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HEALTH SCIENCES

Antimicrobial potential of *Pectis substriata* essential oil (Asteraceae) against drug-resistant *Staphylococcus* strains

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Abstract: Resistant bacterial infections represent one of the major threats in worldwide health services. In this scenario, plant essential oils are considered promising antimicrobial agents. Therefore, this study aimed to evaluate the antimicrobial potential of *Pectis substriata* essential oil alone and in combination with antibiotics, against clinical drug-resistant bacterial strains. The essential oil from the plant aerial parts was obtained by hydrodistillation. Antimicrobial activity was assessed against standard and clinical bacterial strains by broth microdilution method, and the synergistic effect was evaluated by checkerboard microtiter assay. The oil alone showed significant activity against clinical *Staphylococcus warneri* (62.5 $\mu g.mL^{-1}$), and was moderately active on *Staphylococcus aureus* (standard strain) and clinical *Staphylococcus intermedius* (125 and 250 $\mu g.mL^{-1}$, respectively). Synergism was achieved for the combinations of essential oil and ampicillin on *S. warneri* and of oil and kanamycin on *S. intermedius*. Additive effects were also observed. This is the first report of the chemical composition of *P. substriata* essential oil, and the results revealed the presence of compounds with proven antimicrobial activity. The oil proved active against resistant Gram-positive cocci, and showed synergism with antibiotics, revealing its potential use as adjuvant or in the development of new alternative treatments of drug-resistant antimicrobial infections.

Key words: Terpenes, antimicrobial, synergism, perillaldehyde, One Health.

INTRODUCTION

The antibacterial activity of plant essential oils is well documented, and they are described as promising antimicrobial agents (Simões et al. 2009). Recently, their potential has been exploited alone, or in combination with antibiotics, acting as sensitizers or targeting virulence factors, through synergistic effect (Valdivieso-Ugarte et al. 2019, Yu et al. 2020). Synergic effect consists in the biological action triggered by the combination of two or more chemical entities in the treatment of a pathology, in which the activity of a combination of compounds is higher than the sum of the effects of individual compounds (Efferth & Koch 2011, Tyers & Wright 2019). The main mechanisms by which synergy effects are achieved consist in multi-target actions, such as increasing bioavailability, inhibiting or suppressing antibiotic resistance, particularly leading to the use of concentrations above the minimum inhibitory concentration (MIC), also contributing with the reduction of possible adverse effects (Wagner & Ulrich-Merzenich 2009, Yang et al. 2014, Shin et al. 2018). In addition, avoiding the use of first line therapy drugs with a broad spectrum of antibacterial action, and re-sensitizing the bacteria for the most common types of antibiotics, lessens the evolutive pressure and, consequently, antibiotic resistance. Decreasing the amount of antibiotics via synergistic effect also has the advantage

to show less cytotoxicity to human cells and symbiotic gut bacteria. Since the microbiota is closely related to the immune system, the ability to preserve this microbiota is considered a therapeutic priority (Belkaid & Hand 2014).

Plant natural products are considered an important source of bioactive molecules, due to the wide array of complex and structurally diverse molecules produced by these organisms, with great pharmacological potential. Brazilian flora, enclosed in biomes such as Pantanal and Cerrado, represents one of the highest potentials in terms of biological diversity. The Pantanal, considered the word largest wetland´s area, is distributed among the countries of Bolivia, Paraguay, and Brazil, which houses about two-thirds of its area. Although several bioactive molecules have been identified from Pantanal plants (Garcez et al. 2016), the rich flora of this biome still offers a wide biodiversity of species that remains unexplored. Therefore, the Pantanal consists of a promising source of natural products to be investigated regarding their potential synergistic effects in combination with routinely used antibiotics for the treatment of bacterial infections.

Plants belonging to the genus *Pectis* (Asteraceae) attract attention due to their pronounced fragrances, a characteristic trait observed in other genera in Tageteae tribe. The aromatic properties of *Pectis* species have been associated with their use in folk medicine, such as *P. stenophylla*, from which an infusion of the aerial parts is prepared and the hot vapor is inhaled to treating colds (Gentry 1963), and *P. prostrata,* used for colds and tuberculosis (Austin 2004). Plants rich in essential oil are often appreciated for their use for flavoring food, such as *P. elongata* (Maia et al. 2005) and *P. brevipedunculata* (Marques et al. 2013), or in perfumery, such as *P. angustifolia* (Bradley & Haagen-Smit 1949).

Although *Pectis* species are renowned for their noticeable fragrances and are widely distributed in the Americas, most of the members of this large genus, comprising *c.* 90 species (Hansen et al. 2016), have not yet been investigated or are still poorly explored. To the best of our knowledge, the essential oil from *Pectis substriata* has not been previously investigated.

Once antimicrobial resistance is a severe public health problem and a growing phenomenon, for which combat strategies are urgently needed, we aimed to evaluate the antimicrobial potential of the essential oil against a panel of clinical resistant bacterial strains, alone and/or in combination with known antimicrobial agents, and to report for the first time the chemical composition of the essential oil of the aromatic plant *P. substriata* from Pantanal biome, Brazil.

MATERIALS AND METHODS

Plant material

The fresh plant material of *Pectis substriata* Rusby (Asteraceae) (1.2 kg) were collected from Pantanal (Miranda county, Mato Grosso do Sul, Brazil, 19°34'37"S and 57°00'42" W), in May 2019. The plant material was identified by Dr. Arnildo Pott, CGMS Herbarium, Universidade Federal de Mato Grosso do Sul, Brazil, where a voucher specimen (No. 75.359) is deposited.

Essential oil extraction

Fresh aerial parts (leaves and stems) of *P. substriata* (1.030 kg) were extracted for 5 hours using a Clevenger-type apparatus, to yield 4.2 g (yield of 0.41% m/m) of essential oil.

Gas chromatography/mass spectrometry (GC/MS)

The GC/MS analysis was performed using a Shimadzu GC/MS QP-2010 PLUS Gas Chromatograph (Shimadzu Corporation, Kyoto, Japan) coupled to a mass spectrometer operating at 70 eV, Rtx®-5MS Restek fused silica capillary column (5%-diphenyl–95%-dimethylpolysiloxane) of 30 m × 0.25 mm i.d., 0.25 mm film thickness, and equipped with an autosampler AOC-20i (Shimadzu).

Chromatography conditions

The essential oil was dissolved in dichloromethane (1 $mg.mL^{-1}$) and an injection volume of 1 µL was employed, with a split ratio of 1:50. Injector temperature was 250°C, with the carrier gas (Helium 99.999% purity) at a flow rate of 1 $mL.min^{-1}$, and pressure of 87.1 kPa. The oven temperature was programmed from 50°C (isothermal for 1.5 min), with an increase of 3°C/min, to 260°C, ending with a 5 min isothermal at 260°C. A mixture of linear hydrocarbons (C9 to C22 alkanes) was injected under the same experimental conditions. The identification of the constituents in the essential oil was performed by comparing the mass spectra obtained with those of the equipment database (Wiley 7 lib and Nist 08 lib) and by using the Retention Index (RI), calculated for each constituent as previously described (Adams 2017).

Antimicrobial susceptibility assays

All reagents and media for the antibacterial assays were purchased from Sigma Aldrich™. The bacterial strains used were *Staphylococcus aureus* (NEWP0023, sensitive to amoxicillin, amoxicillin + clavulanic acid, gentamicin, cephalexin, cefoxitin, streptomycin and azithromycin), *Escherichia coli* (NEWP0022, sensitive to amoxicillin, amoxicillin + clavulanic acid, gentamicin, cephalexin, cefoxitin, streptomycin and tetracycline), both purchased from NEWPROV™ Company, clinical *S. aureus* (from human intra-abdominal fluid, β-lactamase producer, mecA mediated methicillin resistance), clinical *S. warneri* (from human hemoculture, β-lactamase producer, resistant to ampicillin, erythromycin and tetracycline) and clinical *S. intermedius* (from ulcerated nodule on dog skin, mecA mediated methicillin resistance, resistant to amoxicillin + clavulanic acid, gentamicin, neomycin, azithromycin, cephalexin, cephalothin, streptomycin and marbofloxacin). Human clinical strains were provided by the Center of Clinical Analysis of the University Hospital, Universidade Federal de Mato Grosso do Sul (Campo Grande, Brazil), while the veterinary strain was furnished by the Faculty of Veterinary Medicine and Animal Science of Universidade Federal de Mato Grosso do Sul. The antimicrobial activity of the essential oil alone was determined by broth microdilution method, as described by Manda et al. (2018). Two-fold dilutions were performed in 96-well plates prepared with Mueller-Hinton broth to reach a final concentration of 31.3 $µg.mL^{-1}$ to 4000 $µg.mL^{-1}$, with a 100 µL final volume in each well. The inoculums were overnight cultures of each bacterial species in Mueller-Hinton agar diluted in sterile saline solution (0.45%) to a concentration of approximately 10^8 $CFU.mL^{-1}$ (0.5 in McFarland scale), measured in a MS Tecnopon MCF-500 McFarland turbidimeter. This solution was diluted 1/10 in saline solution (0.45%) and 5 µL were added to each well containing the test samples. All experiments were performed in triplicate and the microdilution trays were incubated at 36°C for 18 h. Then, 20 µL of an aqueous solution (0.5 %) of triphenyl tetrazolium chloride (TTC) were added to each well and the trays were again incubated at 36°C for 2 h. In those wells where bacterial growth did occur, TTC changed from colourless to red. MIC was

defined as the lowest concentration of each substance at which no colour change occurred and was expressed in $\mu g.mL^{-1}$.

Synergistic interactions were evaluated using the checkerboard microtiter test, following the method described by Solarte et al. (2017). Serial two-fold dilutions of the essential oil (EO) were made vertically in 96-well plates prepared with Mueller-Hinton broth, to reach a concentration of 31.3 $\mu g.mL^{-1}$ to 4000 $\mu g.mL^{-1}$, with a 50 µL final volume in each well. Aliquots (50 µL) of antibiotics solutions in Mueller-Hinton broth were added in each well, so the final concentrations varied horizontally from 100 to 0.05 $\mu g.mL^{-1}$. For EO, the final concentrations varied from 15.6 $\mu g.mL^{-1}$ to 2000 $\mu g.mL^{-1}$. Bacterial inoculums were prepared as mentioned above, and 5 µL were added to each well containing the test samples, then the plates were incubated at 36°C for 18 h. After addition of TTC, MIC of the combinations were accessed, and fractional inhibitory concentration (FIC) and fractional inhibitory concentration index (FICI) were calculated by the formulas:

FIC= Combined MIC of EO or antibiotic/
Individual MIC of EO or antibiotic

FICI = FIC of EO + FIC of antibiotic

The FICI value was interpreted as: synergism (FICI ≤ 0.5), additive (0.5 < FICI ≤ 1), indifferent (1 < FICI ≤ 4), and antagonist (FICI > 4) (Lim et al. 2016, Ahumada-Santos et al. 2016, Silva et al. 2019)

RESULTS AND DISCUSSION

The essential oil of *P. substriata* (EO) was first evaluated against *Staphylococcus aureus* (NEWP0023) and *Escherichia coli* (NEWP0022), two sensitive standard strains, by broth microdilution assay, and showed antimicrobial activity only against *S. aureus*, with a minimum inhibitory concentration (MIC) of 125 $\mu g.mL^{-1}$.

This selectivity encouraged us to select a panel of clinical Gram-positive strains, with different sensitivity profiles to antibiotics. The chosen strains were *Staphylococcus aureus* (human pathogen, methicillin mecA-mediated resistance, β-lactamase producer), *S. warneri* (human pathogen, β-lactamase producer) and *S. intermedius* (canine pathogen, methicillin mecA-mediated resistance, resistant to penicillins, aminoglycosides, first-generation cephalosporins and quinolones).

Staphylococcus microorganisms are important targets, as they have a diverse arsenal of pathogenicity factors, represented by adhesins, enterotoxins, hemolysins, leukocidins, biofilm production, ability to invade epithelial cells, among others, which contribute to colonize and damage their hosts (da Costa et al. 2011). *S. aureus* is the major pathogen causing bacterial infection in community settings and hospitals, significantly contributing to morbidity and mortality, as it has the capability to generate a diverse array of infection in different organs or tissues, including skin wound infection, folliculitis, pneumonia, endocarditis, and bacteremia (Yeh et al. 2020). *S. warneri* is a coagulase-negative common commensal colonizing human and animals' skin and mucosal membranes, that are gaining clinical attention. This bacteria can cause sepsis (e.g. in immunocompetent patients with multiple abscesses), infections related to community-acquired native valve endocarditis, it was also detected in orthopaedic cases, and may be responsible for urinary tract infections (Liu et al. 2020, Szemraj et al. 2020). *S. intermedius* is a bacterial strain commonly found in skin and mucosal flora in a variety of animals, including dogs and cats, but rarely isolated from humans (Wang et al. 2013). Once antimicrobial resistance

genes are very promiscuous, circulating through humans, animals, and the environment, the transmission of resistance from animal microorganisms by direct contact between humans and animals is a concern (Wegener 2012). Therefore, the initiatives working within the *One Health* concept (Nyatanyi et al. 2017), including animal pathogens in the research for new antimicrobial drugs, can be seen as a more interesting strategy to mitigate the problem of antibiotic resistance.

The oil was tested alone and in combination with antimicrobial drugs against resistant bacteria, in order to check for possible synergistic interactions. Results can be seen in Table I. The *P. substriata* EO alone showed a significant activity against the human pathogen *S. warneri* (MIC of 62.5 $\mu g.mL^{-1}$), and was moderately active on *S. intermedius* (MIC of 250 $\mu g.mL^{-1}$) (Wamba et al. 2018). Among all staphylococcal strains assayed, only *S. warneri* is a coagulase-negative, characteristic that may be related to the enhanced EO activity against this strain. The coagulase enzyme is considered an indicator of virulence, and most of *S. aureus* and *S. intermedius* are coagulase-positive (da Costa et al. 2011).

The combination effect of the EO and the antibiotics against resistant bacteria were also evaluated. The results can be seen in Table I. All strains evaluated were β-lactamase producers, hence the combination of ampicillin and the EO was tested for all of them. The EO had additive effects on *S. aureus* and *S. intermedius* (FICI=1), while synergism was observed for *S. warneri* (FICI=0.25). Especially for this antibiotic, a remarkable decrease in the MIC values, from >100 to 0.049 $\mu g.mL^{-1}$, was observed for all tested strains. In combination with tetracycline, the oil had an additive affect when tested for *S. warneri*, with FICI of 0.75, lowering the antibiotic MIC from >100 to 25 $\mu g.mL^{-1}$. Four-fold reduction in MICs of kanamycin and EO were observed when assayed in combination against *S. intermedius*, with FICI of 0.5, reflecting synergism.

Essential oils from aromatic plants, such as cinnamon, clove, oregano, lavender and thyme, have shown synergistic effects with antibiotics

Table I. Minimum inhibitory concentration (MIC, in $\mu g.mL^{-1}$) of antibiotics and *Pectis substriata* essential oil, fractional inhibitory concentration (FIC) and fractional inhibitory concentration index (FICI), of antibiotics-essential oil pairs, against drug-resistant bacteria.

Combination	Clinical *S. aureus*				Clinical *S. warneri*				Clinical *S. intermedius*			
	individual MIC	combined MIC	FIC	FICI	individual MIC	combined MIC	FIC	FICI	individual MIC	combined MIC	FIC	FICI
AMP + *EO*	-	-	**-**	**1**	-	-		**0.25**	**-**	**-**	**-**	**1**
AMP	>100	0.049	0.0005	-	>100	0.049	0.0005	-	>100	0.049	0.0005	-
EO	1000	1000	1	-	62.5	15.6	0.25	-	250	250	1	-
TET + *EO*	-	-	-	-	-	-	**-**	**0.75**	**-**	**-**	**-**	**-**
TET	-	-	-	-	100	25	0.25	-	-	-	-	-
EO	-	-	-	-	62.5	31.25	0.50	-	-	-	-	-
KAN + *EO*	-	-	**-**	**-**	-	-	-	-	-	-	**-**	**0.5**
KAN	-	-	-	-	-	-	-	-	100	25	0.25	-
EO	-	-	-	-	-	-	-	-	250	62.5	0.25	-

AMP: ampicillin. TET: tetracycline. KAN: kanamycin. *EO*: Essential oil from aerial parts of *Pectis substriata*. Synergism: FICI≤0.5; additivity: 0.5<FICI≤1; indifference: 1<FICI≤4; antagonism: FICI>4.

against clinically relevant multidrug-resistant bacterial strains, such as β-lactamase producing *Escherichia coli*, *Listeria monocytogenes*, carbapenemase producing *Klebsiella pneumoniae* and *Salmonella enterica* (Cho et al. 2020, Si et al. 2008, Yang et al. 2020), e.g. via mechanisms involving the disruption of the bacterial cytoplasmatic membrane, attributed to their hydrophobicity characteristic (Lambert et al. 2001, Moghimi et al. 2016, Solarte et al. 2017).

The analysis and identification of thirty compounds, representing 98.91% of total oil constitution, was performed by Gas Chromatography coupled to Mass Spectrometry (GC/MS). The essential oil from the aerial parts of *P. substriata* was composed of monoterpenes and aliphatic compounds, with a single component, perillaldehyde, performing 62.15% of the total oil, followed by 4-undecanol (12.05%), limonene (6.46%), α-fenchene (2.89%) and perillyl alcohol (2.51%) (Table II, Supplementary Material - Figure S1, Table SI).

A similar result was observed in the analysis of the chemical composition of an Amazonian specimen of *P. elongata* Kunth leaf oil, which was also characterized by the presence of perillaldehyde (51.7%) and limonene (43.7%) as main compounds (Maia et al. 2005). The monoterpene perillaldehyde has also been defined as the main component of the essential oil from the aerial parts of the Cuban species *P. floribunda* Kunth and *P. prostrata*, representing 44.5% and 70.7% of the total leaf oil, followed by limonene, with values of 9.7% and 16.2%, respectively (Pino et al. 1999, 1996), as well as in the composition of *P. odorata*, collected in Paraguay, which is rich in perillaldehyde and thymol (Hirschmann et al. 1986).

The essential oil of plants belonging to *Pectis* genus, such as *Pectis brevipedunculata*, have shown bactericidal and fungicidal activities (Marques et al. 2013). Although the antimicrobial effects of the *P. substriata* have not been previously investigated, the main compounds found in the essential oil of this species are known to be biologically active and exhibit antimicrobial, anticancer, and anti-inflammatory properties (Duelund et al. 2012). Perillaldehyde efficiently inhibits airborne microbes using an air-washer, contributing to improve environmental health (Sato et al. 2006), and showed antibacterial activity against respiratory tract pathogens, such as *Haemophilus influenza*, *Streptococcus pneumoniae*, *S. pyogenes* [minimum inhibitory dose (MID) of 12.5 $mg.L^{-1}$ air, respectively], and *Staphylococcus aureus* (MID=50 $mg.L^{-1}$ air) (Inouye et al. 2001), and against foodborne bacteria *Escherichia coli*, *E. coli* 0157:H7, *Salmonella typhimurium* (MIC=500 $\mu g.mL^{-1}$, respectively), and *Vibrio vulnificus* (MIC=250 $\mu g.mL^{-1}$) (Kim et al. 1995). Perillyl alcohol proved to be a potent natural chemosensitizing agent against fungal infections, acting by multiple mechanisms of action (Ansari 2016), and has a strong antibacterial effect against the periodontal pathogens *Fusobacterium nucleatum* and *Porphyromonas gingivalis* (Figueiredo et al. 2020), while (+)-limonene has been described as a bactericidal agent to be used in food preservation, effecting Gram-negative bacteria (Espina 2013). The presence of compounds with proven antimicrobial activity reinforces the potential pharmacological use of essential oils, as well as preservative and flavoring agents.

This is the first study regarding the biological activity and chemical composition of *Pectis substriata* essential oil. The use of combinations that have a synergistic or additive antimicrobial effect is an interesting approach, and our results reinforce that essential oils play a prominent role in this scenario. The use of adjuvant antibacterial agents decreases the amount of antibiotics used, therefore decreasing their

Table II. Chemical composition of the essential oil from the aerial parts of *Pectis substriata*, by GC/MS.

Peak	RT	$RI^{+}_{Exp.}$	$RI^{++}_{Ref.}$	Compound	Molecular Formula	Peak area (%)
1	6.430	937	945	α-Fenchene	$C_{10}H_{16}$	2.89
2	6.536	940	939	3-Methyl-valeric acid	$C_6H_{12}O_2$	0.80
3	6.837	950	958	γ-Valerolactone	$C_5H_8O_2$	0.71
4	7.853	983	981	6-Methyl-5-hepten-2-one	$C_8H_{14}O$	0.31
5	9.195	1021	1020	*para*-Cymene	$C_{10}H_{14}$	0.62
6	9.352	1025	1024	Limonene	$C_{10}H_{16}$	6.46
7	10.174	1046	1031	Unknown	$C_7H_8O_2$	0.29
8	11.076	1069	1067	*cis*-Linalool oxide	$C_{10}H_{18}O_2$	0.12
9	11.724	1085	1084	*trans*-Linalool oxide	$C_{10}H_{18}O_2$	0.12
10	11.800	1087	1085	3,7-Dimethyloctan-3-ol	$C_7H_{10}O_2$	0.42
11	12.196	1097	1095	Linalool	$C_{10}H_{18}O$	0.07
12	14.558	1152	1154	Sabina ketone	$C_9H_{14}O$	0.73
13	15.511	1174	1174	Terpinen-4-ol	$C_{10}H_{18}O$	0.13
14	15.962	1185	1187	*trans*-Isocarveol	$C_{10}H_{16}O$	0.27
15	16.087	1187	1198	2-Decanol	$C_{10}H_{22}O$	0.16
16	16.360	1194	1196	*trans* -4-Caranone	$C_{10}H_{16}O$	0.32
17	17.257	1214	1218	Fenchyl acetate	$C_{12}H_{20}O_2$	0.06
18	17.345	1216	1217	β-Cyclocitral	$C_{10}H_{16}O$	0.21
19	17.868	1228	1226	*cis*-Carveol	$C_{10}H_{16}O$	0.05
20	18.301	1238	1235	Neral	$C_{10}H_{16}O$	0.50
21	18.423	1241	1239	Carvone	$C_{10}H_{14}O$	0.51
22	19.625	1268	1264	Geranial	$C_{10}H_{16}O$	0.35
23	19.795	1272	1269	Perillaldehyde	$C_{10}H_{14}O$	62.15
24	20.038	1278	1273	Phellandranal	$C_{10}H_{16}O$	0.80
25	20.179	1281	1294	Perillyl alcohol	$C_{10}H_{16}O$	2.51
26	20.457	1287	1286	4-Undecanol	$C_{11}H_{24}O$	12.05
27	22.142	1327	1325	*para*-Mentha-1,4-dien-7-ol	$C_{10}H_{16}O$	1.70
28	22.558	1336	1332	*cis*-Piperitol acetate	$C_{12}H_{20}O_2$	2.49
29	23.197	1351	1359	9-Decenoic acid	$C_{10}H_{18}O_2$	1.40
30	25.320	1401	1393	Unknown	$C_8H_8O_3$	0.80

The compounds are listed in order of their elution from the Rtx-MS column. RT: retention time of compounds. RI: retention indexes on the Rtx-MS column (relative to n-alkanes). [+]Experimental retention index. [++] Retention index from literature (Adams 2017).

discharge into the environment and resensitizes resistant bacteria, allowing longer life for existing antibiotics.

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REFERENCES

ADAMS RP. 2017. Identification of essential oil components by gas chromatography mass spectroscopy. Ed. 4.1. Carol Stream: Allured Publishing Corporation, 804 p.

AHUMADA-SANTOS YP, SOTO-SOTOMAYOR ME, BAÉZ-FLORES ME, DÍAZ-CAMACHO SP, LOPEZ-ANGULO G, ESLAVA-CAMPOS CA & DELGADO-VARGAS F. 2016. Antibacterial synergism of *Echeveria subrigida* (B. L. Rob & Seaton) and commercial antibiotics against multidrug resistant *Escherichia coli* and *Staphylococcus aureus*. Eur J Integr Med 8: 638.

ANSARI MA, FATIMA Z & HAMEED S. 2016. Anticandidal effect and mechanisms of monoterpenoid, perillyl alcohol against *Candida albicans*. PLoS ONE 11: e0162465.

AUSTIN DF. 2004. Florida Ethnobotany. Boca Raton: Taylor & Francis Group. CRC Press, 952 p.

BELKAID Y & HAND TW. 2014. Role of the microbiota in immunity and inflammation. Cell 27: 121.

BRADLEY CE & HAAGEN-SMIT AJ. 1949. The essential oil of *Pectis papposa*. Econ Bot 3(4): 407.

CHO Y, KIM H, BEUCHAT LR & RYU J. 2020. Synergistic activities of gaseous oregano and thyme thymol essential oils against *Listeria monocytogenes* on surfaces of a laboratory medium and radish sprouts. Food Microbiol 86: 103357.

DA COSTA GM, PEREIRA UP, CUSTÓDIO DAC & DA SILVA N. 2011. Characterization of coagulase-positive *Staphylococcus* by using plasmas from different animal species. Rev Inst Adolfo Lutz 70: 584.

DUELUND L, AMIOT A, FILLON A & MOURITSEN OG. 2012. Influence of the active compounds of *Perilla frutescens* leaves on lipid membranes. J Nat Prod 75: 160.

EFFERTH T & KOCH E. 2011. Complex interactions between phytochemicals. The multi-target therapeutic concept of phytotherapy. Curr Drug Targets 12: 122.

ESPINA L, GELAW TK, DE LAMO-CASTELLVÍ S, PAGÁN R & GARCÍA-GONZALO D. 2013. Mechanism of bacterial inactivation by (+)-limonene and its potential use in food preservation combined processes. PLoS ONE 8: e56769.

FIGUEIREDO RDA, ORTEGA AC, MALDONADO LAG, CASTRO RD, ÁVILA-CAMPOS MJ, ROSSA JUNIOR C & AQUINO SG. 2020. Perillyl alcohol has antibacterial effects and reduces ROS production in macrophages. J Appl Oral Sci 28: e20190519.

GARCEZ FR, GARCEZ WS, YOSHIDA NC & FIGUEIREDO PO. 2016. The chemical diversity from the vegetation of Mato Grosso do Sul and its relevance as a source of bioactive molecules. Rev Virtual Quim 8: 97.

GENTRY HS. 1963. The Warihio Indians of Sonora-Chihuahua: An ethnographic survey. In: Roberts Jr FHH. River basin surveys papers – Inter-agency archeological salvage program n. 26-32. Washington: Smithsonian Institution Bulletin 185.

HANSEN DR, JANSEN RK, SAGE RF, VILLASEÑOR JL & SIMPSON BB. 2016. Molecular phylogeny of *Pectis* (Tageteae, Asteraceae), a C4 genus of the Neotropics, and its sister genus *Porophyllum*. Lundellia 19: 6.

HIRSCHMANN GS, BOHLMONN F & JAKUPOVIC J. 1986. The constituents of *Ambrosia tenuifolia* and *Pectis odorata*. Rev Latinoam de Quimica 17: 200.

INOUYE S, TAKIZAWA T & YAMAGUCHI H. 2001. Antibacterial activity of essential oils and their major constituents against respiratory tract pathogens by gaseous contact. J Antimicrob Chemoth 47: 565.

KIM J, MARSHALL MR & WEI C. 1995. Antibacterial activity of some essential oil components against five foodborne pathogens. J Agr Food Chem 43: 2839.

LAMBERT RJ, SKANDAMIS PN, COOTE PJ & NYCHAS GJ. 2001. A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. J Appl Microbiol 91: 453.

LIM A, SUBHAN N, JAZAYERI JA, JOHN G, VANNIASINKAM T & OBIED HK. 2016. Plant phenols as antibiotic boosters: *In vitro* interaction of olive leaf phenols with ampicillin. Phytother Res 30: 503.

LIU C, ZHAO X, XIE H, ZHANG X, LI K, MA C & FU Q. 2020. Whole genome sequence and comparative genome analyses of multi-resistant *Staphylococcus warneri* GD01 isolated from a diseased pig in China. PLoS ONE 15: e0233363.

MAIA JGS, SILVA MHL & ANDRADE EHA. 2005. The essential oil of *Pectis elongata* Kunth occurring in North Brazil. Flavour Frag J 20: 462.

MANDA BR ET AL. 2018. Synthesis, antibacterial and antitubercular evaluation of cardanol and glycerol-based β-amino alcohol derivatives. J Braz Chem. Soc 29: 639.

MARQUES AM, LIMA CHP, ALVIANO DS, ALVIANO CS, ESTEVES RL & KAPLAN MAC. 2013. Traditional use, chemical composition and antimicrobial activity of *Pectis brevipedunculata* essential oil: A correlated lemongrass species in Brazil. Emir J Food Agr 25: 798.

MOGHIMI R, GHADERI L, RAFATI H, ALIAHMADI A & MCCLEMENTS DJ. 2016. Superior antibacterial activity of nanoemulsion of *Thymus daenensis* essential oil against *E. coli*. Food Chem 194: 410.

NYATANYI T ET AL. 2017. Implementing One Health as an integrated approach to health in Rwanda. BMJ Global Health 2: e000121.

PINO JA, ROSADO A & FUENTES V. 1996. Chemical composition of the leaf oil of *Pectis prostrata* Cav. from Cuba. J Essent Oil Res 8: 579.

PINO JA, ROSADO A & FUENTES V. 1999. Composition of the essential oil of *Pectis floribunda* A. Rich. J Essent Oil Res 11: 31.

SATO K, KRIST S & BUCHBAUER G. 2006. Antimicrobial effect of *trans*-cinnamaldehyde, (-)-perillaldehyde, (-)-citronellal, citral, eugenol and carvacrol on airborne microbes using an airwasher. Biol Pharm Bull 29: 2292.

SHIN J, PRABHAKARAN V & KIM K. 2018. The multi-faceted potential of plant-derived metabolites as antimicrobial agents against multidrug-resistant pathogens. Microb Pathogenesis 116: 209.

SI H, HU J, LIU Z & ZENG ZL. 2008. Antibacterial effect of oregano essential oil alone and in combination with antibiotics against extended-spectrum β-lactamase-producing *Escherichia coli*. FEMS Immunol Med Mic 53: 190.

SILVA DM, COSTA PA, RIBON AOB, PURGATO GA, DIAZ G & DIAZ MAN. 2019. Plant extracts display synergism with different classes of antibiotics. An Acad Bras Cienc 91: e20180117.

SIMÕES M, BENNETT RN & ROSA EAS. 2009. Understanding antimicrobial activities of phytochemicals against multidrug resistant bacteria and biofilms. Nat Prod Rep 26: 746.

SOLARTE AL, ASTORGA RJ, AGUIAR F, GALÁN-RELAÑO Á, MALDONADO A & HUERTA B. 2017. Combination of antimicrobials and essential oils as an alternative for the control of *Salmonella enterica* multiresistant strains related to foodborne disease. Foodborne Pathog Dis 14: 588.

SZEMRAJ M, GRAZUL M, BALCERCZAK E & SZEWCZYK EM. 2020. Staphylococcal species less frequently isolated from human clinical specimens - Are they a threat for hospital patients? BMC Infect Dis 20: 128.

TYERS M & WRIGHT GD. 2019. Drug combinations: a strategy to extend the life of antibiotics in the 21st century. Nat Rev Microbiol 17: 141.

VALDIVIESO-UGARTE M, GOMEZ-LLORENTE C, PLAZA-DÍAZ J & GIL Á. 2019. Antimicrobial, antioxidant, and immunomodulatory properties of essential oils: a systematic review. Nutrients 11: 2786.

WAGNER H & ULRICH-MERZENICH G. 2009. Synergy research: Approaching a new generation of phytopharmaceuticals. Phytomedicine 16: 97.

WAMBA BEN, NAYIM P, MBAVENG AT, VOUKENG IK, DZOTAM JK, NGALANI OJT & KEUTE V. 2018. *Syzygium jambos* displayed antibacterial and antibiotic-modulating activities against resistant phenotypes. Evid Based Complement Alternat Med 2018: 5124735.

WANG N, NEILAN AM & KLOMPAS M. 2013. *Staphylococcus intermedius* infections: case report and literature review. Infect Dis Rep 5: e3.

WEGENER HC. 2012. Antibiotic resistance – linking human and animal health. In: Institute of Medicine (US), Improving food safety through a One Health approach: Workshop Summary. Washington (DC): National Academies Press, A15 p.

YANG S, YUSOFF K, THOMAS W, AKSEER R, ALHOSANI MS, ABUSHELAIBI A, LIM S & LAI K. 2020. Lavender essential oil induces oxidative stress which modifies the bacterial membrane permeability of carbapenemase producing *Klebsiella pneumoniae*. Sci Rep 10: 819.

YANG Y, ZHANG Z, LI S, XIAOLI Y, XUEGANG L & KAI H. 2014. Synergy effects of herb extracts: Pharmacokinetics and pharmacodynamic basis. Fitoterapia 92: 33.

YEH YC, HUANG TH, YANG SC, CHEN CC & FANG JY. 2020. Nano-Based drug delivery or targeting to eradicate bacteria for infection mitigation: A review of recent advances. Front Chem 8: 286.

YU Z, TANG J, KHARE T & KUMAR V. 2020. The alarming antimicrobial resistance in ESKAPEE pathogens: Can essential oils come to the rescue? Fitoterapia 140: 104433.

SUPPLEMENTARY MATERIAL

Figure S1.
Table SI.

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NCY and ACM conceived the study. AP and KMT were responsible for the collection and identification of the plant material. GSJ and KMT extracted the oil and collected the chemical data. ACM and TM realized the biological assays. NCY, ACM and GSJ analysed and interpreted the data. NCY and ACM drafted the manuscript. All authors commented on drafts on the paper. All authors have approved the final draft of the manuscript.