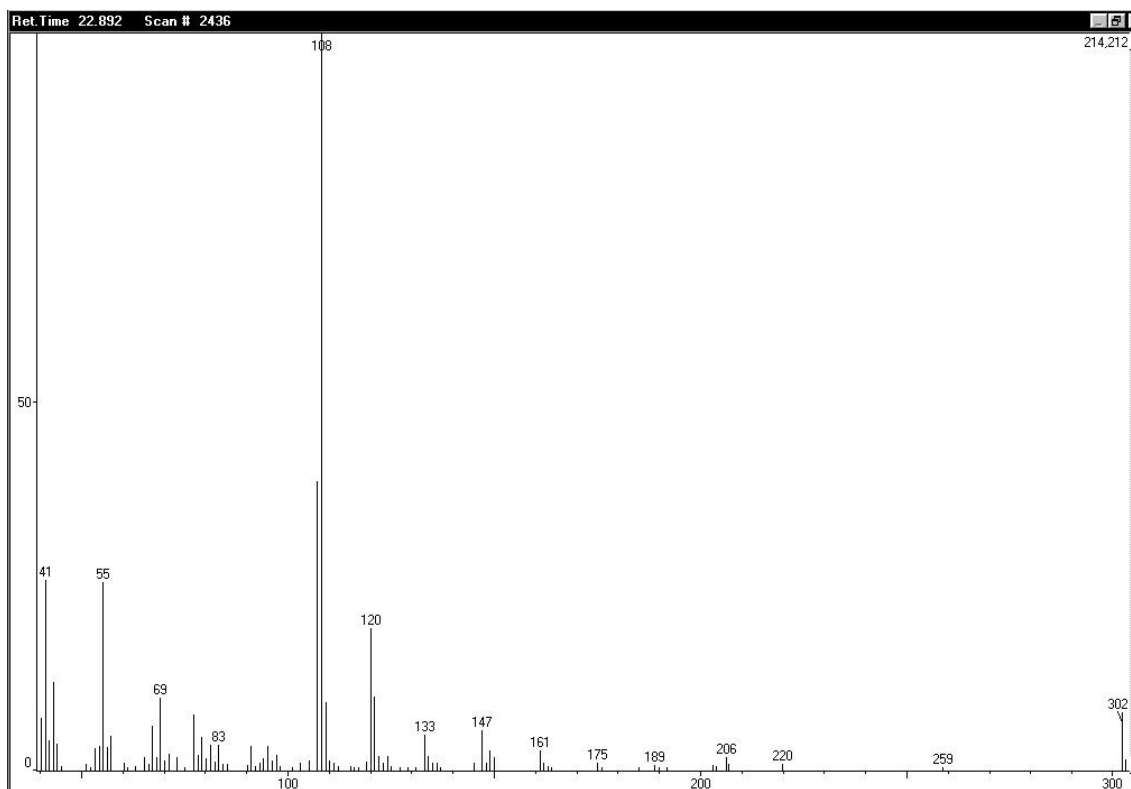


Figure 3. GC-EI-MS of the mass spectrum of 3-(8-pentadecenyl) phenol (12).

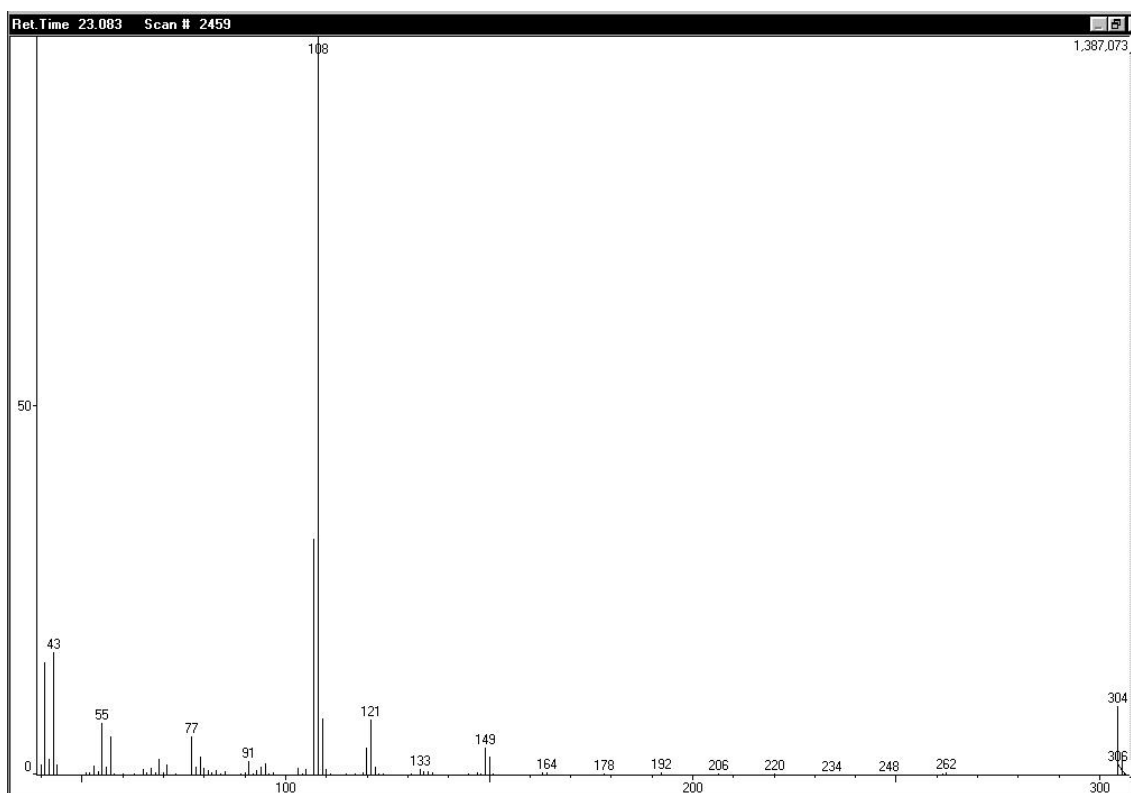


Figure 4. GC-EI-MS of the mass spectrum of 3-pentadecyl phenol or hydrocardanol (13).

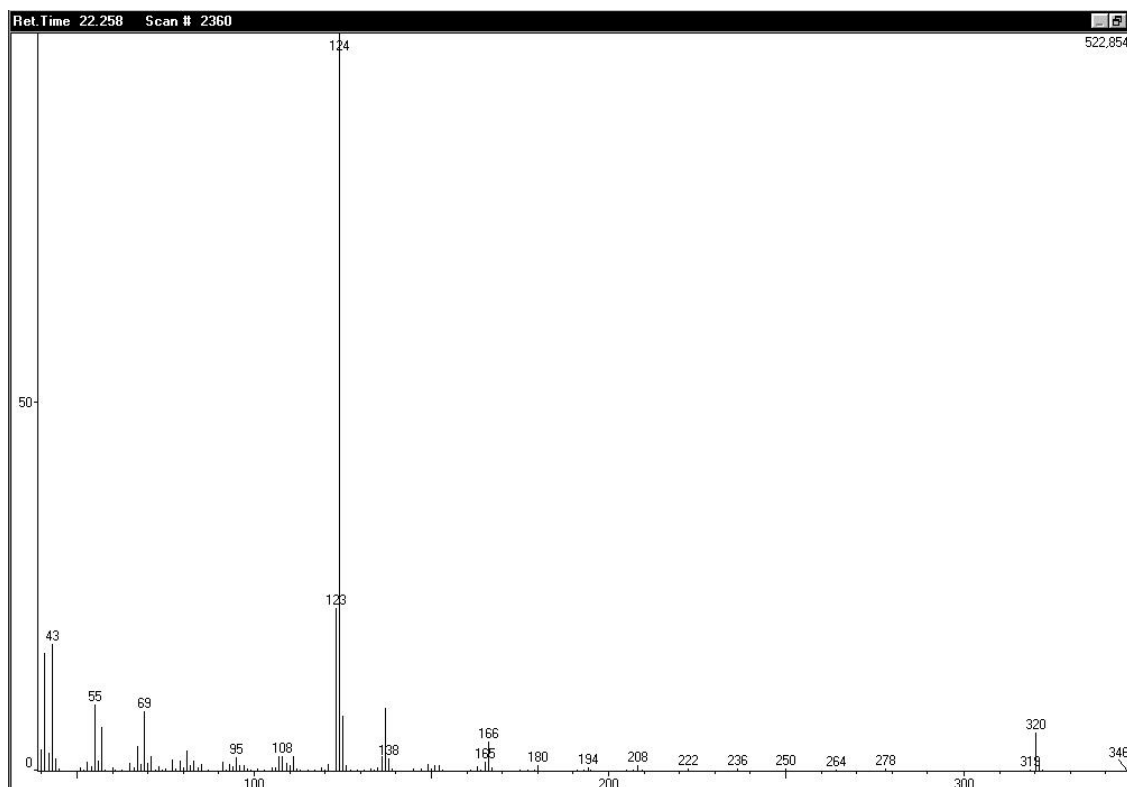


Figure 5. GC-EI-MS of the mass spectrum of 5-pentadecyl resorcinol or cardol (11).

Another sample of geopropolis harvested in Barra do Corda, exhibited an anti-tumoral effect on the solid Ehrlich tumor and on tumor-bearing mice lymphoid organs (Araújo et al., 2010). There are less reports about the chemical composition and biological activity of the *Scaptotrigona* genus than of the *Melipona* genus. Flavonol methyl ethers and methoxychalcones were detected in the geopropolis from *Scaptotrigona aff. depillis* harvested in the State of Rio Grande do Norte, northeastern Brazil, for which the resin source was *Mimosa tenuiflora* (Ferreira et al., 2017). Regional and seasonal differences were observed in the chemical compositions of geopropolis samples from *Scaptotrigona* spp., *Scaptotrigona depillis* and *Scaptotrigona bipunctata*, harvested monthly from two distinct Brazilian states, Maranhão and São Paulo. Diterpene acid derivatives were detected in the three geopropolis samples. However, the chemical profile obtained for the geopropolis from *Scaptotrigona* ssp, harvested in Maranhão State was different from that obtained for the geopropolis from the *Scaptotrigona* species, harvested in the state of São Paulo (Sawaya et al., 2009, 2007). The results obtained by Sawaya et al. (2009) indicated that the geopropolis from *Scaptotrigona* spp., harvested in Maranhão State, probably used *Schinus terebenthifolius* and conifers as the resin sources, while *Hymenaea courbaril* (Caesalpinioideae) was the resin source used for the geopropolis obtained from *Scaptotrigona depillis* and *Scaptotrigona bipunctata*, harvested in São Paulo state. On the other hand, the steroid ethisterone and cardanol were found in the geopropolis from *Scaptotrigona aff. postica* harvested in São Paulo city, which exhibited cytotoxic activity for all cells (Sanches, 2014).

The pollen spectrum of the geopropolis from *S. postica* harvested in Barra do Corda, exhibited 94 pollen types belonging to 35 plant families, the families Fabaceae and Rubiaceae exhibiting the highest pollen contents. The most frequent pollen types found were *Borreria verticillata*, *Anadenanthera* sp. and *Mimosa caesalpiniiifolia* (Souza et al., 2015). Amongst the pollen types, 34 unique pollen types occurred in a given month of the year, which were characterized as seasonal indicators of flowering species, influenced by seasonal and interannual variations in climate (Souza et al., 2015). Much research has been carried out

using cardanol, suggesting different types of applications for this compound and its derivatives (Barbosa et al., 2019; Mubofu & Mgaya, 2018).

Cardanol and cardol are non-polar compounds typical of plants of the genus of the family Anacardiaceae, both in native and cultivated cultures. Anacardic acid, cardanol, cardol and methyl cardol, with different degrees of unsaturation (monoene-15:1, diene-15:2, and triene-15:3), were isolated from cashew (*Anacardium occidentale*), family Anacardiaceae (Morais et al., 2017; Fadeyi et al., 2015; Gómez-Caravaca et al., 2010). Thus, possibly a plant of the Anacardiaceae family, probably *Anacardium occidentale* and/or *Mangifera indica*, could be the resin source for this propolis.

Cardanols, known as phenolic lipids, due to their amphiphilic character derived from a hydrophilic hydroxyl group and a hydrophobic long chain hydrocarbon (Stasiuk & Kozubek, 2010), were detected in fungi, bacteria and in propolis obtained from *Apis mellifera* (Boonsai et al., 2014; Teerasripreecha et al., 2012) and from stingless bees (Araújo et al., 2015; Sanches, 2014). The presence of cardanols in the propolis obtained from Teresina, Piauí State, northeastern Brazil, was attributed to the presence of several cashew trees (*Anacardium occidentale*) around the apiary (Silva et al., 2008). Cardanols were detected in Brazilian green propolis from São Paulo State, (Negri et al., 2003); in propolis from Oman, a country located on the southeastern coast of the Arabian Peninsula in Western Asia (Popova et al., 2013), and in propolis samples harvested in Thailand and in Indonesia (Teerasripreecha et al., 2012). The presence of these compounds in propolis from Thailand, Indonesia and Oman indicated that *Mangifera indica* (Anacardiaceae) was the resin source (Popova et al., 2013; Teerasripreecha et al., 2012).

Thirteen alkenylphenols and nine alkenylresorcinols were detected in propolis from North-Western Cameroon, along with triterpenoids (Kardar et al., 2014). In Thai *Apis mellifera* propolis from different locations triterpenes and three inseparable mixtures of phenolic lipids (cardols, cardanols and anacardic acids) were detected, indicating mango (*Mangifera indica*) as the resin source (Sanpa et al., 2017). Thai *Apis mellifera* propolis is a tropical propolis type, which exhibited considerable antibacterial activities (Sanpa et al., 2017). Beside this, large amounts of cardanols and cardols were detected in the geopropolis produced by *Melipona fasciculata* Smith from Palmeirândia, Maranhão State, northeastern Brazil (Araújo et al., 2015) and in the geopropolis from *Scaptotrigona aff. Postica*, harvested in São Paulo city (Sanches, 2014). Alkenylresorcinols were isolated from the Indonesian propolis from East Java, that used *Macaranga tanarius* L. and *Mangifera indica* L. as the resin sources (Trusheva et al., 2011). Three ent-kaurene diterpenoids were isolated from a sample collected by the native Brazilian bees *Melipona quadrifasciata anthidioides*. Kaurenoic acid, as well as the total extract, exhibited moderate antibacterial activity (Velikova et al., 2000).

Some studies have demonstrated interesting biological activities exhibited by non-polar extracts of geopropolis. The hexane fractions of the geopropolis from *Melipona scutellaris*, harvested in the Atlantic forest of Bahia State (Northeastern Brazil), exhibited considerable antibacterial activity against *Streptococcus mutans*, antitumoral activities against human cancer cell lines (Cunha et al., 2013a) and antinociceptive activity (Franchin et al., 2012). The hexane extract of the geopropolis from *Melipona mondury*, which possesses anacardic acid derivatives as constituents, exhibited antioxidant, antibacterial and antiproliferative activities (Santos et al., 2017a).

Phenolic lipids can be incorporated into erythrocytes and liposomal membranes due to their hydrophilic (water-loving, polar) and lipophilic (fat-loving) properties (Stasiuk & Kozubek, 2010; Kruk et al., 2017) and can be used in pharmaceutical and fine chemical processes (Saladino et al., 2008; Behalo et al., 2016). Beside this, they also exhibited antioxidant (Andrade et al., 2011; Luís et al., 2016), antibacterial (Sibandze et al., 2016), antifeedant, cytotoxic, anticarcinogenic (Kruk et al., 2017), antiproliferative, antileishmanial, antigenotoxic (Parikka et al., 2006), antifungal (Popova et al., 2013) and anti-acetylcholinesterase activities (Oliveira et al., 2011). Cardanols are promising agents for the control of *Aedes aegypti*, the main dengue vector in Brazil, due to their larvicidal activity (Oliveira et al., 2011).

The unsaturated cardanols 3-(4,7-heptadecadienyl) phenol (**5**), 3-(10-heptadecenyl) phenol (**7**) and 3-(8-pentadecenyl) phenol (**12**) were found in large amounts in these non-polar propolis extracts from *S. postica*. According to Stasiuk & Kozubek (2010), cardanols with long unsaturated carbon chains (cardanols C15:1 and C17:1) exhibit more potent activities than those with long saturated chains (cardanols C13:0 and C15:0). The antibacterial activities of these compounds, inhibiting bacterial, fungal, protozoan and parasitic growth, such as *Staphylococcus aureus*, *Escherichia coli*, *Candida tropicalis*, *Candida albicans*, *Mycobacterium smegmatis* and *Mycobacterium aurum*, depend on their interaction with proteins and/or their membrane-disturbing properties (Stasiuk & Kozubek, 2010; Kruk et al., 2017; Sibandze et al., 2016). Cardanol from the Thai *Apis mellifera* propolis, exhibited considerable antibacterial activity (Sanpa et al., 2017), promoting changes in the morphology of *Escherichia coli*, especially in the cell membrane and cell division (Boonsai et al., 2014).

The saturated cardanols, 3-heptadecylphenol (**9**) and 3-pentadecylphenol or hydrocardanol (**13**) were also detected in large amounts in these non-polar extracts. Cardanols C13:0 and C15:0 exhibited the greatest inhibitory effects on the human colon cancer cells HCT-116 and HT-29, and both decreases and increases in the side chain lengths of the cardanol diminished the anticancer activities (Zhu et al., 2012). Cardanols effectively inhibited tyrosinase activities (Yu et al., 2016) and as effective antioxidants exhibited antimutagenic and antitumoral activity. However, despite their chemoprotective capacity, the cardanols exhibited a tendency to induce DNA damage (Schneider et al., 2016).

The cardanol and cardol found in the propolis samples from Thailand and Indonesia exhibited potent anticancer activity (Teerasripreecha et al., 2012). The cardol (C15:0) isolated from *Anacardium occidentale* was cytotoxic to the murine B16-F10 melanoma cells (Kubo et al., 2011). Cardols exhibited many physiological and pathological processes related to the immune system, such as cell signaling and gene regulation (Kozubek & Tyman, 1999). Beside this, they can induce the expression of a pro-inflammatory cytokine and the tumor necrosis factor (TNF- α) and suppress regulatory cytokines, including interleukin (IL-10) and the interferons, IFN- α and IFN- β (Hung et al., 2013). The cytotoxic activity of cardols was demonstrated against the human colon, breast, lung, central nervous, ovarian, cervical and hepatocarcinoma cancer cell lines (Kruk et al., 2017; Zhu et al., 2012). However, anticancer activity was demonstrated against the breast cancer BT-474 cell line and attributed to an increase in the phosphorylation of the extracellular signal-regulated kinases (ERK), JNK and classical MAP kinases (p38 MAPK), which can lead to the obstruction of DNA synthesis (Buahorm et al., 2015). 5-Pentadecatrienylresorcinol, prevented the generation of superoxide radicals catalyzed by xanthine oxidase without the inhibition of uric acid formation (Masuoka et al., 2015). *Ent*-kaurane diterpenoids exhibit a broad spectrum of potential therapeutic effects including anticancer activity (Pham et al., 2016).

4 Conclusions

Propolis from *S. postica*, harvested in Barra do Corda, Brazil, is a natural source of bioactive compounds with promising biological activities. Large amounts of cardanols were found in the non-polar extracts obtained using hexane and chloroform, and the biological activity of cardanols and cardols has been demonstrated in many research projects. These compounds can be used for industrial applications in the food industry and in the pharmaceutical industry for the development of new drugs.

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