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Review

CURBING ANTI-MICROBIAL RESISTANCE OF SYNTHETIC MEDICINAL AGENTS USING HERBAL DRUG ALTERNATIVES: CURRENT TRENDS AND FUTURE INSIGHTS

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ABSTRACT

Anti-microbial resistance represents a critical global health threat, undermining the effectiveness of conventional antibiotics and posing challenges in the treatment of infectious diseases. The increasing resistance to synthetic anti-microbial agents underscores the urgent need to explore alternative therapeutic approaches, particularly through natural and herbal remedies. Unlike synthetic drugs, which are often associated with harmful side effects and toxicity, medicinal plants offer a promising, safer alternative due to their rich array of bioactive compounds. These plant-derived substances have demonstrated significant anti-microbial activity against a variety of pathogens. Traditionally, medicinal plants have been used to treat a wide range of diseases and conditions, but their potential must be validated and standardized through scientific research to ensure both efficacy and safety. The antimicrobial properties of medicinal plants stem from their diverse phytochemical constituents, including alkaloids, flavonoids, terpenoids, and phenolic compounds, which exhibit broad-spectrum activity against bacteria, fungi, and viruses. This review explores the anti-microbial potential of these plant-based compounds, emphasizing their broad-spectrum efficacy in combating resistant pathogens. It also highlights the importance of further research to optimize the use of medicinal plants in modern healthcare, offering a viable strategy to mitigate the growing threat of anti-microbial resistance and provide safer alternatives to conventional antibiotics.

KEYWORDS: Micro-organism, phytoconstituents, medicinal uses, herbal nanoparticles, in-silico studies

1. Introduction

Plants and herbs have been recognized to offer therapeutic benefits since ancient times. Traditionally, people have been using medicinal plants and their natural components to cure a varied array of ailments including infectious diseases. The established herbal medicine practice and current scientific studies provide verification of the effectiveness of medicinal plants in curbing antimicrobial resistance.

Medicinal plants have been employed in healthcare from the time when life began on earth. Medicinal plants are the very first and the safest source of treatment and management for numerous morbidities, principally for chronic diseases. Plants are considered to be the essential source of therapeutic constituents including flavonoids, glycosides, alkaloids, saponins, tannins, tri-terpenoids, coumarins, lignins, organic acids, essential oils etc. These all exhibits a significant role in treating mild fever to the deadliest cancer [1]. Natural components are also significantly used in traditional medicines (TMs), traditional medicine (TCM), ayurveda, neuropathy. homoeopathy, and Unani system of medicine. These systems have developed into well-structured medical systems [2]. Investigations are continuously conducted globally not only in support of the effectiveness but to uncover the hidden therapeutic potential of the medicinal plants. Moreover, natural medicines have remained popular in this modern era owing to safety and cost-effectiveness.

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1.1. Traditional uses of medicinal plants

Plants and natural extracts have been utilized for their therapeutic efficacy in different traditional systems of medicine. These extracts and raw herbs have shown promising analgesic, anti-inflammatory, anti-diabetic, anti-microbial, antioxidant, and anti-cancer activities. They are successfully employed to treat both acute and chronic ailments. Constituents present in plants and other natural sources including animals, microorganisms, marine, insects, and minerals or their analogues have made a remarkable contribution to the efficacious natural origin medicines in current era [3-6].

1.2. Anti-microbial properties of medicinal plants

Infectious diseases have existed since antiquity and are still found challenging to be treated. In the present era, new diseases are emerging owing to mutation in existing microorganisms, environmental changes, animal-human cycles, urbanization, and many others. The emerging and already identified diseases are posing significant threats to the global health and economies therefore, developing the need of potent novel antimicrobial agents to curb the pathetic situation [7]. These pathologies usually occur due to the infections caused by the five major types of causative organisms including viruses (influenza, hepatitis, dengue, corona, measles, rubella, polio, mumps etc.), bacteria (Salmonella, Escherichia coli, Streptococcus pneumonia, Shigella, Staphylococcus aureus, Helicobacter pylori, Vibrio cholera etc.), fungi (Candida albicans, Histoplasma capsulatum), protozoa (plasmodium spp., Giardia lamblia, Leishmania), and worms (hook worm, round worm, flat worm etc.) [8]. The anti-microbial potential of medicinal plants is extensively investigated and not only documented but even utilized broadly in traditional medicine systems. Medicinal plants such as Azadirachta indica (Neem), Ocimum basilicum (basil), Matricaria chamomilla (chamomile), Eucalyptus globules (eucalyptus),

Glycyrrhiza glabra (licorice), Cinchona spp. (quinine), Casia angustifolia (senna), Aloe barbadensis (Aloe), Vaccinium spp. (cranberry), Camellia sinensis (green tree), Punica granatum (pomegranate). However, researchers are continuously putting strenuous efforts in exploring the antimicrobial potential of the other plants as well [9]. This review explores the pharmacognostic properties of selected medicinal plants with their promising antimicrobial activities against pathogenic organisms.

2. Materials and methods

This comprehensive review is comprised of ten years literature survey covering investigations from January 2014 to December 2023. The data was extracted by searching through the web engines of PubMed, Google Scholar, Research Gate, Science Direct, Elsevier, chapters from books, National Institute of Health (NIH) website, PubChem., Drug.com, Medscape.com, WebMD.com, Rxlist.com. The keywords were medicinal plants, antimicrobial agents, anti-microbial resistance, anti-fungal, anti-viral, anti-bacterial, indications, mechanism of antimicrobial action, pharmacological actions, adverse effects, pharmacognostic features, phytochemistry, phytochemical constituents, extracts, toxicity, and doses along with the names of the medicinal plants including Apium graveolens Linn.., Hypericum perforatum Linn., Moringa oleifera Linn., Thymus vulgaris Linn., Zingiber officinale roscoe., Azadirachta indica Linn., Allium sativum Linn., Curcuma longa Linn., Hibiscus sabdariffa L., Tanacetum parthenium, Apocynum cannabinum, Echinacea purpurea, Rosemarinus officinalis Linn., Humulus lupulus Linn., Pistacia lentiscus Linn., Agrimonia pilosa Ledeb., Aniba rosaeodora ducke., Commiphora myrrha, Cichorium intybus L., Momordica charantia L., Eruca vesicaria sativa and Andrographis paniculata. The original research articles, review, systematic reviews and meta-analysis dealing with the pharmacognostic, phytochemical and anti-microbial activity of the above-mentioned medicinal plants were incorporated [10].

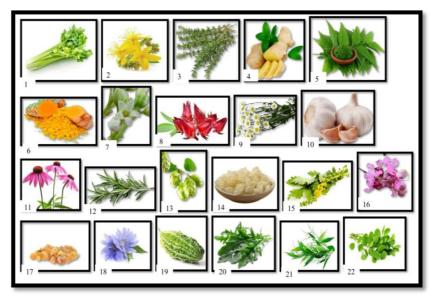


Fig. 1. Photographs of the twenty two medicinal plants. 1: Apium graveolens L., 2: Hypericum perforatum L., 3: Thymus vulgaris L., 4: Zingiber officinale Roscoe., 5: Azadirachta indica Adrien-Henri de Jussieu, 6: Curcuma longa L., 7: Apocynum cannabinum L. 8: Hibiscus sabdariffa L., 9: Tanacetum parthenium L., 10: Allium sativum L., 11: Echinacea purpurea L., 12: Rosemarinus officinalis L., 13: Humulus lupulus L. 14: Pistacia lentiscus L. 15: Agrimonia pilosa Ledeb. 16: Aniba rosaeodora Ducke. 17: Commiphora myrrha Nees. 18: Cichorium intybus L. 19: Momordica charantia L. 20: Eruca vesicaria subsp. sativa Mill. 21: Andrographis peniculata Burm. F. 22. Moringa oleifera Lam.

3. Results

3.1. Pharmacognostic Properties of Medicinal Plants

The medicinal plants were selected after thorough review of the literature owing to their significant antimicrobial activity. The photographs of the 22 medicinal plants discussed in this review article are given in Fig. 1.

The details of each medicinal plant are provided separately as follow:

3.1.1. Apium graveolens L.

A. graveolens L. is native to Europe, Western Asia, and Northern Africa. It is a miraculous herb, with a variety of medicinal characteristics. It is grown under moderate to mildly harsh conditions in different locations of Pakistan. Leafy stems are used to cure bronchitis and seeds are utilized in liver-spleen disorders. Side effects associated with A. graveolens are allergies and dermatitis [11].

3.1.2. Hypericum perforatum L.

St. John's Wort is a perennial herb with unique yellow flowers that grows natively throughout North America, Europe, Asia, Russia, India, and China. It is well-known to have anti-depressant properties. Recent studies suggest that this herb can treat a variety of other ailments from mild cuts and burns to serious cancer and other inflammatory disorders. It has anti-bacterial and anti-viral potential against disease causing micro-organisms showcasing the broad-spectrum efficacy. Photosensitivity, elevated serotonin levels, anxiety, insomnia, headaches, dry mouth, dizziness, gastrointestinal problems, and sexual dysfunction are among the frequent side effects [12, 13].

3,1,3. Moringa oleifera Lam.

Moringa oleifera Lam. is native to Africa and Asia. It is commonly known as the drumstick tree and is grown all over the world for both nutritional and therapeutic purposes. It has been utilised for many years in both conventional and alternative medical practices [14]. Moringa is well known for its ability to strengthen immunity and good health. There are no reported adverse effects to appear from its use. Different dosage forms of Moringa oleifera are available globally. Scientific literature reveales the strong anti-bacterial activities of phytochemical constituents present in the plant [15].

3.1.4. Thymus vulgaris L.

Thymus vulgaris L. is an evergreen perennial herb indigenous to southwestern Europe and southeastern Italy. It belongs to the Lamiaceae family of angiosperm plants having about 400 different species of aromatic herbs. The volatile oils present in the plant include thymol, carvacrol, p-cymene, γ -terpinene, and linalool. Taking excessive amounts of thyme, particularly in the form of thyme oil, could result in headaches, dizziness, upset stomachs, and contact dermatitis [16].

3.1.5. Zingiber officinale Roscoe.

Zingiber officinale (ginger) is a member of the Zingiberaceae family and indigenous to Southeast Asia. Ginger is rich in active compounds like α -Zingiberene, (E,E)- α -farnesene, geranial, β -sesquiphellandrene, and arcurcumene [17]. Adverse consequences may be observed upon excessive intake of ginger rhizome in form of burping,

diarrhea, heartburn, and generalized stomach discomfort [18].

3.1.6. Azadirachta indica L.

Azadirachta indica Linn. (neem) belongs to Meliaceae family. It is native to Indian sub-continent, tropical and subtropical regions. It is distinguished by its significant antimicrobial attributes due to presence of phytochemicals like steroids, tannins, alkaloids, triterpenes, flavonoids, and anthraquinone glycosides [19]. It has been widely used in traditional systems of medicine worldwide for the treatment and prevention of various diseases. Adverse effects related to the use of Azadirachta indica include vomiting, diarrhea, drowsiness, seizures, loss of consciousness, coma, and death [20].

3.1.7. Allium sativum L.

Garlic (Allium sativum L.) is a bulbous plant native to Central Asia. It has a pungent smell due to its high sulfur content. This perennial plant is used to treat various diseases, particularly bacterial infections. The side effects associated with garlic includes bad breath, heartburn, gas, and diarrhea [21].

3.1.8. Curcuma longa L.

Curcuma longa Linn. (turmeric), belongs to a family Zingiberaceae. It is native to Asian countries [22]. It possesses anti-inflammatory, anti-oxidant, and anti-microbial properties. Stomach upset, nausea, dizziness, and diarrhea are some of the adverse effects associated with turmeric [23].

3.1.9. Hibiscus sabdariffa L.

Hibiscus sabdariffa L. (a perennial plant) grows all over the world as it is easy to grow. The plant is well known for its scarlet flowers and calyces as it is the main source of medicinal compounds. Organic acids, phenolic acids, flavonoids, anthocyanins, and dietary fiber are linked to the therapeutic efficacy of H. sabdariffa. It is considered safe if taken according to prescription. Adverse effect associated with irrational use of H. sabdariffa includes spermatogenesis, kidney and liver function disturbances [24].

3.1.10. Tanacetum parthenium L.

Tanacetum parthenium (Feverfew) is herbaceous plant that belongs to the Asteraceae family. Native to Southeastern Europe, central Asia, and west Himalayas, feverfew is recognized for its distinctive yellow and white daisy-like flowers and aromatic leaves. Traditionally, it has been utilized for its medicinal properties, particularly in the management of migraines and other health conditions. Side effects are nausea, digestive problems, and bloating [25, 26].

3.1.11. Apocynum cannabinum L.

Apocynum cannabinum (Indian hemp) is a perennial herbaceous plant native to North America. It belongs to the Apocynaceae family. Indian hemp is characterized by slender stems, opposite leaves, and clusters of small, bell-shaped flowers. Despite its toxicity, some traditional herbal medicine practitioners have explored its narrow spectrum medicinal properties, to be given only on prescription. This herb is considered to have a significant toxicity profile. It is unsafe to take by mouth and can cause irritation in the throat, stomach, and intestines. It may also cause bradycardia and hypertension [27, 28].

3.1.12. Echinacea purpurea L.

Echinacea purpurea (purple coneflower) is a perennial plant native to North America. It is recognized both for its ornamental beauty and traditional medicinal uses. This flowering plant has a distinctive appearance with pink to purple daisy-like flowers featuring a cone-shaped central disc. The side effects include stomach pain, constipation, diarrhea, heartburn, vomiting, and rash [29-31].

3.1.13. Rosemarinus officinalis L.

Rosemarinus officinalis (Rosemary) is an evergreen, aromatic shrub with height up to two meters long. This perennial shrub is indigenous to Europe, Africa, Western Asia, and in the Mediterranean. Rosemary essential oil is commonly utilized in aromatherapy for relieving headache and tension, boost mental activity, reduce stress levels, and support respiratory health [32, 33]. Side effects associated with higher doses or if consumed in essential oil form include dermatitis, infertility, and miscarriage (rare), vomiting, coma, spasm, pulmonary edema. Toxicity is not known but liver and kidney damage (rare) are reported [34].

3.1.14. Humulus lupulus L.

Humulus lupulus (Cannabaceae) is known predominantly to be a raw material with substantial health-promoting qualities. It is native to Europe and Western Asia. It is primarily used to relieve anxiety [35]. Hops have been used in cosmetic and pharmaceutical industries, especially for their antimicrobial and antiviral effect. Side effects were only observed when taken in concentrated form. Sleepiness and slow breathing are two common side effects [36].

3.1.15. Pistacia lentiscus L.

P. lentiscus L. (*Anacardiaceae*) is indigenous to Mediterranean coastal region. It serves as an antioxidant, antifungal, antibacterial, and anti-inflammatory agent. It contains resins as chemical constituents. They are translucent, white or pale-yellow, turning more yellowish and opaquer on aging. The resin is effective in treating gastric ulcers, especially *H. pylori*. It primarily contains volatile oils particularly α-pinene and myrcene, mastic oil, triterpenoids, phytosterols, polyphenols. High consumption of *P. lentiscus* can cause allergic contact dermatitis headache, upset stomach, and dizziness [37, 38].

3.1.16. Agrimonia pilosa Ledeb.

Agrimonia pilosa (Rosaceae) is indigenous to Eastern Europe, Northern Asia and Indochina. It is used to treat diarrhoea, stomach ulcers, gastritis, and other illnesses. A. pilosa Ledeb. contains flavonoids, triterpenoids, and isocoumarin. The pharmacological effects of A. pilosa include anti-oxidant, anti-bacterial, anti-cancer, anti-inflammatory, and anti-tumour activity. Beyond many benefits with optimum safety window, stomach irritation and liver damage are the potential adverse effects [39, 40].

3.1.17. Aniba rosaeodora Ducke.

Aniba rosaeodora (Lauraceae) is native to Amazon and Guyana. It has yellow-brown bark, reaches a height of 30 metres. Rosewood oil is a colourless to pale yellow liquid with a woody floral scent. Its primary ingredient is the monoterpene alcohol, linalool. Although only the trunk wood is collected, the entire aromatic tree is used. Various

species of the plant has been utilized for ornamental and decorative purposes, but on the other hand this medical plant is effectively used to manage epileptic episodes as well. Adverse effects are not reported except allergy [41].

3.2.8. Commiphora myrrha Nees

Commiphora myrrha (Burseraceae) contains oleo gum resins. C. myrrha Nees represents a genus comprised of approximately 150 trees and shrub species found mostly in Africa, India, Yemen, and the southern zones of Saudi Arabia [42]. The oleo gum resins are the best sources of the fragrance. It has strong analgesic action and is extensively used in the treatment of wounds, management of pain, inflammation of the joints, parasitic infections, obesity, and gastro-intestinal diseases. Skin rash, diarrhea, kidney problem, heart rate fluctuation, blood sugar imbalance are some documented adverse effects [42].

3.2.9. Cichorium intybus L.

Cichorium intybus L. (Chicory), a perennial herb of the Asteraceae family within the Cichorium genus, is cultivated worldwide. Chicory is used as a raw material for inulincommercially utilized as a powerful prebiotic. It has some mild side effects like abdominal pain, flatulence, bloating and other digestive problem [43].

3.3.0. Momordica charantia L.

Momordica charantia L. (bitter melon) is native to tropical and subtropical regions, notably in Asia, India, China, and Brazil. It holds traditional significance as a medicinal plant. Scientific investigations have unveiled a broad array of biologically active compounds supporting its therapeutic efficacy. The diverse applications of Momordica charantia make it principal in both traditional medicinal practices and contemporary scientific exploration. Hypoglycemia, fatigue, black stool, fever are the associated adverse effects [44].

3.3.1. Eruca vesicaria subsp. sativa Mill.

Eruca vesicaria sativa (Arugula) is an annual herb in the Brassicaceae family. It is native to North Africa and the Middle East and southern Europe. The young leaves are rich in calcium, iron, and vitamins A, C, and K. The side effects include contact urticaria and anaphylactic shock [45].

3.3.2. Andrographis paniculata Burm. F.

Andrographis paniculata (Green chirata) is a medicinal plant renowned for its therapeutic properties. It is native to south Asia and is conventionally used in various traditional medicine systems, including ayurveda and chinese, for its potential health benefits. Green chirata is recognized for its purported immuno-stimulant, anti-inflammatory, anti-bacterial, and hepato-protective properties. Side effects with the prolonged, unprescribed use of this medicinal plant are disorders affecting the gastrointestinal system, issues related to the skin and subcutaneous tissue, and instances of anaphylaxis [46].

4. Discussion

4.1. Development and anti-microbial potential of herbal nanoparticles

The field of herbal nanoparticles has also advanced significantly, enhancing the medicinal effects of plant extracts. Combining plant extracts with metals such as

silver, gold, copper, and copper oxide boosts therapeutic efficacy. Sustainable green synthesis methods for these nanoparticles improve their bioavailability and stability therefore offering a promising alternative to traditional herbal remedies [47, 48]. Neupane et al. [49] performed an eco-friendly synthesis of Moringa oleifera nanoparticles (MONPs), which showed significant antibacterial activity against Gram-negative but even more higher effectiveness towards Gram-positive bacteria as compared to amoxicillin standard compound. Docking studies further unfolded that most compounds had better binding with 1jij, while luteolin had similar binding to standard ligand 1kzn. The study also confirmed that silver nanoparticles of Moringa oleifera containing flavonoids and polyphenols strongly inhibit DNA gyrase and tyrosyl-tRNA synthetase.

Abdellah and co-workers documented the antibacterial activity of curcumin from *Curcuma longa*. The biocompatible silver nanoparticles of curcuma have been found to improve both their effectiveness and stability many folds [50]. Another study conducted by Fierascu *et al.* [51] explored the effects of *Echinacea purpurea* extracts, obtained through traditional and microwave-assisted methods. The antibacterial properties of these newly synthesized silver nanoparticles were found effective against *Candida albicans* and *Escherichia coli*.

4.2. *In-silico* prediction of the anti-microbial activities of plant-derived compounds

Computational studies and molecular docking are crucial for understanding how plant-derived compounds interact with biological targets to reveal their therapeutic potential. These techniques help to clarify the mechanisms through which complex plant drugs affect protein interactions and biological processes, often overcoming bacterial resistance more effectively than synthetic drugs. They play a vital role in drug discovery by elucidating pharmacokinetics, pharmacodynamics, optimizing drug effects, and predicting interactions and toxicities. Sarwar et al. very recently explored the potential of cinnamon compounds targeting virulent proteins of Helicobacter pylori (virB4, virB8, and virB9). The molecular docking studies identified cinnamyl acetate and benzyl benzoate as promising inhibitors for H. pylori [52]. Likewise, it has been have reported that an ethanolic extract of Hypericum perforatum demonstrated superior anti-microbial activity against Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa compared to many antibiotics. In another investigation, 6-gingerol extracted from Zingiber officinale was evaluated for its antibacterial properties by computational docking [53]. It was revealed that 6gingerol strongly binds to the target and inhibits quorum sensing (QS) receptors, signifying its potential as an antivirulent agent in combination with traditional antibiotics for severe infections. Lahiri et al. also studied the effects of a Curcuma longa (turmeric) extract mixture-curcumin-l and erythromycin on biofilm-forming Staphylococcus aureus and Pseudomonas aeruginosa [54]. It was found that mixtures of phyto-compounds were more effective than single compounds due to synergistic effects. Turmeric extract proved to be a cost-effective alternative to commercial curcumin-I for treating biofilm-forming bacterial infections. Seddogi and co-researcher identified 19 compounds in Pistacia lentiscus L. leaf extract, with catechin gallate and epigallocatechin gallate as major active components. The extract showed high levels of

polyphenols and flavonoids that are held responsible for the potent antioxidant and promising antibacterial activity against both Gram-positive and Gram-negative bacteria [55].

4.3. Current & future prospects of medicinal plants

Past investigations discovered the presence of essential oils, flavonoids, alkaloids, tannins, resins and glycosides constituents in different herbs. In the present study, the structures of the chemical constituents of the studied plants having anti-microbial activity are shown in Fig. 2.

The inclination in the utilization of herbs and medicinal plants is fundamentally owed to the treatment failures using conventional medicines probably due to anti-microbial resistance. This is observed critically in infectious diseases due to escalating issue of anti-microbial resistance. Infections that were once treatable with antibiotics have become untreatable or more difficult to manage, leading to extended hospital stays, higher health-care costs, and elevated mortality rates. There are many reasons for the failure of the synthetic anti-microbial agents as even the broad-spectrum antibiotics are losing their strong killing properties, subsequently hanging at the edge of effectiveness. Various mechanisms are known to revert the inhibitory effect of these potent drugs. Microorganisms have undergone some adaptations, like efflux pump for propelling out the intracellular drug or modify porin channels which help in drug penetration, consequential in reduced accumulation or impermeability of antibiotics. Another significant way is to produce specific enzymes responsible for destruction of antimicrobial agent rendering them ineffective. Production of beta lactamase and carbapenems are grave threats for many potent drugs: penicillin derivatives, amoxicillin, ampicillin, cephalosporins, doripenam, imipenam, meropenam, ertapenam etc. The therapeutic response, however, may be restored by combining β -lactam antibiotics with β lactamase enzyme inhibitors such as clavulanic acid, sulbactam and tazobactam. Other resistance procedures may include the target site modification and mutations (RNA polymerase and DNA gyrase) causing alteration of binding affinity and ultimately making them inert against the administered chemicals, mainly rifamycins and quinolones. Susceptible populations include elderly, infants, and compromised immune systems individuals. Many modern and synthetic chemicals have their roots in the old medicinal plants which have been utilized for ages in a variety of civilizations for their healing abilities. Medicinal plants are a rich source of bio-active constituents, particularly secondary metabolites like flavonoids, phenols, terpenoids, and alkaloids, showing potential activity against infectious pathogens. Fig. 3 represents the common chemical constituents present in majority of medicinal plants with possible mechanism of anti-microbial action [56-58]

Natural anti-microbial agents are not as commonly and frequently used as the synthetic anti-microbial moieties, therefore the resistance against the phytochemicals is found to be negligible. Microorganisms are becoming adapted to routine antibiotics owing to extensive exposure and obviously exert resistance through structural modification and environmental adaptations. Thus, natural anti-microbial compounds offer promising alternatives or adjuncts to conventional antibiotics. Additionally, the adverse effects related to the antibiotics are much higher than the herbal

medicines accompanied with higher clinical safety. Nowadays, the efficacy, safety, and mechanisms of action are subjects of ongoing research, aiming to harness their therapeutic potential while addressing the global challenge of anti-microbial resistance. Integrating these natural agents into healthcare practices requires careful evaluation and standardization to ensure consistent utilization in clinical settings. Despite the promising potential of herbal medicines, further scientific evidence through rigorous clinical trials and molecular investigations is necessary to determine their safety, efficacy, and potential to complement or enhance existing antibiotic therapies in the fight against resistant infections to validate the traditional claims. It is substantial to understand the need for the policy and regulatory

framework to fully support the careful and authentic utilization of medicinal plants in the modern epoch. Integration of the latest findings with the traditional information is deemed to be necessary in order to cope with the evolving issues of anti-microbial resistance, the need for novel therapeutic agents, and the possibilities of natural therapies [59-61].

The pharmacognostic details of the reviewed medicinal plants having anti-microbial potential are provided in Table 1.

These phytochemical ingredients exhibited good to excellent anti-microbial activity against Gram-positive and Gram-negative bacteria and fungi as shown in Table 2.

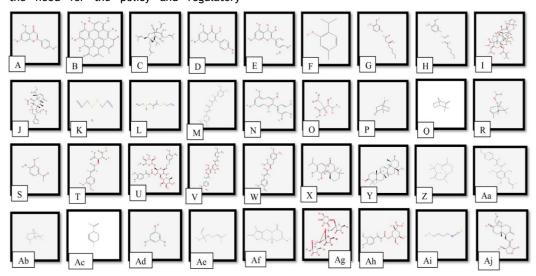


Fig. 2. Phytochemical constituents structures responsible for anti-microbial activity: A - apigenin, B - hypericin, C - hyperforin, D - kaempferol, E - quercetin, F - thymol, G - gingerol, H - hoagols, I - azadirachtin, J - nimbin, K - allicin, L - ajoene, M - curcumin, N - delphinidin, O - hibiscus acid, P - camphor, Q - camphene, R - trans-chrysanthenyl acetate, S - apocynin, T - caftaric acid, U - echinacoside, V - chicoric acid, W - rosemarinic acid, X - carnosol, Y - ursolic acid, Z - humulene, Aa - xanthohumol, Ab - alpha pinene, Ac - limonene, Ad - phloroglucinol, Ae - linalool, Af - commiferin, Ag - inulin, Ah - chlorogenic acid, Ai - erucin, Aj - andrographolide..

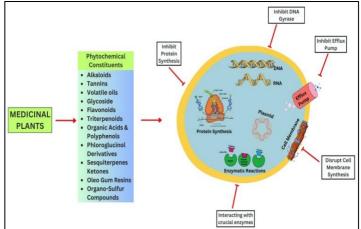


Fig. 3. Medicinal plants containing phytoconstituents including alkaloids, tannins, volatile oils, glycosides, flavonoids, triterpenoids, organic acids, polyphenols, phloroglucinol derivatives, sesquiterpenes ketones, oleo gum resins, organo-sulfur compounds with possible mechanisms of anti-microbial action including inhibition of protein synthesis, DNA gyrase, efflux pump, cell membrane synthesis and interaction with crucial enzymes.

Table 1. Pharmacognostic details of selected medicinal plants with anti-microbial activity.

S. No	Scientific name	Common name	Family	Part used	Pharmacological effects	Indications	Dosage form	Dose	Ref.
1	Apium graveolens Linn.	Celery/ smallage, Ajmoda, ajwain	Apiacaeae/ Umbiliferaceae	Leaf stalk, seeds, roots	Anti-cancer, anti-obesity, anti- hepatotoxic, anti-hypertensive, anti-oxidant, anti-microbial, anti- inflammatory.	Bone defects, gout, arthritis, ulcers, urinary tract infections (UTI), hypertension, flatulence, headache, malnutrition, bronchitis, hyperglycemia and hyperlipidemia, cancers	Fresh herb and seed powder	1-1.5 g of celery seed powder or extracts.	[62-66]
2	Hypericum perforatum Linn.		Hypericaceae/ Clusiaceae/ Guttiferae	Flower, leaves, stem	Anti-depressant (by inhibition of monoamine oxidases), anti-bacterial, anti-viral, anti-inflammatory, anti-oxidant, and neuroprotective	Insomnia, depression, somatic symptom disorder, generalized anxiety disorders, obsessive-compulsive disorder, and other diseases	Hypericin standardized extract (0.3 %, 0.2 %) Hyperforin standardized extract (5 %) Crude extracts	300 mg capsules/extract with 0.3 % hypericin content taken 3 times per day with meals	[67-72]
								250 mg extract with 0.2 % hypericin content taken 2 times daily.	
								300 mg capsules with 5 % hyperforin content taken 3 times daily	
								Crude: 2-4 g orally every day to once in three days	
3	Moringa oleifera	Moringa/Drums tick tree/Suhanjana	Moringaceae	Leaves, pods/ fruits	Hepato-protective, cardio- protective, anti-bacterial, anti- carcinogenic, anti-inflammatory, and anti- oxidant	Depression, Attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder, premenstrual syndrome, psoriasis	Leaves Powder, extracts, seeds, pods	6-10 g of leaf powder	[14, 15, 73-76].
4	Thymus vulgaris linn	Thyme	Lamiaceae (Labiate)	Flowers, leaves	Anti-oxidant, anti-inflammatory, anti-cancer, and anti-microbial.	Cough, patchy hair loss (alopeciaareata), dementia.	Capsules, drops, tablets		[16].
5	Zingiber officinale Roscoe	Ginger, adrak, sonth	Zingiberaceae	Rhizome	Anti-convulsant, analgesic, anti- inflammatory, anti-ulcer, immunomodulatory	Throat infections, inflammation, asthma, dyspepsia, constipation, loss of appetite, palpitation, indigestion constipation, arthritis, colds, nausea, migraines, hypertension	Capsules, tablets, powder 0.5-3 g by mouth daily		[17, 18, 77].
6	Azadirachta indica Linn	Neem, margosa, Indian lilac, Limbo, Nim, Nimba, Medusa and Vempu	Meliaceae	Leaves, flowers, seeds, fruits, roots, and bark	Hypolipidemic, anti-fertility, microbicidal, anti-diabetic, anti-inflammatory, hepatoprotective, anti-pyretic, hypoglycemic, insecticidal, nematocidal, anti-ulcer, anti-oxidant, neuroprotective, cardioprotective, and anti-leishmaniasis	Headache, pyrexia, ulcer, respiratory disorders, diabetes, cancer, leprosy, dengue, malaria, chickenpox, and dermal complications	Powder, capsule, tablet		[78, 79]

7	Allium	Garlic, rason	Liliaceae	Leaves,	Anti-bacterial,	Infections, cardiovascular	Oil,		[21, 80]
	sativum linn.			flowers, and cloves	anti-fungal, anti-viral, anti- parasitic, hypotensive for intraocular pressure, hypotensive, anti-atherosclerotic, anti-thrombotic or anti- aggregatory, hypolipidemic, hypoglycemic, immune- modulator, anti-cancer, anti- diabetic, anti-inflammatory, neuroprotective	diseases, diabetes, high cholesterol, hypertension	powder, tablet, capsule		
8	Curcuma longa Linn	Turmeric, haldi, amba haldi, kurkum	Zingiberaceae	Rhizome	Anti-inflammatory, anti-oxidant, anti-neoplastic, anti-coagulant, anti-diabetic, cardio-protective, anti-ulcer, hypotensive, neuro-protective, anti-venin, hypocholesterolemic, and anti-viral	Fever, gastritis, dysentery, infections, chest congestion, cough, hyper-cholesterolemia, hypertension, rheumatoid arthritis, jaundice, liver and gallbladder problems, urinary tract infections, skin diseases, diabetic wounds, and menstrual discomfort	Tablets, capsule		[22, 23, 81]
9	Hibiscus sabdariffa L.	Roselle, red sorrel	Malvaceae	Calyces, seeds, oils, stems, and flowers	Anti-oxidant, anti-hypertensive, anti-diabetic, hepatoprotective, nephron-protective, antilipidemic, anti-microbial, anticancer, anti-parasitic, antiobesity, diuretic, immunomodulatory	Hypertension, pulmonary hypertension, atherosclerosis, high cholesterol	Tea, extracts, powder	TEA: up to 720 mL daily for up to 6 weeks	[82-85]
10	Tanacetum parthenium L	Feverfew	Asteraceae	Leaf, seed (oil)	Anti-microbial, anti-rheumatic, anti-inflammatory	Inflammation, women's ailments, migraine, headache, psoriasis, toothache, insect bites, asthma rheumatism, and stomach-ache		Extract 50-100 mg PO daily Fresh leaf 2.5 leaves PO daily Freeze-dried leaf 50-150 mg PO qD-BID	[25]
11	Apocynumca nnabinum L.	Indian hemp, dogbane	Apocynacea		Anti-inflammatory, anti-oxidant	Diabetes, arthritis, asthma, bowel disease, ulcer, heart related diseases, and atherosclerosis	Tincture		[27]
12	Echinacea purpurea L	Purple cauliflower	Asteraceae	Leaf, flower	Anti-inflammatory, anti-bacterial, anti-oxidant and lymphocyte activities	Typhoid fever, respiratory infections, prevents development of benign prostate hyperplasia	Capsule		[29, 31]

13	Rosemarinus officinalis L. / Salvia officinalis L.	Rosemary/dew of the sea	lamiaceae or labiatae	Leaves, flower,	Anti-viral, anti-bacterial, anti- fungal, anti-tumor, hepato- protective anti-oxidant, anti- rheumatic, anti-nocioceptive and anti-thrombotic	Neuropathic pain, headache, depression, anxiety, inflammation, dysmennorrhoea, muscle spasms, hyperglycemia and hypercholesterolemia, acne vulgaris, alopecia areata (stimulates circulation to hair follicles), dandruff and greasy hair	Leaf powder/essential oils/mother tinctures in homeopathic medicine	Powder: 1-2 g/day	[32, 33, 86, 87]
				stems, roots				as tea: 1-3 cups/d (steep 1-2g in 150 mL water)	
								Extract: 2-4 mL PO TID (1:1 in 45% alcohol)	
								Essential Oil: doses up to 0.1- 1 mL (6-10% essential oil), massage scalp for 2 minutes.	
14	Humulus lupulus Linn.	Hops	Cannabaceae	dried, flowering parts	Anti-inflammatory effects, anti- microbial, anti-oxidant, anti- proliferative, glucose metabolism and hormonal effects regulating, lipid effects and sedative/hypnotic effects.	Leprosy, bad smell of feet, liver diseases, constipation, sleeping disorders and for purification of blood	Capsules, powder	1-2 g	[35, 36, 88]
15	Pistacia lentiscus	Chios mastic	Anacardiaceae	Resin	Anti-microbial, anti-oxidant, anti-inflammatory, hypolipidemic, and	Dental caries, cardiovascular disease, systemic inflammatory	Capsule, powder		[38, 89]
	Linn.	54			anti-cancer	disorders, cancer, inflammatory bowel diseases			
16	Agrimonia pilosa Ledeb.	Rosacea	Rosacea	Leaves, seeds, flower	Anti-inflammatory, anti-diabetic, anti-tumor, anti-acetylcholinesterase, anti-oxidant, anti-bacterial, and anti-parasitic	Gastritis, gastric ulcer, diarrhea, lung inflammation, liver diseases cholecystitis, cholestasis, intestinal or bladder atony, pyelonephritis, bleeding disorders, skin defects, inflammatory conditions of the oral mucosa, tumors, trichomoniasis, vaginitis, diarrhea, and dysentery.	Capsules	1.5 - 4 g of the drug to be drunk twice or three times a day	[39, 40, 90]
17	Aniba Rosaeodora ducke	Rosewood	Lauraceae [,]	Bark, leaves	Anti-bacterial, anti-fungal, anti- protozoal, anti-oxidant, trypanocidal, sedative, anxiolytic, and anti-convulsant	Bacterial infections, fungal infections, epilepsy, anxiety,	Oil		[41, 91]
18	Commiphora myrrha	Myrrh	Burseraceae	Resin	Expectorant, emmenagogue, carminative, anthelmintic, astringent, antiseptic, antimicrobial, anti-inflammatory, anti-oxidant, analgesic, neuroprotective, anti-diabetic, anti-cancer, and anti-parasitic	Inflammatory illnesses (sinusitis, pharyngitis, gingivitis, and pyorrhea), wounds, mouth ulcers, pains, fractures, stomach problems, and microbiological infections	Capsule	600-1200 mg daily	[42, 92, 93]

19	intybus. L	Chicory/ coffee weed / blue sailor	Asteraceae	Roots, leaves	Anti-oxidant, hepato-protective, anti-inflammatory, anti-diabetic, anti-microbial, and tumor-inhibitory	Tumor, Inflammation	Capsule		[94, 95]	
20	Momordica charantia L	Bitter Melon	Cucurbitaceous	Leaves, seeds	Anti-microbial, anti-oxidant, nutraceutical, and anti- inflammatory	Gastric ulcers and conditions like rheumatism, cancer	Tablet	50-100 mL qD OR 900 mg of fruit TID	[96]	
21		Arugula/ salad rocket	Brassicaceae	seeds, leaves	Anti-microbial, anti-oxidant, anti- proliferative, anti-emetic, and anti-ulcer	Cancer, cardio-vascular diseases, testicular dysfunction, diabetes mellitus, nephroprotective	Capsules	400 mcg/day	[97, 98]	
22	peniculata	Green chiretta/ king of bitter	Acanthaceae	Leaves, seeds	Anti-inflammatory, hepatoprotective, hypotensive and hypoglycemic, anti-bacterial	Urine regulation, for reducing heat and fever, inflammation	Tablet		[99-100]	
	N. A. 11			P. C. H. L. G.						
S. No.	Medicinal herb		ne underlying me obial constituent	dicinal plants.	Antı-mıcrobial spectrum				Ref.	
1	Apium graveolens Volatile oils, flavone glycosides (apigenin) Bacillus aerogenes, B. coagulans, B. megatarium, B. subtilis, Lactobacillus lichmani, Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Kleibsellapheumoniae, Pseudomonas aeruginosa, Salmonella typhi, Shigella, Aspergillus niger, A. flavus, Candida albicans, Cryptococcus neoformans, Trichophyton rubrum								[64, 67, 101]	
2	Hypericum perforatum Linn		Essential oils, hypericin, hyperforin Penicillium expansum, Penicillium citrinum, Penicillium crustosum, S. aureus ATCC, S. epidermidis ATCC 1222							
3	Moringa oleifera Linn.								[76, 105	
4	Thymus vulgaris Linn.	Volatile oi linalool)	ls (thymol, P-cyme	ne, γ- terpinene,	Klebsiella pneumoniae, Pse	Klebsiella pneumoniae, Pseudomonas aeruginosa and Staphylococcus saprophyticus				
5	Zingiber officing	ale Phenolic c shogaols	ompounds, primari	ly gingerols and	cherichia coli, Staphylococcus aureus,	Vibrio cholerae, k	(lebsiella spp. and Salmonella spp	[17, 78]		
6	Azadirachta indi Linn.	compound	flavonoid glycoside s, steroids, triterpe triterpenoids azadi	enoids, carotenoi	ds,	Staphylococcus aureus, Pseudomonas aeruginosa,E-coli,				
7	Allium sativum Linn.	Allicin, ajo	pene, and allyl sulp	hides	·	Bacillus cereus, Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae, Micrococcus flavus, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, Salmonella typhimurium, and Staphylococcus aureus				
8	Curcuma longa Linn.	Curcumin			Pseudomonas aeruginosa, S	Gram-positive and Gram-negative bacterial strains: Staphylococcus aureus and Escherichia coli, Helicobacter pylori, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus mutants,Enterococcus faecalis, Salmonella typhimurium, Bacillus subtilis, Bacillus cereus, Bacillus coagulans and Mycobacterium tuberculosis, Candida species				
9	Hibiscus sabdari Linn.		tannin, phenols, gl coumarins, anthocy		· · ·	Staphylococcus aureus ATCC 25923, Staphylococcus epidermidis ATCC 49461, and Bacillus cereus ATCC 10876, Escherichia coli ATCC 25922, Salmonella enteric ATCC 5174, Klebsiella pneumonia ATCC 27736, Proteus vulgaris ATCC			[24, 85, 86]	

		sambubioside and cyanidin-3-sambubioside), hibiscus acid, volatile oils	49132, and Pseudomonas aeruginosa ATCC 27853;Streptococcus mutans, Staphylococcus aureus and Enterococcus faecalis; E. coli, Salmonella typhimurium, Pseudomonas aeruginosa, Staphylococcus aureus, and Vibrio cholerae	
10	Tanacetum parthenium Linn.	Essential oils, camphor, chrysanthenyl acetate, camphene,chrysanthenone, borneol, and bornyl acetate	Gram-positive and Gram-negative bacteria, fungi	[26]
11	Apocynum cannabinum Linn.	Apocynin oxime ester of undecanoic acid, fatty acid	S. aureus MTCC 96, K. Planticola MTCC 530, Micrococcus luteus MTCC 2470, Staphylococcus aureus MLS-16 MTCC 2940, Escherichia coli MTCC 739, Bacillus subtilis MTCC 121, Klebsiella planticola MTCC 530, Pseudomonas aeruginosa MTCC 2453, Candida albicans MTCC 3017, C. albicans MTCC 3958, C. albicans MTCC 227 and I. hanoiensis MTCC 4755, C. albicans MTCC 854, C. albicans MTCC 183, C. albicans MTCC 3018, C. albicans MTCC 1637, C. Glabrata MTCC 3019, C. krusei MTCC 3020	[27, 28]
12	Echinacea purpurea Linn.	Flavonoids, polyphenolic compounds, caftaric acid, echinacoside, and chicoric acid	E. coli, P. aeruginosa, S. aureus, B. cereus, B. amyloliquefaciens, L. monocytogenes, S. enteritis, E. faecalis, P. aeruginosa, C. albicans, S. cerevisiae, and Penicillium sp., Asp. niger ATCC 1015, Asp. flavus, Rhizopus sp., F. moniliforme ATCC 38932, and Mucor sp., C. albicans NBIMCC 74 and S. cerevisiae	[29]
13	Rosemarinus officinalis Linn.	Essential oil, ursolic acid, rosmarinic acid, rosmaridiphenol, carnosol, epirosmanol, carnosic acid, rosmanol, isorosmanol,	P.aeruginosa and E. coli, Bacillus cereus, Bacillus subtilis and S. aureus, Aspergillus flavus, Candida albicans, C. krusei, C. glabrata, C. parapsilosis, C. tropicalis C. dubliniensis, C. lipolytica	[34, 115- 117]
14	Humulus lupulus Linn.	sesquiterpene ketones (humulene, isohumulone, lupulene, lupulone), xanthohumol, bitter acids	S. aureus, S. mutans, Penicillium and Aspergillus species, Lactobacillus, Streptococcus, Staphylococcus, Micrococcus, and Bacillus, Brucella, Helicobacter pylori.	[35, 36, 118]
15	Pistacia lentiscus Linn	Essential oils, terpene & terpenoids (α -pinene, terpinene, caryophyllene, limonene, and myrcene), oils of mastic resin, flavonoids, phenolic acids	H. pylori, S. aureus, L. plantarum, Pseudomonas spp., S. enteritides, Streptococcus spp., Enterococcus faecalis, Porphyromonasgingivalis, Fusobacterium nucleatum, Actinomyces spp., Tannerella forsythia, Candida albicans and C. glabrata, Klebsiella pneumonia and Pseudomonas aeruginosa, A. niger and A. flavus, B. cereus, L. monocytogens, S. arizona, S. aureus, E. coli, S. typhimurium, K. pneumoniae.	[37, 38, 119-121]
16	Agrimonia pilosa Ledeb.	Flavanoids, phloroglucinol derivatives (agrimol C, agrimol F, agrimol G, and agrimophol)	Staphylococcus aureus, Bacillus cereus, and Gardnerella species	[39, 90]
17	Aniba rosaeodora ducke.	Essential oil (linalool, $\alpha\text{-terpinolene}$, linalool cisoxide	Aeromonas caviae, Enterococcus faecalis, Klebsiella pneumonia, Providenciastuartii	[41].
18	Commiphora myrrha	Oleo-gum-resin, furanosesquiterpenes (furanosesquiterpenoids, 2-methoxyfuranodiene and 2-acetoxyfuranodiene), commiferin	Staphylococcus aureus, Bacillus cereus, Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae, Fusobacterium nucleatum, Paenibacilluspasadenensis NBRC 161214, Micrococcus yunnanensis YIM 65004, Pseudomonas azotoformans NBRC 12693, Rhodococcusqingshengii, Staphylococcus capitis JCM 2420, Staphylococcus epidermidis NBRC 100911, Deinococcusradiodurans R1	[122]
19	Cichorium intybus Linn.	Inulin, sesquiterpene lactones, chlorogenic acid, organic acids (quinolinic, succinic, oxalic and chiquimic acids), chicoric acid	S. aureus and methicillin-resistant S. aureus, P. aeruginosa, and E. coli, Salmonella spp., Streptococcus mutans, Streptococcus sanguinis, Actinomyces naeslundii, Fusobacterium, nucleatum and Prevotella Intermedia, Aspergillus flavus, Aspergillus niger, Aspergillus fumigatus and Fusarium solani, B. subtilis, S. sanguinis, A. naeslundii, F. nucleatum and P. Intermedia, C. albicans, C. lipolytica, C. krusei and F. solani,	[43, 123]
20	Momordica charantia Linn.	Saponins and steroids (triterpenes), triterpenoids, quercetin, flavones	Klebsiella pneumoniae and Proteus mirabilis, Staphylococcus aureus, Staphylococcus epidermidis, Candida albicans, Escherichia coli, Salmonella typhi	[124] [125]
21	Eruca vesicaria sativa	Glucosinolate isothiocyanate, alkaloids, and their derivaties, flavonoid, phenols, tannins, erucin	Escherichia coli HAS, Staphylococcus aureus HAS, Klebsiella pneumonia, Pseudomonas aeruginosa	[98, 126]
22	Andrographis paniculata	Lactones (andrographolide), diterpenes, flavonoids, quinic acid, xanthones, noriridoids	Bacillus cereus, Bacillus thuringiensis, Staphylococcus aureus, and Enterobacter faecalis, Shigella flagella, Salmonella typhimurium, Klebsiella pneumonia, Escherichia coli, Pseudomonas aeruginosa, and Vibrio parahaemolyticus, Aspergillus niger, Trichophyton mentagrophytes, Candida albicans, Candida tropical	[127, 128]

5. Conclusions

Medicinal plants are effectively being explored for their therapeutic efficacy and safety after the development of resistance against most of the antibiotics. Medicinal plants possess significant activity against bacteria, viruses and fungi. The diverse constituents present in these plants have variable modes of action against pathogens. Rigorous research, scientific testing and validation are required to fully harness the anti-microbial potential, safety and broad-spectrum activity of these plants. Traditional knowledge, scientific data, standardization and quality analysis are the tools instantly required in this modern era not only to unlock the potential of the plants but to curb the ineffectiveness of synthetic antimicrobial agents.

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