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Antibacterial activity of Nigerian medicinal plants as panacea for antibiotic resistance: A systematic review

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ABSTRACT

Background & Aim: Antibiotic resistance is one of the global public health threats facing modern health care system. The development of new effective agents has been challenging. Thus, the interest in the use of medicinal plants for the treatment of bacterial infections has increased. Therefore, the aim of this study was to review Nigerian medicinal plants with antibacterial activity.

Experimental: This study retrieved data from published articles on Nigerian medicinal plants with antibacterial activity. The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines were adopted. A systematic search of PUBMED CENTRAL was conducted. The included studies were those published in peer-reviewed English language journals between 1st January 2000 and 31st December 2020 and reported on the key terms; Nigerian medicinal plants with antibacterial activity.

Results: The database searches yielded a total of 817 results, and 765 articles were ineligible. After reviewing relevant titles and abstracts, a total of 52 articles on antibacterial were retrieved for full text review. After extensive review of each article, 13 articles were excluded and a total of 39 articles were retained. Furthermore, 4 articles were also removed due to lack of specific compounds stated. Finally, only 35 articles met the inclusion criteria for the assessment of antibacterial activity of Nigerian medicinal plants. The narrative synthesis of the included studies revealed different plants families with broad activities against gram-positive and gram-negative bacteria. Among the bacterial isolates, *Staphylococcus aureus* was tested more, followed by *Escherichia coli* and *Pseudomonas aeruginosa* and the bacteria were subjected to 97 medicinal plants species for antibacterial activity.

Recommended applications/industries: The results from this study reveal that many Nigerian medicinal plants contain bioactive compounds with potentials of antibacterial activity and suggest that they could be employed as alternative in the treatment of bacterial infections after safety profiles is appraised.

1. Introduction

Antimicrobial resistance has increasingly threatened the global public health. The recent report indicated that death caused by antibiotic resistant-bacteria is far more than deaths caused by Human immunodeficiency Virus (HIV) and Malaria combined (Murray *et al.*, 2022). This further confirmed the previous projection that infection by antibiotic-resistant organisms will be responsible for over 10 million deaths annually worldwide by 2050 if the threat is not subdued (O'Neill, 2016; De Kraker *et al.*, 2016). On the global analysis of the burden, sub-saharan Africa was reported to have highest burden, from seemingly common pathogens; *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa* but now ranked as key pathogens responsible for many deaths (Murray *et al.*, 2022) and some have been placed under World Health Organization's critical priority watch list (WHO, 2015).

However, despite the glaring threat of resistant bacteria, the efficacy of the available antibiotics continues to decline and in the last two decades, no introduction of new class of antibiotic to match the unprecedented rise in antibiotic resistance (Asokan *et al.*, 2019). Slow introduction of new class of antibiotic with new target side could be due to low funding to the antibiotic industry for development and discovery (EMA, 2009). The financial implication of developing new antibiotic is estimated to be over 1 billion dollars (Huttner *et al.*, 2013). This shortage of new antibiotics will continue to fuel the crisis of antibiotic resistance and therefore, necessitate the quest for alternatives to the conventional antibiotics.

The use of plants and plants products for medicinal purposes has long been reported in many traditions in history (Mustapha *et al.*, 2017). Plants have been employed as herbal medicines in many parts of the world, and this tend to gain attention as complementary or alternative to modern medicines due to vast active compounds (Li *et al.*, 2022). The medicinal properties are due to rich secondary metabolites such as alkaloids, amino acids, flavonoids, phenylpropanoids, steroids, volatile oils, glycosides, terpenes, quinones and other compounds with therapeutic properties (Li *et al.*, 2022). Thus, the concept of using plants and plant products based on the knowledge, skills and practices on cultural experiences, theories, and beliefs to maintain and treat illness is regarded as traditional medicine (WHO, 2017).

Nigeria is endowed with vast plants with high medicinal potentials and it used such natural-treasures as traditional medicine, similar practice is used in China and other Asian countries as Traditional Chinese Medicine (TCM) (Ezeorba *et al.*, 2022). The antimicrobial activities of the plants may exhibit synergistic effects in some cases and the different plants parts may provide different phytochemicals (Oladosu *et al.*, 2015).

There is increase interest on complementary medicine study in Nigeria. This paves ways for the screening of active compounds against many pathogens, and will provide better understanding of antimicrobial activities, chemical and safety profiles of active constituent of these medicinal plants. There are records of medicinal plants of Nigerian origin with antibacterial properties, thus, the need for explicitly appraise their efficacy and the nature of compounds. Therefore, the aim of this systematic literature review was to evaluate Nigerian medicinal plants with antibacterial activity.

In this systematic review, we highlight the Nigerian medicinal plants used as antibacterial agents that might potentially be used as alternatives to the conventional antibiotics and pave ways for further research and drug discovery against pathogens of clinical importance.

2. Materials and Methods

A systematic review was conducted on the medicinal plants from Nigeria with antibacterial activity. This systematic review adopted the reporting checklist of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA 2020) (Fig. 1) (Page *et al.*, 2021). Thus, database search was conducted on PUBMED Central to identify studies on medicinal plants with potential antibacterial activities from Nigeria.

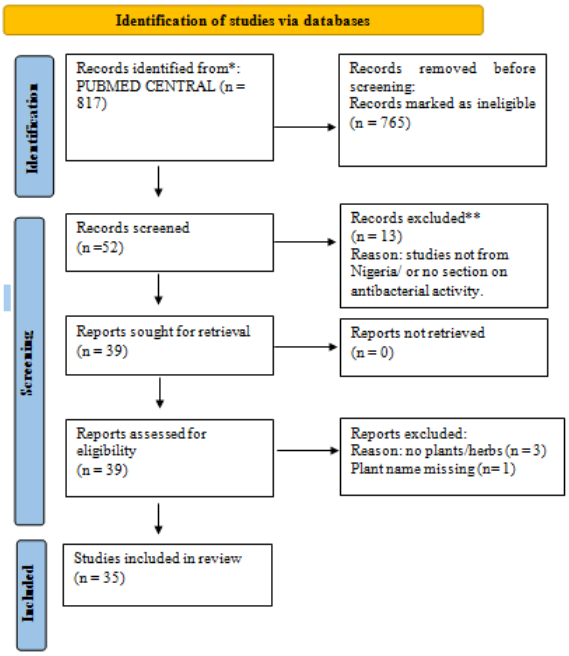

Figure 1. Process flow chart for the identification and review of records. (Adapted from Page *et al.*, 2021).

2.1. Search Strategy

The search approach was structured for the terms "Nigerian medicinal plants and antibacterial activity" targeting the "title" and "abstract" fields. The key words and the application of Boolean operators are presented below:

(Nigerian [All Fields] AND "plants, medicinal"[MeSH Terms] OR "plants"[All Fields] AND "medicinal"[All Fields] OR "medicinal plants"[All Fields] OR "medicinal"[All Fields] AND "plants"[All Fields]) AND "anti-bacterial agents"[All Fields] OR "anti-bacterial agents"[MeSH Terms] OR "anti-bacterial"[All Fields] AND "agents"[All Fields]) OR "anti-bacterial agents"[All Fields] OR "antibacterial"[All Fields] OR "activity"[All Fields] AND ("2000/01/01"[PubDate]: "2020/12/31"[PubDate]).

After the comprehensive search, four authors independently considered studies that meet the eligibility criteria.

2.2. Study design

In the context of population, exposure (intervention), comparator and outcome (PICO) of the review are given underneath: Study subjects (population): bacteria that were used for antibacterial activity of medicinal plants. Intervention: Medicinal plants as whole plants or their parts such as seed, root, flower, bud and leaf extracts used in the experimental groups. The intervention products used were manufactured from a single or combination of medicinal plants, plant extracts, decoctions, or other types of preparations), but not artificially synthesized compounds. The concentration and dose vary on each study. Comparator: Placebo or conventional drugs used as controls. Outcomes: Outcomes were the inhibition or killing by the extracts.

2.3. Eligibility criteria

2.3.1. Inclusion

Studies which were included in this study must be fully focused on Nigeria medicinal plant with antibacterial potentials. The studies (articles, reviews) published in English language within the period of 20 years (1st January, 2000 to 31st December, 2020).

2.3.2. Exclusion

Studies that were not within the period and not from Nigeria even if the authors are Nigerians were excluded, and also newspapers and magazines were not considered.

2.4. Data synthesis

Researchers were paired in four sets to harmonize the retrieved articles for further data synthesis and remove any grey article. Subsequently, an excel sheets was formed to include article's information and further vetting. At the end of thorough screening, 35 documents met the inclusion criteria, comprising 33 original articles and 2 review literatures. All retrieved literature received were perused with rapt attention.

Furthermore, the information extracted include: title, author, year of publication, study duration, type of bacteria used for the study (clinical isolates or reference strains), plant extracts used for activity evaluation, minimum inhibitory concentration (MIC) of extracts/fractions (µg/ml, mg/ml), zone of inhibition (mm), concentrations of crude extracts, type of solvent extracts and fractions used for activity and safety, extraction type and scientific names of the plants. The descriptive reports were turned into narrative findings.

3. Results and discussion

3.1. Overview of studies included

General findings from this systematic review indicated that Nigeria is vast home of medicinal plants with antibacterial activity. It is observed that pathogenic bacteria of public health concern could be tamed with plants and serve as alternative to the conventional antibiotics. However, there was little examination of the safety profile of such crude extracts. In the search of Nigerian medicinal plants with antibacterial activities, a total of 817 relevant articles were independently identified by four authors [Supp.1]. After reviewing relevant titles and abstracts, a total of 52 articles on antibacterial were retrieved for full text review. After extensive review of each article, 13 articles were excluded and a total of 39 articles were retained. Furthermore, 4 articles were also removed for not direct compounds of plants or name of plant is not stated. Finally, 35 articles met the criteria for the assessment of antibacterial activity of Nigerian medicinal plants (Table 1).

Table 1. List of medicinal plants identified from literature search having antibacterial activity.

S/N	Plants Species	Family	Parts Used	Reference
1	*Terminalia. Avicennioides*	*Combretaceae*	Stem	Akinyemi *et al.* (2005)
	Bridella ferruginea	*Euphorbiaceae*	Leaves	
	Ageratum conyzoides	*Compositae*	Leaves	
	Ocimum gratissimum,	*Lamiaceae*	Stem	
	Acalypha wilkesiana and	*Euphorbiaceae*	Stem	
	Phylantus discoideus	*Euphorbiaceae*	Stem	
2	*Strychnos spinosa Lam*	*Loganiaceae*	Leaves	Isa *et al.* (2014)
3	*Mangifera indica*	*Anacardiaceae*	Leaves	Abiala *et al.* (2016)
			Stem	
4	*Calliandra portoricensis*	*Mimosaceae*	Roots	Ogbole *et al.* (2020)
5	*Thymus vulgaris*	*Lamiaceae*	Leaves	Oramadike and Ogunbanwo (2017)
6	*Syzygium aromaticum*	*Myrtaceae*	leaves and young stem	Oluwasina *et al.* (2019)
	Dennettia tripetala	*Annonaceae*		
	Jatropha curcas	*Euphorbiaceae*		
7	*Trichilia heudelotti*	*Meliaceae*	Leaves	Aladesanmi *et al.* (2007)
	Boerhavia diffusa	*Nyctaginaceae*		
	Markhamia tomentosa	*Bignoniaceae*		
8	*Bryophyllum pinnatum and*	*Crassulaceae*	Leaves	Akinsulire *et al.* (2007)
	Kalanchoe crenata	*Crassulaceae*		
9	*Sesame radiatum and*	*Pedaliaceae*	Leaves	Bankole *et al.* (2007)
	Sesame indicum	*Pedaliaceae*		
10	*Cola acuminata*	*Malvaceae*	Leaves	Sonibare *et al.* (2009)
	Cola nitida	*Malvaceae*		
	Cola millenii and	*Malvaceae*		
	Cola gigantea	*Malvaceae*		
11	*Carpolobia lutea*	*Polygalaceae*	Stem and Root	Nwidu *et al.* (2012)
12	*Massularia acuminata*	*Rubiaceae*	Leaves	Oriola *et al.* (2014)
13	*Jatropha multifida*	*Euphorbiaceae*	Stem	Falodun *et al.* (2014)
14	*Khaya senegalensis*	*Meliaceae*	Stem	Ugoh *et al.* (2014)
15	*Annona senegalensis*	*Annonaceae*	Roots	Okoye *et al.* (2012)
16	*Alchornea laxiflora*	*Euphorbiaceae*	Leaves	Akinpelu *et al.* (2015)
17	*Carpolobia lutea*	*Polygalaceae*	Leaves	Anibijuwon *et al.* (2018)

18	*Dialium guineense*	*Leguminosae*	Stem	Olajubu *et al.* (2012)
19	*Tamarindus indica*	*Leguminosae*	fruits, leaves and stem	Nwodo *et al.* (2011)
20	*Crinum jagus*	*Amaryllidaceae*	Bulbs	Udegbunam *et al.* (2015)
21	*G. latifolium*		Leaves	Anyanwu *et al.* (2017)
	A. schimperi		Leave and bark	
	A. indica		Leaves	
	P. corymbosa		Leaves	
	M. lucida		Stem	
	T. avicennioides		Stem	
	A. acalonicum		Leaves	
	T. glaucescens		Stem	
	A. cepa		Bulbs	
	S. longepedunculata		Stem	
	Azadirachta indica		Twigs	
	P. Africana		Leaves	
	D. microcarpum		Leaves	
22	*Gongronema latifolium*	*Apocynaceae*	Leaves	Eleyinmi *et al.* (2017)
23	*Acalypha wilkesiana*	*Euphorbiaceae*	Leaves	Dada *et al.* (2019)
24	*Citrus sinensis*	*Rutaceae*	Leaves	Atolani *et al.* (2020)
	Moringa oleifera	*Moringaceae*	Seeds	
25	*Alchornea cordifolia and*	*Euphorbiaceae*	Fruits	Essien *et al.* (2016)
	Canthium subcordatum	*Rubiaceae*	Fruits	
26	*Vernonia amygdalina*	*Asteraceae*	Leaves	Enemchukwu *et al.* (2019)
27	*Cocos nucifera*	*Aracaceae*	Husk	Akinyele *et al.* (2011)
28	*Parkia biglobosa*	*Fabacea*	Stem	Abioye *et al.* (2013)
29	*Persea americana*	*Lauraceae*	Stem	Akinpelu *et al.* (2015)
30	*Eucalyptus camaldulensis and*	*Myrtaceae*	leaves and stem	Christiana *et al.* (2009)
	Eucalyptus torelliana	*Myrtaceae*		
31	*Abrus precatorius*	*Various*	Various	Ibekwe *et al.* (2014)
	Anogeissus leocarpus			
	Cassia siberiana			
	Combretum molle			
	Erythrina senegalensis			
	Garcinia kola			
	Khaya grandifolia			
	Pentaclethra macrophylla			
	Pterocarpus osun			
	Securidaca longepedunculata			
	Tapinanthus sessifolia			
	Terminalia avicennioides			
	Tetrapleura tetraptera			
32	*Perseaamericana*	*Lauraceae*	Root	Falodun *et al.* (2014)
33	*Ipomoea involucrata*	*Various*	Leaves	Oyedemi *et al.* (2018)
	Acalypha hispida		Leaves	
	Breynia nivosa (BN),		Leaves	
	Jatropha curcas		Leaves	

	Chromolaena odorata		Leaves	
	Macrolobium macrophyllum		Leaves	
	Baphia nitida		Leaves	
	Burkea africana		Leaves	
	Cassia alata		Leaves	
	Eleusine indica		Root	
34	*Aframomum melegueta*	*Zingiberaceae*	Fruits	Olajuyigbe *et al.* (2020)
35	*Argemone mexicana*, *Ficus exasperate*, *Persia Americana*, *Alchornea laxiflora*, *Crinum jagus*, *Adansonia digitate*, *Citrullus colocynthis*, *Cola nitida*, *Dorstenia prorepens*, *Echinacea purpurea*, *Spondias mombin*, *Annona senegalensis*, *Vernonia amygdalina*, *thymus vulgaris*	*Various*	Various	Ugboko *et al.* (2020)

3.2. Excluded articles

Search for this systematic review yielded numerous articles. However, many failed to meet the inclusion criteria for many reasons; i) studies of medicinal plants with antibacterial activity but not from Nigeria; ii) studies focused on other microorganisms (fungal, virus, parasites) other than bacteria; iii) plants are not from Nigerian origin or name of plant not mentioned; iv) authors could be Nigerians but did not conduct the study in Nigeria nor source the pathogens and plants from Nigeria.

3.3. Included articles

A total of 35 articles were eligible for data extraction. The articles included covered period of 20 years (2000-2020). The titles of the studies met the objectives and the body of the studies. Of the 35 studies, 11 used disc diffusion techniques with micro-dilution assay (Minimum Inhibitory Concentration-MIC and Minimum Bactericidal Concentration-MBC), 16 used agar well diffusion method with microdilution assay (MIC and MBC). Three of the studies used plating and agar-well diffusion techniques, while 2 used microbroth dilution methods for minimum inhibitory concentration and minimum bactericidal assays, and 2 other studies used pour plates methods. In the articles retrieved, 2 were review papers which highlighted combination of many assay methods.

3.4. Resistant bacteria

The threat posed by antibiotic resistant bacteria to the global public health is at alarming rate and it continues to grow rapidly. In recent report, deaths related to infection with antibiotic resistant-bacteria has become leading cause of deaths globally (Murray *et al.*, 2022). The top leading pathogens for deaths associated with antibiotic-resistance include *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pneumoniae* and *Acinetobacter baumannii* (Murray *et al.*, 2022). In our systematic review, all of these priority pathogens were observed (Table 2). A total of 179 bacteria were tested in the studies mostly from clinical sources. Among the bacterial isolates, *Staphylococcus aureus* was tested more, followed by *Escherichia coli* and *Pseudomonas aeruginosa.* These bacteria were subjected to 97 medicinal plants for antibacterial activity.

Table 2. List of bacterial isolates identified from literature search.

S/N	Organism	Assay	Extraction solvent	High activity	References
1	Methicillin Resistant *Staphylococcus aureus* (MRSA)	Broth Micro-dilution	Ethanol, water	MIC; 30.4 to 37.0 mcg/mL MBC; 55.4 to 71.0 mcg/mL	Akinyemi *et al*., (2005)
2	*Staphylococcus aureus* *Bacillius cereus* *Enterococcus faecalis* *Escherichia coli*	Broth Micro-dilution	Acetone, methanol and dichloromethane/ methanol	MIC; 0.04 to >1.25 mg/mL	Isa *et al*., (2014)
3	*Escherichia coli, Salmonella enteritidis, Pseudomonas aeruginosa and Klebsiella oxytoca*	ADilM	Methanol	30.60 mm	Abiala *et al*., (2016)
4	*Escherichia coli* (ATCC 25922), *and* Gram-positive Strains Methicillin-Resistant *Staphylococcus aureus* (MRSA), *Staphylococcus aureus (ATCC 6538),*	ADilM	Methanol	13.27 ± 0.00 µg/mL	Ogbole *et al*., (2020)
5	*Vibrio parahaemolyticus and Vibrio fluvialis*	ADilM	Ethanol	23.00 ± 0.0	Oramadike and Ogunbanwo, (2017)
6	*Escherichia coli, Bacillus* sp., *Staphylococcus aureus, Staphylococcus epidermidis, Micrococcus luteus, Streptococcus mutans, Streptococcus pyogenes, Lactobacillus acidophilus*	AWD, ADM	Ethanol	8.33 to 14.4 mm MIC; 2.5 to 20.0 mg/mL,	Oluwasina *et al*., (2019)
7	*Escherichia coli* NCTC 10418, *Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis,*	ADM, DDM	Hexane, chloroform, water	0.25- 5.0 mg/mL	Aladesanmi *et al*., (2007)
8	*Escherichia coli* ATCC 25922, *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Shigella flexneri, Salmonella paratyphi, Citrobacter spp); Staphylococcus aureus* ATCC 25213, *Staphylococcus aureus, Enterococcus faecalis, Bacillus subtilis*	AWD, BDM	Water, methanol, Ethanol	MIC; 8- 32 mg/mL MBC; 64- 256 mg/mL	Akinsulire *et al*., (2007)
9	*Staphylococcus aureus, Streptococcus pneumoniae*	AWD, MDM	Methanol and ethanol	MIC; 70.0µg/ml ZOI; ≥ 10 mm	Bankole *et al*., (2007)
10	*Staphylococcus aureus, Staphylococcus albus, Bacillus subtilis, Klebsiella pneumoniae, Pseudomonas aeruginosa*	AWD	Ethanol	7.3±0.03-16.0±0.0 mm	Sonibare *et al*., (2009)
11	*Eschericia coli* (ATCC 25922), *E. coli* (ATCC10418), *Pseudomonas aeruginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 25923), *Staphyllococus aureus* (ATCC 6571), *Enterococcus faecalis* (ATCC 29212) *and Bacillus subtilis* (NCTC 8853	DDM, Broth Micro-dilution	Ethanol, chloroform, ethyl acetate	>1000 mg/mL	Nwidu *et al*., (2012)
12	*Saphylococcus aureus Clostridium sporogens*	ADM	Ethanol	2 mg/mL	Oriola *et al*., (2014)
13	*Staphylococcus aureus* (ATCC 29213) *S. aureus*, methicillin resistant *S. aureus* (ATCC 33591), *Escherichia coli* (ATCC 35218), *Pseudomonas aeruginosa* (ATCC 27853) *and Mycobacterium intracellulare* (ATCC 23068), *M. intracellulare*	Broth Micro-dilution	Methanol, hexane, ethylacetate	8.7- >200.0 µg/mL	Falodun *et al*., (2014)
14	*Salmonella* Typhi	ADM	Methanol, ethanol and water	14-25 mm	Ugoh *et al*., (2014)
15	*Bacillus subtilis, Escherichia coli Pseudomonas aeruginosa Salmonella paratyphi Staphylococcus aureus*	ADM	Methanol, methylene chloride	10.33 ± 0.06- 17.00 ± 0.00 mm	Okoye *et al*., (2012)
16	*Staphylococcus aureus*(NCIB 8588), *Staph. aureus(*SW*)*, *Staph. aureus* (SS), *Staph. aureus* (NC), *Shigella species* (ST), *Escherichia coli* (ST), *Klebsiella pneumoniae* (NCIB 418), *K. pneumoniae* (SS), *Bacillus polymyxa (*ES), *Clostridium pyogenes* (ES), *Proteus vulgaris* (ES), *Pseudomonas aeruginosa* (ES), *Bacillus anthracis* (ES),*Micrococcus luteus* (NCIB 196), *Pseudomonas fluorescens (*NCIB 3756*), Bacillus cereus* (NCIB6349),*Clostridium*	AWD, Broth Micro-dilution		12± 0.00- 24± 0.50 mm	Akinpelu *et al*., (2015)

	sporogenes(NCIB 532), *Bacillus stearothermophilus* (NCIB 8222), *E. coli* (NCIB 86), *Bacillus subtilis (*NCIB 3610*)*, *Enterococcus faecalis*(NCIB 775), *and Pseudomonas aeruginosa* (NCIB 950).				
17	*Pseudomonas aeruginosa, Salmonella typhi, Escherichia coli, Staphylococcus aureus*	ADM, DDM	Ethanol, n-hexane and hot water	ZOI- 9 – 13 mm MIC- 5-150 mg/ml)	Anibijuwon *et al*., (2018)
18	*Staphylococcus aureusa, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Klebsiella pneumonia, Streptococcus pneumonia Enterohemorrhagic E coli Salmonella typhi, Shigella flexneri, Bacillus subtili*	ADM	Petroleum ether, Chloroform, Acetone, Isopropanol, absolute ethanol, ethanol (50%), water	ZOI-18.0 mm MIC; 0.63 mg/mL, MBC; 5.0 mg/mL	Olajubu *et al*., (2012)
19	*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Bacillus cereus*	AWD	Cold water, hot water, ethanol	MIC; 7.81- 31.25 mg/mL MBC; 125- 250 mg/mL	Nwodo *et al*., (2011)
20	*Staphylococcus aureus, Bacillus subtilis, Pseudomonas areuginosa*	AWD	Methanol	21-25mm	Udegbunam *et al*., (2015)
21	*P. monteilli, P. aeruginosa, E. coli, M. tuberculosis, S. dysenteriae, Flavobacterium* spp, *methicillin-resistant S. aureus, S. mutans, S. typhi, K. pneumoniae, P. vulgaris and Citrobacter* spp	AWD, Broth Micro-dilution, DD	Methanol, ethanol	Various	Anyanwu *et al*., (2017)
22	*E. faecalis, Y. enterolytica, E. aerogenes, B. cereus, E. agglomerans, S. aureus, S. aureus subsp aureus, L. monocytogenes, S. enteritidis, S. cholerasius ser typhimurium and P. aeruginosa.*	DD	Water and 70% methanol	ZOI- 7-22 mm	Eleyinmi *et al*., (2017)
23	*Escherichia coli and Staphylococcus aureus*	AWD	Methanol, ethanol	16-20 mm	Dada *et al*., (2019)
24	*Klebsiella pnamananae, Streptococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis, Salmonella typhi and Escherichia coli*	ADM	Methanol, n-hexane, chloroform, potassium hydroxide, potassium iodide, glacial acetic acid and hydrochloric acid	MIC; 25 mg/mL ZOI-10-20 mm	Atolani *et al*., (2020)
25	*Bacillus cereus* (ATCC No. 14579), *Staphylococcus aureus* (ATCC No. 29213), *Pseudomonas aeruginosa* (ATCC No. 27853), *and Escherichia coli* (ATCC No. 10798)	Broth Micro-dilution	Essential oils	MIC; 156 µg/mL	Essien *et al*., (2016)
26	*Bacillus cereus Staphylococcus aureus, Escherichia coli and Salmonella* spp	AWD	Ethanol	MIC; 3.125–50 mg/mL,	Enemchukwu *et al*., (2019)
27	*Escherichia coli* ATCC 8739, *Pseudomonas aeruginosa* ATCC 19582, *Streptococcus faecalis* ATCC 29212, *Klebsiella pneumoniae* ATCC 10031, *Proteus vulgaris* CSIR 0030, *Bacillus subtilis* KZN, *Enterococcus faecalis* KZN, *Shigella flexineri* KZN, *Micrococcus luteus, Vibrio specie*	AWD	Aqueous and n-hexane	0.6–5.0 mg/mL	Akinyele *et al*., (2011)
28	*Escherichia coli and Pseudomonas aeruginosa*	ADilM	Water and methanol	ZOI;14 ± 0.00 -28 ± 0.71 mm MIC; 0.63-5 mg/mL	Abioye *et al*., (2013)
29	*Bacillus cereus*	ADilM, Broth Micro-dilution	Methanol	ZOI;10 mm and 26 mm MIC- 0.78 and 5.00 mg/mL	Akinpelu *et al*., (2011)
30	*Helicobacter pylori*	ADilM	Chloroform, n-hexane, and methanol	MIC; 12.5 to 400 µg/mL	Christiana *et al*., (2009)
31	*Mycobacterium bovis, BCG and Mycobacterium tuberculosis*	Broth Micro-dilution	Aqueous, methanol	128 µg/mL	Ibekwe *et al*., (2014)
32	*Staphylococcus aureus (*ATCC 29213*)*, methicillin-resistant *S. aureus (*MRSA) (ATCC 33591), *Escherichia coli* (ATCC	Broth Micro-dilution	Aqueous	86.32- 200 µg/mL	Falodun *et al*., (2014)

	35218), *Pseudomonas aeruginosa* (ATCC 27853) *and Mycobacterium intracellulare*				
33	*K. pneumonia, E. coli, P. mirabilis*	DDM, Broth Micro-dilution	Methanol	ZOI;21 and 17 mm MIC- 256 to > 512 µg/ mL	Oyedemi *et al*., (2018)
34	*Aeromonas hydrophila* ATCC 35654 *and Pseudomonas aeruginosa* ATCC 15442,	ADilM	Methanol	ZOI -11 to 40 mm	Olajuyigbe *et al*., (2020)
35	*Mycobacterium spp, Vibrio cholera, Campylobacter jejuni, Helicobacter pylori, Salmonella typhi or paratyphi, Shigella flexneri, Clostridium difficile, and Shiga toxin-producing Escherichia coli, Bacillus subtilis and Staphylococcus aureu*	Various	Various	Various	Ugboko *et al*., (2020)

ADilM-Agar dilution method, DDM -disc-diffusion, MD- micro-dilution, BDM-broth dilution methods.
ADM-agar diffusion method, DD-Disc diffusion method, MIC-Minimum inhibitory concentration.
MBC- Minimum bactericidal concentration, ZOI- Zone of inhibition, AWD-Agar well diffusion method.

3.5. Assays analyzed

Many experimental approaches were used in the evaluation of antibacterial activity. For techniques such as agar well method, agar dilution and disc diffusion assay methods, were recorded in diameter (mm) of the zone of inhibition. While broth microdilution methods to determine MIC and MBC, based on either colour change for colorimetric assays or bacterial growth for non-colorimetric methods and expressed in µg/mL, µl/mL, or mg/mL.

The lowest concentration of *Strychnos spinosa Lam* that inhibited growth of bacteria was 0.04 mg/mL as reported by Isa *et al.* (2014). On the other hand, the highest activity of *Carpolobia lutea* (>1000 mg/m) was reported by Nwidu *et al.* (2012). Similarly, the bacterial growth inhibition, based on values of diameter of zone of inhibition (ZoI) of the respective plant extracts, varied among the extracts and microorganisms. The widest inhibition (30.60 mm) was reported by Abiala *et al.* (2016) which showed the inhibitory zones of methanol extract of *Mangifera indica* (leaves and stem) against *Escherichia coli, Salmonella enteritidis, Pseudomonas aeruginosa and Klebsiella oxytoca*.

3.6. Bias analysis

Proper appraisal was made on all the studies included in the study to make sure they adhere to Good Practice for Microbiology Laboratory and checked the validity of methodological and reporting qualities such as established or modified methods, units and equipment.

This systematic review was aimed to highlight the antibacterial activities of Nigerian medicinal plants. The medicinal plants extracts and their bioactive compounds were assessed for antibacterial potentials as they are commonly used in Nigeria as remedy and cure for diseases. In this systematic review, we analyzed data of Nigerian medicinal plants with antibacterial for a period of 20 years (2000-2020). A total of 35 articles were included in this systematic review, and 97 different plants species exhibited good antibacterial activity over wide range of Gram-negative and Gram-positive bacteria by either inhibiting or killing. These studies revealed the use of various antibacterial assay methods; agar well diffusion method, broth dilution methods and agar dilution method were the most commonly employed methods.

Strikingly, silver nanoparticle from plant; *Acalypha wilkesiana* was investigated against *Escherichia coli and* Staphylococcus *aureus* and demonstrated excellent antibacterial activity and justify that silver nanoparticle can be synthesized from extracts of medicinal plants to enhance activity (Dada *et al.*, 2019). Conversely, Eleyinmi *et al.* (2007) reported no activity of *Gongronema latifolium* against some of the isolates*; Enterococcus faecalis, Yersinia enterolytica, Enterobacter aerogenes, Bacillus cereus* and *Enterobacter agglomerans* but methanolic extracts of *Gongronema latifolium* exhibit activity against some important pathogens such as *S. aureus, Listeria monocytogenes* and *P. aeruginosa*. This explains the activity of different plants extracts in the study and it could be deduced that the activity is organism specific. This review found that *S. aureus, Escherichia coli* and *Pseudomonas aeruginosa* were the common bacteria tested, with only 5 studies did not work on any of them for the antibacterial effect of plants (Christiana *et al.*, 2009;Ugoh *et al.*, 2014; Akindele *et al.*, 2015; Oramadike *et al.*, 2017; Ugboko *et al.*, 2020).

Akinyemi *et al.* (2005) reported six Nigerian medicinal plants *Terminalia avicennioides, Phylantus discoideus, Bridella ferruginea, Ageratum conyzoides,*

Ocimum gratissimum and *Acalypha wilkesiana* against Methicillin resistant *Staphylococcus aureus* (MRSA) and found that both water and ethanol extracts of *T. avicennioides, P. discoideus, O. gratissimum,* and *A. wilkesiana* were effective on MRSA but not on *B. ferruginea* and *A. conyzoides*. These plants extract exhibit bacteriostatic activity.

Isa *et al.* (2014) tested *Strychnos spinosa Lam*. against *Bacillius cereus* (ATCC 14579), *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), and *Escherichia coli* (ATCC 25922); and all the extracts showed moderate activity with MICs ranging from 0.16 to 0.63 mg/L.

Abiala *et al.* (2016) tested methanol extract of *Mangifera indica* for antibacterial effects and the results demonstrated higher efficacy against multi-drug resistant *P. aeruginosa* than *S. enteritidis*. Ogbole *et al.* (2020) assessed fresh roots of *Calliandra portoricensis* on *Staphylococcus aureus* and the results reveled that peptide extract (IC50 = 0.69 ± 0.33 µg/mL) is more effective than the crude methanol extract (IC_{50} = 13.27 ± 0.00 µg/mL), while the crude methanol extract was more active on *Escherichia coli* than the peptide extract. Antibacterial activity of medicinal plants against *Vibro* spp was reported by Oramadike and Ogunbanwo, (2017). Various studies tested medicinal plants against *Bacillus cereus* (Akindele *et al.,* 2015; Nwodo *et al.,* 2011; Enemchukwu *et al.,* 2019) and other *Bacillus* species *(*Aladesanmi *et al.,* 2007; Akinsulire *et al.,* 2007; Sonibare *et al.,* 2009; Akinyele *et al.,* 2011; Nwidu *et al.,* 2012; Okoye *et al.,* 2012; Atolani *et al.,* 2020). These findings demonstrated anti-infective activity from high to moderate efficacy on pathogens of public health importance. Sonibare *et al.* (2009) demonstrated that *Cola acuminate* extract had no antibacterial activity against *Staphylococcus aureus* but it was effective against *Klebsiella pneumoniae*. Antibacterial activity of different plants was reported against wide range of Gram-positive and Gram-negative bacteria. These could be due to the presence of bioactive compounds in different parts of the plants.

4. Conclusion

This study showed that plants extracts used in Nigeria contained bioactive compounds that have potential antibacterial effects. In this review, most of the plants extracts showed broad spectrum activities against both Gram-negative and Gram-positive bacteria. Collections of medicinal plants of different plants families could be explore into discovery and development of compounds with antibacterial potentials against bacterial pathogens of public health importance. It is evident that the plants extracts could be optimized and deployed into modern medicine. This study summarizes the medicinal plants with antibacterial activities in Nigeria in the last 20 years and could serve as plants bank for future reference and for investigation to determine their efficacy as alternative to conventional antibiotics in treatment of bacterial infections. However, this systematic review is limited to only studies from 2000 to 2020, which might have missed important plants with excellent antibacterial activities.

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