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Chemical composition and antimicrobial activity of *Cordia globosa* (JACQ.) essential oil against *Staphylococcus aureus*

Composição química e atividade antimicrobiana do óleo essencial de *Cordia globosa* (JACQ.) contra *Staphylococcus aureus*

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RESUMO

Cordia globosa (Jacq.), conhecida como "maria preta" na região Nordeste do Brasil, é uma planta de ampla utilização no tratamento de doenças gastrointestinais. Este trabalho teve como objetivo obter o perfil químico do óleo essencial da parte aérea de C. globosa, atividade antimicrobiana e antibiofilme contra Staphylococcus aureus. Nas análises de GC/MS foram detectados 47 compostos, dos quais monoterpenos 17,74%, monoterpenos oxigenados 6,84%, sesquiterpenos 40,50%, sesquiterpenos oxigenados 29,87%. Óxido de cariofileno 13,04%, β-Elemeno 12,30% e E-cariofileno 10,13%. Nos resultados, a CIM e o CBM foram de 1 mg/mL e 8 mg/mL, respectivamente. A ação antibiofilme foi confirmada para reduzir a biomassa do biofilme de S. aureus em até 97% entre concentrações de 2mg/mL e 4mg/mL. O óleo essencial de C. globosa demonstrou ser um antibiótico promissor contra S. aureus.

Palavras-chave: *Boraginaceae*; *C. globosa*; Óleo essencial; Cariofileno; Anti-biofilme.

ABSTRACT

Cordia globosa (Jacq.), Known as "maria preta" in the northeastern region of Brazil, is a plant that has widespread use in the treatment of gastrointestinal diseases. This work aimed to obtain the chemical profile of the essential oil of aerial parts of *C. globosa*, antimicrobial activity, and antibiofilm against *Staphylococcus aureus*. In the GC/MS analyses 47 compounds were detected, of which monoterpenes 17.74%, monoterpenes oxygenate 6.84%, sesquiterpenes 40.50%, sesquiterpenes oxygenate 29.87%. Caryophyllene oxide 13.04%, β-Elemene 12.30%, and E-Caryophyllene 10.13%. In the results, MIC and MBC were 1mg/mL and 8 mg/mL, respectively. The antibiofilm action was confirmed to reduce the biofilm biomass of *S. aureus* up to 97% between 2mg/mL and 4mg/mL concentrations. The essential oil of *C. globosa* was shown to be a promising antibiotic against *S. aureus.*

Keywords: *Boraginaceae*; *C. globosa*; Essential oil; Caryophyllene; Anti-biofilm.

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INTRODUCTION

The genus *Cordia* has approximately 100 species in the neotropical regions, are multistemmed shrubs with condensed inflorescence and uniformly serrated leaves with about 30 species of *Cordia* in Brazil, distributed in several biomes with Atlantic forest, cerrado, and caatinga (STAPF, 2010)

Chemical analyses of the essential oil of specimens of the *Cordia* genus have presented monoterpenes and sesquiterpenes, hydrogenated and oxygenated (DE OLIVEIRA; DA CAMARA; SCHWARTZ, 2007; DAS GRACAS et al. 2010; OZA; KULKARNI, 2017).

Cordia globosa (Jacq.) Kunth is a shrub popularly known in northeastern Brazil as "maria-preta" and has it's used in traditional medicine for the treatment of rheumatism, painful menstruation, and dyspepsia (SILVA et al., 2010).

This research aimed to discover the chemical composition of the essential oil of aerial parts *C. globosa* (Jacq.) Kunth and to test its activity antimicrobial activities and antibiofilm activity against strains of clinical interest.

MATERIAL AND METHODS

Collection and identification of botanical material

The aerial parts of *C. globosa* were collected in the Serra da Ibiapaba Ceara Brazil, S – 03º50’02.7” e W – 040º56’35.1”, 877 meters above sea level, in the months April. The plant material was identified by Dr. Elnatan Bezerra de Souza and deposited under accession number 18.083.

Extraction of the essential oil

Aerial parts were air-dried, ground, and submitted to extraction by the hydrodistillation method, from their newly harvested flowers. After heavy flowers were transferred to a volumetric flask of 500 mL, with enough water to cover all the leaves, being subjected to hydrodistillation for 3 hours, after the boiling period. Anhydrous sodium sulfate was used to extract the oil from the aqueous phase and then stored at low temperatures for future analysis.

Analyses of constituents of the essential oil

The chemical composition of the essential oil was analyzed using a gas chromatograph coupled to a mass spectrometer (GC/MS – Shimadzu QP-2010 Plus) equipped with a Factor Four/ VF – 5ms fused-silica capillary column (30 m x 0.25 mm x 0.25 um film thickness), using helium as carrier gas at 1mL/min. The initial oven

temperature was 60 ºC, which after being held constant for 2 min was increased at a rate of 3 ºC min^{-1} to 260 ºC, followed by 10 ºC min^{-1} to 290 ºC, with a final isotherm (290 ºC) for 10 min. The sample injection was 1uL (1:50 split mode). The injector and detector temperatures were of 220 ºC and 250 ºC, respectively. The mass specter was obtained in a range of m/z 10-300, by the electron impact technique at 70 eV.

The quantitative analysis of the oils chemical composition was carried out in gas chromatography coupled to an HP5890 Series II flame ionization detector (FID), using the same operating conditions and the same type of column as in the GC/MS analysis.

The percentage of each constituent was calculated by the integral area under the respective peaks in relation to the total area of all the sample constituents.

The various chemical constituents of the essential oil were identified by visual comparison of their mass spectra with those in the literature (ADAMS, 2017) and spectra supplied by the equipment database (NIST 08), as well as by comparison of the retention indices with those in the literature (ADAMS, 2017). A standard solution of n-alkanes (C8-C20) was injected under the same chromatographic conditions as the sample and used to obtain the retention indices as described by Van Den Dool and Dec. Kratz (1963).

Minimum inhibitory concentration (MIC)

To determine the MICs by means of the microdilution test in broth, the compounds OECg were tested against the strains *S. aureus*. The MIC test was standardized according to the Methods for Dilution Antimicrobial Susceptibility Test for Bacteria That Grow Aerobically; Approved Standard - Tenth Edition (CLSI, 2018) with modifications, as described below.

The minimum inhibitory concentration was determined by the microdilution technique in 96-well polystyrene plates. The calculations for the preparation of the solutions containing OECG were performed based on the densities of the substances. For the assembly of the plates, OECG was prepared at an initial concentration of 14 mg/mL and serially diluted in a culture medium so that the concentrations varied ranged from 0.125 to 4 mg/mL. Then 100 µL of culture medium containing the microorganisms was adjusted to the concentration of 10^6-10^8 CFU/mL and added. The negative control consisted of growing the microorganisms in the TSB culture medium with 2% Tween 20. The lowest concentration of each substance at which no microbial growth was detected was considered the MIC, through a visual reading the lower attention.

Minimum bactericidal concentration (MBC)

The minimum bactericidal concentration was determined by removing a 10µL aliquot from the solutions considered to contain each substance at its MIC. The aliquot, in triplicate, was inoculated in Petri dishes containing TSA, and the dishes were placed in an incubator at 37 °C. Bacterial growth was observed after 24 hours (SA et al., 2012)

Antibiofilm activity

The ability to inhibit biofilm formation was determined by the indirect biomass-quantification technique using crystal violet (CV) and by the colony-forming unit (CFU)-counting technique, which provides data on the viability of the cells contained in the biofilm. The plaques were assembled in a process similar to the MIC test, and after 24 hours, the antibiofilm activity was verified; the bacterium used was *S. aureus*. After the 24-hour incubation, the plates were washed with sterile water (200 µL/well) to remove the loosely adhered and air-dried cells. The adhered cells of the biofilm were fixed in the wells of the plate by the addition of 200 µL of methanol for 15 min. After 15 min, the methanol was removed, and 200 µL of 1% crystal violet was added for 15 min. Then, the plates were washed again and air-dried. Next, 200 µL of ethanol (96%) was added to the wells, and the plates were left shaking for 5 min and then read on a microplate reader at 595 nm (SA et al., 2012). After the incubation period, colony-forming units (CFU mL^{-1}) were determined.

Counting of colony-forming units (CFU)

After the incubation period, the culture medium was removed, and the plates were subjected to three washes with distilled water. Then, 200 µL of 0.9% saline was added to the wells, and the plate was sonicated in an ultrasonic bath (GNATUS Digital Ultrasonic Cleaner) operating at 50 kHz for 10 min. The liquid from the wells was pooled to a total volume of 1 mL, from which a 20 µL aliquot was withdrawn and serially diluted in a volume of 180 µL of saline (10^{-1} to 10^{-6}). In a Petri dish containing TSA, three aliquots of 10 µL were cultured, constituting a triplicate for each concentration. These plates were placed in a greenhouse for 24 hours at 37 °C, and the counting of the colony-forming units was performed by manually counting the visible wells after incubation (SA et al., 2012).

Molecular Docking

Staphylococcal Signal peptidase IB (spsB) crystal structure of the PDB code 4WVJ was used. Docking experiments were performed using AutoDock Vina docking

software version 1.2.0 using exhaustiveness 24. The caryophyllene oxide had its 3D structure was downloaded ZINC15 database, and employed the program MarvinSketch version 18.16, ChemAxon (www.chemaxon.com) for their major microspecies at pH = 7.40. After a careful visual inspection, the compound was optimized utilizing the PM7 semiempirical theory level implemented in MOPAC2016 (HTTP://OpenMOPAC.net). The images were generated with Biovia Studio Discovery Viewer version 21 (BIOVIA, San Diego).

Statistical analysis

The statistical evaluation of the data was performed with the program Prism, GraphPad®, San Diego, California, USA, version 5.0. The statistical test used for multiple comparisons was ANOVA, followed by the Bonferroni test. Values of $p < 0.01$ were considered statistically significant and are indicated by an asterisk. The MBC and CFU tests were performed with three replicates. All tests were performed in three independent experiments.

RESULTS AND DISCUSSIONS

Analysis of essential oil constituents of C. globosa

Table 1 shows the chemical composition of the essential oil of aerial parts of C. globosa. A total of 47 compounds were detected, of which Monoterpenes 17.74%, Monoterpenes oxygenate 6.84%, Sesquiterpenes 40.50%, Sesquiterpenes oxygenate 29.87%. Caryophyllene oxide 13.04%, β-Elemene 12.30 %, and E-Caryophyllene 10.13%.

The result was different from some studies found in the literature. Melissa et al., 2016 analyzed the essential oil of *C. globosa* in Mexico and observed it as a major component of the α-Pinene with 38.4%. de Oliveira et al., 2007 analyzed the essential oil of *C. globosa* and detected it as a major component β-Caryophyllene 39% and caryophyllene oxide 5.9% with total sesquiterpenes of 84.2%. These different chemical compositions may be associated with environmental factors or growing conditions (KURT, 1997).

Table 01 - Chemical composition, retention index of the literature (RI_{Lit}), percentage of the identified components (%) from the essential oil of Cordia *globosa* (EOCg) aerial parts

Compounds	**RI_{Lit}**	**EOCg**
Monoterpenes		**17.74%**
E-Salvene	866	-
Tricycleno	926	0.72
α-Pinene	939	6.03

Canfene	954	0.92
Sabinene	975	2.63
β-Pinene	979	5.87
ρ-Cymene	1024	0.83
Limonene	1029	0.74
Monoterpenes oxygenated		**6.84%**
1,8 – Cineole	1031	3.37
Linalool	1096	1.31
E-Pinocarveol	1139	0.25
Camphor	1146	0.98
Borneol	1169	0.28
Terpinen-4-ol	1177	0.65
Sesquiterpenes		**40.50%**
α-Ylangene	1375	3.82
β-Bourbonene	1388	1.09
β-Elemene	1390	12.30
E-Caryophyllene	1419	10.13
E-α- Caryophyllene	1434	1.10
α-Humulene	1454	1.63
Allo-Aromadendrene	1460	0.75
γ-Muurolene	1479	2.87
Germacrene-D	1485	0.10
β-Selinene	1490	0.44
Viridiflorene	1496	2.24
α-Muurolene	1500	0.24
Germacrene-A	1509	0.31
δ-Cadinene	1523	1.92
Germacrene-B	1561	1.56
Sesquiterpenes oxygenated		**29.87%**
Cubebol	1515	0.49
E-Nerolidol	1563	0.77
Spathulenol	1578	4.76
Caryophyllene oxide	1583	13.04
Viridiflorol	1592	1.35
Humulen epoxide II	1608	1.06
Muurola - 4, 10 (14) - dien-1-β-ol	1631	1.81
Selen-11-en-4-α-ol	1659	3.68
Amorpha-4,9-dien-2-ol	1700	-
14-Hydroxy-α-humulene	1714	0.98
γ-Z-Curcumen-12-ol	1729	-
Vetiselinenol	1731	1.01
γ-Costol	1746	-
2,7(14),10-Bisabolatrien-1-ol-4-one	1845	0.92
Kudtdiol	1912	-
Others		**2.10%**
N-Nonanal	1100	0.37
Cryptone	1185	1.73
Isobaeckeol methyl ether	1778	-
Total		**97.05**

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MIC and MBC tests for essential oils

The result of the antimicrobial activity of EOCg can be seen in table 2.

Table 02 – MIC *and MBC values again Staphylococcus aureus* strain

Specie	MIC	MBC
C. globosa	1 mg/mL	>8 mg/mL

MIC - Minimum Inhibitory Concentration - 1 x 10 7 CFU / mL. MBC- Minimum Bactericidal Concentration. *Staphylococcus aureus* with ATCC record 6538 - Lot 0712039. Concentrations studied: 0.125; 0.25; 0.5; 1.0; 2.0 and 4.0 mg / mL of essential oil. Font: Authors

The bactericidal properties of essential oils are associated, among other factors, with the class of major components or the synergy itself that may occur among minority components (BAKKALI et al., 2008; SAAD; MULLER; LOBSTEIN, 2013)

Essential oils with a higher percentage of monoterpenes are more efficient in inhibiting bacterial growth (MIRANDA et al., 2016). The antimicrobial activity of most terpenoids, such as *p*-cymene, is related to their functional groups, and the hydroxyl group of the phenolic terpenoids and the presence of delocalized electrons are essential elements for their antimicrobial action (NAZZARO et al. 2013).

Melissa et al. (2016) studied the essential oil of *C. globosa*, collected in Mexico concerning the MIC value against *S. aureus*, a matter of 1.00 mg/mL was also observed in our study. It is observed that the variation and the synergy of the chemical composition presented in the chemical analyzes of the constituents present, can interfere with the final result (BAKKALI et al., 2008). On the other hand, terpenes, such as limonene, α-pinene, β-pinene, γ-terpinene, δ-3-carene, (+) - sabinene, and α-terpinene showed very low or no antimicrobial activity against 25 genera of bacteria (DORMAN; DEANS, 2000.

In the case of sesquiterpenes, the antimicrobial and cytotoxic activities of the sesquiterpenes are presented in essential oils with significant values. However, Crevelin et al. (2015) observed low bactericidal activity (MIC> 4mL/mL) of the essential oil of *Plectranthus neochilus*, in which caryophyllene oxide corresponded to 12.8%.

Inhibition of bacterial biofilm formation by Staphylococcus aureus

The results of the percentage inhibition of the biomass of Staphylococcus aureus are observed in table 03.

According to the table, EOCg reduced *S. aureus* biomass from 40% to 97%, when a concentration in the range of 0.125mg/mL to 4mg/mL was used. The EOCg showed

similar results to the controls, chlorhexidine, and vancomycin at concentrations of 2mg/mL and 4mg/mL.

The use of essential oils and by-products has become one of the strategies to combat the formation and development of biofilms. Inhibition of the formation of bacterial biofilms and quorum sensing by essential oils and their major components have been reported (KEREKES et al., 2013; BAI; VITTAL, 2014; KIM et al., 2016), The EOCg showed promise as an inhibitor of biofilm formation by *S. aureus.*

The EOCg induced reduction of the viability of *S. aureus* cells in biofilm concentrations above 1mg/mL, inhibition was 5.66 log CFU/mL and 4.1 logs CFU/mL in the concentrations 2mg/mL and 4mg/mL, respectively (figure 1). When compared to EOCg controls not showed complete inhibition in cellular viability.

The major component β-caryophyllene is a plant compound, a member of bicyclic sesquiterpene, and may occur in nature mainly as trans-caryophyllene mixed with small amounts of its isomers, (Z)-β-caryophyllene (iso-caryophyllene) and α- humulene (α-caryophyllene), as well as its oxidation derivative β-caryophyllene oxide. Dahham et al. (2015) reported antibacterial activity against *S. aureus* bacteria at a concentration of 6,13 mg/mL. The antimicrobial activity of β-caryophyllene could be attributed to its strong antioxidant activities (DORMAN; DEANS, 2000).

Table 03 - C. globosa: inhibition of biofilm formation

Concentration	*C. globosa*	Chlorhexidine (topic)	Vancomycin (oral)
4 mg/mL	95.07±0.14 Aa	95.07±1.45 Aa	97.12±1.15 Aa
2 mg/mL	97.32±0.17 Aa	93.31±2.22 Aa	93.88±1.52 Aa
1 mg/mL	84.97±1.85 Ba	100.0±0.00 Ab	96.55±1.80 Ab
0.5 mg/mL	64.45±2.32 Ca	99.71±0.26 Ab	93.16±2.72 Ab
0.25 mg/mL	47.42±3.14 Da	97.67±1.11 Ab	92.03±2.08 Ab
0.125mg/mL	40.58±3.10 Da	99.83±0.13 Ab	92.49±1.90 Ab

Averages ± standard error followed by the same letter do not differ statistically from one another, upper-case letters correspond to the columns, and lower-case letters correspond to the rows. One-way ANOVA test ($p < 0.05$) with the Bonferroni post-test. Font: Authors

Molecular Docking

Study was performed for Caryophyllene oxide to identify potential protein targets (SAYED et al., 2020). Table 4 arranges the binding energies in kcal/mol of the two compounds against a list of possible targets.

Table 04. Binding energies (kcal/mol) of Caryophyllene oxid against a number of possible staphylococcal targets

Protein	PDB	Caryophyllene oxide (kcal/mol)
UDP-N-acetylenolpyruvoylglucosamine reductase (MURB)	1HSK	-7.4
Peptide deformylase (def)	1Q1Y	-7.3
3-oxoacyl-[acyl-carrier-protein] synthase 2 (FabF)	2GQD	-5.4
D-alanine--D-alanine ligase (ddl)	2I87	-6.3
Dihydrofolate reductase (DHFR)	2W9H	-8.2
DNA gyrase subunit B (Gyr B)	3G7B	-6.2
Enoyl-[acyl-carrier-protein] reductase [NADPH] (fabI)	4CV1	-7.7
Ribosomal RNA large subunit methyltransferase H	4FAK	-5.5
Dna Topoisomerase Iv, B Subunit	4URN	-5.7
Signal peptidase IB (spsB)	4WVJ	-8.8
Sensor protein kinase (WalK)	5IS1	-4.5

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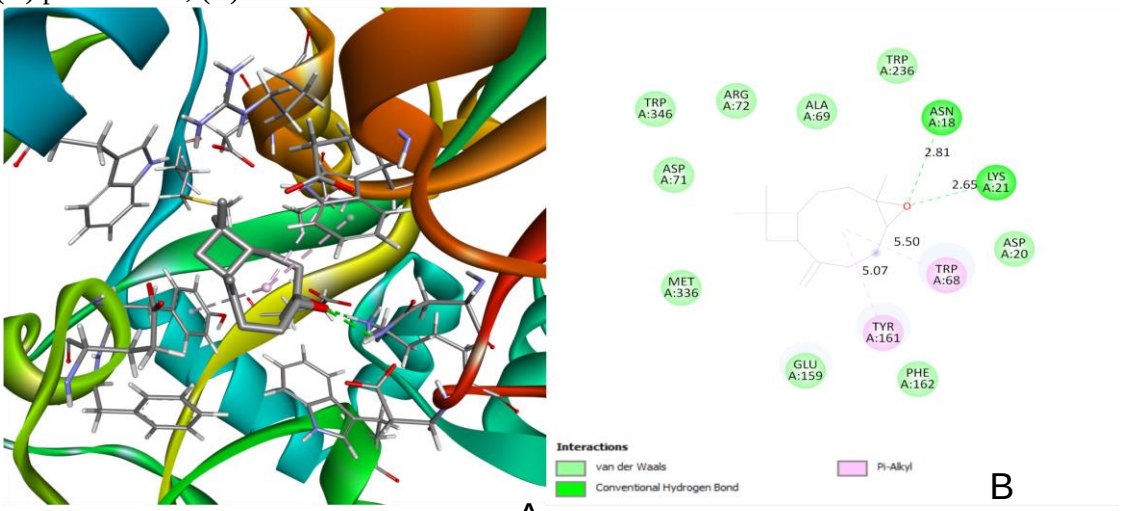
The potential binding modes of spsB crystal structures of the PDB code 4WVJ were chosen for the docking experiments due to their optimum resolution of 1.95 Å. The binding energy was -8.8 kcal/mol showing the highest predicted affinity.

Caryophyllene oxide ligand registered interaction with 13 amino acids (Figure 02). The ligand interacts with the residues Lys21, Asn18, Trp236, Ala69, Arg72, Trp346, Asp71, Met336, Glu159, Phe162, Tyr161, Trp68, Asp20. The hydrogen bond is performed with amino acids Lys21, and Asn18, with 2.65 Å and 2.81 Å respectively.

Two interaction was performed with the benzene ring of Caryophyllene oxide, the pi-alkyl interactions that were established with the Tyr161, and Trp68 with 5.07 Å and 5.50 Å respectively.

Figure 01- Molecular docking caryophyllene oxide molecule and Signal peptidase IB (spsB) 4WVJ. (A) pocket view; (B) 2D view



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The development of biofilm is controlled by a complex global regulatory system. One of the regulatory systems is the quorum-sensing (QS) system, which is responsible for the intercellular communication of bacteria (KONG; VUONG; OTTO, 2006; LU et al., 2019). The agr system, the most essential part of the QS system of S. aureus. that consists of two different operons, RNAII and RNAIII, activated by the promoters P2 and P3, respectively (HARRAGHY; KERDUDOU; HERRMANN, 2007).

The operon RNAII contains agr BDCA genes, encoding AgrBDCA proteins, AgrD, the precursor of AIP, auto-inducing peptides (AIPs), that control the cell population density, is produced and exported on the plasma membrane with AgrB and Spsb (GORDON et al., 2016; GUO et al., 2022). SpsB has been considered an attractive antibacterial target, and inhibitors of the enzyme have been described in the literature (BUZDER-LANTOS et al., 2009; THERIEN et al., 2012). Studies of inhibition of biofilms with isolated Caryophyllene oxide, an enzymatic assay of SpsB, and checkerboard assays are necessary because it is important not to underestimate the significance of minor components on the antibacterial activity of essential oils (MILADINOVIĆ et al., 2021).

CONCLUSIONS

The essential oil of *C. globosa* presented an inhibitory action on the Gram-positive *Staphylococcus aureus* (ATCC 6538), as well as a decrease in the biomass and planktonic cells.

REFERENCES

ADAMS, Robert P. Identification of essential oil components by gas chromatography/mass spectrometry. 5 online ed. **Gruver, TX USA: Texensis Publishing**, 2017.

BAI A, Jamuna; VITTAL, Ravishankar Rai. Quorum sensing inhibitory and anti-biofilm activity of essential oils and their in vivo efficacy in food systems. **Food Biotechnology**, v. 28, n. 3, p. 269-292, 2014.

BAKKALI, Fadil et al. Biological effects of essential oils–a review. **Food and chemical toxicology**, v. 46, n. 2, p. 446-475, 2008.

BUZDER-LANTOS, Peter et al. Substrate based peptide aldehyde inhibits bacterial type I signal peptidase. **Bioorganic & medicinal chemistry letters**, v. 19, n. 10, p. 2880-2883, 2009.

CLSI. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard, 11th ed. CLSI document M07-A11. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA. 2018.

CREVELIN, Eduardo José et al. Antimicrobial activity of the essential oil of Plectranthus neochilus against cariogenic bacteria. **Evidence-Based Complementary and Alternative Medicine**, v. 2015, 2015.

DAHHAM, Saad S. et al. The anticancer, antioxidant and antimicrobial properties of the sesquiterpene β-caryophyllene from the essential oil of Aquilaria crassna. **Molecules**, v. 20, n. 7, p. 11808-11829, 2015.

DAS GRACAS, M. et al. Volatiles of the Cordia Multispicata cham.: A weed medicinal Brazilian plant. **Journal of Essential Oil Research**, v. 22, n. 6, p. 543-545, 2010.

DE OLIVEIRA, José CS; DA CAMARA, Claudio AG; SCHWARTZ, Manfred OE. Volatile constituents of the stem and leaves of Cordia species from mountain forests of Pernambuco (north-eastern Brazil). **Journal of Essential Oil Research**, v. 19, n. 5, p. 444-448, 2007.

DORMAN, HJ–Deans; DEANS, Stanley G. Antimicrobial agents from plants: antibacterial activity of plant volatile oils. **Journal of applied microbiology**, v. 88, n. 2, p. 308-316, 2000.

GORDON, Christopher P. et al. Truncated autoinducing peptides as antagonists of Staphylococcus lugdunensis quorum sensing. **Journal of medicinal chemistry**, v. 59, n. 19, p. 8879-8888, 2016.

GUO, Henan et al. Biofilm and small colony variants—an update on staphylococcus aureus strategies toward drug resistance. **International journal of molecular sciences**, v. 23, n. 3, p. 1241, 2022.

HARRAGHY, Niamh; KERDUDOU, Sylvain; HERRMANN, Mathias. Quorum-sensing systems in staphylococci as therapeutic targets. **Analytical and bioanalytical chemistry**, v. 387, p. 437-444, 2007.

KEREKES, E.-B. et al. Anti-biofilm forming and anti-quorum sensing activity of selected essential oils and their main components on food-related micro-organisms. **Journal of Applied Microbiology**, v. 115, n. 4, p. 933-942, 2013.

KIM, Yong-Guy et al. Essential oils and eugenols inhibit biofilm formation and the virulence of Escherichia coli O157: H7. **Scientific reports**, v. 6, n. 1, p. 36377, 2016.

KONG, Kok-Fai; VUONG, Cuong; OTTO, Michael. Staphylococcus quorum sensing in biofilm formation and infection. **International journal of medical microbiology**, v. 296, n. 2-3, p. 133-139, 2006.

KURT, B. G. Torsell. **Natural product chemistry: a mechanistic, biosynthetic and ecological approach**. Swedish Pharmaceutical Press, 1997.

LU, Lan et al. Developing natural products as potential anti-biofilm agents. **Chinese medicine**, v. 14, n. 1, p. 1-17, 2019.

MELISSA, Miguel et al. Antimicrobial activity of essential oil of Cordia globosa. **African journal of Pharmacy and Pharmacology**, v. 10, n. 11, p. 179-184, 2016.

MILADINOVIĆ, Dragoljub L. et al. The significance of minor components on the antibacterial activity of essential oil via chemometrics. **LWT**, v. 136, p. 110305, 2021.

MIRANDA, Cíntia Alvarenga Santos Fraga et al. Essential oils from leaves of various species: antioxidant and antibacterial properties on growth in pathogenic species. **Revista Ciência Agronômica**, v. 47, p. 213-220, 2016.

NAZZARO, Filomena et al. Effect of essential oils on pathogenic bacteria. **Pharmaceuticals**, v. 6, n. 12, p. 1451-1474, 2013.

OZA, Manisha J.; KULKARNI, Yogesh A. Traditional uses, phytochemistry and pharmacology of the medicinal species of the genus Cordia (Boraginaceae). **Journal of Pharmacy and Pharmacology**, v. 69, n. 7, p. 755-789, 2017.

SA, Nairley Cardoso et al. Antimicrobial and antibiofilm action of casbane diterpene from Croton nepetaefolius against oral bacteria. **Archives of oral biology**, v. 57, n. 5, p. 550-555, 2012.

SAAD, Nizar Y.; MULLER, Christian D.; LOBSTEIN, Annelise. Major bioactivities and mechanism of action of essential oils and their components. **Flavour and Fragrance Journal**, v. 28, n. 5, p. 269-279, 2013.

SAYED, Ahmed M. et al. Discovery of two brominated oxindole alkaloids as Staphylococcal DNA gyrase and pyruvate kinase inhibitors via inverse virtual screening. **Microorganisms**, v. 8, n. 2, p. 293, 2020.

SILVA, Sâmia Andricia S. da et al. Flavanones from aerial parts of Cordia globosa (Jacq.) Kunth, Boraginaceae. **Revista Brasileira de Farmacognosia**, v. 20, p. 682-685, 2010.

STAPF, María Natividad Sánchez de. Nomenclatural notes on Varronia (Boraginaceae sl) in Brazil. **Rodriguésia**, v. 61, p. 133-135, 2010.

THERIEN, Alex G. et al. Broadening the spectrum of β-lactam antibiotics through inhibition of signal peptidase type I. **Antimicrobial agents and chemotherapy**, v. 56, n. 9, p. 4662-4670, 2012.

VAN DEN DOOL, H. A. N. D.; KRATZ, P. Dec. A generalization of the retention index system including linear temperature programmed gas-liquid partition chromatography. **Journal of chromatography**, 1963.