Review

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Review

An Insight into Antimicrobial Properties of *Eucalyptus* Species in Africa: A Systematic Review

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Abstract: The rise of antimicrobial resistance poses a significant challenge to global health, necessitating the exploration for novel antimicrobial agents. *Eucalyptus* species, widely used in traditional African medicine, have shown promise in this regard. This systematic review investigates the antimicrobial potential of Eucalyptus species used in Africa. A systematic search was conducted via PubMed, Scopus, and Embase for African studies investigating the antimicrobial potential of Eucalyptus using the query: "Eucalyptus" AND ("Antimicrobial" OR "Antibacterial") AND (list of African countries). A total of 585 studies were retrieved and exported to Mendeley Desktop for de-duplication. Based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria, only African research on the antibacterial activity of eucalyptus were included in the selection of studies. The included studies covered nine (9) countries across various regions in Africa, and twenty (20) *Eucalyptus* species with the most frequently studied species being *Eucalyptus globulus, Eucalyptus camaldulensis*, and *Eucalyptus torelliana*. The *Eucalyptus* extracts were reported to exhibits good inhibitory actions against a wide range of microorganisms. The findings emphasize the importance of species selection and extraction methods in maximizing antimicrobial efficacy and calls for their exploitation as therapeutic agents in various biomedical applications.

Keywords: antimicrobial potential; traditional medicine; bioactive compounds

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Introduction

Antimicrobial resistance is a growing worldwide health concern, presenting a serious risk to the efficient management of infectious illnesses (Salam et al., 2023; Prestinaci et al., 2015). The World Health Organization (WHO) has highlighted antimicrobial resistance as one of the ten most critical global public health threats confronting humanity (WHO, 2018). This alarming rise in resistance is primarily driven by the overuse and abuse of antibiotics, leading to the evolution of pathogens that are resistant to many antibiotics (Ahmed et al., 2024; Muteeb et al., 2023). Therefore, the search for novel antimicrobial drugs that are capable of successfully combating resistant forms of microbes is urgently needed.

Traditional medicine has long been a valuable resource in the search for new therapeutic agents (Fokunang et al., 2011; Yuan et al., 2016). Throughout the world, in numerous countries, particularly in Africa, plants are used extensively in traditional medicine to manage various ailments, including infectious diseases. Among these plants, *Eucalyptus* species are notable for their widespread use and reported antimicrobial properties (Aleksic Sabo & Knezevic, 2019; Tyagi & Malik, 2011; Salvatori et al., 2023; Sebei et al., 2015). Eucalyptus, a genus of over 700 species native to Australia (Rehman et al.,

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2015) but widely cultivated in Africa, has been traditionally used for its medicinal properties, including its ability to treat respiratory infections, skin conditions, and other ailments.

Previous studies have highlighted the antimicrobial potential of various Eucalyptus species, attributing their efficacy to a range of bioactive compounds (Chandorkar et al., 2021; Nasir Shah et al., 2023; Nortjie et al., 2024). These compounds include tannins, flavonoids, terpenoids, alkaloids, and essential oils, which have demonstrated activity against a variety of microbial pathogens. Despite the potential of this plant, comprehensive reviews specifically focusing on the antimicrobial potential of Eucalyptus species used in Africa are limited.

This study aimed to systematically review and analyze the available evidence on the antimicrobial potential of Eucalyptus species used in Africa.

Methods

Search Strategy

We searched three bibliographic databases PubMed, Scopus and Embase for African studies on antimicrobial potential of Eucalyptus using the search query "Eucalyptus" AND ("Antimicrobial" OR "Antibacterial") AND ("Algeria" OR "Angola" OR "Benin" OR "Botswana" OR "Burkina Faso" OR "Burundi" OR "Cabo Verde" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Democratic Republic of the Congo" OR "Republic of the Congo" OR "Djibouti" OR "Egypt" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea-Bissau" OR "Ivory Coast" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Libya" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Morocco" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome and Principe" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sudan" OR "Tanzania" OR "Togo" OR "Tunisia" OR "Uganda" OR "Zambia" OR "Zimbabwe"). The search result were exported as Research Information Systems (RIS) and BibTeX files from the databases and imported into Mendeley Desktop where duplicates were removed. We did not register a protocol for this study.

Study Selection Criteria

We included only studies conducted in Africa which reported investigating the antimicrobial potential of Eucalyptus plant. Review articles, studies without accessible full texts, and non - African studies were excluded. Study identification, screening and inclusion was guided by the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines.

Data Extraction

Data extraction, de-duplication, was performed by Denis Bahati Lonzima under the supervision of Naheem Adekilekun Tijani and Emmanuel Eilu after which titles and abstract screening was performed independently by Denis Bahati Lonzima and Naheem Adekilekun Tijani. For all studies that met the inclusion criteria, (Denis Bahati Lonzima, Naheem Adekilekun Tijani, and Emmanuel Eilu) accessed the full text and extracted relevant data using a Microsoft Excel (2019) spreadsheet. The spreadsheet had columns labeled as follows: authors' name, year of publication, country of study, plant species used, part of plant used, and solvent used for Extraction and test organism.

Data Analysis

Data analysis of included studies was strictly descripting utilizing frequencies and percentages.

Results

Study Selection and Characteristics

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A Systematic search of PubMed, Embase and Scopus databases from inception through 25th April 2024 returned 585 studies. One hundred and fourty-nine (149) duplicates were removed, and four hundred and thirty-six (n=436) studies were subjected to title and abstract screening. Four hundredn and thirty-six (436) studies were subject to titles and abstracts screening after which two hundred and sixty eight (n = 268) records were excluded for not meeting the inclusion criteria. One hundred sixty eight (n=168) records where screened for accessibility of full text at which point seventy one (n = 71) records inaccessible in full text were excluded. Ninety seven (n = 97) full text were screened for all components of the inclusion criteria were seventy four (n = 74) non-African studies and 7 studies with poorly presented data were excluded, sixteen (n = 16) studies met all components of the inclusion criteria and were included in this study as illustrated in Figure **(1)** below.

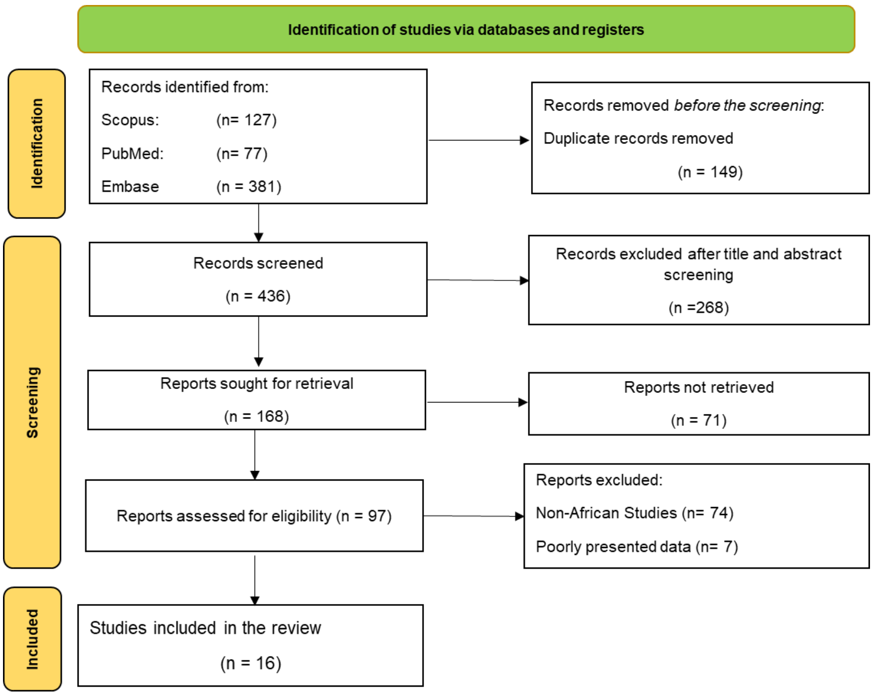

Figure 1. Study Selection Flowchart.

Across 9 African countries, antimicrobial potential of Eucalyptus species have been documented. Majority of the studies exploring the potential of the plant in the management of pathogenic microorganisms were conducted in Nigeria (n=5) followed by Algeria (n=3), and Tunisia (n=2). Egypt, Ethiopia, Morocco, Burkina Faso, Cameroun, and Uganda all have one study (n= 1) each.

Plant Species and Parts Used

The studies investigated twenty (20) Eucalyptus species, with *E. globulus* (n=4), *E. camaldulensis* (n=4), and *E. torelliana* (n=3) being the most frequently studied. Other species included *E. grandis, E. cassia, E. melliodora, E. paniculata, E. transcontinentalis, E. bosistoana, E. salmonopholia, E. sideroxylon, E. gomphocephala, E. cinerea, E. blakelyi, E. griffithsii, E. hemiphloia, E. lesouefii, E. longicornis, E. pyriformis, E. viminalis, and E. wandoo*. The most commonly used plant part was the leaves, though some studies also used stem bark, flowers, inflorescence, and whole plants.

Extraction Methods and Solvents

Various extraction methods were employed across the 16 African studies, including maceration, Soxhlet extraction, decoction, and Hydrodistillation. The solvents used for extraction included methanol, acetone, chloroform, distilled water, N-hexane, ethanol, and aqueous solutions. Methanol (n = 8), and distilled water (n = 5) were the most commonly used solvents.

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Antimicrobial Activity

Across the continent, twenty (n = 20) *Eucalyptus* species (Table 2). The antimicrobial activity of Eucalyptus extracts was tested against a wide range of microorganisms, including Gram-positive and negative bacteria and Fungi. Gram positive test bacteria included *Staphylococcus aureus, Bacillus subtilis, Bacillus cereus, Bacillus polymyxa, Bacillus anthracis, Streptococcus faecalis, Streptococcus pneumoniae, Staphylococcus epidermidis, Listeria monocytogenes, Mycobacterium tuberculosis, and Mycoplasma bovis*. Gram-negative bacteria tested include; *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus stuartii, Proteus vulgaris, Helicobacter pylori, Enterobacter aerogenes, Acinetobacter baumannii.* In regards to antifungal potential of Eucalyptus, the fungal species tested include: *Candida albicans, Aspergillus sp., and Rhizopus nigricans*

Minimum Inhibitory Concentration (MIC)

The MIC values of the extracts varied widely, depending on the *Eucalyptus* species, solvent, and microorganism. The lowest MIC recorded was 0.39 µg/ml for *E. grandis* stem bark extract against *H. pylori*, while the highest was 50mg/ml for *E. gomphocephala* leaves extract against *P. aeruginosa*.

Bioactive Compounds

The studies identified a range of bioactive compounds (Table 1) responsible for the antimicrobial activity, including: Tannins, Saponins, Flavonoids, Terpenoids, Alkaloids, Phenolic compounds, Eucalyptol, α-Pinene, trans-Pinocarveol, p-cymene, neoverbanol, Monoterpenoids, Sesquiterpenoids, Glycosides, Phloroglucinols, Polyphenols, Cardiac glycosides, Reducing sugars, Carbohydrates and Anthraquinones

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Table 1. Characteristics of Included Studies.

Author	Year	Country	Plant Specie	Part of Plant used	Organisms tested	Solvent used	Type of extraction	Extract MIC (mg/ml)	Positive Control	Control Conc. (µg/ml)	Bioactive Compounds
Ikinyom et al	2024	Uganda	*E. globulus Labill*	Leaves	*S. pneumoniae* *K. pneumoniae*	Acetone	Maceration	1.25 2.5	Ciprofloxacin	0.04 0.04	Tannins, saponins, terpenoids, glycosides, alkaloids, phenolic compounds, cardiac glycosides, terpenes, reducing sugars, carbohydrates, flavonoids.
Evans et al	2002	Nigeria	*E. cassia*	Leaves Stem inflorenscence	*S. typhi*	Distilled water Ethanol	Decoction	1 2	Not reported	Not reported	Saponins, Alkaloid Tannins
Kouki et al	2022	Tunisia	*E. melliodora, E. paniculata, E. transcontinentalis E. bosistoana E. salmonophoila*	Leaves	*S. aureus L.monocytogenes, P. aeruginosa E. coli, A. baumannii*	N-hexane	Hydrodistillation	0.026 - 0.032	Tetracycline	23-27 µL/mL	Eucalyptol, α-Pinene, trans-Pinocarveol, p-cymene, neoverbanol, Monoterpenoids, Sesquiterpenoids.
Adeniyi et al	2009	Nigeria	*E. camaldulensis* *E. torelliana*	Leaves Stem bark	*H. pylori*	Chloroform Methanol	Soxhlet extraction	0.0125 – 0.4	Clarithromycin	0.5	Tannins saponins, cardenolides
Bouharb et al	2014	Morocco	*E. gomphocephala*	Leaves	*P. aeruginosa*	Distilled water	Maceration	Aq = 6.25-12.5 Hex = 9.37- 50	Gentamicin	15	tannins, flavonoids, saponins triterpenes
Adeniyi et al	2009	Nigeria	*E. grandis*	Stem bark	*H. pylori*	N-Hexane Methanol	Soxhlet extraction	0.00039 - 0.00156	Bismuth citrate	25	Tannins, essential oils and saponins

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Gemechu et al	2013	Ethiopia	*E. camaldulensis*	Leaves	*M. tuberculosis* *M. bovis*	Methanol	Maceration	0.00625-0.1	Rifampicin	32	Tannins and saponins
Okba et al	2021	Egypt	*E. sideroxylon*	Flowers	*B. subtilis* *S. aureus* *E. coli* *P. aeruginosa* *C. albicans*	Methanol	Maceration	0.5-1.2 1.2 1.2 3.0	**Gentamicin**	**10**	Phloroglucinols, Flavonoids Tannins.
Ouattara et al	2022	Burkina-Faso	*E. camaldulensis*	Whole plant	*E. coli* *K. pneumoniae* *S. aureus* *S. epidermidis* *S. saprophyticus* *C. albicans* *Aspergillus sp*	Methanol	Maceration	0.156 - 5	**Ciprofloxacin**	**5**	Tannins Flavonoids Saponins
Naili et al	2022	Algeria	*E. globulus*	Leaves	*E. coli* *K. pneumoniae* *P. aeruginosa* *E. aerogenes* *S. aureus* *B. subtilis*	Ethanol & Distilled water	Maceration	6.25	Tetracycline Vancomycin, Oxacillin.	30 30 5	Flavonoids Tannins, free quinones Terpenoids
Lawal et al	2012	Nigeria	*E. camaldulensis* *E. torelliana*	Leaves Stem bark	*M. tuberculosis*	N-hexane, Chloroform Methanol	Maceration	0.0495 0.04699	Rifampicin	4–0.0156	Tannins Triterpenes saponins, Anthraquinones Glycosides
Boulekbache-Makhlouf et al	2013	Algeria	*E. globulus*	Fruits	*S. aureus* *B. subtilis* *K. pneumoniae*	Acetone & distilled water	Maceration	0.03 0.08	Gallic and tannic acids	none	Phénols Tannins Flavonoids
Khedhri et al	2022	Tunisia	*E. griffithsii* *E. hemiphloia* *E. lesouefii* *E. longicornis* *E. pyriformis,* *E. viminalis* *E. wandoo*	Leaves	*A. baumannii* *P. aeruginosa* *E. coli* *S. aureus* *L. monocytogenes*	N-hexane	Hydrodistillation	25-38 µL/mL	tetracycline	23- 24 µL/mL	The oxygenated monoterpenes, hydrocarbon monoterpenes, Eucalyptol, Eucalyptol, α-pinene, o-cymene,

											trans-pinocarveol, neo-verbenol, α-terpineol, cumin aldehyde, terpinene-4-ol, dihydrocarveol, pinocarvone, p-menth-1-en-7-al, carvacrol, p-cymene, iso-menthol, β-pinene, m-cymen-8-ol, sabina ketone, spathulenol, sabina ketone, pinocarvone, cryptone, acetate, pinocarvone, sesquiterpenes, β-eudesmol, rosifoliol, α-eudesmol.
Tankeo et al	2014	Cameroon	*E. robusta*	Leaves	*P. stuartii* *P. aeruginosa* *K. pneumoniae* *E. coli* *E. aerogenes* *E. cloacae*	Methanol	Soxhlet extraction	0.064	Chloramphenicol	2.5	Alkaloids Anthocyanins, anthraquinones, Flavonoids Phenols saponins sterols tannins triterpenes
Lawal et al	2012	Nigeria	*E. torelliana*	Leaves Stem bark	*H. pylori*	N-Hexane Chloroform Methanol	Soxhlet extraction	0.050 to 0.1	Clarithromycin	0.25–0.0625	tannins, triterpenoid

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											saponins and cardiac glycosides
Bouras et al	2016	Algeria	*E. golobulus*	Leaves	*K. pneumoniae*	Distilled water	decoction	0.3 – 0.4	dimethylsulfoxid (DMSO)	10	Not reported

E (plant species column) = Eucalyptus**;** **MRSA**: Methicillin resistant staphylococcus aureus; **MDR**: Multidrug resistant; Streptococcus pneumoniae ; Klebsiella pneumoniae; Salmonella typhi; Staphylococcus aureus; Listeria monocytogenes; Pseudomonas aeruginosa; Escherichia coli; Acinetobacter baumannii; Helicobacter pylori ; Mycobacterium tuberculosis; Mycoplasma bovis ; Bacillus subtilis; Candida albicans; Staphylococcus epidermidis ; Staphylococcus saprophyticus; Aspergillus sp; Enterobacter aerogenes; Streptococcus faecalis; Bacillus stearothermophelus; Bacillus cereus; Bacillus polymyxa; Bacillus anthracis; Pseudomonas fluorescens; Enterococcus feacalis; Listeria innocua; Klebsiella oxytoca; Rhizopus nigricans; Providencia stuartii ; Enterobacter cloacae.

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Discussion

The findings of this systematic review highlight the substantial antimicrobial potential of various *Eucalyptus species* used in Africa, corroborating earlier studies that have demonstrated the efficacy of Eucalyptus extracts against a broad spectrum of pathogens (Takahashi et al., 2004; Elbhnsawi et al., 2023; Elaissi et al., 2012; Gilles et al., 2010; De Siqueira Mota et al., 2015; Aleksic Sabo & Knezevic, 2019; Ameur et al., 2021; Sebei et al., 2015; Siddique et al., 2018). Notably, *Eucalyptus globulus, and E. camaldulensis* emerged as the most frequently studied species, showing significant antimicrobial activity. These results are consistent with previous research, which has also reported similar efficacy for these species against common bacterial strains, including *Staphylococcus aureus* and *Escherichia coli* (Ghareeb et al., 2018; Elaissi et al., 2012). The low minimum inhibitory concentration (MIC) values, particularly for *E. grandis* against *Helicobacter pylori*, suggest a strong potential for therapeutic applications, aligning with findings from studies in other regions that have documented the antimicrobial properties of *Eucalyptus* species against this pathogen (Parreira et al., 2017; Nayim et al., 2023; Safavi et al., 2015)

Extraction Methods and Solvents

A noteworthy aspect of this review is the variety of extraction methods employed across the studies. While maceration and Soxhlet extraction were the most commonly used methods, studies that utilized Hydrodistillation reported varying results in antimicrobial efficacy. For instance, Kouki et al., (2022) observed that Hydrodistillation yielded essential oils with potent activity against multi-drug resistant bacteria, whereas studies using maceration predominantly extracted phenolic compounds. This discrepancy underscores the importance of extraction techniques in determining the bioactive profile and resultant antimicrobial activity of Eucalyptus extracts (Shekar et al., 2015). The use of methanol as a solvent in many studies further emphasizes its effectiveness in solubilizing a broad range of polar compounds, including flavonoids and tannins, which are known for their antimicrobial properties (Plaskova & Mlcek, 2023; Muhamad et al., 2014).

Bioactive Compounds and Mechanisms

In addition to highlighting the efficacy of *Eucalyptus* species, this review identified a diverse array of bioactive compounds that contribute to their antimicrobial properties. Compounds such as tannins, flavonoids, and Eucalyptol, α-Pinene, trans-Pinocarveol, p-cymene, neoverbanol, Monoterpenoids, Sesquiterpenoids for essential oils have been previously documented for their ability to disrupt microbial cell membranes, inhibit protein synthesis, and exhibit antioxidant properties (Parham et al., 2020; Nwabor et al., 2021; A. Shaaban, 2020).The presence of these compounds in Eucalyptus extracts provides a scientific basis for their traditional use in treating infections. Comparatively, other studies on medicinal plants have shown similar bioactive compounds with antimicrobial properties, reinforcing the notion that plants serve as a rich source of natural antimicrobials (Sharma et al., 2020). This similarity indicates that the mechanisms through which these compounds exert antimicrobial effects may be conserved across different plant species, suggesting that *Eucalyptus* can be further investigated alongside other medicinal plants (Barbieri et al., 2017).

While the findings from this review are promising, they also raise several questions regarding the mechanisms of action of *Eucalyptus* extracts and their potential to overcome antimicrobial resistance. The ability of *Eucalyptus* compounds to synergize with conventional antibiotics, as reported in studies by Pereira et al., (2014) and (Elangovan & Mudgil, 2023), may offer a strategic approach to enhance therapeutic efficacy and mitigate resistance. Furthermore, the application of nanotechnology in enhancing the bioavailability of bioactive compounds from Eucalyptus extracts represents a significant advancement in this field. Recent studies have demonstrated that encapsulating plant extracts in nanoparticles can improve their solubility, stability, and controlled

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release, ultimately leading to enhanced antimicrobial activity (Matouskova et al., 2016; Hajibonabi et al., 2023). This innovative approach could maximize the therapeutic potential of Eucalyptus species and address the limitations of current antimicrobial treatments.

Implications for Drug Discovery and Antimicrobial Resistance

The findings from this review highlight the potential of *Eucalyptus* species as sources of new antimicrobial agents, which could help in the fight against antimicrobial resistance. The diverse range of bioactive compounds in *Eucalyptus* extracts suggests that they could be developed into effective treatments for various infections, including those caused by drug-resistant pathogens.

Limitations and Future Directions

While this review provides valuable insights, we observed a variability in study methodologies and the lack of standardization in reporting MIC values. Future research should focus on standardizing extraction and testing protocols, as well as conducting in vivo studies to confirm the efficacy and safety of Eucalyptus-based antimicrobial agents.

Conclusion

This systematic review provides evidence for the antimicrobial potential of Eucalyptus species used in Africa, with significant implications for drug discovery and public health. The presence of different bioactive compounds highlight the importance of these plants in combating microbial infections. Future research should focus on standardized extraction methods, in vivo studies to validate efficacy, and the application of nanotechnology to optimize the bioavailability of Eucalyptus extracts.

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