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Review Paper

Myrtaceae family: an update on plant-derived bioactive compounds against bacteria that affect the respiratory system

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Abstract

Respiratory bacterial infections are a cause of morbidity and mortality worldwide; most of these infections respond well to antibiotic therapies, although several factors cause bacteria to become increasingly resistant, leading to a concerning public health problem. Hence, researchers have sought new antibiotics that can replace or enhance the effectiveness of existing drugs. Given this scenario, this review is based on original articles from the PubMed and Science Direct databases published from May 2015 to February 2022 that reported the potential of essential oils, extracts, and formulations containing Myrtaceae and nanoparticles against bacteria that affect the respiratory system.

Key words: antibacterial, Myrtaceae, phytochemistry, respiratory infection, therapy.

Resumo

As infecções bacterianas do sistema respiratório são causa de morbidade e mortalidade em todo o mundo. A maioria dessas infecções responde bem às terapias antibióticas, porém, diversos fatores fazem com que as bactérias se tornem cada vez mais resistentes, causando um grave problema de saúde pública no mundo. Devido a este problema, têm-se procurado novos antibióticos que possam substituir ou aumentar a eficácia dos fármacos existentes. Esta revisão é baseada em artigos originais obtidos através de buscas nas bases de dados PubMed e Science Direct publicados no período de maio de 2015 a fevereiro de 2022, que relataram o potencial de óleos essenciais, extratos e formulações contendo Myrtaceae e nanopartículas contra bactérias que afetam o sistema respiratório.

Palavras-chave: antibacteriano, Myrtaceae, fitoquímica, infecção respiratória, terapia.

Introduction

Respiratory infections are among the most common diseases, causing morbidity and mortality worldwide. Most of these infections respond well to antibiotic therapies, although several factors cause the pathogens to develop resistance, including the indiscriminate use of this type of medication, cross-resistance, and lack of new drugs, among others (Torres *et al.* 2021; Troeger *et al.* 2018).

The emergence of multidrug-resistant (MDR) bacteria increases morbidity and mortality rates, hospital stay lengths, and patient treatment costs, making bacterial antibiotic resistance a major public health problem (Woolhouse *et al.* 2016). In 2017, the World Health Organization published a list of antibiotic-resistant "priority pathogens" containing a variety of microorganisms, including bacteria involved in respiratory infections, that

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pose the greatest threat to human health (WHO 2017). Each year, 700,000 people worldwide die of MDR infections, and if no action is taken, over 10 million deaths are estimated to occur by 2050 (Tillotson & Zinner 2017). Therefore, searching for new antibiotics capable of overcoming microbial resistance is critical.

Given these circumstances, bioprospection research has sought to identify plants from which new drugs may be produced using essential oils, crude plant extracts, isolating active components, combinations of antibiotics, nanotechnology, and other approaches. In the research and development sector of the pharmaceutical industry, phytochemicals are a source of new molecules leading to new drug development, and it is estimated that 30–50% of modern drugs are based on natural products, especially plants (Boucher *et al.* 2017; Newman & Cragg 2020).

Various plant species from the Myrtaceae family are used for medicinal purposes, including the treatment of infectious diseases, and the underlying mechanism of action is thought to be related to the plants' astringent properties. Given this context, this study will review the essential oils, extracts, and nanoproducts synthesized from plants of the Myrtaceae family and employed against respiratory infection-causing bacteria.

Material & Methods

A search was performed in the PubMed and Science Direct databases for original scientific articles published from May 2015 to February 2022, and 'Myrtaceae used as a clinical antibacterial' was used as the search term. The articles included in this review were selected based on studies with plants of the Myrtaceae family that evaluated the *in vitro* antibacterial activity against bacteria involved in respiratory infections.

Results & Discussion

Myrtaceae family

Myrtaceae is a family of plants present in the main group of angiosperms, comprising 145 genera and 5,970 species (The Plant List 2013). The species that make up this family are predominantly distributed in the Southern Hemisphere and mostly found in the Neotropical and Australian regions (Fig. 1) (Sytsma *et al.* 2004; Heywood *et al.* 2007). In Brazil, there are 140 genera within the Myrtaceae family and 6,000 species (Proença *et al.* 2022). Due to its chemical composition, this family has numerous bioactive properties, comprising phenolic and polyphenol compounds such as flavonoids, phenolic acids, tannins, stilbenes, lignans, coumarins, tocopherols, functional lipids, and carotenoids (Fig. 2) (Duarte & Paull 2015).

The Myrtaceae family consists of various species, including *Eucalyptus globulus* Labill. (eucalyptus), *Eugenia uniflora* L. (pitanga), *Campomanesia adamantium* (Cambess.) O. Berg (guabiroba), *Melaleuca alternifolia* (Maiden & Betche) Cheel (tea tree), *Psidium guajava* L. (guava), *Psidium cattleianum* Sabine (araçá), *Syzygium cumini* (L.) Skeels (jambolan), and *Syzygium aromaticum* (L.) Merr. & L. M. Perry (clove) (The Plant List 2013).

1. Bioactive species of Myrtaceae and their identified compounds in treating respiratory infection-causing bacteria

1.1 Essential oils

Essential oils (EO) are natural volatile compounds present in plants, with over 3,000 secondary metabolites. Among these metabolites, about 500 are volatile compounds, including mono- and sesquiterpenes, terpenoids, aldehydes, and phenols (Schelz *et al.* 2006). Some of these constituents have proven biological properties, such as anti-inflammatory and antibacterial effects (Lazarini *et al.* 2018; Schelz *et al.* 2006). The chemical constituents and activity of EOs of different species of the Myrtaceae family against respiratory infection-causing bacteria are described throughout the text and in Table S1 (available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>).

1.1.1 Genus *Eucalyptus*

The genus *Eucalyptus*, popularly known as eucalyptus, represents over 700 species worldwide. Luís *et al.* (2016) investigated *Eucalyptus globulus*

Figure 1 – Geographic distribution of plants in the Myrtaceae family.

EO and, through gas chromatography coupled with mass spectrophotometry (GC-MS), found 45 constituents in their chemical composition, the main ones being 1.8-cineol (eucalyptol) (63.81%), α-pinene (16.06%), and aromadendrene (3.68%). Salem *et al.* (2018) found 67 volatile constituents in *E. globulus* EO and differences depending on the plant stage; eucalyptol (13.23%) was observed in the vegetative stage, while p-cymene was found as the major compound in the full flowering (32.19%) and fruiting stages (37.82%) (Tab. S1, available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>). The authors also tested the antibacterial activity of *E. globulus* and *E. radiata* Hook. EOs against several microorganisms, and the *E. globulus* EO showed promising activity against *Acinetobacter baumannii* ATCC 17978 with a minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of 4 μL mL^{-1}, while *E. radiata* EO presented a MIC and MBC of 8 μL mL^{-1} against this bacterium.

The researchers evaluated the combination of *E. globulus* EO with conventional antibiotics (cefoperazone, piperacillin, ciprofloxacin, tetracycline, chloramphenicol, and gentamicin) and found that this was effective against *A. baumannii*. In fact, the authors noted that the best fractional inhibitory concentration indices (FICI) were achieved by combining chloramphenicol with *E. globulus* EO, leading to modal values of 0.12 (*A. baumannii* ATCC 17978) and 0.09 (*A. baumannii* ATCC 19606), followed by combining the same antibiotic with *E. radiata* EO, leading to modal values of 0.12 against *A. baumannii* ATCC 17978 and 0.06 against *A. baumannii* ATCC 19606. Salem *et al.* (2018) identified a MIC of 4 mg mL^{-1} in the *E. globulus* EO against *Staphylococcus aureus* ATCC 6816 in all the tested stages of the plant; for methicillin-resistant *S. aureus* (MRSA), the researchers found an even lower MIC of 2 mg mL^{-1} in the vegetative stage and 4 mg mL^{-1} in the other stages. For *Klebsiella pneumoniae* CIP 104727, the MIC was 4 mg mL^{-1} in all EOs of the different parts of the plant tested. The antibacterial activity of this EO can occur due to its chemical composition since 1.8-cineol and p-cymene can act synergetically, potentiating the effects (Veras *et al.* 2012). In the checkerboard test, when testing *E. globulus* EO with ampicillin, the authors found partial synergism with a FICI of 0.53 μg mL^{-1} compared to MRSA and FICI of 1μg mL^{-1} compared to *K. pneumoniae* CIP 104.727, showing additivity (Salem *et al.* 2018).

Seventy-two compounds were found in *E. radiata* EO, of which most were limonene (68.51%), α-terpineol (8.60%), and α-terpinyl acetate (6.07%) (Luís *et al.* 2016). The authors tested the antibacterial potential of *E. globulus* and *E. radiata* EOs against standard strains: *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 13883, *A. baumannii* ATCC 17978, and *A. baumannii* ATCC 19606 and three more clinical isolates: *P. aeruginosa* PA 08, *P. aeruginosa* PA 12/08, and *K. pneumoniae* KP 08, and the MIC test revealed that the *E. radiata*

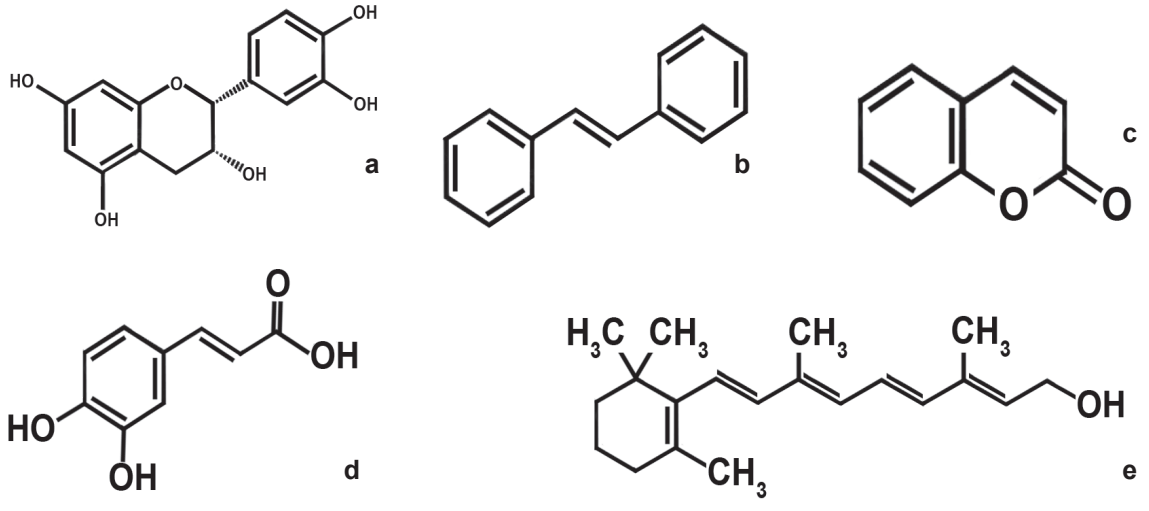

Figure 2 – a-e. Molecular representation of the main compounds present in the chemical composition of plants in the Myrtaceae family – a. Flavonoid; b. Stilbene; c. Coumarin; d. Phenolic acid; e. Carotenoid.

EO had better antibacterial activity, proving to be bactericidal, as the MIC were lower than the *E. globulus* EO against *P. aeruginosa* PA 08 and *K. pneumoniae* KP 08. Furthermore, Luís *et al.* (2016) tested the combination of conventional antibiotics (cefoperazone, piperacillin, ciprofloxacin, tetracycline, chloramphenicol, and gentamicin) with *E. radiata* EO and found modal values of 0.12 and 0.06 against *A. baumannii* ATCC 17978 and *A. baumannii* ATCC 19606, respectively.

E. camaldulensis is also a species within the genus *Eucalyptus* with biological properties, in addition to being tested against MDR strains such as *A. baumannii* (Jazani *et al.* 2012). Knezevic *et al.* (2016) evaluated two types of *E. camaldulensis* EOs collected from two coastal areas of Montenegro (Europe - Herceg Novi (EuHN) and Bar (EuB)). Fourty-three compounds were identified in these EO, and the most representative were spatulenol (EuHN - 18.90%; EuB: 21.39%), krypton (EuHN - 7.59%; EuB - 12.15%), p-cymene (EuHN - 5.35%; EuB - 7.56%), and 1.8-cineole (EuHN - 7.62%; EuB - 1.95%). The antibacterial activity was assessed against three standard strains: *A. baumannii* ATCC 19606, *A. baumannii* ATCC BAA747, and *A. baumannii* NCTC 13420, and twenty more *A. baumannii* MRD isolated from clinical and outpatient wounds. The authors found that MIC for the reference bacteria ranged from 1 to 2 μL mL^{-1} and from 0.5 to 2 μL mL^{-1} for the isolates in both tested EOs. In addition, the researchers observed a synergistic interaction when combining the *E. camaldulensis* EO with ciprofloxacin, producing FICI values below 0.5 μL mL^{-1} against two *A. baumannii* isolates (Aba-4914 and Aba-5055) and an additive effect against Aba-6673. Moreover, a synergistic interaction occurred when the EO was tested with gentamicin against Aba-4914, decreasing the concentrations of the antibiotic, as was shown by combining the EO and polymyxin B, which showed synergistic potential against three multi-resistant microorganisms (Knezevic *et al.* 2016).

1.1.2 Genus *Melaleuca*

The species of *Melaleuca alternifolia* is used as a topical antiseptic and anti-inflammatory agent (Saller *et al.* 1998). The EO extracted from this plant has antibacterial activity against Gram-positive and Gram-negative bacteria (Carson *et al.* 1995, 2000). Oliva *et al.* (2018) employed the GC-MS technique and identified three main constituents in *M. alternifolia* EO, namely: terpinene 4-ol (35.4%), eucalyptol (15.2), and α-pinene (12.4%). Imane *et al.* (2020) utilized the same approach and found terpinene 4-ol (13.5%) and α-pinene (13.1%), although in smaller quantities, with α-carene (17.4%) being the major compound. When determining the antimicrobial activity, the following microorganisms were used: methicillin-sensitive *S. aureus* (MSSA) ATCC 29213, MRSA - clinical isolate (skin), extended-spectrum beta-lactamases producer carbapenem-sensitive *Klebsiella pneumoniae* (ESBL-CS-Kp) - clinical isolate (urine), carbapenem-resistant *K. pneumoniae* (ESBL-CR-Kp) - clinical isolate (urine), carbapenem-resistant *A. baumannii* (CR-Ab) - clinical isolate (sputum), and carbapenem-resistant *P. aeruginosa* (CR-Pa) - clinical isolate (bronchoalveolar lavage). The results showed that *M. alternifolia* EO was active, with MIC and MBC of 0.25 μg mL^{-1} for CR-Ab and ESBL-CR-Kp, 0.50 μg mL^{-1} for ESBL-CS-Kp, and MIC of 0.50 μg mL^{-1} and MBC of 2.0 μg mL^{-1} for MRSA. The EO was active against MSSA ATCC 29213, with MIC and MBC of 1.0 and 2.0 μg mL^{-1}, respectively, and CR-Pa MIC of 1.0 μg mL^{-1} and MBC of 1.0 μg mL^{-1}; however, it was possible to note that the EO was bactericidal against all the tested bacteria (Oliva *et al.* 2018).

Imane *et al.* (2020) also observed antibacterial activity against the microorganisms evaluated, with a MIC of 4.42 mg mL^{-1} against MRSA NCTC 12493 and 2.21 mg mL^{-1} against a *S. aureus* isolate, both being bactericidal. When evaluating the same EO against *K. pneumoniae* ATCC 700603, the authors obtained a MIC of 8.84 mg mL^{-1}. These findings highlight how *M. alternifolia* EO is a promising alternative in treating infections caused by MDR Gram-negative microorganisms, considering that various infections, such as hospital pneumonia, are caused by these bacteria (especially *A. baumannii* and *K. pneumoniae*). In addition, this EO is a promising inhalable alternative for local therapy in the case of respiratory infections (Ekren *et al.* 2018; Li *et al.* 2016; Oliva *et al.* 2018).

In the checkerboard assay, Oliva *et al.* (2018) tested some antibiotics, including amikacin, oxacillin, cefazolin, vancomycin, and rifampicin for MSSA (ATCC 29213) and MRSA; for the other bacteria, the combination of EO with amikacin, meropenem, and colistin was evaluated. The results showed a synergistic effect in subinhibitory concentrations of the combinations of *M. alternifolia* EO and amikacin, oxacillin, and cefazolin against both Gram-positive bacteria and when tested with amikacin, meropenem, and colistin against all Gram-negative microorganisms.

The chemical characterization of the *M. leucadendra* EO was analyzed by GC-MS, revealing 45 compounds, which accounted for 99.73% of the total oil composition. Monoterpenoids dominated the EO (77.43%), with four primary compounds: α-pinene (9.06%), limonene (32.00%), 1,8-cineole (17.32%), and viridiflorol (14.89%) (Bautista-Silva *et al.* 2020).

Bautista-Silva *et al*. (2020) achieved a broad spectrum of antibacterial activity against Gram-positive and Gram-negative bacteria using *M. leucadendra* EO. Among the microorganisms tested, *K. pneumoniae* ATCC 13883 had one of the highest MIC (62.5 mg mL^{-1}), while the EO showed the lowest antibacterial activity (31.2 mg mL^{-1}) against *P. aeruginosa* ATCC 27853 and *S. aureus* ATCC25923. The authors evaluated the activity of the *M. leucadendra* EO against the tested strains (exponential stage) during the different periods, in which it was possible to observe a reduction in cell viability, decreasing bacterial growth for *K. pneumoniae* at concentrations below the MIC (62.5 mg mL^{-1}).

1.1.3 Genus *Syzygium*

Imane *et al.* (2020) also evaluated the EO of cloves, as it is popularly known, despite receiving the scientific name of *Syzygium aromaticum* L. Merr. & L. M. Perry (The Plant List 2013). In the chemical characterization of the *S. aromaticum* EO, the authors found 3-allyl guaiacol (42.6%), eugenol acetate (15.9%), and caryophyllene (15.5%) as the three main compounds. This EO showed antibacterial activity against MRSA NCTC 12493, *K. pneumoniae* ATCC 700603, and a *S. aureus* isolate with MIC and MBC of 0.21 mg mL^{-1} (Tab. S1, available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>) (Imane *et al.* 2020).

1.1.4 Genus *Pimenta*

The genus *Pimenta* has various medicinal purposes; *Pimenta dioica* (L.) Merr. and *Pimenta racemosa* (Mill.) J.W. Moore are the most recognized species within this genus as they have pharmacological effects due to their rich EO composition (Chaverri & Cicció 2015; Ismail *et al.* 2020). Ismail *et al.* (2020) tested EO extracted from *P. dioica* and *P. racemosa* leaves and berries and found β-myrcene as the main constituent in the chemical composition of *P. dioica* leaves (44.1%), 1.8-cineol (18.8%), and limonene (11.7%). The EO extracted from the berry had similar major compounds: β-myrcene (13.9%), limonene (4.6%), and β-linalool (3.6%), although β-myrcene and limonene were found in smaller quantities. These authors tested the four EO against the standard strain of *A. baumannii* ATCC 19606 and fourteen MDR clinical isolates of *A. baumannii* and observed that the *P. dioica* EO extracted from leaves and berry presented MIC ranging from 0.51 to 5.2 μg mL^{-1} against the fifteen microorganisms evaluated. Thus, the EO of this plant showed a more substantial antimicrobial potential in terms of lower MIC than the other EO tested.

The *P. racemosa* EO was also analyzed by Ismail *et al.* (2020); they identified three main compounds: β-myrcene, limonene, and β-cis-ocimene in the EO extracted from leaves and berries, although in different amounts (39.6, 15.5, and 2.8% for the former and 42.3, 14.3, and 4.6% for the latter). All EOs tested showed a bactericidal effect after 24 h incubation; both EO prepared with *P. racemosa* leaves and berries exhibited the same bactericidal activity at 2.08 and 2.76 μg mL^{-1}, respectively, although the *P. racemosa* EO had less pronounced action than the *P. dioica* EO (Ismail *et al.* 2020).

1.1.5 Genus *Rhodamnia*

Rhodamnia dumetorum (DC.) Merr. & L.M. Perry is a plant species originally from Cambodia. In the study by Houdkova *et al.* (2018), the chemical characterization of EO extracted from *R. dumetorum* leaves was evaluated by GC-MS equipped with two capillary columns of different polarities (HP-5MS and DB-17MS). In addition, a flame ionization detector coupled to a quadrupole selective mass detector, in which 72 constituents were identified, was equivalent to 91.37% (HP-5MS) and 90.48% (DB-17MS) of the total content. The major volatile compounds were caryophyllene epoxide (33.29/4.51%), α-pinene (26.09/73.53%), and humulene-1,2-epoxide (2.48/0.39%) (Tab. S1, available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>). Antibacterial activity was performed against bacteria related to respiratory tract infections (*Haemophilus influenzae* ATCC 49247, *S. aureus* ATCC 29213, and *Streptococcus pneumoniae* ATCC 49619). Concentration values of >1024 μg mL^{-1} were found against all tested microorganisms. The *R. dumetorum* EO showed moderate cytotoxicity (IC_{50} 1.98 ± 1.17 μg mL^{-1}) against pulmonary fibroblast cells (MRC-5) (Houdkova *et al.* 2018).

1.1.6 Genus *Eugenia*

Pereira *et al.* (2017a) evaluated *Eugenia jambolana* Lam. EO (EjEO) and found 26 compounds in its composition (98.93%), with α-pinene (48.09%) and nerolidol (8.73%) as the major constituents. The authors analyzed the antibacterial activity of EjEO against *S. aureus* ATCC 25923, *P. aeruginosa* ATCC25853, and isolates of *S. aureus* SA 358 and *P. aeruginosa* PA 03, observing that the EO had a better effect against the strain of *S. aureus* (128 μg mL^{-1}) according to the *in vivo* assays. In the technique of modulating antibiotic activity by direct contact, the combination of EjEO with amikacin or gentamicin increased the MIC against *S. aureus*, obtaining an antagonistic effect; in the gaseous contact method with the same EO and amikacin or erythromycin against *P. aeruginosa*, the halos decreased, thus having a synergistic activity (Pereira *et al.* 2017a). When assessing EO with ciprofloxacin and norfloxacin using the same technique, however, with exposure to red and blue light-emitting diodes (LED), the halo increased, indicating synergism. Phototherapy combined with EO may be an option to reduce the excessive use of antimicrobials, as the application of LED lights positively affected Gram-positive and Gram-negative microorganisms (Pereira *et al.* 2017a; Wagner 2011).

Eugenia uniflora L. is a native species of Brazil and popularly known as "pitangueira," "pitanga," and "pitanga-vermelha," occuring throughout Brazil (Fouqué 1981; Villachica 1996; Mazine *et al.* 2022). Pereira *et al.* (2017b) chemically characterized *E. uniflora* EO (EuEO) and found isofuran-germacrene (65.80%) as the main compound, followed by germacra-3,7,9-trien-6-one (16.19%) and β-element (4.47%). In the antibacterial assay using the broth microdilution technique for *S. aureus* ATCC 25923, the researchers obtained a MIC of 256 μg mL^{-1}; however, in the test of bacterial resistance modulation by direct contact against the same microorganism, when the EuEO was combined with commercial antimicrobials (amicanine and gentamicin), there was a reduction in the concentration of the antibiotic, resulting in synergism. This is the opposite of what occurred for *P. aeruginosa*, which presented antagonism when combining EuEO with amikacin and erythromycin (Pereira *et al.* 2017b). The antagonism resulting from the combination of EuEO with aminoglycosides against *P. aeruginosa* may occur due to a complex barrier system formed by the membrane (phospholipids, lipopolysaccharides, and proteins) that allows a high degree of impermeability to antimicrobials (Lambert *et al.* 2001).

Essential oils are a viable alternative to antibiotics in the fight against microorganisms (Tab. S1, available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>). The antimicrobial activity of these EO seems more potent than the sum of their separate components, demonstrating the synergy between the numerous constituents present in their chemical composition. Therefore, using EO extracted from plants is an important research theme given the need to find substances that are not resistant to antibiotics, as they have specific antimicrobial agents and, therefore, could be used to treat numerous infections, thereby contributing to reducing existing bacterial resistance.

1.2 Extracts

Traditional medicine has been accepted as an alternative form of health care. The ever-increasing microbiological resistance to available antibiotics has led researchers to investigate the antimicrobial activity of medicinal plants. Numerous extracts from different plants of the Myrtaceae family have been tested due to their antimicrobial activities, as their antimicrobial agents are increasingly potent against MDR bacteria. Therefore, medicinal plants and extracts from such plants are often recognized as a source of new drugs and complementary medicines for synthetic drugs and their versatile applications against microorganisms that cause respiratory tract infections.

Natural extracts are chemical compounds with biological activities from parts of medicinal plants (*e.g.*, leaves, stems, fruits, and roots). These extracts have important biological properties, such as antioxidant, antifungal, antibacterial, and antiparasitic activity (Chakraborty *et al.* 2014; Njimoh *et al.* 2015). Multiple studies have analyzed chemical compounds and the antibacterial activity of extracts from different Myrtaceae family plants (Tab. S2, available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>).

1.2.1 Genus *Syzygium*

Syzygium cumini (L.) Skeels, also commonly known as "jambolão," plum java, and black plum, is native to tropical Asia, mainly India (Singh *et al.* 2016). Singh *et al.* (2016) evaluated the ethanolic extract of *S. cumini* and via high-performance liquid chromatography (HPLC) and found various

phenolic compounds, namely: caffeic acid (65.6 mg mL^{-1}), gallic acid (41.4 mg mL^{-1}), synaptic acid (21.3 mg mL^{-1}), delphinidin (20.2 mg mL^{-1}), and quercetin acid (14.9 mg mL^{-1}). Analysis of the antibacterial activity of the extract against pathogenic strains revealed MICs between 0.5 and 2 mg mL^{-1} against *S. aureus* (MTCC-740), *K. pneumoniae* (MTCC-109), and an MRSA isolate (Tab. S2, available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>). The *S. cumini* extract showed greater inhibitory potential, with MIC equal to 0.5 mg mL^{-1} compared to the reference strain of *S. aureus*, while for the other bacteria, it reached a MIC of 2 mg mL^{-1}.

Panda *et al*. (2020) investigated the antibacterial activity of a *Syzygium praecox* (Roxb.) Rathakr. & N.C. Nair extract prepared with the leaves of the plant and acetone as a solvent and found terpenoids and alkaloids as the major phytochemicals. Nonetheless, this extract could not inhibit *Staphylococcus* MDR isolates and *S. aureus* strain ATCC 6538.

1.2.2 Genus *Eucalyptus*

Moradi *et al*. (2020) investigated the antibacterial effect of an extract of *S. aromaticum* and *Eucalyptus camadulensis* Dehnh. against *P. aeruginosa* (isolated from a patient with cystic fibrosis) and obtained bactericidal activity with MIC/MBC of 0.78/6.25 and 0.39/3.1 mg mL^{-1}, respectively.

1.2.3 Genus *Myrtus*

Myrtus communis L. is native to the Mediterranean region and other countries in the Middle East, such as Jordan, Iraq, and Saudi Arabia (Mir *et al*. 2020). Mir *et al*. (2020) identified, in the ethanolic extract of *M. communis* leaves, 50 constituents via GC-MS, the dominant compounds being 1.1.8a-trimethylocta-hydro-2.6-naphthalenedione (27.6%), pyrogallol (9.1%), and 1.8-cineole (3.9%). The antibacterial effect of the extract was evaluated against *P. aeruginosa* ATCC 9027 and isolates of *S. aureus* and *K. pneumoniae*, in which the standard strain tested and *K. pneumoniae* were resistant to the extract; only the isolate of *S. aureus* was inhibited (MIC of 9.7 µg mL^{-1}). In addition, the authors analyzed the MICs for several antimicrobials (colistin, vancomycin, tetracycline, and levofloxacin) alone and combined with the ethanolic extract of *M. communis* leaves, finding a MIC of 0.61 µg mL^{-1} from the plant extract against *S. aureus*.

1.2.4 Genus *Eugenia*

Eugenia brasiliensis Lam. is popularly known as "grumixama," "grumixameira," and "Brazilian cherry"; this species has several varieties, although the most common is the yellow fruit (Silva *et al.* 2014; Teixeira *et al.* 2015). In one study, the ethanol extract of *E. brasiliensis* had a content of total phenolic compounds of 389.88 ± 3.48 mg of GAE/g, and in the LC-MS/MS, catechins, ellagitannins, flavonoids, and anthocyanins were identified (Lazarini *et al.* 2018). The *E. brasiliensis* extract showed a better antibacterial effect against *S. aureus* ATCC 25923 (MIC of 62.5 µg mL^{-1}) than MRSA ATCC 33591, and *P. aeruginosa* ATCC 27853 obtained a MIC of 250 µg mL^{-1}; the extract proved to be bactericidal for all microorganisms tested, with an MBC of 500 µg mL^{-1}. This extract did not present toxic effects on *Galleria mellonella* larvae at doses of 0.025 g/kg; therefore, the ethanol extract of *E. brasiliensis* should be further investigated for its safety in therapeutic uses, as natives have described it being effective in treating many diseases, including inflammatory and infectious diseases (Lazarini *et al.* 2018; Pietrovski *et al.* 2010; Silva *et al.* 2014).

Ramhit *et al.* (2018) researched extracts of plants endemic to Mauritania (Africa). The extracts of *Eugenia elliptica* Lam., *Eugenia orbiculate* Lam., and *Eugenia tinifolia* Lam. demonstrated significant differences in phenolic compounds, flavonoids, and proanthocyanidins. In the chemical characterization by HPLC, two flavonoids were found in *E. tinifolia* (kaempferol and quercetin) and only one in *E. orbiculata* (quercetin), as well as the polyphenol epigallocatechin. The authors noted that all the extracts had activity against the tested microorganisms in the antibacterial assays. The three extracts of the genus *Eugenia* presented a MIC of 19.5 µg of fresh weight (FW) mL^{-1} against *P. aeruginosa* ATCC 27853. When tested against *Klebsiella oxytoca* ATCC 43086, this bacterium was more sensitive to *E. orbiculata* extracts (MIC = 4.9 µg FW mL^{-1}) and *E. tinifolia* (MIC = 9.7 µg FW mL^{-1}). The extracts showed MIC lower than at least one tested antibiotic (amoxicillin, chloramphenicol, and tetracycline) against the microorganisms. The difference in the effect of extracts and conventional antimicrobials may be in the penetrating power and levels of active compounds that interfere with the bacteria, which can lead to death (Ramhit *et al.* 2018).

1.2.5 Genus *Campomanesia*

Campomanesia adamantium (Cambess.) O. Berg is a plant in Brazil, native to the Cerrado biome, and popularly known as "guabiroba-do-campo" (Lima *et al.* 2011). Sá *et al.* (2018) evaluated the antimicrobial activity of several *C. adamantium* extracts, including crude ethanolic extract, hexane (HF), dichloromethane, ethyl acetate, and aqueous extracts. The HF extract was fractionated, resulting in fractions HF1, HF2/2, HF2/6, and HF9/3/1/2/1, which were analyzed by GC-MS. Caryophyllene oxides (HF1), isoaromadendrene (HF2/2), octadecanoic acid (HF2/6), and cubenol (HF9/3/1/2/1) were the chemical compounds found. All extracts tested showed antibacterial activity. Of all the extracts evaluated, HF had the best activity against *S. aureus* ATCC 6538 (MIC = 31.25 μg mL^{-1}). Afterward, the MIC for *S. aureus* ATCC 25923 was 62.5 μg mL^{-1}; for the clinical isolate of *P. aeruginosa* SPM1, MIC = 500 μg mL^{-1}. The other extracts obtained higher MIC, including when tested against *K. pneumoniae* ATCC 700603 (MIC >1000 μg mL^{-1}), in which the extract was less active.

1.2.6 Genus *Callistemon*

Callistemon citrinus (Curtis) Skeels is popularly known as bottlebrush and is widely distributed in Australia, South America, and tropical Asia, although it can also be found in other regions around the world (Oyedeji *et al.* 2009). Shehabeldine *et al.* (2020) evaluated the crude extract of *C. citrinus* against MRSA ATCC 33591 and MSSA ATCC 25923 and found a MIC of 125 and 62.5 μg mL^{-1}, respectively, while both presented MBC of 250 μg mL^{-1}. However, the MIC revealed bacteriostatic activity for the crude extract against MSSA and bactericidal activity against MRSA (Shehabeldine *et al.* 2020).

1.2.7 Genus *Psidium*

The species *Psidium guayaquilense* Landrum & Cornejo and *Psidium rostratum* Mc Vaugh (also known as "guayabas") come from Ecuador. These species were evaluated by María *et al.* (2018), who conducted quantification tests of the total phenolic compounds; they found 941.97 ± 30.69 mg of GAE/g of dry extracts for the *P. guayaquilense* ethanolic extract and 591.34 ± 24.31 mg of GAE/g of dry extracts for the *P. rostratum* extract. Regarding antibacterial activity, both extracts were effective against *S. aureus* ATCC 25923, with a MIC of 50 μg mL^{-1}.

Within the genus *Psidium* is the species *P. guajava* L. (guava). Valle *et al.* (2015) evaluated ethanolic extracts of this species in the Philippines and observed antibacterial effects against *S. aureus* ATCC 25923, *P. aeruginosa* ATCC 27853, *K. pneumoniae* ATCC BAA-1705, *K. pneumoniae* carbapenem-resistant, *K. pneumoniae* producer of extended-spectrum β-lactamase (ESβL), *A. baumannii* metallo-β-lactamase (MβL), *P. aeruginosa* MβL, MRSA 1 (wound isolate), MRSA 2 (wound isolate), MRSA 3 (blood isolate), and MRSA 4 (sputum isolate). In the disc diffusion method, only MRSA isolates were sensitive to the extract, and the inhibition halos ranged from 13 to 18 mm (Valle *et al.* 2015). In contrast, Chakraborty *et al.* (2018) analyzed the effect of a *P. guajava* ethanolic extract against ten clinical MRSA isolates and ten non-clinical MRSA isolates and found that the inhibition zone in a non-clinical MRSA culture was 29.69 ± 0.78 mm compared to 24.73 ± 0.55 mm for clinical MRSA isolates. The results of Valle *et al.* (2015) for the antibacterial activity using the guava ethanolic extract only showed action against *S. aureus* ATCC 25923 and against all MRSA. The extract did not present any activity against the other microorganisms. The lowest MIC (625 μg mL^{-1}) were found against MRSA 1 and 4. The extract tested against MRSA 4 was bactericidal at the same concentration of MIC; however, for MRSA 1, it needed a higher concentration (2500 μg mL^{-1}) to inhibit bacterial growth (Valle *et al.* 2015).

Fu *et al.* (2016) tested the phenolic compounds in the methanolic extract of *P. guava* and found six constituents: catechin (391.93 ± 15.08 mg kg^{-1}), quercetin (122.23 ± 10.14 mg kg^{-1}), gallic acid (99.15 ± 1.62 mg kg^{-1}), epicatechin (58.43 ± 4.70 mg kg^{-1}), luteolin (51.39 ± 3 mg kg^{-1}), and kaempferol (38.06 ± 2.00 mg kg^{-1}). When testing the methanolic extract of guava against microorganisms, the best results were obtained against *P. aeruginosa* ATCC 27853, as it reached lower MIC and MBC (312.5/312.5 mg mL^{-1}) compared to *S. aureus* CMCC(B)26003 (1250/2500 mg mL^{-1}). The authors evaluated the compounds found in the extract separately and observed that the polyphenol catechin, the major constituent in the extract, presented MIC and MBC of 1.25 mg mL^{-1} against *S. aureus* and 2.50 mg mL^{-1} against *P. aeruginosa*. When tested separately, the compound with the best antibacterial activity was gallic acid against *S. aureus*, with activity at 0.63 mg mL^{-1} (MIC/MBC), a constituent also found in the *P. guava* extract (Fu *et al.* 2016).

Psidium cattleianum Sabine is popularly known as "araçá," "araçá-do-mato," "araçá-do-campo," "yellow araçá," "red araçá," "araçazeiro," and "araçazeiro-da-praia" (Coradin *et al.* 2011; Raseira *et al.* 2004). This plant originated in Brazil and can be found in Bahia, Rio Grande do Sul, and Santa Catarina States (Biegelmeyer *et al.* 2011). Many studies have demonstrated the use of *P. cattleianum* in various areas (Dacoreggio *et al.* 2019; Medina *et al.* 2011; Scur *et al.* 2016). However, few studies have evaluated *P. cattleianum*, especially against bacteria associated with respiratory infections (*i.e.*, MDR).

Dacoreggio *et al.* (2019) obtained aqueous extracts of *P. cattleianum* leaves harvested in winter and summer. The researchers employed water + ultrasound (WU) extraction and water + enzyme – cellulase complex (WE) extraction. Regarding the number of total phenolics, there was no statistically significant difference ($p < 0.05$), considering how the extracts were obtained; nonetheless, the phenolic content presented differences in terms of the season in which the leaves were collected. The results in determining the total phenolic content were expressed as gallic acid equivalents (GAE) per g of dry vegetal material. Values of 101 mg of GAE g^{-1} (WU) were observed in the extract that the leaves were harvested in the summer and a higher content of phenolic compounds in those harvested in the winter (WU - 144 mg of GAE g^{-1}). The same was observed in the WE extract; in the summer, the authors found 121 mg of GAE g^{-1}, while in the winter, 123 mg of GAE g^{-1} of phenolic compounds. The outliers of the number of phenolic compounds in each extract can vary depending on several environmental factors, such as the temperature difference in the seasons (Dacoreggio *et al.* 2019).

When testing the antibacterial activity of the aqueous extract of *P. cattleianum*, the authors obtained MIC ranging from 12.6 to 18 μg mL^{-1} against *S. aureus*. The two extracts showed lower MIC than the extracts made with leaves collected in the summer season (WU = 12.6 μg mL^{-1} and WE = 15.1 μg mL^{-1}) (Dacoreggio *et al.* 2019).

1.3 Formulations containing Myrtaceae and nanoparticles

Nanotechnology has been applied in various areas. As a delivery system, it has been investigated to contribute to the control and release of drugs, improve the effectiveness and selectivity of drugs, and assist in treating infectious diseases (Flores *et al.* 2011; Gupta & Gupta 2005). Table 3 (available on supplementary material <https://doi.org/10.6084/m9.figshare.22318294.v1>) shows nanoparticles synthesized with extracts from different plant species of the Myrtaceae family.

Asghar *et al.* (2020) investigated the antibacterial activity of synthesizing chitosan functionalized silver nanoparticles using ethanolic bud extract of *S. aromaticum* against resistant microorganisms, such as vancomycin-resistant *S. aureus* (VRSA) LT 4312 and MRSA LT 0531, and found a MIC of 64 μg mL^{-1}. Nickel oxide nanoparticles (NiO-NPs) have also been suggested as antibacterial agents; Saleem *et al.* (2017) synthesized NiO-NPs with *Eucalyptus globulus* leaf extracts (ELE), presenting an average NiO-NP size of 19 nm. The antimicrobial activity of the NiO-NPs synthesized was tested with 1 mM NiNO3 and ELE with distilled water (1:8 v/v) using diffusion technique against the clinical isolate of *P. aeruginosa* ESβL (48 and 64), MSSA (MS-2 and MS-6), and MRSA (MR-10 and MR-31), in which they found zones of inhibition that varied between 13–15 mm. In contrast, the MIC presented against all microorganisms was 0.8 mg mL^{-1} and MBC was 1.6 mg mL^{-1}. In addition, the combination of the nanoparticle and ELE inhibited biofilm formation depending on the tested dose. The antibiofilm concentrations tested were 0, 0.1, 0.2, 0.4, 0.8, and 1.6 mg mL^{-1} of NiO-NPs. The best results were obtained for the MRSA isolate (32, 62, 72, 73, 76, and 83% inhibition, respectively). The results of Saleem *et al.* (2017) are positive, allowing NiO-NPs associated with *E. globulus* extract to be applied against bacterial infections, protecting human health from pathogenic microorganisms.

Although some studies have already investigated the green synthesis of silver nanoparticles, there is currently no alternative treatment for infection by MDR microorganisms. Wintachai *et al.* (2019) investigated the potential of silver nanoparticles synthesized with ethanolic extract of *E. critriodora* leaves as an inhibitor of MDR *A. baumannii* infection. The spherical size of the nanoparticle ranged from 8 to 15 nm. Antibacterial assays (MIC) were performed against clinical isolates of MDR *A. baumannii* (n = 10), in which the MIC and MBC varied from 0.05 to 0.18 μg mL^{-1} and 0.36 to 0.72 μg mL^{-1}, respectively. A reference strain of *A. baumannii* ATCC 19606 was used, which obtained MIC and MBC of 0.09 and 0.36 μg mL^{-1}. The antibiofilm

activity of the silver nanoparticle associated with *E. critriodora* extract was analyzed against five clinical isolates of *A. baumannii* MDR plus the standard strain in parallel with colistin. When testing 1/8 to 1/2 of the MIC (0.012–0.045 μg mL^{-1}) of silver nanoparticles, the best result for the reduction in biofilm formation was the one presented in 1/8 MIC (0.012 μg mL^{-1}). The silver nanoparticle synthesized with the *E. critriodora* extract did not show significant cytotoxicity at the maximum concentration of 0.72 μg mL^{-1} when tested against the human lung epithelial cell line (A549). The authors also analyzed that the clinical isolates of *A. baumannii* MDR in A549 cells were sensitive when treated with concentrations varying from 1/8 to 1/2 MIC (0.012–0.045 μg mL^{-1}). After checking the results, nanoparticles synthesized with the ethanolic extract of *E. critriodora* may be a potential alternative therapy to reduce respiratory infections, such as those caused by MDR *A. baumannii* (Wintachai *et al.* 2019).

Hashemi *et al.* (2020) prepared iron (ZVINPs) and silver (AgNPs) nanoparticles, in which the biosynthesis of both was using an aqueous extract of *Feijoa sellowiana* fruit. Through HPLC, five phenolic acids were detected in the extract: catechin 1 (188.5 mg g^{-1} of extract), gallic acid 2 (18.5 mg g^{-1} of extract), caffeic acid 3 (3.2 mg g^{-1} of extract), rutin 4 (15.8 mg g^{-1} of extract), and *p*-coumaric acid 5 (4.7 mg g^{-1} of extract). The authors investigated the antibacterial activity of the nanoparticles against pathogenic bacteria (*S. aureus* ATCC 29213, *A. baumannii* ATCC 29606, *K. pneumonia* ATCC 700603, and *P. aeruginosa* ATCC 27853) and clinical isolates from the same species. The tested concentrations of each nanoparticle ranged from 125 to 0.25 μg mL^{-1} of AgNPs and from 30 to 0.15 μg mL^{-1} of ZVINPs. The ZVINPs showed the best antibacterial potential against three standard strains tested (*A. baumannii* ATCC 29606, *K. pneumonia* ATCC 700603, and *P. aeruginosa* ATCC 27853); for *S. aureus* ATCC 29213, the AgNPs had a more significant effect, resulting in a MIC of 2 μg mL^{-1}. Both nanoparticles proved bactericidal against the strains evaluated (Hashemi *et al.* 2020).

Hashemi *et al*. (2020) also tested the antibacterial activity of nanoparticles against clinical isolates of *S. aureus*, *A. baumannii*, *K. pneumoniae*, and *P. aeruginosa*, in which AgNPs showed better activity against *A. baumannii* (3.5 μg mL^{-1}) and *S. aureus* (4 μg mL^{-1}). In contrast, ZVINPs against *P. aeruginosa* and *K. pneumoniae* presented a MIC of 15 μg mL^{-1} for both bacteria. The two nanoparticles were bactericidal, although the lowest concentrations of MBC found were for the ZVINPs. The mechanism of action of silver nanoparticles synthesized with the *F. sellowiana* extract is due to the presence of phenolic compounds in the extract reacting with the silver nanoparticles and forming a complex, fighting microorganisms (Ebrahimzadeh *et al.* 2019; Hashemi *et al.* 2020).

Ali *et al*. (2015) performed the green synthesis of AgNPs with an aqueous ELE by developing a solution with both products (1:4 v/v) and irradiating them with microwaves. The ELEAgNPs were approximately 1.9–4.3 nm in size with microwave treatment and 5–25 nm without treatment. The ELEAgNPs were evaluated for antibacterial activity against *P. aeruginosa* ESβL, MRSA (MR-6), and MSSA (MS-6). In the diffusion test, when ELEAgNPs were tested, the inhibition zones ranged from 19 to 21 mm compared to the values tested only with ELE (8–10 mm). The MIC and MBC with ELEAgNPs against MRSA were 27 and 30 μg mL^{-1} and against MSSA were 30 and 33 μg mL^{-1}, while for *P. aeruginosa* ESβL, were 27 and 36 μg mL^{-1}. The authors performed antibiofilm activity with a concentration of 30 μg mL^{-1}, showing 82 ± 3% and 81 ± 5% biofilm inhibition against *S. aureus* and *P. aeruginosa*, respectively. This inhibition can occur due to the polyphenol compounds in the chemical characterization of the *E. globulus* leaf extract, which can capture the iron in the medium, killing the microorganisms (Ali *et al.* 2015).

The formulation of iron nanoparticles (FeNP) synthesized with an aqueous extract of *E. robusta* leaves with various concentrations of iron salt in the proportion of 1:1 was evaluated by Vitta *et al.* (2020). As for the quantification of phenolic and flavonoid compounds, *E. robusta* extract showed 158.47 ± 0.64 mg gallic acid (GAE)/g extract and 131.12 ± 4.49 (mg quercetin (QE)/g extract, respectively, while FeNP showed 98.21 ± 10.34 mg GAE/g and 40.54 ± 6.87 mg QE/g, respectively. The antibacterial activity through the agar diffusion method evaluated the FeNP obtained under various forms of synthesis in the following concentrations (FeNP I = 0.01 g mL^{-1} extract + 1 mM [Fe]; FeNP II = 0.01 g mL^{-1} extract + 5 mMe [Fe]; FeNP III = 0.005 g mL^{-1} + 0.005 mM [Fe]) against *P. aeruginosa* and *S. aureus*, and as the size of the nanoparticle decreased, increased the size of the inhibition halos. It is believed that the chemical composition of E. robusta extract contributed to

the antibacterial potential, in addition to the fact that the size of the nanoparticle interfered with the mechanism of action because the smaller the particle, the greater the power of penetration into the bacteria. Thus, nanoparticles are promising alternatives for application as antibacterial agents in clinical practice(Vitta *et al.* 2020).

Given the growing problem of bacterial resistance with each passing year, it is becoming increasingly difficult to contain the microorganisms that cause respiratory tract infections that eventually become MDR. One of the leading causes is the indiscriminate and excessive use of conventional drugs the market offers, thereby emphasizing the need and urgency to develop new antimicrobials that serve as a strategy for conventional antibiotics, enabling researchers and industry professionals to control and eliminate these microorganisms (especially MDR bacteria), or even antibacterial agents that enhance the action of existing drugs.

This review provided studies performed in recent years with plants of the Myrtaceae family, presenting their chemical composition and *in vitro* antibacterial activity against microorganisms that cause respiratory infection, including *A. baumannii*, *S aureus*, *P. aeruginosa*, *H. influenzae*, *K. pneumoniae*, and *K. oxytoca*. As for the chemical characterization, the essential oils found in most studies present terpenoid constituents, while research with Myrtaceae extracts showed phenolic compounds, especially phenolic acids, and flavonoids. Plants of this family have various constituents with antimicrobial activity and can be used to treat bacteria that cause respiratory infections. In addition, few clinical studies were conducted with plants of the Myrtaceae family and tested against pathogens involved in MDR respiratory infections. Hence, it is crucial to encourage the scientific community to continue seeking new and effective therapeutic agents so that they are applied clinically against the microorganisms that cause respiratory tract infections, as numerous studies have demonstrated the promising results of employing species of the Myrtaceae family.

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Ali K, Ahmed B, Dwivedi S, Saquib Q, Al-Khedhairy AA & Musarrat J (2015) Microwave accelerated green synthesis of stable silver nanoparticles with *Eucalyptus globulus* leaf extract and their antibacterial and antibiofilm activity on clinical isolates. Plos One 10: 1-20. <https://doi.org/10.1371/journal.pone.0131178>.

Asghar MA, Yousuf RI, Shoaib MH & Asghar MA (2020) Antibacterial, anticoagulant and cytotoxic evaluation of biocompatible nanocomposite of chitosan loaded green synthesized bioinspired silver nanoparticles. International Journal of Biological Macromolecules 160: 934-943. <https://doi.org/10.1016/j.ijbiomac.2020.05.197>.

Bautista-Silva JP, Seibert JB, Amparo TR, Rodrigues IV, Teixeira LFM, Souza GHB & Santos ODH (2020) *Melaleuca leucadendra* essential oil promotes loss of cell membrane and wall integrity and inhibits bacterial growth: an *in silico* and *in vitro* approach. Current Microbiology 77: 2181-2191. <https://doi.org/10.1007/s00284-020-02024-0>.

Biegelmeyer R, Andrade JMM, Aboy AL, Apel MA, Dresch RR, Marin R, Raseira MCB & Henriques AT (2011) Comparative analysis of the chemical composition and antioxidant activity of red (*Psidium cattleianum*) and yellow (*Psidium cattleianum* var. *lucidum*) strawberry guava fruit. Journal of Food Science 76: C991-C996. <https://doi.org/10.1111/j.1750-3841.2011.02319.x>

Boucher HW, Ambrose PG, Chambers HF, Ebright RH, Jezek A, Murray BE, Newland JG, Ostrowsky B & Rex JH (2017) White paper: developing antimicrobial drugs for resistant pathogens, narrow-spectrum indications, and unmet needs. Journal of Infectious Diseases 216: 228-236. <https://doi.org/10.1093/infdis/jix211>.

Carson CF, Cookson BD, Farrelly HD & Riley TV (1995) Susceptibility of methicillin-resistant *Staphylococcus aureus* to the essential oil of *Melaleuca alternifolia*. Journal of Antimicrobial Chemotherapy 35: 421-424. <https://doi.org/10.1093/jac/35.3.421>.

Chakraborty B, Nath A, Saikia H & Sengupta M (2014) Bactericidal activity of selected medicinal plants against multidrug resistant bacterial strains from clinical isolates. Asian Pacific Journal of Tropical

Medicine 7: S435-S441. <https://doi.org/10.1016/S1995-7645(14)60271-6>.

Chakraborty S, Afaq N, Singh N & Majumdar S (2018) Antimicrobial activity of *Cannabis sativa*, *Thuja orientalis* and *Psidium guajava* leaf extracts against methicillin-resistant *Staphylococcus aureus*. Journal of Integrative Medicine 16: 350-357. <https://doi.org/10.1016/j.joim.2018.07.005>.

Chaverri C & Cicció JF (2015) Leaf and fruit essential oil compositions of *Pimenta guatemalensis* (Myrtaceae) from Costa Rica. Revista de Biología Tropical 63: 303-311. <https://doi.org/10.15517/rbt.v63i1.14580>.

Coradin L, Siminski A, Reis A & Reis A (2011) Espécies nativas da flora brasileira de valor econômico atual ou potencial - plantas para o futuro - Região Sul. Centro de Informação e Documentação Luís Eduardo Magalhães - CID Ambiental. MMA, Brasília. 934p.

Cox SD, Mann CM, Markham JL, Bell HC, Gustafson JE, Warmington JR & Wyllie SG (2000) The mode of antimicrobial action of the essential oil of *Melaleuca alternifolia* (tea tree oil). Journal of Applied Microbiology 88: 170-175. <https://doi.org/10.1046/j.1365-2672.2000.00943.x>.

Dacoreggio MV, Moroni LS & Kempka AP (2019) Antioxidant, antimicrobial and allelopathic activities and surface disinfection of the extract of *Psidium cattleianum* Sabine leaves. Biocatalysis and Agricultural Biotechnology 21: 101295. <https://doi.org/10.1016/j.bcab.2019.101295>.

Duarte O & Paull R (2015) Exotic fruits and nuts of the New World. CABI, Wallingford. 332p. <https://doi.org/10.1079/9781780645056.0000>.

Ebrahimzadeh MA, Biparva P, Mohammadi H, Tavakoli S, Rafiei A, Kardan M, Badali H & Eslami S (2019) Highly concentrated multifunctional silver nanoparticle fabrication through green reduction of silver ions in terms of mechanics and therapeutic potentials. Anti-Cancer Agents in Medicinal Chemistry 19: 2140-2153. <https://doi.org/10.2174/1871520619666191021115609>.

Ekren PK, Ranzani OT, Ceccato A, Li Bassi G, Conejero EM, Ferrer M, Niederman MS & Torres A (2018) Evaluation of the 2016 Infectious Diseases Society of America/American Thoracic Society guideline criteria for risk of multidrug-resistant pathogens in patients with hospital-acquired and ventilator-associated pneumonia in the ICU. *In*: American Journal of Respiratory and Critical Care Medicine 197: 826-830. <https://doi.org/10.1164/rccm.201708-1717LE>.

Flores FC, Ribeiro RF, Ourique AF, Rolim CMB, Bona SC, Pohlmann AR, Beck RCR & Guterres SS (2011) Nanostructured systems containing an essential oil: protection against volatilization. Quimica Nova 34: 968-972. <https://doi.org/10.1590/S0100-40422011000600010>.

Fouqué A (1981) Les plantes médicinales présentes en forêt guyanaise. Vol. 36. Fruits, Paris. Pp. 223-240.

Fu L, Lu WQ & Zhou XM (2016) Phenolic compounds and *in vitro* antibacterial and antioxidant activities of three tropic fruits: Persimmon, Guava, and Sweetsop. BioMed Research International 2016: 4287461. <https://doi.org/10.1155/2016/4287461>.

Gupta AK & Gupta M (2005) Cytotoxicity suppression and cellular uptake enhancement of surface modified magnetic nanoparticles. Biomaterials 26: 1565-1573. <https://doi.org/10.1016/j.biomaterials.2004.05.022>.

Hashemi Z, Ebrahimzadeh MA, Biparva P, Mortazavi-Derazkola S, Goli HR, Sadeghian F, Kardan M & Rafiei A (2020) Biogenic silver and zero-valent iron nanoparticles by *Feijoa*: biosynthesis, characterization, cytotoxic, antibacterial and antioxidant activities. Anti-Cancer Agents in Medicinal Chemistry 20: 1673-1687. <https://doi.org/10.2174/1871520620666200619165910>.

Heywood VH, Brummit RK, Culham A & Seberg O (2007) Flowering plant families of the world. Firefly Books, Canadá. Pp. 225-226.

Houdkova M, Urbanova K, Doskocil I, Rondevaldova J, Novy P, Nguon S, Chrun R & Kokoska L (2018) *In vitro* growth-inhibitory effect of Cambodian essential oils against pneumonia causing bacteria in liquid and vapour phase and their toxicity to lung fibroblasts. South African Journal of Botany 118: 85-97. <https://doi.org/10.1016/j.sajb.2018.06.005>.

Imane NI, Fouzia H, Azzahra LF, Ahmed E, Ismail G, Idrissa D, Mohamed KH, Sirine F, L'Houcine O & Noureddine B (2020) Chemical composition, antibacterial and antioxidant activities of some essential oils against multidrug resistant bacteria. European Journal of Integrative Medicine 35: 101074. <https://doi.org/10.1016/j.eujim.2020.101074>.

Ismail MM, Samir R, Saber FR, Ahmed SR & Farag MA (2020) *Pimenta* oil as a potential treatment for acinetobacter baumannii wound infection: *in vitro* and *in vivo* bioassays in relation to its chemical composition. Antibiotics 9: 1-16. <https://doi.org/10.3390/antibiotics9100679>.

Jazani NH, Mikaili P, Shayegh J, Haghighi N, Aghamohammadi N & Zartoshti M (2012) The hydro-alcoholic extract of leaves of *Eucalyptus camaldulensis* Dehnh. has antibacterial activity on multi-drug resistant bacteria isolates. Journal of Applied Biological Sciences 6: 37-40.

Knezevic P, Aleksic V, Simin N, Svircev E, Petrovic A & Mimica-Dukic N (2016) Antimicrobial activity of *Eucalyptus camaldulensis* essential oils and their interactions with conventional antimicrobial agents against multi-drug resistant *Acinetobacter baumannii*. Journal of Ethnopharmacology 178: 125-136. <https://doi.org/10.1016/j.jep.2015.12.008>.

Lambert RJW, Joynson J & Forbes B (2001) The relationships and susceptibilities of some industrial,

laboratory and clinical isolates of *Pseudomonas aeruginosa* to some antibiotics and biocides. Journal of Applied Microbiology 91: 972-984. <https://doi.org/10.1046/j.1365-2672.2001.01460.x>.

Lazarini JG, Sardi JCO, Franchin M, Nani BD, Freires IA, Infante J, Paschoal JAR, Alencar SM & Rosalen PL (2018) Bioprospection of *Eugenia brasiliensis*, a Brazilian native fruit, as a source of anti-inflammatory and antibiofilm compounds. Biomedicine and Pharmacotherapy 102: 132-139. <https://doi.org/10.1016/j.biopha.2018.03.034>.

Li M, Zhu L, Liu B, Du L, Jia X, Han L & Jin Y (2016) Tea tree oil nanoemulsions for inhalation therapies of bacterial and fungal pneumonia. Colloids and Surfaces B: Biointerfaces 141: 408-416. <https://doi.org/10.1016/j.colsurfb.2016.02.017>.

Lima DF, Goldenberg R & Sobral M (2011) O gênero *Campomanesia* (Myrtaceae) no estado do Paraná, Brasil. Rodriguésia 62: 683-693.

Luís Â, Duarte A, Gominho J, Domingues F & Duarte AP (2016) Chemical composition, antioxidant, antibacterial and anti-quorum sensing activities of *Eucalyptus globulus* and *Eucalyptus radiata* essential oils. Industrial Crops and Products 79: 274-282. <https://doi.org/10.1016/j.indcrop.2015.10.055>.

María R, Shirley M, Xavier C, Jaime S, David V, Rosa S & Jodie D (2018) Preliminary phytochemical screening, total phenolic content and antibacterial activity of thirteen native species from Guayas province Ecuador. Journal of King Saud University - Science 30: 500-505. <https://doi.org/10.1016/j.jksus.2017.03.009>.

Mazine FF, Bünger M, Faria JEQ, Fernandes T, Giaretta A, Valdemarin KS, Santana KC, Souza MAD & Sobral M (2022) *Eugenia in* Flora e Funga do Brasil. Jardim Botânico do Rio de Janeiro. Available at <https://floradobrasil.jbrj.gov.br/FB10338>. Access on 30 June 2022.

Medina AL, Haas LIR, Chaves FC, Salvador M, Zambiazi RC, Silva WP, Nora L & Rombaldi CV (2011) Araçá (*Psidium cattleianum* Sabine) fruit extracts with antioxidant and antimicrobial activities and antiproliferative effect on human cancer cells. Food Chemistry 128: 916-922. <https://doi.org/10.1016/j.foodchem.2011.03.119>.

Mir MA, Bashir N, Alfaify A & Oteef MDY (2020) GC-MS analysis of *Myrtus communis* extract and its antibacterial activity against gram-positive bacteria. BMC Complementary Medicine and Therapies 20: 1-9. <https://doi.org/10.1186/s12906-020-2863-3>.

Moradi F, Hadi N & Bazargani A (2020) Evaluation of quorum-sensing inhibitory effects of extracts of three traditional medicine plants with known antibacterial properties. New Microbes and New Infections 38: 100769. <https://doi.org/10.1016/j.nmni.2020.100769>.

Newman DJ &Cragg GM (2020) Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. Journal of Natural Products 83: 770-803. <https://doi.org/10.1021/acs.jnatprod.9b01285>.

Njimoh DL, Assob JCN, Mokake SE, Nyhalah DJ, Yinda CK & Sandjon B (2015) Antimicrobial activities of a plethora of medicinal plant extracts and hydrolates against human pathogens and their potential to reverse antibiotic resistance. International Journal of Microbiology 2015: 547156. <https://doi.org/10.1155/2015/547156>.

Oliva A, Costantini S, Angelis M, Garzoli S, Božović M, Mascellino MT, Vullo V & Ragno R (2018) High potency of *Melaleuca alternifolia* essential oil against multi-drug resistant gram-negative bacteria and methicillin-resistant *Staphylococcus aureus*. Molecules 23: 1-14. <https://doi.org/10.3390/molecules23102584>.

Oyedeji OO, Lawal OA, Shode FO & Oyedeji AO (2009) Chemical composition and antibacterial activity of the essential oils of *Callistemon citrinus* and *Callistemon viminalis* from South Africa. Molecules 14: 1990-1998. <https://doi.org/10.3390/molecules14061990>.

Panda SK, Das R, Lavigne R & Luyten W (2020) Indian medicinal plant extracts to control multidrug-resistant *S. aureus*, including in biofilms. South African Journal of Botany 128: 283-291. <https://doi.org/10.1016/j.sajb.2019.11.019>.

Pereira NLF, Aquino PEA, Júnior JGAS, Janyketchuly SC, Filho MAV, Moura FF, Ferreira NMN, Silva MKN, Nascimento EM, Correia FMA, Cunha FAB, Boligon AA, Coutinho HDM, Ribeiro-Filho JMIF (2017a) Antibacterial activity and antibiotic modulating potential of the essential oil obtained from *Eugenia jambolana* in association with led lights. Journal of Photochemistry and Photobiology B: Biology 174: 144-149. <https://doi.org/10.1016/j.jphotobiol.2017.07.027>.

Pereira NLF, Aquino PEA, Júnior JGAS, Janyketchuly SC, Filho MAV, Moura FF, Ferreira NMN, Silva MKN, Nascimento EM, Correia FMA, Cunha FAB, Boligon AA, Coutinho HDM & Matias EFFMIF (2017b) *In vitro* evaluation of the antibacterial potential and modification of antibiotic activity of the *Eugenia uniflora* L. essential oil in association with led lights. Microbial Pathogenesis 110: 512-518. <https://doi.org/10.1016/j.micpath.2017.07.048>.

Pietrovski EF, Magina MDA, Gomig F, Pietrovski CF, Micke GA, Barcellos M, Pizzolatti MG, Cabrini DA, Brighente IMC & Otuki MF (2010) Topical anti-inflammatory activity of *Eugenia brasiliensis* Lam. (Myrtaceae) leaves . Journal of Pharmacy and Pharmacology 60: 479-487. <https://doi.org/10.1211/jpp.60.4.0011>.

Proença CEB, Amorim BS, Antonicelli MC, Bünger M, Burton GP, Caldas DKD, Costa IR, Faria JEQ,

Fernandes T, Gaem PH, Giaretta A, Lima DF, Lourenço ARL, Lucas EJ, Mazine FF, Meireles LD, Oliveira MIU, Pizzardo RC, Rosa PO, Santana KC, Santos LLD, Santos MF, Souza MC, Souza MAD, Stadnik A, Staggemeier VG, Tuler AC, Valdemarin KS, Vasconcelos TNC, Vieira FCS, Walter BMT, Sobral M (2022) *Myrtaceae in* Flora e Funga do Brasil. Jardim Botânico do Rio de Janeiro. Available at <https://floradobrasil.jbrj.gov.br/FB171>. Access on 30 June 2022.

Ramhit P, Ragoo L, Bahorun T & Neergheen-Bhujun VS (2018) Multi-targeted effects of untapped resources from the Mauritian endemic flora. South African Journal of Botany 115: 208-216. <https://doi.org/10.1016/j.sajb.2018.01.020>.

Raseira MCB, Antunes LEC, Emerson RT & Gonçalves ED (2004) Espécies frutíferas nativas do Sul do Brasil. Documento, 129. Embrapa Clima Temperado, Pelotas. 124p.

Sá S, Chaul LT, Alves VF, Fiuza TS, Tresvenzol LMF, Vaz BG, Ferri PH, Borges LL & Paula JR (2018) Phytochemistry and antimicrobial activity of *Campomanesia adamantium*. Revista Brasileira de Farmacognosia 28: 303-311. <https://doi.org/10.1016/j.bjp.2018.02.008>.

Saleem S, Ahmed B, Khan MS, Al-Shaeri M & Musarrat J (2017) Inhibition of growth and biofilm formation of clinical bacterial isolates by NiO nanoparticles synthesized from *Eucalyptus globulus* plants. Microbial Pathogenesis 111: 375-387. <https://doi.org/10.1016/j.micpath.2017.09.019>.

Salem N, Kefi S, Tabben O, Ayed A, Jallouli S, Feres N, Hammami M, Khammassi S, Hrigua I, Nefisi S, Sghaier A, Limam F & Elkahoui S (2018) Variation in chemical composition of *Eucalyptus globulus* essential oil under phenological stages and evidence synergism with antimicrobial standards. Industrial Crops and Products 124: 115-125. <https://doi.org/10.1016/j.indcrop.2018.07.051>.

Saller R, Berger T, Reichling J & Harkenthal M (1998) Pharmaceutical and medicinal aspects of Australian tea tree oil. Phytomedicine 5: 489-495. <https://doi.org/10.1016/s0944-7113(98)80048-2>.

Schelz Z, Molnar J & Hohmann J (2006) Antimicrobial and antiplasmid activities of essential oils. Fitoterapia 77: 279-285. <https://doi.org/10.1016/j.fitote.2006.03.013>.

Scur MC, Pinto FGS, Pandini JA, Costa WF, Leite CW & Temponi LG (2016) Antimicrobial and antioxidant activity of essential oil and different plant extracts of *Psidium cattleianum* Sabine. Brazilian Journal of Biology 76: 101-108. <https://doi.org/10.1590/1519-6984.13714>.

Shehabeldine AM, Ashour RM, Okba MM & Saber FR (2020) *Callistemon citrinus* bioactive metabolites as new inhibitors of methicillin-resistant *Staphylococcus aureus* biofilm formation. Journal of Ethnopharmacology 254: 112669. <https://doi.org/10.1016/j.jep.2020.112669>.

Silva NA, Rodrigues E, Mercadante AZ & Rosso VV (2014) Phenolic compounds and carotenoids from four fruits native from the Brazilian Atlantic forest. Journal of Agricultural and Food Chemistry 62: 5072-5084. <https://doi.org/10.1021/jf501211p>.

Singh JP, Kaur A, Singh N, Nim L, Shevkani K, Kaur H & Arora DS (2016) *In vitro* antioxidant and antimicrobial properties of jambolan (*Syzygium cumini*) fruit polyphenols. Lwt 65: 1025-1030. <https://doi.org/10.1016/j.lwt.2015.09.038>.

Sytsma KJ, Litt A, Zjhra ML, Pires JC, Nepokroeff M, Conti E, Walker J & Wilson PG (2004) Clades, clocks, and continents: historical and biogeographical analysis of Myrtaceae, Vochysiaceae, and relatives in the Southern hemisphere. International Journal of Plant Sciences 165: S85-S105. <https://doi.org/10.1086/421066>.

Teixeira LDL, Bertoldi FC, Lajolo FM & Hassimotto NMA (2015) Identification of Ellagitannins and Flavonoids from *Eugenia brasilienses* Lam. (Grumixama) by HPLC-ESI-MS/MS. Journal of Agricultural and Food Chemistry 63: 5417-5427. <https://doi.org/10.1021/acs.jafc.5b01195>.

The Plant List (2013) Version 1.1. Published on the Internet. Available at <http://www.theplantlist.org/>. Access on 21 november 2020.

Tillotson GS & Zinner SH (2017) Burden of antimicrobial resistance in an era of decreasing susceptibility. Expert Review of Anti-Infective Therapy 15: 663-676. <https://doi.org/10.1080/14787210.2017.1337508>.

Torres A, Cilloniz C, Niederman MS, Menéndez R, Chalmers JD, Wunderink G & Poll TVD (2021) Pneumonia. Nature Reviews Disease Primers 7: 25. <https://doi.org/10.1038/s41572-021-00259-0>.

Troeger C, Blacker BF, Khalil IA, Rao PC, Cao S, Zimsen SRM, Albertson S, Stanaway JD, Deshpande A, Farag T, Forouzanfar MH, Abebe Z, Adetifa IMO, Adhikari TB, Akibu M, Lami FHA, Al-Eyadhy A, Alvis-Guzman N, Amare AT, Amoako YA, Antonio CAT, Aremu O, Asfaw ET, Asgedom SW, Atey TM, Attia EF, Avokpaho EFGA, Ayele HT, Ayuk TB, Balakrishnan K, Barac A, Bassat Q, Behzadifar M, Behzadifar M, Bhaumik S, Bhutta ZA, Bijani A, Brauer M, Brown A, Camargos PAM, Castañeda-Orjuela CA, Colombara D, Conti S, Dadi AF, Dandona L, Dandona R, Do HP, Dubljanin E, Edessa D, Elkout H, Endries AY, Fijabi DO, Foreman KJ, Fullman N, Garcia-Basteiro AL, Gessner BD, Gething PW, Gupta R, Gupta T, Hailu GB, Hassen HY, Hedayati MT, Heidari M, Hibstu DT, Horita N, Ilesanmi OS, Jakovljevic MB, Jamal AA, Kahsay A, Kasaeian A, Kassa DH, Khader YS, Khan EA, Khan MN, Khang YH, Kim YJ, Kissoon N, Knibbs LD, Kochhar S, Koul PA, Kumar GA,

Lodha R, El Razek HMA, Malta DC, Mathew JL, Mengistu DT, Mezgebe HB, Mohammad KA, Mohammed MA, Momeniha F, Murthy S, Nguyen CT, Nielsen KR, Ningrum DNA, Nirayo YL, Oren E, Ortiz JR, Mahesh PA, Postma MJ, Qorbani M, Quansah R, Rai RK, Rana SM, Ranabhat CL, Ray SE, Rezai MS, Ruhago GM, Safiri S, Salomon JA, Sartorius B, Savic M, Sawhney M, She J, Sheikh A, Shiferaw MS, Shigematsu M, Singh JA, Somayaji R, Sufiyan MB, Taffere GR, Temsah M-H, Thompson MJ, Tobe-Gai R, Topor-Madry R, Tran BX, Tran TT, Tuem KB, Ukwaja KN, Vollset SE, Walson JL, Weldegebreal F, Werdecker A, West TE, Yonemoto N, Zaki MES, Zhou L, Zodpey S, Vos T, Lim SS, Naghavi M, Murray CJL, Mokdad AH, Hay SI & Reiner Júnior RC (2018) Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infection Diseases 18: 1191-1210. <https://doi.org/10.1016/S1473-3099(18)30310-4>.

Valle DL, Andrade JI, Puzon JJM, Cabrera EC & Rivera WL (2015) Antibacterial activities of ethanol extracts of Philippine medicinal plants against multidrug-resistant bacteria. Asian Pacific Journal of Tropical Biomedicine 5: 532-540. <https://doi.org/10.1016/j.apjtb.2015.04.005>.

Veras HNH, Rodrigues FFG, Colares AV, Menezes IRA, Coutinho HDM, Botelho MA & Costa JGM (2012) Synergistic antibiotic activity of volatile compounds from the essential oil of *Lippia sidoides* and thymol. Fitoterapia 83: 508-512. <https://doi.org/10.1016/j.fitote.2011.12.024>.

Villachica LH (1996) Frutales y hortalizas promisorios de la Amazonía. Spt-Tca, 44. TCA, Lima. 344p.

Vitta Y, Figueroa M, Calderon M & Ciangherotti C (2020) Synthesis of iron nanoparticles from aqueous extract of *Eucalyptus robusta* Sm and evaluation of antioxidant and antimicrobial activity. Materials Science for Energy Technologies 3: 97-103. <https://doi.org/10.1016/j.mset.2019.10.014>.

Wagner H (2011) Synergy research: approaching a new generation of phytopharmaceuticals. Fitoterapia 82: 34-37. <https://doi.org/10.1016/j.fitote.2010.11.016>.

Wintachai P, Paosen S, Yupanqui CT & Voravuthikunchai SP (2019) Silver nanoparticles synthesized with *Eucalyptus critriodora* ethanol leaf extract stimulate antibacterial activity against clinically multidrug-resistant *Acinetobacter baumannii* isolated from pneumonia patients. Microbial Pathogenesis 126: 245-257. <https://doi.org/10.1016/j.micpath.2018.11.018>.

WHO - World Health Organization (2017) WHO publishes list of bacteria for which new antibiotics are urgently needed. Geneva. Available at <https://www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed/>. Access on 15 October 2022.

Woolhouse M, Waugh C, Perry MR & Nair H (2016) Global disease burden due to antibiotic resistance - state of the evidence. Journal of Global Health 6: 1-5. <https://doi.org/10.7189/jogh.06.010306>.

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