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POTENTIAL OF *EUGENIA UNIFLORA* AS A NATURAL ANTIBACTERIAL AGENT: A SYSTEMATIC REVIEW

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ABSTRACT

Background: *Eugenia uniflora* (family Myrtaceae), a medicinal plant traditionally used for the treatment of infectious and inflammatory diseases, has attracted increasing interest due to its potential antibacterial properties. **Objectives:** This systematic review aimed to comprehensively evaluate and synthesize published evidence on the antibacterial activity of *E. uniflora*. **Methods:** A systematic review was conducted following the PRISMA guidelines by searching Scopus, ScienceDirect, PubMed, and Google Scholar for English-language original studies published between 2015 and 2025 that evaluated the antibacterial activity of *Eugenia uniflora*. Of the 296 records identified, nine studies met the eligibility criteria and were included in the final analysis. **Results:** Nine included studies consistently demonstrated antibacterial activity of *E. uniflora* against both Gram-positive and Gram-negative bacteria. Gram-positive bacteria were generally more susceptible than Gram-negative bacteria, while antibacterial activity varied according to the plant part, extraction method, solvent, and extract concentration. Several studies also reported low minimum inhibitory concentration (MIC) values and broad-spectrum antibacterial activity, supporting the therapeutic potential of *E. uniflora*. **Conclusions:** The findings of this systematic review support the antibacterial potential of *E. uniflora*; however, further standardized and well-designed studies are necessary to confirm its efficacy and support its use and development as a natural antibacterial agent.

Keywords: *Eugenia uniflora*; Antibacterial activity; Medicinal plants; Systematic review

INTRODUCTION

Bacterial infections remain a significant cause of morbidity and mortality worldwide, and their impact has become increasingly severe with the rapid spread of antimicrobial resistance (AMR)[1]. In 2021 alone, AMR was associated with millions of deaths, with more than one million deaths directly attributable to resistant bacterial infections. Pathogens such as *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumoniae* are among the leading contributors to this burden, posing serious challenges to clinical management[2]. As the effectiveness of conventional antibiotics against these organisms continues to decline, alternative or complementary antibacterial strategies are urgently needed to address the escalating problem of drug resistance.

Plants have long been recognized as important sources of antibacterial agents due to their rich content of bioactive secondary metabolites, such as alkaloids, flavonoids, tannins, and terpenoids[3]. These compounds are widely recognized for their antimicrobial properties and play a crucial role in

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inhibiting the growth of pathogenic microorganisms[4].

Among the plants known for these properties is *Eugenia uniflora*, a member of the family Myrtaceae[5]. This plant originated in South America and has traditionally been used to treat various ailments[6]. Notably, several studies have demonstrated that *E. uniflora* possesses antibacterial effects against a variety of pathogenic bacteria [7-8].

The antibacterial activity of *E. uniflora* is closely associated with its high content of bioactive compounds, particularly flavonoids, tannins, and terpenoids[9],[10]. These compounds act through multiple mechanisms against bacterial cells and collectively contribute to the observed antibacterial effects[11],[12]. In particular, flavonoids are known to interfere with essential cellular processes, including major enzymes involved in DNA replication and transcription, such as DNA gyrase and topoisomerase IV, which are crucial for DNA unwinding during cell division[13]. In addition, flavonoids may act synergistically with other constituents of *E. uniflora*, including tannins and terpenoids, by increasing bacterial cell membrane permeability and facilitating the entry of other compounds into the cell[8].

Despite numerous studies reporting the antibacterial activity of *E. uniflora* and identifying its bioactive compounds, the available findings remain scattered and inconsistent with respect to extraction methods, tested bacterial strains, and experimental designs. Therefore, a systematic review is needed to integrate existing research, clarify current evidence, and identify knowledge gaps that may guide future antibacterial studies and development of *E. uniflora* as a potential antibacterial agent.

METHODS

PRISMA

The PRISMA guideline is widely recognized for describing and documenting systematic reviews, especially in evaluating the strengths and limitations of healthcare interventions[14]. Accordingly, the present review on the antibacterial properties of *E. uniflora* was conducted in line with the PRISMA, which served as the guiding protocol.

Resources

The literature search was carried out using four major databases: Scopus, ScienceDirect, PubMed, and Google Scholar. These platforms were chosen because they are well-established sources that provide broad coverage and full-text access to numerous high-impact medical journals. The search approach was adjusted for each database, as summarized in Table 1.

Table 1. Search Strategies Used Across Four Major Databases

Database Search and/or terms
Scopus (“eugenia uniflora”) AND (“antibacterial”)
ScienceDirect “eugenia uniflora” AND “antibacterial”
PubMed #1 Eugenia uniflora #2 “antibacterial” OR “Agents, Anti-Bacterial” OR “Anti-Bacterial Agents” OR “Antibacterial Agents”
Google Scholar Search manually from previous studies.

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Study Selection

Studies were eligible if they investigated the antibacterial activity of *E. uniflora* extracts. The inclusion criteria were limited to journal articles presenting original empirical data. Eligible studies were further required to be written in English, published between 2015 and 2025, and involve either *in vitro* or *in vivo* experiments assessing the antibacterial effects of *E. uniflora*. Exclusion criteria applied to publications such as review articles, books, letters to the editor, systematic reviews, meta-analyses, and conference proceedings. Studies were also excluded if they were not written in English or unrelated to the antibacterial evaluation of *E. uniflora*.

Systematic Review Process and Data Extraction

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two independent reviewers performed the study selection and data extraction, while any disagreements were resolved through discussion and consultation with a third reviewer.

The review process consisted of five stages. First, relevant search keywords were identified based on previous literature concerning *Eugenia uniflora* and antibacterial activity. Second, duplicate records were identified and removed. Third, titles and abstracts were screened according to the predefined eligibility criteria. Fourth, the full texts of potentially eligible studies were assessed for eligibility. Finally, only original research articles published in English between 2015 and 2025 that investigated the antibacterial activity of *E. uniflora* using in vitro or in vivo experimental designs were included in the qualitative synthesis.

Data were extracted independently by the two reviewers using a standardized data extraction form. The extracted information included the first author and publication year, bacterial species tested, plant part used, extraction solvent and method, extract concentration, antibacterial assay, inhibition-zone diameter, minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), reference antibiotic used as the positive control, statistical significance (where reported), and the main antibacterial findings. The extracted data were synthesized descriptively to compare the antibacterial activity of *E. uniflora* across the included studies.

RESULTS

The systematic review process is summarized in Figure 1. Database searches using the selected keywords initially identified 296 articles: Scopus (n=33), ScienceDirect (n=241), PubMed (n=13), and Google Scholar (n=9). After removing 13 duplicate records, 283 articles remained. Of these, 178 were excluded for the following reasons: non-English publications (n=1), published prior to 2014 (n=83), and review articles (n=94). The titles and abstracts of the remaining records were screened, and 24 full-text articles were assessed for eligibility. A full-text assessment was subsequently performed to evaluate compliance with the inclusion criteria, and 9 studies were ultimately included in the final analysis.

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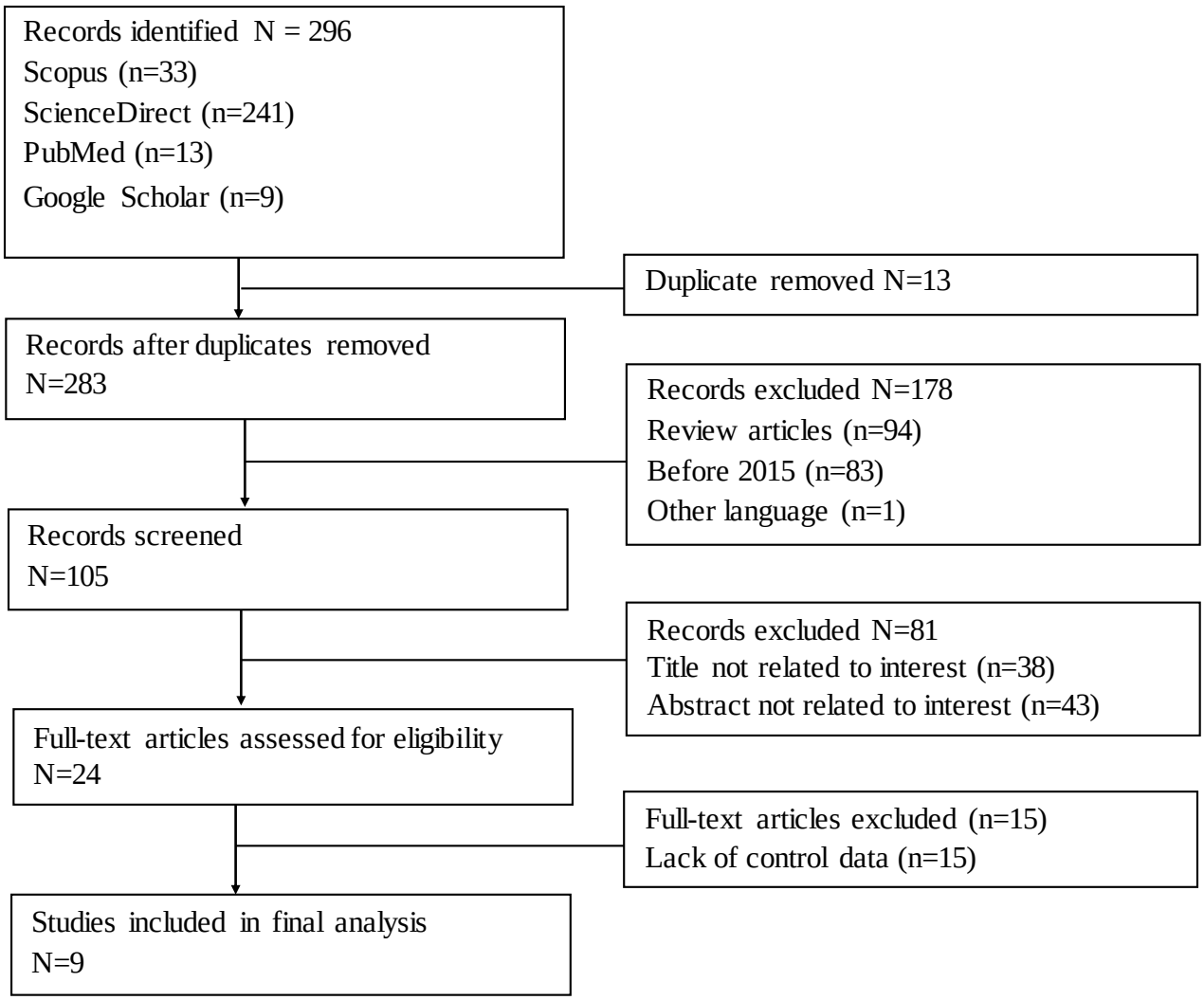

Figure 1. PRISMA Flowchart of The Study Selection Process

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The characteristics of the included studies are summarized in Table 2.

Table 2. Characteristics of The Included Articles

Reference	Microorganism tested	Plant parts	Antibacterial assay	Main results
[8]	*Escherichia coli*.	Leaves.	Kirby-Bauer disk diffusion.	*E. uniflora* leaf extract showed antibacterial activity against *E. coli*. The 80% extract produced the largest inhibition zone (15.33 ± 1.58 mm), while gentamicin showed the highest activity (25.67 ± 1.15 mm). Significant differences were observed among treatment groups ($p < 0.05$). MIC and MBC were not reported.
[15]	*Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, and* a methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli, Salmonella enteritidis, Pseudomonas aeruginosa.*	Leaves.	Broth microdilution method	*E. uniflora* crude extract and its fractions exhibited antibacterial activity against several Gram-positive bacteria and *S.enteritidis,* and *P. aeruginosa*, with the lowest MIC observed for *S. epidermidis* (0.313 µg/mL). No activity was detected against *E. coli*. Cephalothin, gentamicin, and vancomycin were used as reference antibiotics. MBC and inhibition-zone diameters were not reported.
[16]	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Listeria monocytogenes, Bacillus cereus, Chromobacterium violaceum.*	Fruit pulp.	Plate (well) diffusion assay and broth microdilution assay.	*E. uniflora* fruit pulp phenolic extract exhibited antibacterial activity against all tested bacteria, with inhibition zones up to 14.67 ± 0.58 mm and MIC values of <490 mg GAE/L for all tested bacteria except *C. violaceum* (115.76 mg GAE/L).

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Reference	Microorganism tested	Plant parts	Antibacterial assay	Main results
[17]	*Pseudomonas aeruginosa.*	Leaves.	Disc diffusion and broth dilution methods.	*E. uniflora* leaf ethanolic extract exhibited antibacterial activity against *P. aeruginosa*, with inhibition zones ranging from 6.0-13.7 mm, MICs of 0.83-1.33 mg/mL, and MBCs of 8.33-13.33 mg/mL, indicating a bacteriostatic effect. Amikacin was used as the reference antibiotic, and significant synergistic effects were observed with piperacillin and ceftazidime ($P < 0.05$).
[18]	*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*.	Leaves (essential oil).	Broth microdilution method.	*E. uniflora* leaf essential oil exhibited antibacterial activity against *S. epidermidis*, *S. aureus*, *P. aeruginosa*, and *E. coli*, with MIC values of 153.93 mg/mL for all tested bacteria except *E. coli* (307.96 mg/mL). Ampicillin and sulfamethoxazole were used as reference antibiotics.
[19]	*Pseudomonas aeruginosa, Escherichia coli, Micrococcus varians, Klebsiella pneumoniae, Staphylococcus aureus.*	Leaves.	Agar well diffusion.	*E. uniflora* leaf methanol extract and its fractions exhibited antibacterial activity against *P. aeruginosa, S. aureus, M. varians*, and *K. pneumoniae*. The ethyl acetate and aqueous fractions showed the strongest antibacterial activity, with inhibition zones up to 24.5 mm and MIC values ranging from 0.625 to 5.00 mg/mL. Cloxacillin was used as the reference antibiotic.

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Reference	Microorganism tested	Plant parts	Antibacterial assay	Main results
[20]	*Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa.*	Leaves.	Agar well diffusion assay.	Methanolic leaf extract, fractions, and essential oil of *E. uniflora* exhibited antibacterial activity against *S. aureus, K. pneumoniae*, and *P. aeruginosa*. The ethyl acetate fraction demonstrated the strongest activity, with inhibition zones up to 25.0 ± 1.0 mm, MICs of 6.25-100 mg/mL, and MBCs of 12.5-100 mg/mL. All extracts were tested at 100 mg/mL; ciprofloxacin served as the reference antibiotic, and significant differences were observed ($P < 0.05$).
[21]	*Helicobacter pylori.*	Leaves.	Broth microdilution method.	Methanolic leaf extract of *E. uniflora* exhibited antibacterial activity against *H. pylori*, with an MIC of 128 µg/mL, while no MBC was detected up to 1024 µg/mL, indicating a bacteriostatic effect. Inhibition-zone diameter was not reported. Metronidazole and amoxicillin were used as reference antibiotics.
[22]	*Bacillus megaterium, Enterococcus faecalis, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella enteritidis, Serratia marcescens, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus,*	Leaves.	Broth microdilution method, modulation assay, and checkerboard assay	Crude leaf extract and solvent fractions of *E. uniflora* exhibited antibacterial activity against multidrug-resistant Gram-positive and Gram-negative bacteria. The ethyl acetate fraction showed the highest antibacterial activity, with MIC values ranging from 7.81-250 µg/mL and MBC values ranging from 7.81-500

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Reference	Microorganism tested	Plant parts	Antibacterial assay	Main results
	Streptococcus agalactiae, and Streptococcus pyogenes.			µg/mL, depending on the bacterial strain. Inhibition-zone diameters were not reported. The antibacterial activity was evaluated using crude extract and hexane, ethyl acetate, and aqueous fractions. Ampicillin, azithromycin, ciprofloxacin, and gentamicin were used as reference antibiotics. Significant synergistic interactions were observed between the extracts/fractions and selected antibiotics, as confirmed by checkerboard assays (FICI ≤ 0.5).

Overall, all included studies consistently demonstrated that *E. uniflora* possesses antibacterial activity against a wide range of Gram-positive and Gram-negative bacteria, although the magnitude of activity varied depending on the bacterial species, plant part, extraction method, and extract type. Most studies evaluated leaf extracts, whereas Rodrigues et al. investigated the phenolic extract of the fruit. Despite these differences, antibacterial activity was consistently observed, supporting the broad-spectrum antimicrobial potential of *E. uniflora*.

The antibacterial efficacy of *E. uniflora* was influenced by the extraction solvent and fractionation process. Setiyanto et al. demonstrated concentration-dependent antibacterial activity of the ethanolic leaf extract against *E. coli*, with the 80% extract producing the greatest inhibition zone[8]. Similarly, Olugbuyiro et al. and Obuotor et al. reported that methanolic leaf extracts exhibited antibacterial activity against several clinically important bacteria, including *S. aureus, P. aeruginosa*, and *K. pneumoniae*[19],[20]. However, the effect of fractionation was not entirely consistent across studies. Olugbuyiro et al., Obuotor et al., and Ferreira et al. found that the ethyl acetate fraction exhibited the strongest antibacterial activity, characterized by larger inhibition zones and lower MIC values than the crude extracts[18-19],[22]. In contrast, Falcão et al. reported that the crude extract showed lower MIC values than its corresponding fractions, suggesting that synergistic interactions among phytochemical constituents may contribute substantially to the antibacterial activity[15].

Differences in antibacterial susceptibility were also observed among bacterial species. Gram-positive bacteria, particularly *S. aureus, S. epidermidis, B. cereus*, and *M. varians*, generally exhibited greater susceptibility than Gram-negative

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bacteria. Conversely, *E. coli* frequently showed lower susceptibility or required higher extract concentrations to achieve bacterial inhibition[8],[18-19]. This trend is commonly reported in phytochemical research and can be attributed to structural differences in bacterial cell walls. Gram-negative bacteria possess an outer membrane that acts as an additional permeability barrier, limiting the penetration of bioactive compounds, whereas Gram-positive bacteria lack this feature, making them more vulnerable to plant-derived antimicrobials[24]. Nevertheless, several studies demonstrated promising antibacterial activity against clinically important Gram-negative pathogens, including *P. aeruginosa, K.pneumoniae,* and *H. pylori*, indicating that the antibacterial spectrum of *E. uniflora* extends beyond Gram-positive bacteria[16],[18-21].

Although most studies focused on solvent extracts, Souza et al. demonstrated that hydrodistilled essential oil also inhibited bacterial growth, although *E. coli* exhibited lower susceptibility than the other tested bacteria[18]. These findings suggest that both volatile and non-volatile phytochemicals contribute to the antibacterial properties of *E. uniflora*, although differences in chemical composition may influence their antibacterial potency.

Another important observation is the growing evidence supporting the use of *E. uniflora* as an adjuvant to conventional antibiotic therapy[27]. Bobadilla et al. demonstrated synergistic interactions between the leaf extract and piperacillin and ceftazidime against *P.aeruginosa*[17]. Likewise, Ferreira et al. reported synergistic effects between *E. uniflora* extracts and several conventional antibiotics, including ampicillin, azithromycin, ciprofloxacin, and gentamicin, against multidrug-resistant bacteria[22]. These findings suggest that *E. uniflora* may not only function as a direct antibacterial agent but also enhance the efficacy of existing antibiotics, thereby representing a promising strategy to combat antimicrobial resistance. Collectively, the available evidence indicates that the antibacterial activity of *E. uniflora* is influenced by multiple factors, including the extraction solvent, fractionation procedure, plant material, and bacterial species.

Despite these promising findings, several limitations should be acknowledged. First, all included studies were conducted exclusively under in vitro conditions, limiting the direct translation of the findings into clinical applications. Experimental conditions, including standardized bacterial strains, controlled incubation periods, and simplified laboratory environments, do not adequately represent the complexity of in vivo infections. Second, considerable methodological heterogeneity was observed among the included studies, including differences in extraction solvents, plant parts, extraction procedures, antibacterial assays, bacterial strains, and outcome measures. This variability makes direct comparisons difficult and precludes quantitative synthesis of the available evidence. Furthermore, most studies evaluated crude extracts or partially purified fractions without comprehensive phytochemical characterization or identification of the bioactive compounds responsible for the antibacterial activity. Consequently, the mechanisms underlying the observed antibacterial effects remain poorly understood, while reproducibility and standardization of extract composition continue to represent major challenges.

Future research should therefore prioritize standardized extraction protocols, comprehensive phytochemical profiling, and the isolation and structural characterization of active compounds. In addition, mechanistic studies, toxicity evaluations, pharmacokinetic investigations, and well-

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designed in vivo experiments are needed to validate the antibacterial efficacy and safety of *E. uniflora*. Such studies will be essential for supporting its potential development as a safe and effective antibacterial agent or as an adjuvant to conventional antibiotic therapy.

CONCLUSION

This systematic review demonstrates that *E. uniflora* possesses promising broad-spectrum antibacterial activity against both Gram-positive and Gram-negative bacteria. Despite variations in extraction methods and antibacterial assays, the available evidence consistently supports its antibacterial potential. However, the predominance of in vitro studies and methodological heterogeneity limit the current evidence. Future research should focus on standardized methodologies, phytochemical characterization, and in vivo validation to facilitate the development of *E. uniflora* as a potential antibacterial agent.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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