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REVIEW ON ANTI-MICROBIAL PROPERTIES OF MEDICINAL PLANTS IN ETHIOPIA

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ABSTRACT: Infectious diseases are one of the major problems in the world. After the discovery of penicillin, many classes of the antimicrobial agent were introduced and most infectious diseases were brought under control. However, the increased use of these antimicrobial agents in clinical practice was soon followed by the emergence of antibiotic resistance. Because of multiple drug resistance and adverse effects of these antimicrobial agents on the host, there is the need to discover and develop natural antimicrobials that are safe and with better therapeutic effects. Medicinal plants have been used as an alternative source of medicine to treat infectious diseases due to their rich antimicrobial activity. These Plants contain bioactive compounds such as quinines, phytoalexins, phenols, alkaloids, flavonoids, terpenoids, steroids, tannins, glucosinolates and pathogenesis-related proteins, which exert antimicrobial activity by different mechanisms, such as destruction of the cell membrane, inhibition of protein synthesis and enzymes impregnated on the cell membrane. There are various extracts of medicinal plants with minimum inhibitory concentration against pathogenic microorganisms that are safe and effective as therapeutic agents. In this review, data on 91 medicinal plants from Ethiopia distributed in 49 families against 27 species of bacteria, 11 species of fungi were assessed, to provide information, and opportunity for further analysis of medicinal plant extracts for the development of effective antimicrobial agents.

INTRODUCTION: In spite of the tremendous progress in drug development, infectious diseases remain a major public health problem, and the impact of infectious diseases is serious in sub-Saharan African countries [1]. There is a great concern about antimicrobials currently in use for the treatment of infectious diseases because of increasing costs of the synthetic anti-microbials, side effects, and rapidly emerging resistance of pathogenic microorganisms to these antimicrobials.

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Plant-derived anti-microbials offer a great therapeutic benefit and are less expensive treatment options [2, 5]. Natural products such as medicinal plants represent a major reservoir of novel compounds for new drug identification. Several medicinal plant-derived bioactive compounds are used for the management of a variety of chronic disorders and infectious diseases.

The healing effects of medicinal plant extracts had long been discovered and widely used before pathogenic microbes recognized as a causative agent of infectious diseases [2, 3]. Bioactive compounds derived from these plants have continued to play crucial roles in the management of many human ailments since ancient times [3]. These bioactive substances, which are non-

nutritive, have been found to protect the plant from pathogenic microbes. It is, therefore, crucial to screen a variety of medicinal plants for their bioactive substances as the basis for further research into the discovery of new antimicrobials. With technological advances in areas of analytics, metabolomics, biotechnology, proteomics, and genomics it is now possible to isolate and purify numerous bioactive substances from different medicinal plants and used as essential synthetically improved therapeutic agents. Among these bioactive substances are alkaloids, terpenoids, glycosides, flavonoids, phenols, and tannins, which are important raw materials for the production of life- saving antimicrobials [4 - 6].

Today, more than 50% of drugs released into the world market, and a great number of novel pharmaceutical agents derived from natural products and their derivatives that used in herbal medicine [3, 4, 7, 8]. Of these drugs, 25% derived from higher plants. Due to this reason, today pharmaceutical companies pay more attention to research on safer bioactive substances isolated from medicinal plants, which have elsewhere been used in traditional folklore medicine with acceptable safety for the development of new drugs with a novel mechanism of action [5, 6].

Globally, between 250,000 to 500,000 species of plants are known of which 35,000 to 50,000 are medicinal plant species. Out of these, 4000 and 6000 have been introduced into the pharmaceutical markets, but only about one hundred medicinal plant species have been used as a source of a drug as shown in **Table 1** [7].

TABLE 1: MOST COMMONLY CLINICAL USED PLANTS DERIVED DRUGS

Drug name	Bioactive compound	Name of the plant [family]	Therapeutic use
Atropine	Alkaloid	*Atropa belladonna* [solanaceae]	Abdominal colics, bradyarrhythmias, mydriatics
Artemisinin	Sesquiterpene	*Artemisia annua* [compositae]	Anti-malaria agent
Apomorphine	Alkaloid	*Papaver somniferum* [papaveraceae]	Parkinson's disease
Arecoline	Alkaloids	*Areca calechu* [Polmoae]	Parasympathomimetic
Cannabidiol, Dronabinol	Terpenoids	*Cannabis sativa* [cannabaceae]	Anti-pain, glaucoma
Capsaicin	alkaloid	*Capsicum annuum* [solanaceae]	Anti pain
Caffeine	Alkaloid	*Camellia sinensis* [rubiaceae]	CNS stimulant.
Colchicine	Alkaloid	*colchicum autumnale* [iridaceae]	Anti-gout
Camphor	terpenoide	*Cinnamomum camphora* [Lauraceae]	Rubefacient
Camptothecin	Alkaloid	*Camptotheca acuminate* [nyssaceae]	Anti-cancer
Cocaine	Alkaloid	*Erytroxylum coca* [erythroxylaceae]	Local anesthetic.
Coumarin	Coumarin glycosides	*Dipteryx odorata* [leguminosae]	Anti-coagulants
Crofelemer	condensed tannins	*Croton lechleri* [euphorbiaceae]	Anti diarhea
Danthron	anthraquinon	Cassia species	Laxative
Digitoxin, digoxin, digitalin	Steroidal-glycoside	*Digitalis purpurea* [plantaginaceae]	Heart failure, atrial flutter, atrial fibrillation, paroxysmal atrial tachycardia
Demecolcine		*Colchicum autumnale* [iridaceae]	Anti-tumour agent
Elliptinium		*Bleekeria vitensis* [Apocynaceae]	Anti-tumour agent
Emetine	Alkaloid	*Hedera helix* [araliaceae)] *Cephaelis ipecacuanha* [rubiaceae]	Anti-amebic , Emesis
Ephedrine	Alkaloid	*Ephedra sinica* [ephedraceae]	Sympathomimetic
Etoposide	Lignans	*Podophyllum peltatum* [berberidaceae]	germ-cell testicular tumours Small-cell lung carcinoma
Galanthamine	Alkaloide	*Leucojum oestivum* [Amoryllidoceoe]	Anti-Alzheimer's disease.
Glycyrrhizin	Triterpenoid	*Glycyrrhiza glabra* [Leguminosae]	Sweetener,
Gossypol	Sesquiterpen	Cotton plant [malvaceae]	Male contraceptive
homoharringtonine	cephalotaxine alkaloid	*Cephalotaxus harringtonia* [Cephalotaxaceae]	Anti-cancer
Hyoscyamine	Alkaloid	*Hyoscyamus niger*	Peptic ulcers and GIT disorder

		[solanaceae]	Caused by spasm
Irinotecan	Alkaloid	*Camptotheca acuminate* [nyssaceae]	Colorectal cancer
Lanatosides A, B	cardiac glycoside	*Digitalis lanata* [Scrophulariaceae]	Cardiotonic
L-dopa	Alkaloid	*Mucuna pruriens* [fabaceae]	Anti-parkinson
Morphine, codeine	Alkaloid	*Papaver Somniferum* [papaveraceae]	Narcotic analgesics
Noscapine			
mycophenolate			immunosuppression
galegine	Alkaloid	*Galega officinalis* [fabaceae]	Type 2 diabetes mellitus
Nicotine	Alkaloid	*Nicotiana tabacum* [solanaceae]	Insecticide
Ouabain	Steroid glycosides	*Strophanthus gratus* [apocynaceae]	Heart failure
Paclitaxel	Diterpenoid	*Taxus brevifolia* [taxaceae]	Ovarian cancer and metastatic Breast cancer
Papavarine	Alkaloid	*Papaver somniferum* [papaveraceae]	Smooth muscle relaxant
Physostigmine	Alkaloid	*Physostigma venenosum* [leguminosae]	Increases intestinal and bladder motility, Glaucoma, esotropia
Podophyllotoxin	Terpenoids	*Podophyllum peltatum* [berberidaceae]	Wart, anti-cancer
Pilocarpine	Alkaloid	*Pilocarpus jaborandi* [rutaceae]	Glaucoma, xerostomia
Picrotoxin	Lactone	*Anamirta cocculus* [menispermaceae]	Analeptic
Psoralen	Furanocoumarin glycosides	*Psoralea corylifolia* [leguminosae]	
Quinidin	Alkaloid	*Cinchona succirubra* [rubiaceae]	Anti-arrhythmic
Quinine	Alkaloid	*Cinchona ledgeriana* [rubiaceae]	Malaria
Reserpine	Alkaloid	*Rauvolfia serpentine* [apocynaceae]	Anti-hypertensive
Rutin	Flavonol glycosides	*Fagopyrum esculentum* [polygonaceae]	Reduce capillary bleeding
Scopolamine	Alkaloid	*Datura stramonium* [solanaceae]	Motion sickness, antispasmodic Preanaesthetic
Salicin *(aspirin)*	Phenolic glycosides	*Salix alba* [salicaceae]	Anti Pain anti inflammatory, and anti-clotting agent
Strychnine	Alkaloid	*Strychnos nux-vomica* [loganiaceae]	Cns stimulant
Tiotropium	Alkaloid	*Atropa belladonna* [solanaceae]	Anti-asthma
Teniposide	polyphenol	*Podophyllum peltatum* [berberidaceae]	Anti-cancer
Theophylline	Alkaloids	*Camellia sinensis* [theaceae]	Bronchodilator
Tetrahydrocannabinl	Terpinoid	*Cannabis sativa* [cannabaceae]	Anti-emetic, decreases occular tension
Tubocurarine	Alkaloid	*Strychnos castelnaei* [loganiaceae]	Skeletal muscles relaxant
Vinblastine vincristine	Alkaloid	*Catharanthus roseus* [apocynaceae]	Anti-cancer
Yohimbine	Alkaloid	*Pausinystalia yohimbe* [rubiaceae]	Aphrodisiac

Ethiopia, a tropical country known for its rich flora and fauna biodiversity, is home to more than 7,000 species of higher plants, out of which 12% are indigenous to the country, making it one of the most diverse floristic regions in the world [7, 8]. Being a land of diverse climatic and edaphic potentials, more than 800 species of medicinal plants are distributed in different parts of the country. The knowledge and the therapeutic use of these medicinal plants have played a significant role, as an alternative source of medicinal drugs to treat a variety of human and livestock diseases, in supporting the fragile health care system of the country [8, 9].

There are written and oral pharmacopeias about the therapeutic use of medicinal plants in the country as the therapeutic uses of plant-based remedies have been practiced for a very long time. At present, more than 80% of the human population in Ethiopia and 90% of livestock population depend on traditional remedies that mainly (95%) involves the therapeutic use of medicinal plants [10]. The demand for medicinal plants increase in the future due to the trust the communities have in the medical values of the medicinal plants, affordability, safety of the plants and the readily available traditional healers in the communities in contrast to the modern orthodox healthcare systems

which are expensive, with few trained health care professionals, and limited number of healthcare facilities [9, 10]. The scientific researches on medicinal plants in Ethiopia have given evidence-based alternative medicines, which has formed the basis of the herbal drug industry and isolation of drug targets in the pharmaceutical industry [11]. In the last few years, several medicinal plants have been evaluated in Ethiopia for their antimicrobial activities against different pathogenic micro-organisms [12-52]. Many of them were found to be effective against resistant microbial strains [13, 14, 39, 40, 52]. To the best of our knowledge, there are no reviews on medicinal plants with antimicrobial effects in Ethiopia. This review provides up-to-date information on medicinal plants, with highlights on the need for experimental research that will analyze the extracts of these plants for the future development of effective antimicrobial agents.

Methodology:

Systematic Search: A systematic literature review was conducted on pre-reviewed papers on herbal medicines and their phytochemical antimicrobial activity shown on the scientific database; Medline, Pub Med, Science Direct, Springer Link, Embase, Hinari and Google Scholar. To identify the recent studies not published, we also searched abstracts presented at conferences.

The search was restricted to studies with abstracts published in English. Literature Database search was performed using the following keywords; Ethiopia / Ethiopian plants / Ethiopian medicinal plants/Ethiopian anti-microbial plants / Traditional knowledge / Traditional Medicine / Traditional medicinal plants, Medicinal Plants / Medicinal herbs, Plants / Herbal / Medicine / Remedies, Folk Medicine / Folk remedies / Home remedies / Herbal remedies, Ethnobotanical. However, the search excluded the papers on the antimicrobial activity of derivatives from bioactive compounds.

Collection of Studies and Abstraction of Data: The author assessed studies for eligibility and extracted details of the medicinal plants from each article by using a structured abstraction forms, which contains the botanical and local name, the plant part, the solvent used for extraction, activity against microorganism and their minimum inhibitory concentration.

Selection of Articles: A total of 243 articles were obtained from the search. After accounting for duplicates, 128 articles were excluded leaving 115 articles. Of these, 42 articles were further excluded because they did not satisfy the inclusion criteria following review of their abstracts and were therefore considered irrelevant. Six additional articles were however selected by searching the references of the retrieved articles. A total of 79 articles were reviewed in detail but 39 were further excluded after the detailed review because they did not contain the required information. Eventually, only 40 articles were reviewed for this paper.

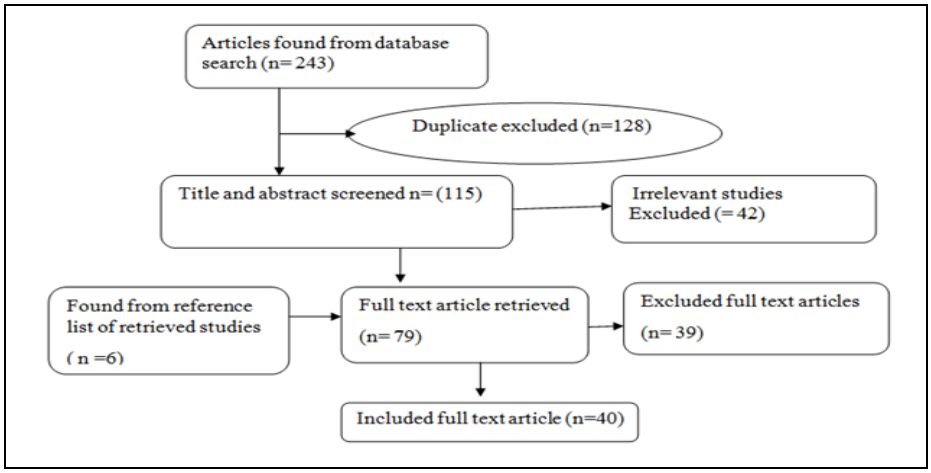

FIG. 1: FLOW DIAGRAM OF PUBLISHED ARTICLE SEARCH RESULTS

DISCUSSION:

Historical Development of Medicinal Plants: The use of medicinal plants as drug dated back to prehistoric times. The oldest known medical record is a Sumerian clay tablet that mentioned the use of plants about the 3rd millennium BC. In the time of

the Egyptian civilization, the therapeutic use of medicinal plants was documented in the Papyrus Ebers in 1500 BC [53]. In China Pun-Tsao, a pharmacopeia that was written around 1600, which list thousands of medicinal plants that helped to the works of Shen-Nung, China's emperor and father of Chinese medicine lived over 4500 years ago [54]. Hippocrates (460 - 377 BC), the father of medicine, described 400 medicinal plants. Theophrastus (371-286 BC) who wrote the book Historia Plantarum that mentioned more than 500 medicinal plants (55). Dioscorides (78 AD), a Roman physician wrote: "De Materia Medica" which described more than 600 medicinal plants [56].

Claudius Galen (135 - 201 AD) was a pharmacist in Rome who wrote about 400 works covering all aspects of medicine. He prepares drugs in a complex mixture of more than 30 ingredients called ''galenicals''. In the fourth century, after the fall of the Roman Empire, the cultural center shifted to the Byzantine Empire, and then to the Arab world [57]. Ebne Sina, known in the West as Avicenna (980-1037) a famous scientific figure of the Arabian world who wrote the Canon Medicinae compendium, which describes the therapeutic use of 750 medicines [58]. Drugs used before 1800 were prepared with water plant extracts as infusions, tinctures, decoctions, but their chemical structure was unknown. In the nineteenth century, with the emergence of organic chemistry and chemical analysis the isolation of bioactive compounds from plant extract was opened. The first discovery was the isolation of morphine from opium in 1806 by Serturner [57]. Between 1820 and 1850, several compounds were isolated and evaluated for medicinal applications. In Paris, Pierre Joseph Pelletier and his collogues isolated emetine from ipecacuanha root and strychnine from the seed of *Strychnos nux vomica*, quinine sulfate from cinchona bark [57, 58]. Chinese researchers identified Artemisinins in 1972 from *Artemisia annua* L [59].

Determination of Antimicrobial Efficacy of Medicinal Plant Extracts: Anti-microbial susceptibility testing methods are vital tools used to determine the antimicrobial efficacy of medicinal plant extracts against different microorganisms through the determination of the Minimum Inhibitory Concentration (MIC) and minimum bactericidal concentration (MBC) and comparing with available antimicrobial agents as control. Antimicrobial susceptibility testing methods can be categorized into dilution (broth microdilution, broth macro dilution) methods and diffusion (disc diffusion, agar diffusion) methods [60].

Diffusion Methods: These are common and simple methods for determining the antibacterial activity of medicinal plant extracts against microorganisms. In the agar diffusion method, it involves the use of wells cut into the agar plates that have been streaked with a standardized inoculum of bacteria. A known concentration or volume of the extracts is poured into the well and allowed to diffuse out to inhibit bacterial growth after incubating inappropriate atmosphere. The zone of inhibition (in mm) around the well is then measured and estimated as the antibacterial activity of the extracts when compared with the zone of inhibition of a known antibiotic or a standard. The agar diffusion method was replaced by paper discs impregnated with extracts or antibiotics (disc diffusion method), but the lack of standardization of this method resulted in unreliable and non-reproducible results [60, 61]. Therefore, disc diffusion method is not a suitable method for determining the antibacterial activity of medicinal plant extracts.

Dilution Methods: Dilution methods are assays used to determine the minimum concentration of antimicrobial agents or extracts that result in either killing (minimum bactericidal concentration, MBC) or inhibition (minimum inhibitory concentration, MIC) of the growth of microorganisms. Dilution tests can be broth microdilution, broth macro dilution (tube dilution), or agar dilution methods. The final volume of the test defines whether the method is macro dilution, *i.e.* if done using 2 ml tube or microdilution when performed using ≤500 µl per well. In both the agar and broth dilution techniques, the lowest amount of the antimicrobial agent or extract that inhibits the visible growth of microorganisms under known conditions is termed the MIC. The advantages of dilution over diffusion methods include increased sensitivity for smaller extracts, quantitative analysis, and differentiation of bacteriostatic and bactericidal effects of the extracts or anti-microbial agents. Dilution methods considered the reference methods for *in-vitro* susceptibility testing and used to evaluate the performance of other techniques [60-62].

TABLE 2: ETHIOPIAN MEDICINAL PLANT EXTRACTS WITH THEIR MINIMUM INHIBITORY CONCENTRATION (MIC) AGAINST DIFFERENT MICROORGANISMS

Botanical name [Family]	local name (Parts used)	Extract	MIC	Activity Against microorganism	Ref
Curcuma longa [Zingiberaceae]	ERD (Rhizome)	Oil	>25 mg/ml 25 mg/ml	*E. coli* *S. aureus, P. aeruginosa*	[12]
Aframomum corrorima [Zingiberaceae]	Kororima (Fruit)	Ac	>25 mg/ml 25 mg/ml	*S. aureus, E. coli,* *P. aeruginosa*	
Asparagus africanus [Asparagaceae]	Yefurded (Leaf)	ETOH	.512 mg/ml	*E. faecalis*	[13]
Guizoti aschimperi [Asteraceae]	Mocho (Leaf)	ETOH	.128 mg/ml .512 mg/ml	*S. aureus, E. Faecalis* *C. albicans*	
Lippia adoensis [Verbenaceae]	Kessie (Leaf)	ETOH	.256 mg/ml .512 mg/ml	*S. aureus, E. faecalis* *C. albicans*	
Premna schimperi [Lamiaceae]	Teqoqi (Leaf)	ETOH	.512 mg/ml	*S. aureus, E. faecalis*	
Rhamnus prinoides [Rhamnaceae]	Gesho (Leaf)	MEOH	2.03 mg/ml 4.06 mg/ml 8.13 mg/ml	*S. aureus* *S. pyogen, S. typhi* *P. aeruginosa, E. coli,*	[14]
Ranunculus multifidus [Ranunculaceae]	Gubducaffee (Leaf)	MEOH $CHCl_3$	16.5 mg/ml	*P. aeruginosa, S. typhi,* *E. coli, S. aureus*	[15]
Leucasmartinicensis [Lamiaceae]	Mata burusa (Leaf)	MEOH $CHCl_3$	16.5 mg/ml 5.6 mg/ml	*S. typhi, E. coli,* *P. aeruginosa* *S. aureus*	
Kosteletzkya begonifolia [Malvaceae]	Ingiccee (Leaf)	MeOH $CHCl_3$	16.5 mg/ml 5.6 mg/ml	*S. typhi , P. aeruginosa* *S. aureus*	
Achyranthes Aspera [Amaranthaceae]	Elenj/Qaytelenj (Leaf)	MEOH	15.6 mg/ml 7.81 mg/ml	*S.aureus, P. aeuruginosa, E. coli, P. vulgaris* *S. pyogens*	[16]
Bruceaanti dysenterica [Simaroubaceae]	Waginos/Yedega Abalo (Root)	MEOH	15.6 mg/ml 7.81 mg/ml 62.5 mg/ml	*S. aureus, E. coli* *S. pyogens* *P. aeuruginosa*	
Phytolaca Dodecandra [Phytolaccaceae]	Indodi (Root)	MEOH	1.96 mg/ml 15.6 mg/ml	*S. pyogens* *P. aeuruginosa*	
Solanum incanum [Solanaceae]	Inbuay (Leaf)	MEOH	31.3 mg/ml 62.5 mg/ml 125 mg/ml	*S. aureus* *S. pyogens* *P. aeuruginosa*	
Rumex nepalensis [Polygonaceae]	Tult (Leaf)	Ac	3.13 mg/ml 6.26 mg/ml	*E. coli, S. typhi* *S. aureus*	[17]
Phytolac adodecandra [Phytolaccaceae]	Indodi (Fruits)	Ac	12.5 mg/ml 25.1 mg/ml	*E. coli, S. typhi* *S. aureus , P. aeruginosa*	
Grewia ferruginea [Tiliaceae]	Lenkoata (Bark)	Ac	3.13 mg/ml 25.1 mg/ml 12.5 mg/ml	*E. coli* *S. aureus, P. aeruginosa* *S. typhi*	
Aloe vera [Xanthorrhaeceae]	ERET (Aerial part)	MEOH	.098 mg/ml .02 mg/ml .42 mg/ml .10 mg/ml	*S. typhi, S. agalactia* *E. coli* *S. aureus* *S. agalactia*	[18]
Zingiber officinale [Zingiberaceae]	Jinjible (Rhizome)	MEOH	.093 mg/ml .05 mg/ml .16 mg/ml .19 mg/ml	*S. aureus* *S. typhi* *E. coli* *S. agalactia*	
Allium ursinium [Amaryllidaceae]	Yejibshinkurt (Bulb)	MEOH	250 mg/ml	*M. tuberculosis*	[19]
Pterolobium stellatum [Fabaceae]	Kentefa (Leaf)	MEOH	250 mg/ml	*M. tuberculosis*	
Dodonaea anguistifolia [Sapindaceae]	Kitkita (Leaf)	MEOH	12.5 mg/ml	*M. tuberculosis*	
Calpurnia aurea [Fabaceae]	Digita (Leaf)	MEOH	.063 mg/ml	*S. aureus, P. aeruginosa, E. coli.*	[20]

Croton macrostachyus [Euphorbiaceae]	Bissana (Leaf)	MEOH $CHCl_3$	7.5 mg/ml 3.75 mg/ml	*E. coli* *S. aureus*	[21]
Lippia adoensis [Verbenaceae]	Kesse / Koseret (Leaf)	MEOH $CHCl_3$	2.5 mg/ml 10 mg/ml	*S. aueres, P. aeroginosa, S. typhi* *E. coli*	[22]
Acokanthera schimperi [Apocynaceae]	Merztekil (Leaf)	MEOH	7.81 mg/ml 15.6 mg/ml	*S. pyogens* *E. coli, P. aeuruginosa P. vulgaris, S. aureus*	[16]
Brucea Antidysenterica [Simaroubaceae]	Waginos/Yedega Abalo (Root)	MEOH	15.6 mg/ml 7.8 mg/ml 62.5 mg/ml	*S. aureus* *S. pyogens* *P. aeuruginosa*	
Phytolacca Dodecandra [Phytolaccaceae]	Endodi (Root)	MEOH	1.95 mg/ml 15.6 mg/ml	*S. pyogens* *P. aeuruginosa*	
Solanum incanum [Solanaceae]	Imbuay (Leaf)	MEOH	31.3 mg/ml 62.5 mg/ml 125 mg/ml	*S. aureus* *S. pyogens* *P. aeuruginosa*	
Verbena officinalis [Verbenaceae]	Atuch (Leaf)	MEOH	31.3 mg/ml 7.81 mg/ml 250 mg/ml	*S. aureus* *S. pneumoniae* *E. coli*	[22]
Hypericum revolutum [Hypericaceae]	Amija (Leaf)	MEOH	125mg/ml 250 mg/ml	*Shigella* *P. aeuroginosa*	[23]
Peterollobium stellatum	Kentefa (Roots)	MEOH	250 mg/ml 125 mg/ml	*S. typhi, S. aureus* *E. coli*	
Thymus serrulatus [Lamiaceae]	Tosign (Leaf)	ETOH	4 mg/ml 2 mg/ml	*B. cereus, S. aureus* *E. coli*	[24]
Terminalia brownii [Combretaceae]	Weba (Leaf)	ETOH	4 mg/ml	*S. typhi*	
Oliniaro chetiana [Penaeaceae]	Tife (Leaf)	MEOH	5 mg/ml 2.5 mg/ml 10 mg/ml	*S. aureus* *P. aeruginosa* *E. coli, C. albicans*	[25]
Calpurinia aurea [Fabaceae]	Digita (Leaf)	MEOH	25 mg/ml 100 mg/ml	*S. aureus* *S. dysgalactiae, D. congolensis*	[26]
Croton macrostachyus [Euphorbiaceae]	Bissana (Leaf)	MEOH	12.5 mg/ml 25 mg/ml	*S. aureus* *S. dysgalactiae, D. congolensis*	
Nicotiana tabacum [Solanaceae]	Zeka-keba (Leaf)	MEOH	25 mg/ml 50 mg/ml	*S. aureus*, S. *dysgalactiae* *S. agalactia, D. congolensis*	
Achyranthes aspera [Asparagaceae]	Leaf (Mechalo)	MEOH	6.25 mg/ml 50 mg/ml	*E. coli, S. hycus, S. aureus* *K. pneumonae, S. intermedi*	
Salvia schimperi [Lamiaceae]	Leaf (Yahiya Joro)	MEOH	31.3mg/ml 62.5mg/ml 125 mg/ml	*S. typhi*, S.aureus *S. paratyphi, Shigella* *E. coli, P. aeuroginosa*	[38]
Foenculum vulgare [Apiaceae]	Leaf (Insilal)	Aqueous extract	.01mg/l 0.1 mg/ml	*P. gallinarum, S. agalactae* *M. haemolyticum*	[39]
Lyonitesocymifolia [Lamiaceae]	Aerial part (Raskimir)	MEOH	0.1 mg/ml 1 mg/ml	*P. gallinarum* *M. haemolyticum, S. typhi*	
Jasminum abysinicum [Oleaceae]	Leaf (Tembelel)	Aqueous extract	0.1 mg/ml 0.01 mg/ml	*P. gallinarum, S. gallinarum, M. haemolyticum, S. agalactae* *S. typhimurium*	
Myrsine Africana [Myrsinaceae]	Leaf (Kechemo)	MEOH	0.1 mg/ml 0.01 mg/ml	*P. gallinarum, S. agalactae* *S. aureus*	
Moring astenopetala [Moringaceae]	Shiferaw (Seeds)	MEOH	1.25 mg/ml 10 mg/ml 5 mg/m	*S. aureus* *E. coli* *S. boydii*	[40]
Oliniaro chetiana [Oliniaceae]	TIFE (Leaf)	MEOH	2.5 g/ml 5 g/ml 10 g/ml	*P. aeuroginosac, T. mentagrophytes* *S. aureus* *E. coli, Candida albica*	[26]
Combretum molle [Combretaceae]	Yekolaavalo (Stem bark)	MEOH	0.1 mgml 0.2 mg/ml 0.05 mg/ml 0.8 mg/ml	*E. coli, V. cholerae* *S. typhi, B. pumilus* Shigella dysentery C.albicans	[41]

			1.5 mg/ml	*P. notatum, P. citrinum*	
Albizia gummifera [Fabaceae]	Seed	Butanol	.125 mg/ml	*N. gonorrhea*	[42]
Achyranthes aspera	Leaf	MEOH	12.3 mg/ml	*E. coli, P. aeruginosa, S. aureus*	[43]
[Asparagaceae]	(Mechalo)		6.26 mg/ml	S. boydii, S. typhi	
Aloe elegans	Leaf	ETOH	1.56 mg/ml	*E. coli, S. aureus*	[44]
[Aloeacea]			6.25 mg/ml	*P. aeruginosa, C. albicans*	
			12.5 mg/ml	*K. pneumonia, S. typhi*	
Lepidium sativum	Seed	ETOH	6.5 mg/ml	*E. coli*	[45]
[Brassicaceae]	(Fetto)		12.5 mg/ml	*P. aeruginosa,*	
Ocimum lamiifolium	Leaf	Aqueous	10 mg/ml	*E. coli, P. aeruginosa, S. aureus,*	[46]
[lamiaceae]	(Damakesse)	extract		*S. boydii*	
Taverniera abyssinica	Root	MEOH	12.5 mg/ml	*S. aureus, E. faecalis, A. flavus*	[47]
[Fabaceae]	(Dingetegna)		6.5 mg/ml	*C. albicans*	
Rosmarinus officinalis	Leaf	MEOH	15.8 mg/ml	*S. epidermidis*	[48]
[Lamiaceae]	(Sigametibesha)		31.3 mg/ml	*S. pyogenes, E. coli, S. typhi, S. aureus*	
Eucalyptus globules	Leaf	MEOH	15.8 mg/m	*S. epidermidis, S. aureus,*	
[Myrtaceae]	(Nechbahirzaf)		20.6 mg/ml	*S. pyogene*, Shigella, *E.coli*	
Vernonia Auriculifera	Leaf	$CHCl_3$	200 mg/ml	*S. aureus*	
[Compositae]	(Grawa)	MEOH			[49]
Verbena officinalis	Leaf	MEOH	7.8 mg/ml	*S. boydii*	[24]
[Verbenaceae]	(Atuch)		15.8 mg/ml	*S. aureus*	
			3.9 mg/ml	*S. pneumonia*	
			62.5 mg/ml	MRSA	
Punica Granatum	Leaf	MEOH	6.25 mg/ml	*S. aureus, S. pneumonia*, Shigella	[50]
[Punicaceae]	(Yeromanzaf)		12.5 mg/ml	MRSA, *E. coli, C. albican*	
Plectranthus caninus	Aerial part	Essential oil	0.03 mg/ml	*E. coli, S. typhi, Shigella, S. aureus, V. cholera, B. pumilus*	[51]
[Lamiaceae]	(Endifdif)				
Aloe sinana	Latex	MEOH	5 µg/ml	*Shigella boydii*	[52]
[Xanthorrhaeceae]	(Rate)		10 µg/ml	*E. coli, V. cholera, S. typhi*	
			25 µg/ml	*S. aureus, S. enterica*	
			0.8 mg/ml	*A. niger, C. albica*	
			1.5 mg/ml	*P. funiculosum, P. notatum*	

Abbreviation: Methanol: MEOH, ethanol: ETOH, $CHCl_3$: Chloroform, PE: Petroleum ether, Ac: Acetone Methicillin resistant *Staphylococcus aureus*, MRSA

TABLE 3: MEDICINAL PLANT EXTRACTS WITH THEIR CONCENTRATION ACTIVE AGAINST DIFFERENT MICRO ORGANISM

Botanical name [Family]	local name (Parts used)	Extract	Extract concentration	Activity against microorganism	Ref
Clematis simensis	Azohareg	MEOH	5 mg/ml	*S. aureus, E. coli, S. typhi, P. aeruginosa*	[28]
[Ranunculacae]	(Leaf)				
		PE	5 mg/ml	*E. coli, S. typhi*	
Ruta graveolens	Tena Adam	$CHCl_3$	5 mg/ml	*S. aureus, B. subtilis,*	[29]
[rutaceae]	(Leaf)	MEOH		*E. coli,* P. aeruginosa	
Syzygeum guineense [Myrtaceae]	Dokma (Leaf)	MEOH	.25 mg/ml	*N. gonorrhea, E.coli*	[30]
Laggerato mentosa	Keskeso	MEOH	2 mg/ml	*N. gonorrhea, S.*	
[Compositae]	(Areal part)			*pyogenous, S. pneumonia*	
Artemisia abyssinica	Chikugn	ETOH/	2 mg/ml	*B. cereus, N. gonorrhea,*	
[Compositae]	(Areal)	PE		*S. aureus*	
Dovyalis abyssinica	Koshim	MEOH	2 mg/ml	*B. cereus, N. gonorrhea,*	
[Flacourtiaceae]	(Leaf)			*S. aureus, Shigella*	
Warburgia ugandensis	Bifti	MEOH	2 mg/ml	*B. cereus, N. gonorrhea,*	
[Canaleaceae]	(Leaf/stem bark)			*S. aureus*	
Syzygeum guineense	Dokma	MEOH	1 mg/ml	*N. gonorrhea, S. aureus S.*	
[Myrtaceae]	(Leaf)			*pyogene S. pneumonia*	
Bersama abyssinica	Azamir	MEOH	1 mg/ml	*B. cereus, Shigella*	
[Melianthaceae]	(Root bark)				
Ferula communis	Doge	MEOH	1 mg/ml	*N. gonorrhea, S. aureus S.*	
[Umbelliferae]	(Root)			*pyogene, S. pneumonia*	

Gardenia lutea [Rubiaceae]	Gambilo (Stem bark)	MEOH	2 mg/ml	*B. cereus, N. gonorrhea, S. aureus, Shigella*	
Myricasalci folia [Myricaceae]	Shinet (Leaf)	MEOH	1 mg/ml	*B. cereus, N. gonorhea S. aureus, Shigella*	
Discopodiu peninervum [Solanaceae]	Ameraro (Leaf)	MEOH	2 mg/ml	*N. gonorrhea, S. aureus S. pyogene, S. pneumonia*	
Olea europea [Oleaceae]	Woyera (Stem bark)	MEOH	1 mg/ml	*N. gonorrhoea, S. aureus S. pyogene, S. pneumonia*	
Trichila emetica [Melianthaceae]	Roka (Fruit)	MEOH	2 mg/ml	*B. cereus, N. gonorrhea, S. aureus, S. typhi*	
Combertum molle [Combretaceae]	Yekolaabola (Leaf)	ETOH	1 mg/ml	*B. cereus N. gonorrhea, S. aureus, S. typhi*	
Maesa lanceolata [Myrsinaceae]	Kelewo (Fruits)	MEOH	250 mg/ml	*S. aureus, E. coli*	[31]
Cissus quadrangularis [Vitaceae]	Yezhonanjent (Aerial part)	MEOH	250 mg/ml	*S. aureus*	
Dodonae angustofolia [Sapindaceae]	Kitkita (Leaf)	MEOH	250 mg/ml	*S. aureus, E. coli*	
Artemisia afra [Asteraceae]	Ariti (Leaf)	MEOH PE	100mg/ml	*S. aureus , E. coli, B. subtilis, shigella*	[32]
Nicotia natabacum [Solanaceae]	Zeka-keba (Leaf)	MEOH $CHCl_3$	50 mg/ml	*E. coli, S. aureus, P. aeruginosa*	[20]
Croton macrostachyus [Euphorbiaceae]	Bissana (Leaf)	MEOH $CHCl_3$	50 mg/ml	*S. aureus E. coli, P. aeruginosa*	
Calpurnia aurea [Fabaceae]	Digita (Leaf)	MEOH $CHCl_3$	50 mg/ml	*S. aureus, E. coli, P. aeruginosa*	
Withania somnifera [Solanaceae]	Giziewa (Root)	MEOH $CHCl_3$	50 mg/ml	*S.aureus, E. coli, P. aeruginosa*	
Datura stramonium [Solanaceae]	Astenagir (Leaf)	ETOH & Ac	20 mg/ml	*S. aureus, B. subtilis, S. typi, E. coli, F. solani, F. oxysporum, A. niger*	[33]
Commicarpus pedenculosus [Nyctaginaceae]	Tihuantila (Leaf)	MEOH	2.5 mg/ml	*S. aureus*	[34]
Rosmarinus officinalis [Lamiaceae]	YetibsKitel (Leaf)	Oil extract	10 µl	*S. aureus, E. coli, F. oxysporum*	[35]
Eculaptus Globulus [Myrtaceae]	nechbahirzaf (leaf)	Oil extract	20 µl	*S. typhi, E. coli, B. subtilis S. aureus*	[36]
Hagenia abyssinica [Leucosidea]	Kosso (Flower, Fruit)	MEOH ETOH	50 mg/ml	*S. aureus, S. typhi*	[37]
Combertum molle [Combretaceae]	Yekolaavalo (Bark)	An	50 mg/ml	*E. coli, Shigella, C. albican*	[38]
Acokanthera schimperi [Apocynaceae]	Mrenz (Leaf)	MEOH	25 mg/ml	*S. aureus, P. aeruginosa, T. mentagrophytes*	[26]
Kalanchoe petitiana [Crassulaceae]	Endohahila (Leaf)	MEOH	25 mg/ml	*S. aureus, P. aeruginosa, E. coli*	
Malva parviflora [Malvaceae]	Lit (Root)	MEOH	25 mg/ml	*T. mentagrophytes, S. aureus*	
Verbascumsinaiticum [Scrophulariaceae]	Ketetina (Leaf)	MEOH	25 mg/ml	*S. aureus, P. aeruginosa*	

Abbreviation: Methanol: MEOH, ethanol: ETOH, $CHCl_3$: Chloroform, PE: Petroleum ether, Ac: Acetone Methicillin-resistant *Staphylococcus aureus*: MRSA

Anti-microbial Studies of Medicinal Plant Extracts in Ethiopia: Several *in-vitro* antimicrobial studies on crude extracts of medicinal plant species have been done in Ethiopia with promising results against pathogenic micro-organisms. Approximately 91 medicinal plants in Ethiopia, distributed in 49 families, showed important anti-microbial activity in **Table 1** and **2**. From these medicinal plant families, the most common representatives are Lamiaceae, Solanaceae, Fabaceae, Compositae, and Myrtaceae, which contain nine, six, four, three, and three plant species respectively. About 109 extracts belonging to these medicinal plants have been evaluated for

their antimicrobial effect against 27 species of bacteria and 11 species of fungi. The findings showed that methanol extracts of *Guizoti aschimperi* [13], *Combretum molle* [14], *Foenculum vulgare* [39], *Myrsine Africana* [40] and *Aloe sinana* [52], showed the highest growth inhibition against the microorganism evaluated with the anti-microbial activity ranged between 5 μg/ml and 250 mg/ml.

Phytochemical Compounds from Medicinal Plants with Anti-microbial Actions: Phytochemical compounds are bioactive substances found in medicinal plants. Phytochemical screening is a simple and cheap procedure that gives a rapid response to the different types of phytochemicals in a mixture and is a vital tool in identifying bioactive compounds of medicinal and industrial value. The antimicrobial effect of these medicinal plants is attributed to the presence of several classes of bioactive compounds such as quinines, phytoalexins, phenols, alkaloids, flavonoids, terpenoids, tannins, glucosinolates and pathogenesis-related proteins [49, 50].

Alkaloids are heterocyclic nitrogen bioactive compounds synthesized from amino acid building blocks that exert their antimicrobial effect due to their ability to intercalate with DNA thereby interfering with cell division, and also by disrupting cell membranes leading to increase membrane permeability in the bacteria. Morphine, quinine, caffeine, strychnine, narcotine, and emetin are well-known alkaloids that have medicinal value. Besides, berberine, piperine, palmatine, and tetrahydropalmatine are examples of alkaloids with antimicrobial, anthelmintic and anti-diarrhoeal activity [63]. Phenols are bioactive compounds that have one or more unsaturated rings with one or more hydroxyl groups, responsible for the color of fruits of plants and as well as defense against pathogenic microorganisms. Phenol acid exerts its antimicrobial activity by diffusion across the membrane, leading to acidification of the cytoplasm and also cause a reduction in adherence of organisms to the cell lining. Catechol, epicatechin and cinnamic acid are examples of phenol with antimicrobial activity [64].

Flavonoids are another group of phenolic compounds that contain more than one benzene ring in its structure, provide colors attractive to plant pollinators, and are well known for their antioxidant or free radical scavenging activities. Flavonoids have antimicrobial, antiviral, anti-allergic, and anti-inflammatory properties. Their antimicrobial activity is through inhibition of bacterial virulence factors such as toxins, quorum-sensing signal receptors and enzymes, destabilization, and permeabilization of the cytoplasmic membrane, inhibition of extracellular microbial enzymes and deprivation of the substrates required for microbial growth such as iron and zinc. Quercetin, rutincatechin, chrysin, kaempferol, flavones, and calchones are some of the other important flavonoids with anti-microbial activity [64, 65].

Anthraquinones are aromatic compounds with a 9, 10-dioxoanthracene. The antimicrobial activity of Anthraquinones occurs through different mechanisms including destabilization of the cell wall and alterations of metabolic pathways. For example, emodin disrupts cell wall and membrane, intercalates into DNA base pairs and inhibits the activity important enzymes, which generally affect transcription, repress expression and cause cell death. Aloe-emodin, hypericin, 1, 8-dihydroxyanthraquinone, chrysophanol, emodin, physcion, and rhein are some of the Anthraquinones with antimicrobial activity [63, 66]. Terpenoids are bioactive compounds that confer characteristic smell on plants. They are effective against bacteria, fungi, viruses, and protozoa. Terpenoids exert their antimicrobial activity by disturbing the cell membrane, disrupting the proton motive force and coagulation of cell contents. Typical examples include menthol, citral, camphor, and salvinorin [64, 67].

The essential oil contains about 500 different compounds like terpenoids, aliphatic and aromatic compounds such as aldehydes and phenols. Essential oils have a hydrophobic property that disturbs cell membrane, electron flow, and coagulation of cell contents, which are the possible mechanisms of their antimicrobial activity. Carvacrol, eugenol, and thymol are some examples of essential oil with anti-microbial activity [68]. Tannin is a polyphenolic bioactive compound with the astringent effect that helps to protect against a variety of illnesses by enhancing the immune system through activation of phagocytic cells.

Tannin also exerts its effect by inhibiting microbial essential enzymes, deprivation of the substrates needed for microbial growth, and inhibition of oxidative phosphorylation, which affects microbial metabolism. Condensed tannins bind to the cell wall of bacteria thereby inducing bacterial stasis and protease activity.

Ellagitannin is a typical tannin with antimicrobial activity [69]. Saponins are bioactive compounds derived from triterpenoid glycosides with 'soap like' property in water. It is a poisonous compound that causes hemolysis of red blood cells. Saponins exert antimicrobial activity by altering the permeability of cell walls to elicit changes in cell morphology leading to cell lysis, as well as immunostimulant activity [70]. Glucosinolates are bioactive compounds that consist of sulfur and nitrogen. Glucosinolates such as glucoiberverine, sinigrin, glucoiberin, glucoerucin, and isothiocyanates have significant antifungal, anticancer antimicrobial, antioxidant and anti-inflammatory activity [70, 71]. Anti-microbial peptides are used as host defenses against different micro-organisms. Anti-microbial peptides are more potent than conventional antibiotics because they have different targets and mechanisms of actions.

They inhibit the growth of bacteria by interacting with cellular membranes. The cationic amino acids bind to negatively charged compounds such as teichoic acid, phospholipids, and lipo-polysaccharide. This leads to membrane destabilization and leakage of cytoplasmic contents, loss of membrane potential, the entry of peptides and the occlusion of anionic cell components or the activation of autolytic enzymes.

Thionins, hevein-like peptides, defensins, lipid transfer proteins, α-hairpinin families, snakins, knottin-type peptides, and puroindolines are examples of antimicrobial peptide families of plant origin that are classified based on their Cys motifs, sequence similarity and distinctive disulfide bond patterns [63, 71].

CONCLUSION: Medicinal plants have provided important sources of antimicrobial drugs. This review reveals that in Ethiopia, medicinal plants from over 90 species extracted with different solvents showed promising anti-microbial activity. The traditional uses of medicinal plants for the management of microbial infections in Ethiopia have been supported by *in-vitro* and *in-vivo* studies. Based on the anti-microbial assay from this review, *Staphylococcus aureus* was found to be more susceptible to the plant extracts than *Escherichia coli* or *Pseudomonas aeruginosa*.

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