European Journal of Medicinal Plants

31(18): 1-14, 2020; Article no.EJMP.63182
ISSN: 2231-0894, NLM ID: 101583475

Antimicrobial Activity from Species *Plectranthus amboinicus* (Lour.) Spreng, a Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author JMSS designed the study, performed the analysis and wrote the first draft of the manuscript. Authors CSA, LAR and APO supervised the study and analysed the data. Authors JRGSA, CSCA, DAN and LMOD managed the literature search writing of the final manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/EJMP/2020/v31i1830337
Editor(s):
(1) Dr. Patrizia Diana, University of Palermo, Italy.
(2) Prof. Marcello Iriti, University of Milan, Italy.
Reviewers:
(1) Someshwar Dattatraya Mankar, Pravara Rural College of Pharmacy, India.
(2) Okoronkwo, Samuel Okafor, Ebonyi State University, Nigeria.
Complete Peer review History: http://www.sdiarticle4.com/review-history/63182

Review Article

Received 15 September 2020
Accepted 21 November 2020
Published 11 December 2020

ABSTRACT

Introduction: Nowadays, several bacteria have acquired resistance to available antimicrobial agents making necessary the search for new therapeutic alternatives. *Plectranthus amboinicus* L. is a succulent and aromatic herb, popularly known as thick leaf mint, used in popular medicine for the treatment of colds, digestive diseases, asthma, headache and to fight pathogenic bacteria activity. In view the antimicrobial activity of *P. amboinicus* this study had as aim to review publications involving researches about antimicrobial activity of this species.

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Materials and Methods: For this, PubMed, Scopus, Science Direct and Scielo databases were consulted in November 2020 using the keywords *Plectranthus amboinicus* and antimicrobial activity. In vitro and/or in vivo studies on the antimicrobial activity of the species in the last 10 years were considered.

Results: The main microorganisms evaluated were: *Klebsiella pneumoniae*, *Mycobacterium tuberculosis*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and some Candida species. The essential oils had carvacrol, germacrene D, thymol and camphor as main constituents. Most studies evaluated the antimicrobial activity using broth dilution and agar diffusion methods. In most studies essential oil, extracts and/or isolated substances showed significant antimicrobial activity. Synergistic activity was also observed through association with antibiotics.

Conclusion: *P. amboinicus* has therapeutic potential for antimicrobial treatments and can be an alternative to the treatment of resistant microorganisms and that further *in vivo* and clinical studies with the species are still needed.

Keywords: Lamiaceae, aromatic herbs; in vitro studies; in vivo studies; biological activities.

1. INTRODUCTION

Microbial resistance is an adaptive and natural process to selective pressure from the environment that occurs through genetics modifications [1]. However, the irrational use of antimicrobial agents by humans as well the indiscriminate administration in animals has speed up this process [2,3]. Different resistance mechanisms acquired by microorganisms can be transferred to humans through to direct intake or to food products made with this animals and all these practices makes the microbial resistance a public health problem [2-5].

In view the microbial resistance to therapeutic agents available nowadays, is necessary the searches by new alternatives and medicinal plants are an extensive source for this discovery. Antimicrobial activity of medicinal plants extracts and their essential oils have been seen place over the years, and among species with proven antimicrobial potential, we have the specie *Plectranthus amboinicus* (Lour.) Spreng (Lamiaceae) [6–10].

P. amboinicus is a succulent and aromatic herb (Fig. 1) know in Brazil as malvarisco, french oregano and thick leaf mint and widely used in folk medicine to treat constipations, digestive disorders, asthma, headaches [11]. In Brazil, this species is so important which even nowadays in one of the most cited medicinal species by the indigenous population Munduruku – Ipaupixuna, Brazil for treatment of asthma, eye cleansing, flu, inflammation and injuries [12]. Studies carried out with extracts from several parts of this specie showed its antioxidant, anti-inflammatory, analgesic, antitumor and antiplatelet activities [13]. Its essential oil has antimicrobial potential and presents, in general, the compounds carvacrol and transcarophyllene as main [13–17]. In view of human health problems this study has as aim to reach an overview about studies carried out with *P. amboinicus* involving antimicrobial activity in the least 10 years.

Fig. 1. *Plectranthus amboinicus* (Lour.) Spreng

2. EXPERIMENTAL PART

2.1 Methodology

Research it was carried out in November of 2020 in specialized data bases PubMed, Scopus, Science Direct and Scielo using the key-words *P. amboinicus* and antimicrobial activity, with search terms throughout the manuscript. For data acquisition, it was considered whole and available articles published in Portuguese or English containing in vitro and or in vivo studies about antimicrobial activity from extracts or essential oils of *P. amboinicus* from the least 10 years.

3. RESULTS AND DISCUSSION

3.1 Agar Diffusion Methods

Agar diffusion methods are used in laboratories to assess the microorganisms' susceptibility to different substances. In the disc-diffusion method, drugs impregnated in a special paper disc have the antimicrobial potential evaluated through its diffusion capacity over the agar plate. In view of its practicality, the disc-diffusion method is widely employed in antibiogram qualitative assays. A second alternative also very employed consist in drill wells into agar plate with sterilized apparatus followed of the direct solution drug apply [18,19].

In Agar diffusion assays, drugs with antimicrobial potential show a growth inhibition halo with diameter proportional at its antimicrobial potential and, strong antimicrobial potentials are considered when halos with at least 15 mm of diameter are achieved [20]. According to with this parameter, *P. amboinicus* essential oils have strong antimicrobial activity against several strains as *Staphylococcus aureus* [21-26], *MRSA*, *S. epidermidis*, *Enterococcus faecalis* [25], *Aeromonas caviae* [21], *Proteus vulgaris* [21], *Escherichia coli* [22,23,25,26], *Pseudomonas aeruginosa* [22,25], *Salmonela sp*. [26] *Aspergillus niger* [21] and *Candida albicans* [22] showing halos which range to 17-42 mm with concentration-dependent profile.

In developed studies, *S. aureus* including multi-drugs resistant *S. aureus* has been show as the most sensible strains to *P. amboinicus* essential oils. This bacterial is a common pathogen that is associated with serious community infections and known as major cause of food poisoning due to the production of enterotoxins [27].

For studies raise and in many cases, the growth inhibition potential of *P. amboinicus* essential oil was higher than standard drugs as [22,26], where *P. amboinicus* essential oil showed most efficiency that than the drugs Cefepime and Gatifloxacin [22]. Another study showed higher inhibition zones for the essential oil in relation to vancomycin against gram-positive bacteria and cefotaxime against *E. coli* [25]. For *S. aureus* strains collected from foods, *P. amboinicus* essential oil and its main compound were able to inhibit the bacteria growth of all 35 strains including among these, the 28 strains oxacillin or vancomycin resistant [24].

A common point observed in studies carried out *P. amboinicus* essential oil was the positive correlation between carvacrol or thymol concentrations and growth inhibition potential. Essential oils where carvacrol or its isomer was main compound showed, in general lines, the higher inhibition halos [21,22,24,25]. To prove the correlation between carvacrol and the growth inhibition [24] tested this chemical compound against the 35 strains from foods and as expected, the carvacrol showed strong and superior activity to essential oil with 88.17% of carvacrol in its chemical constitution [24].

Carvacrol (5-isopropyl-2-methylphenol) and thymol (2-isopropyl-5-methylphenol) are phenolic terpenoids and isomers of position known by its antibacterial and antifungal activities [27,28]. In view the strong antimicrobial activity, studies were carried out to understand its action mechanism and the results showed that both, carvacrol and thymol, act causing changes in surface electrostatic of the cell membranes and damages in the membrane integrity of fungi and bacteria in a short time interval [28]. In addition, for *S. aureus* it was proved that carvacrol and thymol suppress coagulase and lipase enzymatic activities inhibiting, as consequence, the production of staphylococcal enterotoxins. The authors agree that the this founding are linked to prevention of protein secretion promoted by changes in the membrane integrity, once that the intercalation of active plant compounds into the cytoplasmic membrane may interfere with the process of membrane associated signal transduction and impair the function of some membrane proteins, resulting in changes to the architecture and composition of the cell wall [27].

Extracts from different parts from *P. amboinicus* have been also evaluated, using agar diffusion methods, against several bacteria and the fungus *C. albicans*. As observed to essential oils *S. aureus* was the most susceptible strain, but in general, the extracts efficiency is lower than the observed to essential oils because even using higher concentrations the growth inhibition halo are lower diameter when compared to essential oils [22,29–34]. This nature can be linked to the complexity of extracts where even having compounds with proved activity, its concentrations become too low to reach their potential effectiveness.

Several solvents are used to obtain *P. amboinicus* extracts but the extractions with methanol and ethanol showed the better results [22,29–34]. It was observed in study developed by [32] a significant decrease in antibacterial activity when the extracts were obtained with more diluted hydroalcoholic solutions [32].

In an interesting study, the crude *P. amboinicus* was used to prepare a mouthwash and the formulation coating only 3% of crude extract was able to inhibit the *S. aureus* and *S. mutans* growth, but similar to others studies with extracts the authors can't identify the/or compound(s) responsible by results. In general, the antimicrobial activity is linked, but not conclusively, to presence of phenolic compounds [31] and flavonoids [33], showed to us that further studies about chemical composition and antimicrobial activities for extract are necessary.

3.2 Broth Dilution Methods

Broth dilution methods consist in evaluating cell growth, in liquid culture media, against antimicrobial agents in different dilutions and against different standard antibiotics. It is can be classified in macro or microdilution according to culture media volume used. Macrodilutions was carried out using 1-10 mL of culture media while microdilutions with only 0.1-0.2 mL, but in both methods, the bacterial inoculums have a standardized concentration. These methods have as an advantage its practicality and the ability to provide quantitative and more representative results of antimicrobial activity because are able to provide the concentration where the cell growth is inhibited and also the death concentration though minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) [19].

Despite is advantages studies of antimicrobial potential from natural products by broth dilution methods are susceptible to misinterpretation because no parameters are really set for extracts, essential oils or phytochemical compounds by reference agencies as the Clinical and Laboratory Standards Institute (CLSI). In all articles used in this review, no cut-points used as references values it was showed, the authors to attribute a classification of its results as strong or weak but don't show to readers which parameters were been used.

Several authors have draws attention for this problem and suggest that results are considered relevant when IC_{50} values below 100 $\mu g.mL^{-1}$ for extracts and below 25 µM for pure compounds are achieved [35]. However, as evidenced in literature these criteria don't is a useful one that most studies are expressed its results as MIC. In this same paper the author suggest a new criteria where activity of plant extracts will be classified as significant (MIC < 100 $\mu g.mL^{-1}$), moderate (100 < MIC ≤ 625 $\mu g.mL^{-1}$) or weak (MIC > 625 $\mu g.mL^{-1}$). In addition, significant activity (MIC < 10 $\mu g.mL^{-1}$),moderate (10 < MIC ≤ 100 $\mu g.mL^{-1}$) and low or negligible (MIC > 100 $\mu g.mL^{-1}$) to isolated compounds and this values it was based in its literature review [36].

For *P. amboinicus* essential oils and extracts was often investigated concerning its antimicrobial capacity against bacteria gram-positives and gram-negatives as well as against fungi strains. In include papers of this review, the bacteria most studied are *S. aureus* and *E. coli*, bacteria gram-positives and gram-negatives respectively, while *Candida* species are the main responsible for the fungi.

According to Kuete criteria [36], *P. amboinicus* essential oils showing antibacterial activity that vary among strong and weak activity. In Ceará Brazilian state, essential oils from leaves and steam, and the carvacrol, your main compound with 88.17% (Table 1) had it moderate antibacterial potential prove against two *S. aureus* strains: ATCC 6538 and, oxacillin and vancomycin-resistant (OVRSA). *P. amboinicus* essential oil showed 0.25 $mg.mL^{-1}$ and 0.5 $mg.mL^{-1}$ as MICs values for standard and resistant strains respectively, while carvacrol showed 0.25 $mg.mL^{-1}$ MICs values against both [24,37]. In others studies where carvacrol or its isomer thymol were among the main chemical compounds, strong antimicrobial activities it was observed and in general lines, the authors attribute the observed results to the major components of essential oils [22,23,38]. Interestingly, the essential oil with higher carvacrol content showing a moderate potential [24] while the others had strong potentials with MIC values range to 32-50 μg.mL^{-1} [22,23,38] but, although these results and the authors' justifications seem to be at variance, the inoculums concentration used in assays can be the key. In study carried out by [24] the cell suspension it was started at 1.25 x 10^{7} UFC/mL while for others, the cell suspension it was started at 10^{6} UFC/mL this differences reinforce, and the same results profile to *E. coli*, one more time, the standardization necessity in order that the results can be compared.

The importance of carvacrol and its isomers presence in *P. amboinicus* essential oils for antibacterial activity gains reinforcement when comparing the following studies. A essential oil containing germacrene D as main compound, in study carried out by Aguiar et al. [39], the MIC value against *S. aureus* and *E. coli* increased in 10 and 2.56 times respectively, when compared to value found by Manjamalai et al. [22] against the same strain. Questions about inoculum suspension can be raised, but for study where the sesquiterpene germacrene D it was the main compound, with inoculum suspension starting into only 10^{5} UFC/mL, an lowest antibacterial activity it was found.

P. amboinicus essential oils had showing also synergic effect when associated to standard drugs. In the study where *P. amboinicus* essential oil had 54.4% of carvacrol the MIC initial were: *E.coli* (MIC 256 μg.mL^{-1}), *P. vulgaris* (MIC 64 μg.mL^{-1}), *B. cereus* (CIM 512 μg.mL^{-1}), *P. aeruginosa* (MIC 128 μg.mL^{-1}), *S. aureus* (MIC 128 μg.mL^{-1}) e *S. aureus* (multiresistant) (MIC 32 μg.mL^{-1}) and only *P. aeruginosa* showed resistance (MIC ≥ 1024 μg.mL^{-1}). However, when the same essential oil it was associated to aminoglycosides amikacin, kanamycin and gentamicin the antibacterial potential it was increased and the MIC values it was reduced to the half [38]. This synergism can be observed even at low concentrations of carvacrol. The association among sample with 17% of carvacrol and ciprofloxacin, streptomycin and chloramphenicol promoted reduction in MICs values for *S. aureus* and the association with the same oil it was able to promoted synergistic effect against *S. aureus* (multiresistant) and *B. spizizenii* [37].

Similar results it was noted when *P. amboinicus,* containg germacrene D (38.6%) as main compound, it was associated to amikacin and gentamicin. The synergism between essential oil and standard drugs reduced the MICs values to 30, 60 e 15 μg.mL^{-1} for *S. aureus*, *E. coli* and *P. aeruginosa* respectively, for amikacin. When the association it was made with gentamicin, the MIC it was reduced to 15, 20 and 9 μg.mL^{-1} for *S. aureus*, *E. coli* and *P. Aeruginosa* respectively [40,39].

A probable explanation to results showed before, can be linked to fact that terpenes as carvacrol, thymol and germacrene D are able to alter the cell wall or disrupt the cell membrane facilitating drug uptake, but studies about this suggestion are necessary.

About antimicrobial activity from *P. amboinicus* extracts it is possible to affirm that extracts have less potential than essential oils. In selected papers for this review, only the study carried out with specie collected in Egypt had good results against gram-positives strains. The alcoholic and aqueous extracts and lyophilized juice of the leaves against *S. mutans* and *L. Acidófilo*, had powerful MICs values range 3.85-100 μg.mL^{-1} [29]. But, as view in most other studies, the authors made no relation between the chemical composition and observed results.

3.3 Antiparasitic Activity

P. amboinicus essential oils and extracts studied about its antiparasitic activity. The antileishmanial activity of *P. amboinicus* essential oil it was evaluated *in vitro* against *Leishmania (Viannia) braziliensis* and after 48 h of treatment with 2.5% of essential oil, a reduction in promastigotes growth like amphotericin it was observed. In view the promising results, studies *in vivo* it was carried out, but no positives result it founded, whereas no differences were observed between the treated and untreated related to lesion thickness. The authors associated the results *in vivo* to variables as: used concentration, administration form, treatment time and/or necessity of association of essential oil to other vegetable materials to efficacy increase [40]. Despite the authors' suggestion, the concentration variable can apparently be discarded since the behaviour of *P. amboininus* essential oil, also containing carvacrol as a majority compound, varies concerning different species of organisms. Against other organisms the essential oil and carvacrol presented strong growth inhibition. For example, very low IC_{50} values it was observed against *Plasmodium falciparum* (IC_{50} = 5.9 µg.mL^{-1}), *Trypanosoma brucei* (IC_{50} = 34.9 µg.mL^{-1}) and *L. amazonensis* (IC_{50} = 58.2 µg.mL^{-1}) and this results shown to us that the organism specie is probably the main factor [41].

Against *P. berghei* the antimalarial activity, it was evaluated in several concentrations. Prophylactically the extract at concentrations of 50, 200 and 400 mg.kg^{-1} showed a capacity to reduce parasitic load, which not observed for the dose of 1000 mg.kg^{-1}. In curative and suppression assays, the parasitemia not significantly reduced. The extract did not present a toxic risk in acute tests and the authors conclude that the extract may have the potential to be used as preventive against malaria [42].

3.4 Action Mechanism Investigations

The most studies to attribute the essential oil antimicrobial activity to its hydrophobic characteristics. Hydrophobic compounds can permeate and promote destabilization of the cell membrane and this mechanism, is widely cited in the literature [43]. To *P. amboinicus* essential oils these permeation and destabilization abilities are attributed to main compounds as carvacrol, thymol and germacrene D [24,39,44]. However, the most articles used in this review, do not carry out assays to prove the really action mechanism of its samples.

Against *K. pneumonia* (ATCC and clinical isolates) using violet crystal and urease assays, *P. amboinicus* essential oil with 98.03% of carvacrol and controls (ciprofloxacin and EDTA) have its permeability and enzymatic potential evaluated. As results, the authors could verify the capture potential of violet crystal of essential oil at one concentration twice higher that MIC (0.16%), and a significant enzymatic activity for all tested concentrations. The capsule expression it was evaluated at the same concentrations and reductions in this parameter it was observed out 1/8 MIC and when 1/4 MIC it was used only cellular debris was observed [17]. These results show to us the mechanisms possible to *P. amboinicus* essential oil when carvacrol is the main compound, but as the chemical composition in essential oils are variable, the action mechanism turning out an interesting point to be more researched.

3.5 *In vivo* Assays

Hydroalcoholic and ethyl acetate fractions from *P. amboinicus* promote a fast-wound healing of mice in skin infection model using *S. aureus* (MRSA) as infectious agent. The hydroalcoholic extract it was able to reduce the cell viability and to promote fast wound healing at 500 mg/kg/dose while ethyl acetate fraction to promote fast wound healing at 250 and 500 mg/kg/dose, showing results superior to vancomycin and according authors, the promising results can be attributed to antimicrobial potential of *P. amboinicus* [45]. Only one study founded with *in vitro* tests using the species, making evident the need for further research.

3.6 Main Active Substances Identified

In Table 1, we bring a resume of main chemical compounds founded in *P. amboinicus* essential oils. Among the main compounds, the carvacrol isolated it was the most used in antimicrobial assays for being considered the chemical compound responsible by antimicrobial potential of essential oils. The Table 2 shows the plant segments used for extracts preparations in founded studies. Both for studies with essential oil and with extracts of different types, important information are missing. Some provide incomplete information about place and time collection of vegetable material and the most used extracts do not submitted to adequate chemical characterization, for identification of compounds with possible biological activity.

3.7 Studies Using Drug-Delivery Systems

Nanoparticles are considered molecules with promising biological properties due to its physico-chemical characteristics as its reduced size. The synthesis can occur by chemical, physical, electrochemical methods, among others, but green synthesis has been widely used due to its lower environmental impacts [58–60]. Six studies using *P. amboinicus* extracts in nanoparticles systems it was founded.

Table 1. Main compounds founded in *P. amboinicus* essential oils

Main compound	(%) by GC-MS	Collection local	Plant segment	Season	Reference
Carvacrol	88.17	Cariri, CE, Brazil	Leaves and stems	Fall (2014)	[24]
Carvacrol	90.0-98.0	Fortaleza, CE, Brazil	Leaves	-	[17]
Thymol	61.5	Fortaleza, CE, Brazil	Leaves	-	[44]
Germacren-D; Carvacrol	38.60; 90.55	Crato and Fortaleza, CE, Brazil	Fresh leaves	-	[46]
Thymol	64.3	Crato, CE, Brazil	Fresh leaves	Spring (2007)	[9]
Germacrene-D	38.6	Crato, CE, Brazil	Fresh leaves	-	[39]
Carvacrol	54.4	Crato, CE, Brazil	Aerial parts	Spring (2010)	[38]
Carvacrol; Camphor	23.0; 22.2	Comoros Archipelago, West Africa	Dried leaves	Fall (2008)	[23]
Carvacrol	-	Lavras da Mangabeira, CE, Brazil	-	-	[40]
Thymol	18.09	Siruvani Falls, India	Fresh leaves	-	[22]
-	-	Campina Grande, PB, Brazil.	Leaves	-	[47]
Carvacrol	37.7	Nova Odessa, SP, Brazil	Leaves	Fall (2014)	[48]
Carvacrol and δ-3-carene	17.9; 15.2	Monvert, Mauritius Island	Leaves	Summer (2018)	[37]
Carvacrol	51.3	Bago City, Negros Occidental, Philippines	Dried leaves	-	[25]
Carvacrol	71.0	Havana, Cuba	Aerial parts	2017	[41]

CE: Ceará state; PB = Paraíba state; SP = São Paulo state.

Table 2. Characteristics of *P. amboinicus* extracts used in studies of antimicrobial activity

Extraction method	Solvent	Country	Plant segment	Season	Identified compounds	Reference
Decoction	Water	India	Fresh leaves	-	-	[49]
Decoction	Water	India	Fresh leaves	-	-	[50]
Decoction	Water	India	Leaves	Winter (2015)	-	[51]
Decoction	Wates	India	Dried leaves	-	-	[52]
Soxhlet	Methanol	India	Dried plant	Summer (1998-2001)	-	[30]
Maceration	Ethanol 70%	Brazil	Dried plant	Winter (2007) and summer (2008)	-	[20]
Maceration	Ethanol	Brazil	Dried plant	-	Tannins and flavonoids	[53]
Percolation	Ethanol 70%	Egypt	Dried leaves	2008-2010	Caffeic acid, eriodictinol, rosmanic acid, coumaric acid, luteolin, chrysoeriol, quercetin	[29]

Extraction method	Solvent	Country	Plant segment	Season	Identified compounds	Reference
-	Ethanol 30%, 35%, 40% and 70%	Mexico	Dried leaves	-	-	[32]
Turbolysis	Water	-	Dried leaves	-	-	[54]
Maceration	Ethanol 96%	-	Dried leaves		Flavonoids, glycosides, saponins, tannins, triterpenes and steroids	[33]
-		Brazil	Leaves	-	-	[47]
Maceration	Ethanol 70% and 99%	Brazil	Fresh leaves	-	-	[45]
Maceration	Ethanol 95%	Malaysia	Fresh leaves	Dry season (2011)	Flavonoids	[42]
Maceration	Water	India	Fresh leaves	2011	Phenolic compounds, flavonoids, coumarins and monosaccharides. Gallic acid, chlorogenicacid, caffeicacid, coumaric acid, rutin and rosmarinic acid	[55]
Mechanical agitation	methanol, acetone and hexane	Malaysia	Dried leaves	Tropical and rainy weather (2015)	Tetracontane, Tetrapentacontan, Acetone extract: Squalene, phytool, carvacrol, tetrapentacontane	[30]
Mortar milling	Ethanol	India	Fresh leaves	-	-	[56]
Sonication	Methanol	Truro, United Kingdom	Dried leaves	Fall (2015) and spring (2016)	Phenolic compounds	[57]

In the synthesis of silver nanoparticles, extracts from the leaves of *P. amboinicus* were used as reducing agent of $AgNO_3$ salt. In further, the antimicrobial potential of nanoparticles it carried out using agar disc-diffusion method. *E. coli* and *Penicillium spp.* it were the species most susceptible showing inhibition zones with 9 mm and 7 mm, respectively using only 16 µL of nanoparticles solution [49]. In other study, better results it was observed for higher tested concentration (200 $\mu g.mL^{-1}$) against *S. mutans* (10.89 ± 0.89 mm) and *L. acidophilis* (11.13 ± 0.31 mm) very close to observed to vancomycin 15.17 ± 1.1 and 15.69 ± 1.3 mm to *S. mutans* and *L. acidophilis* respectively [48]. From 100 $\mu g.mL^{-1}$ [51] observed inhibition zones similar to [48] for *S. aureus* (10 mm), *B. subtilis* (10 mm), *P. vulgaris* (15 mm), *P. aerogenosa* (11 mm) and *C. albicans* (12 mm). In this article, the authors considered sensitive the strains with inhibition zones ≥ 19 mm, when the concentration was doubled only *P. vulgaris* (19 mm) showed sensitivity.

P. amboinicus extracts were used also in development and antimicrobial evaluation of zinc, CuO and NiO nanoparticles. The obtained nanoparticles were able to inhibit the cell grown of *S. aureus* (MRSA) ATCC 33591 at 8 and 10 $\mu g.mL^{-1}$ with 11 and 13 mm of inhibition zone respectively, using agar disc-diffusion method. The authors highlight still the strong anti-biofilm and larvicidal activities against bacteria *S. aureus* (MRSA) and instar mosquito larvae *Anopheles stephensi*, *Culex quinquefasciatus* and *C. tritaeniorhynchus* [50]. Similar inhibition zone results were observed by Ramesh et al. (2020) [52] in study using NiO nanoparticles against *Proteus spp.* and *Candida spp.* (11 mm). CuO nanoparticles were tested against six strains of bacteria and four strains of fungi. At 150 $\mu g.mL^{-1}$ the largest inhibition zones were observed for *E. coli* (13.65 ± 0.88 mm), *K. pneumonia* (13.40 ± 0.86 mm) and *P. aeruginosa* (13.05 ± 0.84 mm) [61].

4. CONCLUSION

P. amboinicus essential oils and extracts from different regions showed antimicrobial activity with concentration dependence. The monoterpene carvacrol it was the main compound founded in the most studies and showed antimicrobial activity. Its antimicrobial activity superior to essential oils in some moments make the authors relate its presence to antimicrobial activity although it is necessary to develop further studies with isolated compounds and mechanisms of action. The main methods used by authors were agar disc-diffusion method and microdilution, but the comparison among results it is very hard given the lack of standardization in the methodologies used as well as the absence in chemical characterization and vegetable data collection. Even in view of the species' proven antimicrobial activity, most of the studies developed are simple with *in vitro* tests. It observed also that studies about development of technological products using *P. amboinicus* are scarce. Therefore, this review highlights the need for continued research to further study in vivo and clinical trials with the species.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

To the foundation of support for science and technology of the state of Pernambuco (FACEPE) for the grant for the development of this work.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Santos NQ. A resistência bacteriana no contexto da infecção hospitalar. Texto Context - Enferm [Internet]. 2004;13(spe): 64-70. Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-07072004000500007&lng=pt&tlng=pt
2. Wannmacher L. Uso indiscriminado de antibióticos e resistência microbiana: Uma guerra perdida? In: Uso racional de medicamentos: temas selecionados [Internet]; 2004. Available:https://extensao.cederj.edu.br/material_didatico/sau2203/pdfs/aula05_LC.pdf

3. WHO. Antimicrobial resistance [Internet]; 2018. Available:https://www.who.int/en/news-room/fact-sheets/detai https://www.who.int/en/news-room/fact-sheets/detail/antimicrobial-resistance
4. Mota RA, Silva KPC da, Freitas MFL de, Porto WJN, Silva LBG da. Utilização indiscriminada de antimicrobianos e sua contribuição a multirresitência bacteriana. Brazilian J Vet Res Anim Sci [Internet]. 2005;42(6):465. Available:http://www.revistas.usp.br/bjvras/article/view/26406
5. Peixoto LJ, SÁ MC, Gordiano L, Costa MM. Aeromonas spp.: Fatores de virulência e perfis de resistência a antimicrobianos e metais pesados. Arq Inst Biol (Sao Paulo) [Internet]; 2012; 79(3):453-61. Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1808-16572012000300020&lng=pt&tlng=pt
6. Saraiva RMC. Atividade antibacteriana de plantas medicinais frente á bactérias multirresistentes e a sua interação com drogas antimicrobianas [Internet]. 2012; 94. Available:http://www.ppgcf.propesp.ufpa.br/ARQUIVOS/dissertacoes/rosamarcia.pdf
7. Araújo CDS. Estudo fitoquímico e atividade biológica *in vitro* de Annona vepretorum MART. (ANNONACEAE) [Internet]. 2013;196. Available:http://www.cpgrnsa.univasf.edu.br/uploads/7/8/9/0/7890742/estudo_fitoquÍmico_e_atividade_biolÓgica_in_vitro_de_annona.pdf
8. Silva EEDS. Estudo fitoquímico e atividade biológica *in vitro* de Alternanthera brasiliana (L.) KUNTZE (Amaranthaceae) [Internet]; 2013. Available:http://www.cpgrnsa.univasf.edu.br/uploads/7/8/9/0/7890742/dissertação_reunida.pdf
9. Bezerra JWA, Costa AR, da Silva MAP, Rocha MI, Boligon AA, da Rocha JBT, et al. Chemical composition and toxicological evaluation of *Hyptis suaveolens* (L.) Poiteau (LAMIACEAE) in *Drosophila melanogaster* and *Artemia salina*. South African J Bot [Internet]. 2017;113:437-42. Available:https://doi.org/10.1016/j.sajb.2017.10.003
10. Freire NB. Atividade antimicrobiana do extrato de *Hymenaea martiana* Hayne (Fabaceae) e compostos antimicrobianos frente a isolados clínicos de *Staphylococcus aureus* [Internet]. 2018;83. Available:http://www.cpgrnsa.univasf.edu.br/uploads/7/8/9/0/7890742/dissertação_naiana_versaofinal.pdf
11. Ferreira TF. Revisão sistemática do óleo essencial da espécie *Plectranthus amboinicus* (Lour.) Spreng. [Internet]. 2015;44. Available:https://repositorio.ufpb.br/jspui/bitstream/123456789/948/1/TFF18052015.pdf
12. Oliveira PC, Sou BCOQ. Traditional knowledge of forest medicinal plants of munduruku indigenous people - ipaupixuna. European J Med Plants [Internet]. 2020;20-35. Available:https://www.journalejmp.com/index.php/EJMP/article/view/30309
13. Menéndez Castillo Rosa A PGV. *Plecthranthus amboinicus* (Lour.) Spreng. Rev Cuba Plantas Med [Internet]. 1999; 4(3):110-5. Available:http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1028-47961999000300006
14. Morais SM de, Dantas JDP, Silva ARA da, Magalhães EF. Plantas medicinais usadas pelos índios Tapebas do Ceará. Rev Bras Farmacogn [Internet]. 2005;15(2):169-77. Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-695X2005000200017&lng=pt&nrm=iso&tlng=pt
15. Murthy PS, Ramalakshmi K, Srinivas P. Fungitoxic activity of Indian borage (Plectranthus amboinicus) volatiles. Food Chem [Internet]. 2009;114(3):1014-8. Available:https://linkinghub.elsevier.com/retrieve/pii/S030881460801282X
16. Bandeira J, Barbosa F, Barbosa LM, Rodrigues IC, Bacarin M, Peters J, et al. Composição do óleo essencial de quatro espécies do gênero Plectranthus. Rev Bras Plantas Med [Internet]. 2011; 13(2):157-64. Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1516-05722011000200006&lng=pt&tlng=pt
17. Gonçalves TB, Braga MA, de Oliveira FFM, Santiago GMP, Carvalho CBM, Cabral PB e, et al. Effect of subinihibitory and inhibitory concentrations of *Plectranthus amboinicus* (Lour.) Spreng essential oil on *Klebsiella pneumoniae*.

Phytomedicine [Internet]. 2012;19(11): 962-8.
Available:https://linkinghub.elsevier.com/retrieve/pii/S0944711312001912

18. Sejas LM, Silbert S, Reis AO, Sader HS. Avaliação da qualidade dos discos com antimicrobianos para testes de disco-difusão disponíveis comercialmente no Brasil. J Bras Patol e Med Lab [Internet]. 2003;39(1).
Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1676-24442003000100006&lng=pt&nrm=iso&tlng=pt

19. Ostrosky EA, Mizumoto MK, Lima MEL, Kaneko TM, Nishikawa SO, Freitas BR. Métodos para avaliação da atividade antimicrobiana e determinação da Concentração Mínima Inibitória (CMI) de plantas medicinais. Rev Bras Farmacogn [Internet]. 2008;18(2):301-7.
Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-695X2008000200026&lng=pt&nrm=iso&tlng=pt

20. Almeida CFCBR, Cabral DLV, Almeida CCBR, Amorim ELC, Araújo JM, Albuquerque UP. Comparative study of the antimicrobial activity of native and exotic plants from the Caatinga and Atlantic Forest selected through an ethnobotanical survey. Pharm Biol [Internet]. 2012;50(2):201-7.
Available:http://www.tandfonline.com/doi/full/10.3109/13880209.2011.596205

21. Costa JGM, Pereira CKB, Rodrigues FFG, de Lima SG. Chemical composition, antibacterial and fungicidal activities of leaf oil of *Plectranthus amboinicus* (Lour.) Spreng. J Essent Oil Res [Internet]. 2010; 22(2):183-5.
Available:http://www.tandfonline.com/doi/abs/10.1080/10412905.2010.9700298

22. Manjamalai A, Tom Alexander VMBG. Bioactive evaluation of the essential oil of *Plectranthus amboinicus* by GC-MS analysis and its role as a drug for microbial infections and inflammation. Bioact Eval Essent oil *Plectranthus amboinicus* by GC-MS Anal its role as a drug Microb Infect Inflamm. 2012;4(3):205-11.

23. Hassani MS, Zainati I, Zrira S, Mahdi S, Oukessou M. Chemical composition and antimicrobial activity of *Plectranthus amboinicus* (Lour) Spring. Essential Oil from Archipelago of Comoros. J Essent Oil Bear Plants [Internet]. 2012;15(4):637-44.
Available:http://www.tandfonline.com/doi/abs/10.1080/0972060X.2012.10644098

24. Vasconcelos SECB, Melo HM, Cavalcante TTA, Júnior FEAC, de Carvalho MG, Menezes FGR, et al. *Plectranthus amboinicus* essential oil and carvacrol bioactive against planktonic and biofilm of oxacillin and vancomycin-resistant *Staphylococcus aureus*. BMC Complement Altern Med [Internet]. 2017;17(1): 462.
Available:http://bmccomplementalternmed.biomedcentral.com/articles/10.1186/s12906-017-1968-9

25. Bugayong AM, Cruz P, Padilla PI. Antibacterial activity and chemical composition of essential oils from leaves of some aromatic plants of Philippines. J Essent Oil Bear Plants [Internet]. 2019; 22(4):932-46.
Available:https://www.tandfonline.com/doi/full/10.1080/0972060X.2019.1682683

26. Dao TP, Nguyen DC, Nguyen DT, Tran TH, Nhan Nguyen PT, Hong Le NT, et al. Extraction process of essential oil from *Plectranthus amboinicus* using microwave-assisted hydrodistillation and evaluation of it's antibacterial activity. Asian J Chem [Internet]. 2019;31(5):977-81.
Available:http://www.asianjournalofchemistry.co.in/User/ViewFreeArticle.aspx?ArticleID=31_5_1

27. Souza EL, Oliveira CEV, Stamford TLM, Conceição ML, Gomes Neto NJ. Influence of carvacrol and thymol on the physiological attributes, enterotoxin production and surface characteristics of *Staphylococcus aureus* strains isolated from foods. Brazilian J Microbiol [Internet]. 2013;44(1):29-36.
Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1517-83822013000100004&lng=en&nrm=iso&tlng=en

28. Ahmad A, Khan A, Akhtar F, Yousuf S, Xess I, Khan LA, et al. Fungicidal activity of thymol and carvacrol by disrupting ergosterol biosynthesis and membrane integrity against Candida. Eur J Clin Microbiol Infect Dis [Internet]. 2011; 30(1):41-50.
Available:http://link.springer.com/10.1007/s10096-010-1050-8

29. El-hawary SS, El-sofany RH, Abdel-Monem AR, Ashour RS, Sleem AA.

Polyphenolics content and biological activity of *Plectranthus amboinicus* (Lour.) spreng growing in Egypt (Lamiaceae). Pharmacogn J [Internet]. 2012;4(32):45-54.
Available:http://linkinghub.elsevier.com/retrieve/pii/S0975357512800095

30. Samy RP, Manikandan J, Qahtani MA. evaluation of aromatic plants and compounds used to fight multidrug resistant infections. Evidence-Based Complement Altern Med [Internet]. 2013; 1-17.
Available:http://www.hindawi.com/journals/ecam/2013/525613/

31. Swamy MK, Arumugam G, Kaur R, Ghasemzadeh A, Yusoff MM, Sinniah UR. GC-MS based metabolite profiling, antioxidant and antimicrobial properties of different solvent extracts of Malaysian *Plectranthus amboinicus* Leaves. Evidence-Based Complement Altern Med [Internet]. 2017;2017:1-10.
Available:https://www.hindawi.com/journals/ecam/2017/1517683/

32. Itza-Ortiz M, Carrera-Chávez JM, Aguilar-Urquizo E, Parra-Suescún JE. Phytobiotic Activity Of *Larrea tridentata*, *Origanum vulgare* and *Plectranthus amboinicus* in gram positive and gram negative bacterias. Interciencia. 2019;44(5).

33. Nazliniwaty N, Laila L. Formulation and antibacterial activity of *Plectranthus amboinicus* (Lour.) spreng leaves ethanolic extract as herbal mouthwash against halitosis caused bacteria. Open Access Maced J Med Sci [Internet]. 2019; 7(22):3900-3903.
Available:https://www.id-press.eu/mjms/article/view/oamjms.2019.529

34. Mokni RE, Majdoub S, Jlassi I, Joshi RK, Hammami S. Gas chromatography-mass spectrometry profile and antimicrobial activities of *Ballota bullata* Pomel and *B. nigra* L. subsp. uncinata (Fiori & Bég.): A comparative analysis. Int J Mass Spectrom. 2020;450.

35. Cos P, Vlietinck AJ, Berghe D Vanden, Maes L. Anti-infective potential of natural products: How to develop a stronger *in vitro* 'proof-of-concept.' J Ethnopharmacol [Internet]. 2006;106(3):290-302.
Available:https://linkinghub.elsevier.com/retrieve/pii/S0378874106001851

36. Kuete V. Potential of Cameroonian plants and derived products against microbial infections: A review. Planta Med [Internet]. 2010;76(14):1479-91.
Available:http://www.thieme-connect.de/DOI/DOI?10.1055/s-0030-1250027

37. Jugreet BS, Mahomoodally MF. Essential oils from 9 exotic and endemic medicinal plants from Mauritius shows *in vitro* antibacterial and antibiotic potentiating activities. South African J Bot [Internet]. 2020;132:355-62.
Available:https://linkinghub.elsevier.com/retrieve/pii/S0254629920309078

38. Rodrigues FFG, Costa JGM, Rodrigues FFG, Campos AR. Study of the Interference between Plectranthus Species Essential Oils from Brazil and Aminoglycosides. Evidence-Based Complement Altern Med [Internet]. 2013;1-7.
Available:http://www.hindawi.com/journals/ecam/2013/724161/

39. Aguiar JJS, Sousa CPB, Araruna MKA, Silva MKN, Portelo AC, Lopes JC, et al. Antibacterial and modifying-antibiotic activities of the essential oils of *Ocimum gratissimum* L. and *Plectranthus amboinicus* L. Eur J Integr Med [Internet]. 2015;7(2):151-6.
Available:https://linkinghub.elsevier.com/retrieve/pii/S1876382014003084

40. Lima SCG, Teixeira MJ, Lopes Júnior JEG, de Morais SM, Torres AF, Braga MA, et al. *In vitro* and *in vivo* leishmanicidal activity of *Astronium fraxinifolium* (Schott) and *Plectranthus amboinicus* (Lour.) Spreng against *Leishmania* (Viannia) *braziliensis*. Biomed Res Int [Internet]. 2014;2014:1-7.
Available:http://www.hindawi.com/journals/bmri/2014/848293/

41. Monzote L, Scherbakov AM, Scull R, Gutiérrez YI, Satyal P, Cos P, et al. Pharmacological assessment of the carvacrol chemotype essential oil from *Plectranthus amboinicus* growing in Cuba. Nat Prod Commun [Internet]. 2020; 15(10):1934578X2096223.
Available:http://journals.sagepub.com/doi/10.1177/1934578X20962233

42. Taher M, Ramli N, Ahamed PS, Elhady H. Antimalarial activity of Malaysian *Plectranthus amboinicus* against Plasmodium berghei. Pharmacognosy Res [Internet]. 2014;6(4):280.
Available:http://www.phcogres.com/text.asp?2014/6/4/280/138248

43. Andrade MA, Cardoso M das G, Batista LR, Mallet ACT, Machado SMF. Óleos essenciais de *Cymbopogon nardus*, *Cinnamomum zeylanicum* e *Zingiber officinale*: composição, atividades antioxidante e antibacteriana. Rev Ciência Agronômica [Internet]. 2012;43(2):399-408.
    Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1806-66902012000200025&lng=pt&nrm=iso&tlng=en
44. Mota APP, Dantas JCP, Frota CC. Antimicrobial activity of essential oils from *Lippia alba*, *Lippia sidoides*, *Cymbopogon citrates*, *Plectranthus amboinicus*, and *Cinnamomum zeylanicum* against Mycobacterium tuberculosis. Ciência Rural [Internet]. 2018;48(6).
    Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0103-84782018000600453&lng=en&tlng=en
45. Oliveira FFM, Torres AF, Gonçalves TB, Santiago GMP, Carvalho CBM, Aguiar MB, et al. Efficacy of *Plectranthus amboinicus* (Lour.) Spreng in a murine model of methicillin-resistant *Staphylococcus aureus* skin abscesses. Evidence-Based Complement Altern Med [Internet]. 2013;2013:1-9.
    Available:http://www.hindawi.com/journals/ecam/2013/291592/
46. Santos FAV, Serra CG, Bezerra RJAC, Figueredo FG, Edinardo, Matias FF, et al. Antibacterial activity of *Plectranthus amboinicus* Lour (Lamiaceae) essential oil against *Streptococcus mutans*. Eur J Integr Med [Internet]. 2016;8(3):293-7.
    Available:https://linkinghub.elsevier.com/retrieve/pii/S1876382015300627
47. Nogueira JCR, Diniz MFM, Lima EO. Atividade antimicrobiana *in vitro* de produtos vegetais em otite externa aguda. Rev Bras Otorrinolaringol [Internet]. 2008; 74(1):118-24.
    Available:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-72992008000100019&lng=pt&tlng=pt
48. Santos NO, Mariane B, Lago JHG, Sartorelli P, Rosa W, Soares MG, et al. Assessing the chemical composition and antimicrobial activity of essential oils from Brazilian plants - *Eremanthus erythropappus* (Asteraceae), *Plectrantuns barbatus* and *P. amboinicus* (Lamiaceae). Molecules. 2015;20(5):8440-52.
49. Ajitha B, Ashok Kumar Reddy Y, Reddy PS. Biosynthesis of silver nanoparticles using *Plectranthus amboinicus* leaf extract and its antimicrobial activity. Spectrochim Acta Part A Mol Biomol Spectrosc [Internet]. 2014;128:257-62.
    Available:https://linkinghub.elsevier.com/retrieve/pii/S1386142514002923
50. Vijayakumar S, Vinoj G, Malaikozhundan B, Shanthi S, Vaseeharan B. *Plectranthus amboinicus* leaf extract mediated synthesis of zinc oxide nanoparticles and its control of methicillin resistant *Staphylococcus aureus* biofilm and blood sucking mosquito larvae. Spectrochim Acta Part A Mol Biomol Spectrosc [Internet]. 2015; 137:886-91.
    Available:https://linkinghub.elsevier.com/retrieve/pii/S1386142514012554
51. Niveditha K, Sukirtha TH. green synthesis, characterization and antimicrobial activity of silver nanoparticles from *Plectranthus amboinicus* plant extracts. Indian J Med Res Pharm Sci. 2018;5(3):41-51.
52. Ramesh R, Yamini V, Sundaram SJ, Khan FLA, Kaviyarasu K. Investigation of structural and optical properties of NiO nanoparticles mediated by *Plectranthus amboinicus* leaf extract. Mater Today Proc [Internet]; 2020.
    Available:https://linkinghub.elsevier.com/retrieve/pii/S2214785320323622
53. Costa JG, Campos A, Brito S, Pereira CK, Souza E, Rodrigues FF. Biological screening of araripe basin medicinal plants using *Artemia salina* Leach and pathogenic bacteria. Pharmacogn Mag [Internet]. 2010;6(24):331.
    Available:http://www.phcog.com/text.asp?2010/6/24/331/71792
54. Manojkanna K, Nasim Iffat, Gayathri R, Priya VV. Synthesis and characterization of silver nanoparticles from *Plectranthus amboinicus* extract and its antimicrobial activity against *Streptococcus mutans*, Lactobacillus. Drug Invent Today. 2019; 12(6):1236-8.
55. Shubha JR, Bhatt P. *Plectranthus amboinicus* leaves stimulate growth of probiotic L. plantarum: Evidence for ethnobotanical use in diarrhea. J Ethnopharmacol [Internet]. 2015;166:220-7.
    Available:https://linkinghub.elsevier.com/retrieve/pii/S0378874115001439

56. Suneetha DV, Vuppu, Indhumathi SV, Swetha S, Janani LR, Preethi KK. Evaluation of culinary plants by using ABST And MIC For Pharmacological Studies. Int J Sci Technol Res. 2019; 8(12):3840-3.
57. Zhang B, Wijesundara NM, Abbey, Lord, Rupasinghe HPV. Growing medium amendments effect on growth, secondary metabolites and anti-streptococcal activity of two species of Plectranthus. J Appl Res Med Aromat Plants [Internet]. 2017;5:53–9.
Available:https://linkinghub.elsevier.com/retrieve/pii/S2214786116300705
58. Mohanraj VJ, Chen Y. Nanoparticles - A review. Trop J Pharm Res [Internet]. 2007; 5(1).
Available:http://www.ajol.info/index.php/tjpr/article/view/14634
59. Rani PU, Rajasekharreddy P. Green synthesis of silver-protein (core–shell) nanoparticles using *Piper betle* L. leaf extract and its ecotoxicological studies on *Daphnia magna*. Colloids Surfaces A Physicochem Eng Asp [Internet]. 2011; 389(1–3):188-94.
Available:https://linkinghub.elsevier.com/retrieve/pii/S0927775711005267
60. Bhattacharyya S. Rapid green synthesis of silver nanoparticles from silver nitrate by a homeopathic mother tincture *Phytolacca decandra*. J Chinese Integr Med [Internet]. 2012;10(5):546-54.
Available:http://www.jcimjournal.com/en/showAbstrPage.aspx?articleID=jcim20120510
61. Velsankar K, Vinothini V, Sudhahar S, Kumar MK, Mohandoss S. Green Synthesis of CuO nanoparticles via *Plectranthus amboinicus* leaves extract with its characterization on structural, morphological, and biological properties. Appl Nanosci [Internet]. 2020;10(10):3953-71.
Available:http://link.springer.com/10.1007/s13204-020-01504-w

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/63182