Plant Science Review

PLANT SCIENCE REVIEW

ISSN No: 3041-7279

Review Article

Journal homepage: https://psr.crcjournals.org/

Check for updates

Phytochemical Profiling and Microbial Targeting of Medicinal Plants in the Development of Alternative Antimicrobial Therapies

Vinayaka K. S

Department of Botany, Sri Venkataramana Swamy College, Vidyagiri, Bantwal-574211, Dakshina Kannada, Karnataka, India

Received 09 July 2024 | Revised 06 September 2024 | Accepted 14 October 2024 | Available Online October 16 2024

*Corresponding Author: **Vinayaka K. S** | Email Address: **ks.vinayaka@gmail.com**

Citation: Vinayaka K. S (2024). Phytochemical Profiling and Microbial Targeting of Medicinal Plants in the Development of Alternative Antimicrobial Therapies. ***Plant Science Review***. **DOI: https://doi.org/10.51470/PSR.2024.05.02.07**

Abstract

The increasing prevalence of multidrug-resistant (MDR) pathogens has necessitated the search for novel antimicrobial agents. Medicinal plants, long used in traditional healing systems, offer a rich reservoir of bioactive compounds with therapeutic potential. This review explores the phytochemical profiling of medicinal plants and their targeted antimicrobial activity against a wide range of pathogenic microbes. By identifying key secondary metabolites such as alkaloids, flavonoids, terpenoids, and phenolic acids, researchers have been able to elucidate their roles in disrupting microbial growth and biofilm formation. The integration of advanced analytical tools like GC-MS, LC-MS, and NMR has enabled detailed chemical characterization of these compounds. Furthermore, this paper discusses the mechanisms by which plant-derived compounds exert antimicrobial effects, including membrane disruption, inhibition of nucleic acid synthesis, and interference with quorum sensing. The synergistic effects observed between plant extracts and conventional antibiotics also highlight the potential of phytochemicals as resistance-modifying agents. Finally, the review addresses current challenges and future perspectives in translating these findings into clinically viable therapies.

Keywords: *alkaloids, flavonoids, terpenoids, and phenolic acids, nucleic acid synthesis, traditional healing systems.*

1. Introduction

The rapid and relentless emergence of antimicrobial resistance (AMR) has become a global public health crisis, threatening the effectiveness of modern medicine. Once easily curable infections are becoming difficult to treat, with rising rates of resistance observed in pathogens responsible for common illnesses such as pneumonia, tuberculosis, urinary tract infections, and sepsis [1]. The World Health Organization (WHO) has identified AMR as one of the top ten global public health threats facing humanity. This alarming trend is largely driven by the overuse, misuse, and inappropriate prescription of antibiotics in both human and veterinary medicine, as well as the widespread use of antimicrobials in agriculture and animal husbandry [2]. As conventional antibiotics continue to lose their efficacy, there is an urgent need to explore new sources of antimicrobial agents that are effective, sustainable, and safe.

One promising yet underutilized approach lies in the exploration of medicinal plants, long revered in traditional medicine systems across cultures for their therapeutic potential. From Ayurveda and Traditional Chinese Medicine to indigenous healing systems in Africa and South America, plant-based remedies have played a crucial role in managing infections and promoting overall health [3].

The pharmacological value of these plants is largely attributed to the diverse array of secondary metabolites they produce—commonly referred to as phytochemicals. These bioactive compounds, including alkaloids, flavonoids, terpenoids, saponins, phenolic acids, and tannins, are not only central to plant defense mechanisms but also exhibit potent biological activities against a wide range of human pathogens.

Unlike synthetic antibiotics that typically target specific bacterial components, phytochemicals often exert multi-targeted mechanisms of action. For example, some disrupt microbial cell walls and membranes, others inhibit vital enzymes or interfere with DNA and RNA synthesis [4]. This multi-faceted activity reduces the likelihood of resistance development, making plant-derived antimicrobials especially valuable in the context of AMR. Additionally, several phytochemicals have been shown to interfere with quorum sensing—bacterial communication systems that regulate virulence and biofilm formation—thereby neutralizing pathogenicity without necessarily killing the microbes outright. This anti-virulence approach may further reduce selective pressure for resistance.

Over the past two decades, scientific interest in plant-based antimicrobials has surged, fueled by advances in phytochemical analysis, microbiology, and molecular biology. Techniques such as gas chromatography-mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and nuclear magnetic resonance (NMR) spectroscopy have enabled precise identification and quantification of phytochemicals in plant extracts. Concurrently, in vitro and in vivo studies have demonstrated the antimicrobial efficacy of numerous medicinal plants against both gram-positive and gram-negative bacteria, as well as fungi [5]. For instance, *Allium sativum* (garlic) and *Nigella sativa* (black seed) have shown broad-spectrum antimicrobial activity, while *Azadirachta indica* (neem), *Ocimum sanctum* (holy basil), and *Curcuma longa* (turmeric) have been investigated for their action against multi-drug resistant (MDR) pathogens.

Importantly, the interest in medicinal plants extends beyond mere antimicrobial potency. These natural products are often more accessible and affordable in resource-limited settings where healthcare infrastructure is lacking and antibiotic availability is constrained. Moreover, plant-based therapies align with the growing public interest in "green" medicine—remedies that are perceived to be more holistic, eco-friendly, and sustainable [6]. With proper scientific validation and standardization, plant-based antimicrobials can serve both as standalone treatments and as adjuvants that restore or enhance the efficacy of existing antibiotics.

However, despite their immense promise, medicinal plants remain underexplored in mainstream antimicrobial drug development. Major challenges include variability in plant composition due to environmental and genetic factors, lack of standardized extraction methods, limited clinical trial data, and concerns about toxicity and side effects when consumed in high doses or for prolonged periods. Furthermore, regulatory hurdles and gaps in intellectual property protection for traditional knowledge often hinder the integration of plant-based remedies into conventional healthcare systems [7].

This review seeks to bridge the gap between ethnobotanical knowledge and modern pharmaceutical science by providing a comprehensive overview of the antimicrobial potential of medicinal plants. It focuses on phytochemical profiling, mechanisms of microbial inhibition, and the role of these compounds in combating drug-resistant infections [8-9]. By highlighting both the scientific evidence and practical considerations surrounding plant-derived antimicrobials, this work underscores the importance of integrating traditional wisdom with modern innovation to tackle one of the most formidable challenges of our time—antimicrobial resistance.

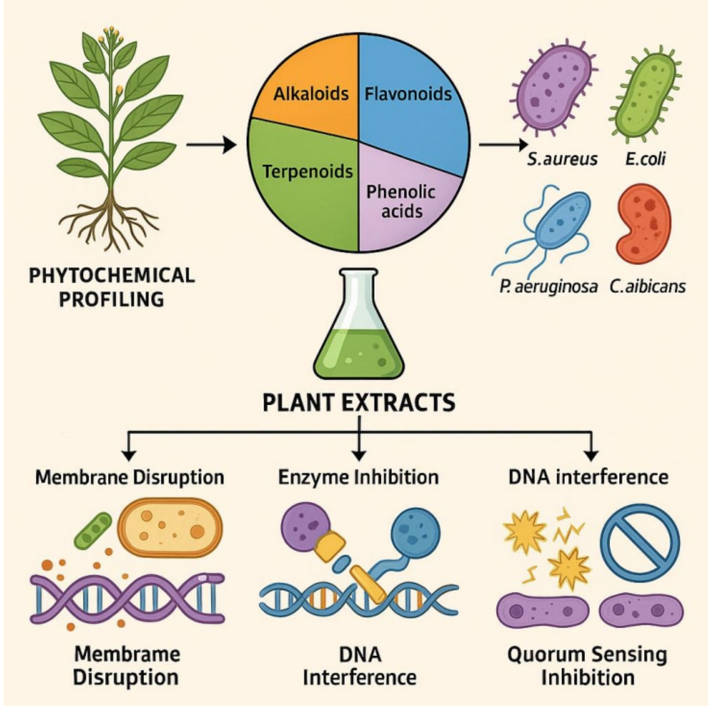

Figure. 1 Schematic Overview of Phytochemical-Based Antimicrobial Mechanisms from Medicinal Plants.

This fig 1. illustrates the key steps in utilizing medicinal plants for antimicrobial therapy. It highlights phytochemical extraction, profiling techniques like LC-MS and NMR, and major bioactive compounds such as alkaloids, flavonoids, terpenoids, and phenolics. The diagram also demonstrates their antimicrobial mechanisms—including membrane disruption, enzyme inhibition, DNA interference, and quorum sensing inhibition—targeting pathogens like *E. coli*, *S. aureus*, and *Candida albicans*. This integrated approach underscores the potential of plant-derived compounds in combating antimicrobial resistance.

2. Phytochemical Profiling of Medicinal Plants

Phytochemicals are a diverse class of naturally occurring compounds in plants that play a central role in their defense mechanisms against microbial invasion, herbivory, and environmental stress. These secondary metabolites are not directly involved in primary metabolic processes such as growth or reproduction but contribute significantly to the plant's adaptive survival and, importantly, to their therapeutic potential in humans. Among their many bioactivities, antimicrobial properties have drawn increasing attention in the context of developing alternative strategies to combat antimicrobial resistance [10-11]. The most prominent classes of phytochemicals with antimicrobial potential include alkaloids, flavonoids, terpenoids, and phenolic acids.

Alkaloids are nitrogen-containing compounds that exhibit a broad spectrum of bioactivities, including antibacterial, antifungal, and analgesic effects. They act by interfering with DNA replication, protein synthesis, and membrane function in microbial cells. Flavonoids, a large group of polyphenolic compounds, are renowned for their antioxidant activity, but they also possess potent antimicrobial effects. They exert their action through mechanisms such as inhibition of nucleic acid synthesis, disruption of microbial membranes, and inactivation of enzymes [12].

Terpenoids, also known as isoprenoids, are structurally diverse lipophilic compounds that often disrupt microbial membranes, impair energy metabolism, and interfere with signal transduction pathways in bacteria and fungi. Their ability to penetrate lipid-rich microbial cell walls makes them particularly effective against certain gram-positive and gram-negative organisms. Phenolic acids, such as caffeic and gallic acid, inhibit microbial growth by binding to proteins, altering membrane permeability, and disrupting essential enzyme systems, thereby affecting microbial metabolism and viability [13-14]. To harness the therapeutic potential of these phytochemicals, accurate and reproducible phytochemical profiling is essential. Advanced analytical technologies enable researchers to identify, isolate, and quantify individual compounds from complex plant extracts. Gas chromatography-mass spectrometry (GC-MS) is widely used for volatile and semi-volatile compounds, offering high sensitivity and precise molecular identification. For non-volatile and thermally unstable compounds, liquid chromatography-mass spectrometry (LC-MS) provides robust separation and detection, particularly for flavonoids, alkaloids, and phenolic acids. Additionally, nuclear magnetic resonance (NMR) spectroscopy is indispensable for structural elucidation and confirmation of isolated phytochemicals, complementing mass spectrometric techniques.

These analytical platforms, often used in combination, have dramatically improved our understanding of the chemical complexity of medicinal plants. They not only aid in the discovery of new antimicrobial candidates but also support standardization of herbal formulations for clinical application. The integration of phytochemical profiling with biological screening against microbial strains has further enabled the identification of bioactive markers responsible for therapeutic effects [15]. As the global scientific community intensifies efforts to find alternatives to conventional antibiotics, phytochemical profiling serves as a critical bridge between traditional medicine and modern pharmacological research. Continued exploration of plant-derived compounds through advanced analytical methods will be vital in identifying novel antimicrobial agents and in supporting the development of safe, effective, and standardized plant-based therapies.

Table 1: Major Classes of Phytochemicals and Their Antimicrobial Mechanisms

Phytochemical Class	Examples	Mechanism of Action	Target Pathogens
Alkaloids	Berberine, Sanguinarine	DNA intercalation, protein synthesis inhibition	*E. coli*, *S. aureus*, *Mycobacterium spp.*
Flavonoids	Quercetin, Catechin	Enzyme inhibition, membrane disruption	*P. aeruginosa*, *C. albicans*
Terpenoids	Limonene, Thymol, Menthol	Cell membrane lysis, efflux pump inhibition	*S. aureus*, *Salmonella spp.*
Phenolic Acids	Caffeic acid, Ferulic acid	Oxidative stress induction, enzyme disruption	*Listeria monocytogenes*, *E. coli*
Saponins	Dioscin, Glycyrrhizin	Membrane permeabilization, surface tension disruption	*Candida spp.*, *Bacillus subtilis*

Table 2: Selected Medicinal Plants with Antimicrobial Activity

Plant Name	Active Compounds	Microbial Targets	Activity Type
Azadirachta indica	Nimbin, Azadirachtin	*S. aureus*, *E. coli*, *C. albicans*	Antibacterial, Antifungal
Allium sativum	Allicin	*H. pylori*, *Candida spp.*, *E. coli*	Broad-spectrum
Ocimum sanctum	Eugenol, Ursolic acid	*S. aureus*, *P. aeruginosa*	Antibacterial, Antifungal
Camellia sinensis	Epigallocatechin gallate	*E. coli*, *MRSA*, *Salmonella typhi*	Antibacterial
Curcuma longa	Curcumin	*Bacillus spp.*, *Fusarium spp.*	Antimicrobial, Anti-inflammatory

Table 3: Techniques for Phytochemical Profiling and Their Applications

Technique	Principle	Application in Phytochemistry
Gas Chromatography–Mass Spectrometry (GC-MS)	Separates and identifies volatile compounds	Terpenoids, essential oils profiling
Liquid Chromatography–Mass Spectrometry (LC-MS)	Detects non-volatile compounds	Flavonoids, alkaloids, phenolics
Nuclear Magnetic Resonance (NMR)	Structural elucidation of organic molecules	Confirmation of molecular structures of phytochemicals
High-Performance Liquid Chromatography (HPLC)	Separation based on polarity	Quantification and purity assessment
UV-Visible Spectroscopy	Absorbance-based detection of compounds	Preliminary screening of phenolic and flavonoid content

3. Antimicrobial Activities of Plant Extracts

Medicinal plant extracts have demonstrated significant antimicrobial activity against a broad spectrum of human pathogens, including both gram-positive and gram-negative bacteria, as well as opportunistic fungal species. These bioactivities are largely attributed to the complex mixture of phytochemicals inherent to each plant, which often act synergistically to inhibit microbial growth and survival. Notably, many plant-derived compounds have shown efficacy against clinically relevant pathogens such as *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans*—microorganisms commonly associated with skin infections, urinary tract infections, respiratory diseases, and candidiasis, respectively [16]. One widely studied medicinal plant is *Azadirachta indica*, commonly known as neem. Neem extracts are rich in bioactive compounds like nimbin, nimbidin, and azadirachtin, which have been reported to exert strong antibacterial effects.

These compounds work by disrupting bacterial membrane integrity, interfering with biofilm formation, and modulating quorum sensing pathways. *Azadirachta indica* has demonstrated broad-spectrum antimicrobial activity and is traditionally used in treating skin infections, dental conditions, and gastrointestinal disturbances.

Ocimum sanctum, also known as holy basil or *Tulsi*, is another plant with well-documented antimicrobial potential. Its essential oils contain eugenol, a phenolic compound with potent antifungal and antibacterial properties. Eugenol acts by permeabilizing microbial cell membranes, leading to leakage of cellular contents and eventual cell death [17]. In addition to *S. aureus* and *E. coli*, *Ocimum sanctum* extracts have been effective against *Candida* species, making it a promising candidate for natural antifungal therapy.

Allium sativum, commonly referred to as garlic, is perhaps one of the most extensively studied antimicrobial plants. The compound allicin, released when garlic cloves are crushed or chopped, is known for its robust antimicrobial activity. Allicin reacts with thiol groups in microbial enzymes, inhibiting essential metabolic pathways and leading to microbial cell lysis [18]. Garlic extracts have shown effectiveness against multidrug-resistant strains of *P. aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA), highlighting their potential as adjunctive agents in antibiotic-resistant infections.

Numerous other medicinal plants also exhibit significant antimicrobial activity. For instance, Curcuma longa (turmeric) contains curcumin, which possesses antibacterial and antifungal properties through disruption of microbial cell division and suppression of inflammatory pathways. Similarly, Punica granatum (pomegranate) peel extracts, rich in tannins and polyphenols, have shown inhibitory effects on *E. coli*, *Salmonella*, and various fungal strains by damaging microbial membranes and interfering with nutrient uptake [19], the antimicrobial potential of plant extracts is not limited to individual compounds, but often results from the synergistic action of multiple phytochemicals. This complexity provides an advantage over conventional antibiotics by making it more difficult for microbes to develop resistance. Continued exploration of plant-derived antimicrobials, supported by rigorous pharmacological and microbiological evaluation, offers a promising path toward the development of novel, effective therapies to combat antimicrobial resistance and infectious diseases.

4. Mechanisms of Action of Phytochemicals

Phytochemicals exert their antimicrobial activity through a variety of molecular mechanisms that target the structural and functional integrity of microbial cells. The complexity and diversity of these mechanisms are key advantages of plant-derived compounds, often resulting in broad-spectrum activity and a reduced risk of resistance development.

One of the primary modes of action is membrane disruption. Lipophilic compounds such as terpenoids and saponins integrate into the lipid bilayer of microbial membranes, compromising membrane integrity. This leads to increased permeability, resulting in leakage of essential intracellular components, including ions, nucleotides, and proteins. Such disruption often culminates in osmotic imbalance and eventual microbial cell death. The ability of these compounds to destabilize microbial membranes is particularly significant in overcoming resistance mechanisms related to drug efflux pumps and reduced permeability [20]. Another important mechanism is enzyme inhibition. Polyphenolic compounds such as flavonoids and tannins are known to bind and inactivate microbial enzymes, particularly those involved in vital metabolic pathways. By forming complexes with bacterial proteins and metal ions, these phytochemicals interfere with enzyme structure and function. For example, tannins may precipitate membrane-bound proteins, while flavonoids can disrupt energy metabolism by inhibiting ATP synthesis or bacterial DNA gyrase activity.

Some phytochemicals, particularly alkaloids, interfere directly with microbial genetic material. These compounds can intercalate into microbial DNA, distorting the double helix and inhibiting replication and transcription processes. In addition, they may inhibit DNA topoisomerases, further disrupting nucleic acid synthesis and cell division. The capacity of alkaloids to interfere with nucleic acids makes them especially effective against rapidly dividing bacterial and fungal cells [21]. A more recently recognized mechanism is quorum sensing inhibition (QSI). Quorum sensing is a microbial communication system that regulates gene expression in response to population density, controlling processes such as virulence factor production and biofilm formation. Several plant-derived compounds, including certain flavonoids and phenolic acids, have been shown to interfere with this signaling. By blocking quorum sensing pathways, these phytochemicals can reduce microbial pathogenicity without necessarily killing the cells, which may help prevent the development of resistance, these mechanisms reflect the multifaceted strategies employed by phytochemicals to combat microbial pathogens. Their ability to target different cellular structures and processes simultaneously makes them promising candidates in the search for novel antimicrobial therapies, particularly in the face of rising antimicrobial resistance [22]. Future research should continue to explore these mechanisms in greater molecular detail, including structure–activity relationship (SAR) studies and synergy with existing antimicrobial agents.

5. Synergistic Effects with Conventional Antibiotics

One of the most promising applications of plant-derived phytochemicals lies in their ability to act synergistically with conventional antibiotics. This synergy can enhance the antimicrobial potency of existing drugs, particularly against resistant pathogens. For example, flavonoids from *Camellia sinensis* (green tea) have demonstrated the capacity to enhance the activity of antibiotics such as ciprofloxacin against *Escherichia coli* and *Staphylococcus aureus*. The mechanisms underlying these synergistic effects include increased antibiotic uptake, inhibition of efflux pumps, and modulation of bacterial stress responses. This not only restores antibiotic efficacy against resistant strains but may also allow for lower dosages of antibiotics, thereby reducing the risk of side effects and slowing the development of resistance. Moreover, phytochemicals may help disrupt biofilms or interfere with quorum sensing, making bacteria more susceptible to antibiotics [23]. These findings open up possibilities for combination therapies in which plant extracts are used as adjuvants to conventional drugs.

6. Challenges and Future Prospects

Despite the growing interest and demonstrated potential of phytochemicals in antimicrobial therapy, several challenges hinder their full-scale development and clinical translation. A major obstacle is the lack of standardization in herbal extracts. The chemical composition of plant extracts can vary significantly depending on species, geographical origin, growth conditions, and harvesting time, leading to inconsistent therapeutic outcomes. This variability poses a serious problem for quality control and reproducibility in both research and clinical settings [24].

Another significant challenge is the toxicity and safety evaluation of phytochemicals. While many compounds are derived from traditionally used medicinal plants, their effects at therapeutic doses, interactions with human cells, and long-term safety profiles require rigorous toxicological assessments and clinical trials. This is often complicated by the complexity of plant extracts, which may contain dozens of active compounds with diverse pharmacodynamics [25]. In addition, regulatory barriers related to herbal medicine and natural products further complicate commercialization. The lack of harmonized regulatory frameworks across countries delays the approval and integration of phytochemical-based therapeutics into mainstream healthcare. Nevertheless, the future of phytochemical antimicrobials appears promising. Advances in metabolomics, bioinformatics, and synthetic biology offer new tools to tackle current limitations. Metabolomic profiling allows for the identification and quantification of bioactive compounds in complex plant matrices. Bioinformatics can predict biological targets, resistance mechanisms, and synergistic potential. Synthetic biology enables the biosynthesis of key phytochemicals in microbial hosts, ensuring consistency and scalability, while numerous hurdles remain, the integration of modern scientific techniques with traditional knowledge holds great potential to harness medicinal plants in the global fight against antimicrobial resistance. Continued interdisciplinary research and investment are essential to unlocking the full therapeutic potential of plant-based antimicrobials.

7. Conclusion

Phytochemical profiling and microbial targeting of medicinal plants represent a promising and increasingly vital approach to addressing the global crisis of antimicrobial resistance (AMR). With conventional antibiotics rapidly losing their efficacy against multidrug-resistant pathogens, there is an urgent need to explore alternative therapeutic avenues. Medicinal plants, which have been utilized for centuries in traditional systems of medicine, offer a rich reservoir of bioactive compounds with proven antimicrobial properties.

Advancements in analytical technologies such as GC-MS, LC-MS, and NMR have significantly improved our ability to identify, characterize, and quantify plant-based phytochemicals. These compounds—including alkaloids, flavonoids, terpenoids, phenolic acids, and tannins—demonstrate diverse mechanisms of action such as membrane disruption, enzyme inhibition, DNA intercalation, and interference with microbial communication pathways like quorum sensing. Moreover, when used in combination with conventional antibiotics, many phytochemicals exhibit synergistic effects, potentially restoring drug sensitivity in resistant strains and enhancing treatment outcomes. Such synergy may also reduce required dosages, minimize side effects, and decrease the selective pressure that drives resistance. Despite these advantages, challenges such as standardization, toxicity assessment, and regulatory hurdles must be addressed. Interdisciplinary research integrating pharmacognosy, microbiology, pharmacology, and biotechnology is crucial to translate these findings into clinically viable solutions, harnessing the antimicrobial potential of medicinal plants through systematic phytochemical and microbiological studies can lead to the development of innovative, safe, and effective treatments for infectious diseases. As AMR continues to threaten global health, plant-based therapies offer a sustainable and powerful complement to modern antimicrobial strategies.

References

1. Kebede, T., Gadisa, E., & Tufa, A. (2021). Antimicrobial activities evaluation and phytochemical screening of some selected medicinal plants: A possible alternative in the treatment of multidrug-resistant microbes. *PloS one*, *16*(3), e0249253.

2. AlSheikh, H. M. A., Sultan, I., Kumar, V., Rather, I. A., Al-Sheikh, H., Tasleem Jan, A., & Haq, Q. M. R. (2020). Plant-based phytochemicals as possible alternative to antibiotics in combating bacterial drug resistance. *Antibiotics*, *9*(8), 480.

3. Khare, T., Anand, U., Dey, A., Assaraf, Y. G., Chen, Z. S., Liu, Z., & Kumar, V. (2021). Exploring phytochemicals for combating antibiotic resistance in microbial pathogens. *Frontiers in pharmacology*, *12*, 720726.

4. Anand, U., Jacobo-Herrera, N., Altemimi, A., & Lakhssassi, N. (2019). A comprehensive review on medicinal plants as antimicrobial therapeutics: potential avenues of biocompatible drug discovery. *Metabolites*, *9*(11), 258.

5. Vaou, N., Stavropoulou, E., Voidarou, C., Tsigalou, C., & Bezirtzoglou, E. (2021). Towards advances in medicinal plant antimicrobial activity: A review study on challenges and future perspectives. *Microorganisms*, *9*(10), 2041.

6. Suganya, T., Packiavathy, I. A. S. V., Aseervatham, G. S. B., Carmona, A., Rashmi, V., Mariappan, S., ... & Ananth, D. A. (2022). Tackling multiple-drug-resistant bacteria with conventional and complex phytochemicals. *Frontiers in cellular and infection microbiology*, *12*, 883839.

7. Enioutina, E. Y., Teng, L., Fateeva, T. V., Brown, J. C., Job, K. M., Bortnikova, V. V., & Sherwin, C. M. (2017). Phytotherapy as an alternative to conventional antimicrobials: combating microbial resistance. *Expert review of clinical pharmacology*, *10*(11), 1203-1214.

8. Borges, A., Abreu, A. C., Dias, C., Saavedra, M. J., Borges, F., & Simões, M. (2016). New perspectives on the use of phytochemicals as an emergent strategy to control bacterial infections including biofilms. *Molecules*, *21*(7), 877.

9. Shriram, V., Khare, T., Bhagwat, R., Shukla, R., & Kumar, V. (2018). Inhibiting bacterial drug efflux pumps via phyto-therapeutics to combat threatening antimicrobial resistance. *Frontiers in microbiology*, *9*, 2990.

10. Arip, M., Selvaraja, M., R, M., Tan, L. F., Leong, M. Y., Tan, P. L., & Jubair, N. (2022). Review on plant-based management in combating antimicrobial resistance-mechanistic perspective. *Frontiers in Pharmacology*, *13*, 879495.

11. Nortjie, E., Basitere, M., Moyo, D., & Nyamukamba, P. (2022). Extraction methods, quantitative and qualitative phytochemical screening of medicinal plants for antimicrobial textiles: a review. *Plants*, *11*(15), 2011.

12. Bhatia, P., Sharma, A., George, A. J., Anvitha, D., Kumar, P., Dwivedi, V. P., & Chandra, N. S. (2021). Antibacterial activity of medicinal plants against ESKAPE: An update. *Heliyon*, *7*(2).

13. Castronovo, L. M., Vassallo, A., Mengoni, A., Miceli, E., Bogani, P., Firenzuoli, F., & Maggini, V. (2021). Medicinal plants and their bacterial microbiota: a review on antimicrobial compounds production for plant and human health. *Pathogens*, *10*(2), 106.

14. Efferth, T., Kadioglu, O., Saeed, M. E., Seo, E. J., Mbaveng, A. T., & Kuete, V. (2021). Medicinal plants and phytochemicals against multidrug-resistant tumor cells expressing ABCB1, ABCG2, or ABCB5: a synopsis of 2 decades. *Phytochemistry Reviews*, *20*(1), 7-53.

15. Savoia, D. (2012). Plant-derived antimicrobial compounds: alternatives to antibiotics. *Future microbiology*, *7*(8), 979-990.

16. Lillehoj, Hyun, Yanhong Liu, Sergio Calsamiglia, Mariano E. Fernandez-Miyakawa, Fang Chi, Ron L. Cravens, Sungtaek Oh, and Cyril G. Gay. "Phytochemicals as antibiotic alternatives to promote growth and enhance host health." *Veterinary research* 49, no. 1 (2018): 76.

17. Wijesundara, N. M., & Rupasinghe, H. V. (2019). Bactericidal and anti-biofilm activity of ethanol extracts derived from selected medicinal plants against Streptococcus pyogenes. *Molecules*, *24*(6), 1165.

18. Tuyiringire, Naasson, Serawit Deyno, Anke Weisheit, Casim Umba Tolo, Deusdedit Tusubira, Jean-Pierre Munyampundu, Patrick Engeu Ogwang, Claude Mambo Muvunyi, and Yvan Vander Heyden. "Three promising antimycobacterial medicinal plants reviewed as potential sources of drug hit candidates against multidrug-resistant tuberculosis." *Tuberculosis* 124 (2020): 101987.

19. Reddy, S., Barathe, P., Kaur, K., Anand, U., Shriram, V., & Kumar, V. (2022). Antimicrobial resistance and medicinal plant products as potential alternatives to antibiotics in animal husbandry. In *Antimicrobial resistance: Underlying mechanisms and therapeutic approaches* (pp. 357-384). Singapore: Springer Nature Singapore.

20. Gadisa, E., Weldearegay, G., Desta, K., Tsegaye, G., Hailu, S., Jote, K., & Takele, A. (2019). Combined antibacterial effect of essential oils from three most commonly used Ethiopian traditional medicinal plants on multidrug resistant bacteria. *BMC Complementary and Alternative Medicine*, *19*(1), 24.

21. Das, R., & Mehta, D. K. (2018). Microbial biofilm and quorum sensing inhibition: Endowment of medicinal plants to combat multidrug-resistant bacteria. *current drug targets*, *19*(16), 1916-1932.

22. Mulat, M., Pandita, A., & Khan, F. (2019). Medicinal plant compounds for combating the multi-drug resistant pathogenic bacteria: a review. *Current pharmaceutical biotechnology*, *20*(3), 183-196.

23. Sisay, M., Bussa, N., Gashaw, T., & Mengistu, G. (2019). Investigating in vitro antibacterial activities of medicinal plants having folkloric repute in Ethiopian traditional medicine. *Journal of evidence-based integrative medicine*, *24*, 2515690X19886276.

24. Heliawati, L., Lestari, S., Hasanah, U., Ajiati, D., & Kurnia, D. (2022). Phytochemical profile of antibacterial agents from red betel leaf (Piper crocatum Ruiz and Pav) against bacteria in dental caries. *Molecules*, *27*(9), 2861.

25. Alhazmi, H. A., Najmi, A., Javed, S. A., Sultana, S., Al Bratty, M., Makeen, H. A., & Khalid, A. (2021). Medicinal plants and isolated molecules demonstrating immunomodulation activity as potential alternative therapies for viral diseases including COVID-19. *Frontiers in immunology*, *12*, 637553.

26. Wangchuk, P., Keller, P. A., Pyne, S. G., Taweechotipatr, M., Tonsomboon, A., Rattanajak, R., & Kamchonwongpaisan, S. (2011). Evaluation of an ethnopharmacologically selected Bhutanese medicinal plants for their major classes of phytochemicals and biological activities. *Journal of Ethnopharmacology*, *137*(1), 730-742.