IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 3, June 2025
Impact Factor: 7.67

Antibacterial and Antifungal Activity of Medicinal Important Medicinal Plant

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Abstract: *Medicinal plants have been playing an essential role in the development of human culture. As a source of medicine, Medicinal plants have always been at forefront virtually all cultures of civilizations. Medicinal plants are regarded as rich resources of traditional medicines and from these plants many of the modern medicines are produced. For thousands of years medicinal plants have been used to treat health disorders, to add flavour and conserve food and to prevent diseases epidemics. The use of plant compounds for the therapy of fungal and bacterial diseases is effective due to their unique biocompatible and bioavailable. The trend toward new antifungal and antibacterial agents being introduced to the market remains small, while resistance too many antibiotics is emerging, especially in patients receiving long-term treatment. Recently, various studies about the antibacterial and antifungal activities of these metabolites have been reported. For this purpose, in this review, antibacterial and antifungal activities of endophytes of Pestalotiopsis genus and medicinal plant species of Zingiber and Hydnora genera have been discussed according to recent studies*

Keywords: Antimicrobial Activities, Natural Compounds, Primary Metabolites, Secondary Metabolites, Drug-Resistance**.**

I. INTRODUCTION

Systemic bacterial and fungal infections in recent years due to the increasing number of debilitating diseases immune system such as AIDS, blood malignancies, overdose, corticosteroid drugs, broad-spectrum antibiotics specifically in the case of multidrug-resistant bacteria, etc [1-4], especially for hospitalized patients has been raised. For instance, there is a prevalence of acute and subsequent candida infections with drug-resistance properties such as fluconazole. Pestalotiopsis As mentioned in the introduction section, endophytes can contribute to their host plant species by producing various metabolites to protect and survive the plant [10]. Some studies reported antifungal metabolites of this genus include a new lactone monoterpene, (3R, 4R, 6R, 7S) -7- hydroxy-3,7-dimethyl-oxabicyclo nonan-2- one, with a combination A known related 3 R, 4R-3- (7-methyl cyclohexenyl) -propanoic acid) was discovered from the endophytic fungus Pestalotiopsis foedan obtained from Bruguiera sexangula, a mangrove tree or shrub, in Hainan. These compounds showed antifungal activity against Botrytis cinerea and Phytophthora nicotianae at minimum inhibition concentration (MIC) values of 3.1 and 6.3 µg/ml, while the known antifungal drug, ketoconazole showed comparable activity (MIC 3.1 µg/ml). The effects of Candida albicans at MIC 50 µg/ml show positive efficacy while ketoconazole MIC at 6.3 µg/ml has positive efficacy. In addition to inflammation, anti-cancer, neuroprotective/neurotrophic, cosmetic, and antifungal/antibacterial activities, a review of the clinical effects of various formulations using Plai (Z. cassumunar) on pain relief, acne treatment, and antihistamines has been performed. But there has been no previous report summarizing the accumulated studies in the phytochemicals literature and the in vitro and in vivo biological properties of Z. cassumunar, including our previous studies that have contributed to the discovery of chemical diversity and biological activity of this plant [21]. The oil of Z. cassumunar rhizomes has high antifungal activity (inhibition zone of 11.7-15.7 mm) and its effectiveness is much higher than the five strains of yeast, Saccharomyces cerevisiae, Cryptococcus neoformans, C. albicans, and Candida tropicalis.

DOI: 10.48175/568

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MEDICINAL PLANTS

Zingiber genus Zingiber cassumunar Roxb. Belongs to the Zingiberaceae family and is a perennial herbaceous plant that consists of an underground part consisting of rhizomes. In Thailand, Indonesia and other Asian countries, Z. cassumunar is traditionally used as a medicinal plant in folk remedies, for example, to treat various diseases such as inflammation, including arthritis, rheumatism, sprains, Respiratory problems such as asthma and cough and pain due to musculoskeletal disorders, menstruation or gastrointestinal tract are main medicinal applications of these plants.

Camellia genus Many studies have shown the health benefits of several species of camellia, namely C. sinensis, C. oleifera and C. japonica. These species have antimicrobial (antibacterial, antifungal, and antiviral) and antitumor activity and are a huge source of polyphenols such as catechins. (Especially epicatechin (EC), epigallocatechin (EGC), epicatechin-3- gallate (ECG) and especially epigallocatechin3-gallate (EGCG), the main polyphenols of green, white, and black tea.

Hydnora genus The genus Hydnora (Hydnoraceae) is one of the basic angiosperms in the order Piperales, which is found in the semi-arid regions of Africa and the South Arabian Peninsula. As various studies have shown, plants in this genus play an essential role in communities around the world. There are currently eight species of the genus Hydnora.

According to World health organization (WHO) more than 80% of the world population relies on traditional medicine for their primary health care needs1.The use of medicinal plants as a source for relief from illness can be traced back over five mellenia to written documents of the early civilization in China, India and the north east, but it is thoughtless as art as old as mankind2. The potential of higher plants as a source for new drugs is still largely unexplored. Among the estimated 250'000- 500,000 plant species, only a small percentage have been investigated phytochemically and the fraction submitted to biological or pharmacological screening. Compound of natural or synthetic origin has been the source of innumerable therapeutic agents 2, 3, 4. Medicinal plants are rich sources of antimicrobial agents. Plants are used medicinally in different countries and are the source of potential and powerful drugs5. Human beings have depended on nature for their simple requirements as being the sources for medicines, shelters, food stuffs, fragrances, clothing, flavours, fertilizers and means of transportation throughout the ages. For the large proportions of world's population medicinal plants continue to show a dominant role in the healthcare system and this is mainly true in developing countries, where herbal medicine has continuous history of long use. The development and recognition of medicinal and financial aids of these plants are on rise in both industrialized and developing nations. The traditional medicine practice is widespread in China, India, Japan, Pakistan, Sri Lanka and Thailand. About 40% of the total medicinal consumption is attributed to traditional tribal medicines alone by China. In Thailand, herbal medicines make use of legumes encountered in the Caesalpiniaceous, the Fabaceae, and the Mimosaceae. It is estimated that in mid-90s, more than US$2.5 billion have resulted from the sales of herbal medicines. The herbal medicinal preparations are more in demand than mainstream pharmaceutical products in Japan.

Lymphoedema is a chronic illness that has a major physical and psychological effect on patients and lowers the quality of patient life substantially. Neglected tropical diseases (NTDs) such as podoconiosis, lymphatic filariasis, and leprosy are the most common causes of lower limb lymphoedema in the tropics. Suffering can be aggravated by frequent painful episodes of acute bacterial limb infection known as "acute attacks. Cellulitis and erysipelas are typical wound complications, with the majority of infections caused by group A, C, or G streptococci and *Staphylococcus aureus* species. However, *Aeromonas hydrophila/caviae, Acinetobacter lwoffii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Shewanella algae, Staphylococcus aureus, Streptococcus pyogenes, Streptococcus dysgalactiae, Staphylococcus haemolyticus, Streptococcus agalactiae* and *Staphylococcus simulans* have recently been found to be involved in colonising wounds of lymphoedematous limbs in patients from Ethiopia. Lymphoedema caused by the aforementioned NTDs is progressive if not treated. In the early stages oedema can be reversed overnight, but with disease progression there can be serious impairment and loss of independence. Patients are excluded from society because of their incapacitating and stigmatized impairments which cause significant economic effects, intergenerational poverty, and alienation from society. In Ethiopia, an estimate of 5.6 and 34.9 million peoples are at risk of lymphatic filariasis and podoconiosis respectively. There are 1.5 million cases of podoconiosis across 345 districts of Ethiopia, and the country has the highest prevalence of podoconiosis in the world. The use of medicinal plants has a long history in the treatment of a range of diseases, including infectious diseases, and these days hundreds

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of thousands of plant species have been tested for their medicinal properties. However, the phytochemical and pharmacological activities of many more plants remain to be studied. Plant-derived substances are tolerated and accepted by patients and seem a reliable source of antimicrobial compounds.

Medicinal plants are commonly used worldwide as alternative treatments for mental and physical illnesses. Herbal formulated medicines and traditional health practices are considered more affordable and accessible to most rural societies than modern drugs. The World Health Organization (WHO) estimated that about 65% of the world population use medicinal plants for their primary health care. In addition, approximately 39% of the drugs developed since 1980 have been derived from plants and their derivatives.

Traditional medicine has long been established in the culture of Ethiopian communities. In rural areas this includes the use of plant-based treatments of inflammation, wounds and infection. Records from as far back as the fifteenth century detail traditional medical practices and remedies obtained from oral tales, early medico-religious manuscripts, and traditional pharmacopeia. The antimicrobial activities of these traditional medicinal plants are based on their secondary metabolites such as alkaloids, terpenoids, flavonoids, tannins and glycosides.

Many *in vitro* antibacterial and antifungal studies have been conducted on the safety and efficacy of Ethiopian medicinal plants used to treat bacterial and fungal infections. However, data on the efficacy and safety of these medicinal plants in the management of wound infection have not yet been summarized. This systematic review draws together up-to-date information on Ethiopian medicinal plants used as antibacterial and antifungal agents that might potentially be used for the management of wound infections in lymphoedema.

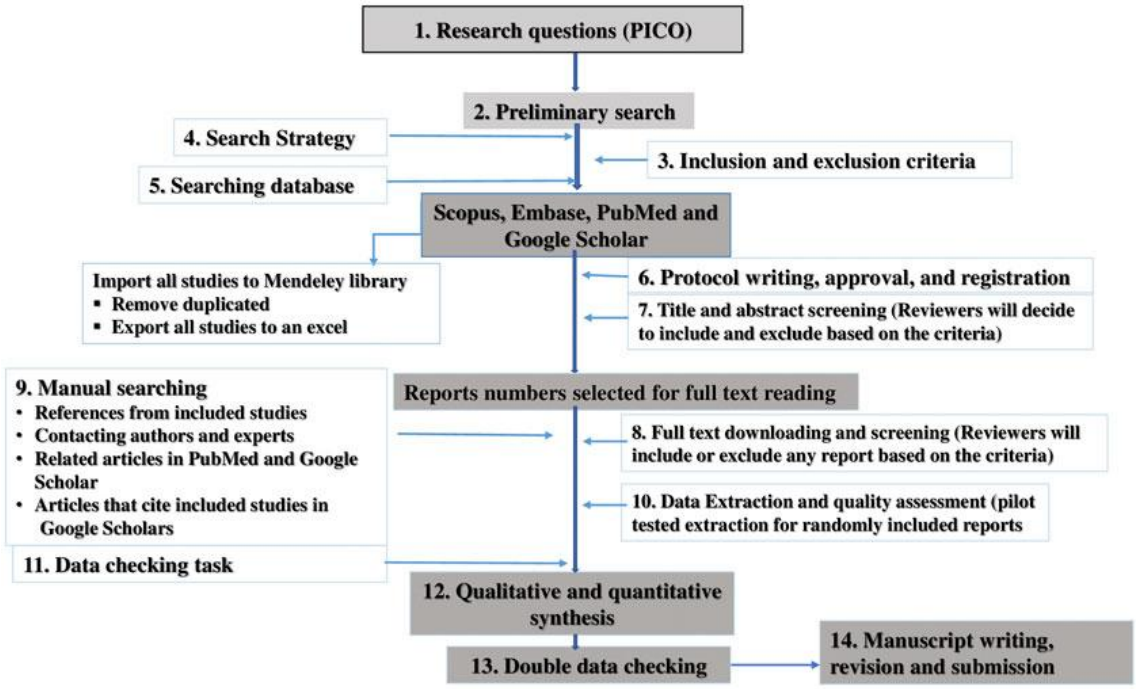

FIGURE 1. A step by step flow diagram to conduct the systematic.

Mauritius is a tropical island in the South West IndianOcean that has numerous plant resources. The peopleof Mauritius have a very long standing tradition in theuse of ethnomedicine and the practice of traditionalmedicine is still very strong in the treatment of minorailments. However, the use of the flora had beenrestricted mainly to exotic plants brought by immi-grants from Africa, Madagascar, India and China, nearly a century and a half ago. In a survey carried outon the traditional uses of plants both in Mauritius and Rodrigues, only a small percentage (ca. 5%) of the endemics were being used as medicinal plants.

It is well established that plant-derived compounds offer potential sources of new antibiotics, anticancer agents and anti-HIV agents amongst other pharmaceu-tical agents. As part of a systematic study on the floraof Mauritius for new

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biologically active compoundsfrom higher plants, 43 extracts from 18 plants belong-ing to 14 different families were screened for theirantibacterial and antifungal properties. This prelimi-nary study of 18 plants constitutes the first assessmentof the antibacterial and antifungal properties of Mau-ritian medicinal plants. Appendix 1 highlights the usesof these plants in the traditional pharmacopeia and theirdifferent properties as reported in the literature. Reportsare also available on the traditional medicinal uses ofsome native plants of Mauritius. Many tisanes are sold in the markets in Mauritiusand such information has also been collected from laypeople. An attempt has been made to validate the usesof such tisanes which are sometimes made up of manyplants.It is well known that tannins influence the antibac-terial and antifungal properties of plant extracts. Inorder to ascertain that components other than tanninsare responsible for the activities, the tannins were pre-cipitated out of the solutions with gelatin and the fil-trates were re-tested for antibacterial and antifungalproperties. Systemic bacterial and fungal infections in recent years due to the increasing number of debilitating diseases immune system such as AIDS, blood malignancies, overdose, corticosteroid drugs, and broad-spectrum antibiotics has been raised. There is a prevalence of acute and subsequent candida infections with drug-resistance properties such as fluconazole. Due to the prevalence and spread of fungal and bacterial diseases, the effort to find treatments has increased more than before. The use of plant compounds for the therapy of fungal and bacterial diseases is effective due to their unique biocompatible and bioavailable. The trend toward new antifungal and antibacterial agents being introduced to the market remains small, while resistance too many antibiotics is emerging, especially in patients receiving long-term treatment. Considering the enormous antimicrobial potentials of natural compounds isolated from plants and endophytes and screening of new antibiotics for various pharmaceutical applications as an alternative source remains largely unknown. Endophytes and medicinal plant species have main primary and secondary metabolites suitable to hindrance or inactivation of pathogens. Recently, various studies about the antibacterial and antifungal activities of these metabolites have been reported. For this purpose, in this review, antibacterial and antifungal activities of endophytes of *Pestalotiopsis* genus and medicinal plant species of *Zingiber* and *Hydnora* genera have been discussed according to recent studies.

RESULTS

In the search of medicinal plants used for their anti-fungal, wound healing or anti-infective activities, a total of 2,330 relevant articles were independently identified by two reviewers for preliminary review from electronic and manual searches. After removal of duplicates by reviewing relevant titles and abstracts, a total of 330 articles on antibacterial and antifungal activities were retrieved for full text review. After a detailed review of each article, 234 articles were excluded and a total of 96 articles were retained: anti-bacterial activity and anti-fungal activity. Most of the plants, except for Ayapana triplinervis,showed reasonable activity against Gram 1 andGram 2 bacteria. A. triplinervis showed antifungalproperties only against Aspergillus niger. It wouldappear that A. triplinervis extracts have a very narrowrange of activity as the only activity reported so far hasbeen against Bacillus subtilis (Appendix 1) (Verpoorteet al., 1987).It was very interesting to note that 30% of the testedplants with the most promising antibacterial propertieswere the endemic/indigenous species: Erythroxylumlaurifolium, E. macrocarpum, Faujasiopsis flexuosassp. erecta, F. flexuosa ssp. flexuosa, Polygonumpoiretii, and Terminalia bentzoe ssp. bentzoe. Tris-temma mauritianum, P. poiretii and Terminalia bentzoealso showed antifungal properties.Among these endemic plants, only the Erythroxylumspp. Have been studied previously. The ethanol extractof E. laurifolium contains polyphenols and shows ACEinhibitory properties. E. macrocarpum contains tropane alkaloidswhile E. sideroxyloides has not been studied so far.However, they all showed good activity against theGram positive and Gram negative bacteria.Both endemic varieties of Faujasiopsis flexuosa arebeing used often by the lay people against dysenteryand interestingly, both of them showed activity againstall the bacteria tested. Faujasiopsis flexuosa has beenstudied for its antisickling properties. Polygonum poiretii and Terminalia bent-zoe are used against diarrhea and dysentery, respec-tively, and they also showed reasonable activity againstthe tested bacteria and fungi in vitro. Tristemma mau-ritianum and Ficus pumila showed promising activityagainst the bacteria in vitro.After removal of the tannins from the extracts, onlyFaujasiopsis flexuosa and Ficus pumila continued tohave antibacterial activities (Appendix 3). This wouldtherefore suggest that other components besides tan-nins are responsible for the antibacterial properties inthese two species.The water extract of the tisanes also showed anti-microbial activity. Since the antimicrobial activity wasfound using the same preparation as

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prescribed by thehealers, these results would support the way people usethese herbal remedies. The methanol extracts showedmore pronounced activity especially against P. aerugi-nosa thus confirming that the active components arepolar.

DISCUSSION

The purpose of this review was to demonstrate the activities of Ethiopian medicinal plants as antimicrobial agents that might potentially be used for limb care (particularly, of tropical lymphoedema and associated wounds). This section discusses the efficacy of plant extracts and their secondary metabolites investigated as antibacterial and antifungal, and the most frequently used models. This systematic review identified a total of 96 articles covering two different experimental models, i.e., 79 antibacterial activity and 17 antifungal activity models. Overall, medicinal plant extracts tested for these two conditions in *in vitro* were shown to have good activity. Despite the heterogeneity of the studies, all plant extracts investigated succeeded in inhibiting bacterial and fungal growth.

In this review of antibacterial activity, a total of 144 medicinal plant species and four compounds were investigated against 25 gram-negative and 17 gram-positive bacteria using agar well diffusion, paper disc diffusion, broth micro/macro-dilution and agar dilution method. A summary of plant species whose extracts and their isolated compounds were shown to have significant *in vitro* activity against bacteria is the focus for our discussion.

Minale et al. performed anti-bacterial activity tests on *Aloe sinana* Reynolds and its compounds (Microdontin, Aloin and Aloinoside) against 21 strains of bacteria using the disk diffusion method. The leaf latex showed high inhibitory activities against *B. pumillus 82, B. subtilis ATCC 6633 and S. aureus ML 267, E. coli K99, E. coli K88, E. coli CD/99/1, E. coli LT37, E. coli 306, E. coli 872, E. coli ROW 7/12, E. coli 3:37C, S. enterica TD 01, S. typhi Ty2, S. boydii D13629, S. dysentery 8, S. flexneri Type 6, S. soneii 1, V. cholerae 85, V. cholerae 293, V. cholerae 1,313 and V. cholerae 1,315* at a concentration of 200 µg/ml, which showed comparable activity to the standard drug ciprofloxacin. Similarly, compounds isolated from *Aloe sinana* Reynolds were shown to have high activity against *E. coli, S. typhi Typ 2, Shigella, S. aureus and V. cholerae*, comparable to the reference drug, ciprofloxacin. The leaf latex's action was due to the secondary metabolite anthraquinones, which possess a range of functional groups and have the ability to disrupt bacterial cell wall permeability and inhibit nucleic acid synthesis and then cause death of the microorganism. In another anti-microbial study, the leaf and stem bark extracts of *Azadirachta indica* A. Juss. Exhibited significant antibacterial activity against a wide range of bacteria due to the tricyclic diterpenoids isolated from stem bark, and azadirachtins, quercetin and β-sitosterol isolated from the leaves. Many studies have been carried out to screen medicinal plants for their antifungal activity, and various groups of researchers have initiated antifungal programs for traditionally used plants. Classes of compounds from plant metabolites, such as terpenoids (isoprenoids), saponins, phenolic compounds, flavonoids, coumarins, alkaloids, proteins and peptides showed anti-fungal activity against different fungal species. Under this review, 15 studies were included comprising 42 species of plant extracts against 50 species of fungus using agar well diffusion, disc diffusion, macro/microdilution and agar dilution methods. Alcoholic extracts (methanol and ethanol) of *E. kebericho* Mesfin were tested by Ameya et al. against *A. flavus* and *C. albicans* using disc diffusion and agar dilution methods, and shown to cause significant inhibition at low concentration, comparable to the reference drug ketoconazole. The alcoholic solvents have the ability to extract phenolic compounds such as flavonoids, anthocyanins and phenolic acids which may contribute to the antifungal activity of the extracts.

Kasparaviciene et al. tested the activity of oleo-gels, formulated with different concentrations of thyme essential oil against *C. albicans* by broth dilution method, which showed significant activity with MIC value of 0.25%. Thymol was reported the major constituent of the thyme essential oil in this study. The biological activity of thyme essential oil depends on its yield and chemical composition, and the essential oils have several chemical names depending on the main constituents they have, such as thymol, carvacrol, terpineol, and linalool.

Future prospects of Medicinal Plants

There is a promising future of medicinal plants as there are about half million plants around the world, and most of them are not investigated yet for their medical activities and their hidden potential of medical activities could be decisive in the treatment of present and future studies.

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In the development of human culture medicinal plants have played an essential role, for example religions and different ceremonies. Among the variety of modern medicines, many of them are produced indirectly from medicinal plants, for example aspirin. Many food crops have medicinal effects, for example garlic. Studying medicinal plants helps to understand plant toxicity and protect human and animals from natural poisons. The medicinal effects of plants are due to secondary metabolite production of the plants. Keeping this in consideration there have been increased waves of interest in the field of research in natural product chemistry. This interest can be due to several factors, including therapeutic needs, the remarkable diversity of both chemical structure and biological activities of naturally occurring secondary metabolites, the utility of novel bioactive natural compounds as biochemical probes, the development of novel and sensitive techniques to detect biologically active natural products, improved techniques to isolate, purify, and structurally characterize these active constituents, and advances in solving the demand for supply of complex natural products. The importance of traditional medicine has also recognized by World Health Organization (WHO) and has created strategies, guidelines and standards for botanical medicines. For the cultivation, processing of medicinal plants and the manufacture of herbal medicines agro-industrial technologies need to be applied. Medicinal plants are resources of new drugs and many of the modern medicines are produced indirectly from plants.

II. CONCLUSION

The advancement of human development has been significantly influenced by medicinal plants. Medicinal plants have long been used as a source of medicine in almost every society. Many modern medications are made from medicinal plants, which are considered to be abundant sources of traditional medicines.In this review *Calpurnia aurea* (Aiton) Benth., *Croton macrostachyus* Hochst. Ex Delile, *Withania somnifera* (L.) Dunal*Achyranthes aspera* L., *Datura stramonium* L., *Solanum incanum* L., *Verbascum erianthum* Benth., *Nigella sativa* L., *Gymnanthemum amygdalinum* (Delile) Sch. Bip., *Olinia rochetiana* A. Juss., *Sida rhombifolia* L, *Bersama abyssinica* Fresen and *Azadirachta indica* A. Juss are the most studied plants species against bacteria, and *Azadirachta indica* A. Juss and *Lawsonia inerms* L. against fungal species. Thymoquinone, a constituent of the black seed of *Nigella sativa* L., alcoholic extract of *Echinop skebericho* Mesfin, *Aloe sinana* Reynolds and its compounds (Microdontin, Aloin and Aloinoside), alcoholic extract of *Azadiractha indica* A. Juss and *Lawsonia inerms* L. are the most effective plant materials against gram negative and gram-positive species. In addition, *Azadiractha indica* A. Juss and *Lawsonia inerms* L. have activity against a wide range of gram-negative and positive bacterial strains. Similarly, methanol extract of *Echinops kebericho* Mesfin and oleo-gels formulated with different concentrations of thyme essential oil are the most effective against different fungal species.

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ISSN: 2581-9429
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