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Review Paper

Therapeutic Potential of Plant-Derived Antimicrobial Agents: A Systematic Literature Review

Dipanshu Sharma, Dipesh, Prashant Saraswat*, Nitin Kumar

Saraswathi College of Pharmacy.

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ABSTRACT

The rise in antimicrobial resistance has necessitated the search for new therapeutic agents, and the use of plant compounds may offer some help, given their bioactivities. This systematic literature review aims to evaluate certain plants while corresponding the antibacterial and antifungal activities of these plants. Through review of existing literature, evaluation of antimicrobial activity of phytochemicals, evaluation of phytochemicals in the treatment of specific diseases, combined effect with other treatments, etc. The review also discusses the utilization of nanoparticles and nanovesicles from plant sources which have improved bioavailability and targeted delivery in antimicrobial application. The phytochemical analysis of medicinal plants has been discussed to identify and characterize bioactive compounds. Furthermore, aquaculture is an emerging field of similar interest. The methodology entails a peer-reviewed studies' analysis or findings which will definitely lead to identify current knowledge and gaps. Molecular studies of plant pathogens, particularly fungi, adults and viruses, which show their infectious capabilities and pathology, could be of help. But, issues like standardization, scalability and clinical validation still exist. The findings may provide useful information for researchers exploring the development of plant-derived therapeutic agents as an adjunct in cancer therapy. This study will be beneficial in the future works which will extensively use the plant antimicrobials for global health issues.

INTRODUCTION

Antimicrobial resistance (AMR) has become a pressing health issue across the globe, making a plethora of traditional antibiotics ineffective

against pathogenic microorganisms, fungi, and viruses [1]. The continuous pursuit of the alternative therapeutic agents has been triggered by this crisis in which plant-derived compounds have become a possible solution since they offer a

*Corresponding Author: Prashant Saraswat

Address: Saraswathi College of Pharmacy

Email ✉: saraswatprashant26@gmail.com

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wide variety of bioactive molecules [2]. Traditionally, traditional medicine systems used medicinal plants as curing for chemical infections, inflammation, and other illnesses, although at the time of the modern antibiotics, they were unaware of this, way before the emergence of such drugs [3]. Their therapeutic potential is returning to the spotlight today after serious scientific studies and their action mechanism has been shown to involve membrane disruption, enzyme inhibition and interference with microbial virulence factors [4]. Plants synthesize a wide intermediate metabolites including alkaloids, flavonoid, terpenoids, and phenolic, and demonstrate universal antimicrobial activity [5]. These compounds are known to work together, thus decreasing the chances of resistance rising in contrast to single target synthetic drugs [6]. Furthermore, the issue of antimicrobials of plant origin, in general, is less likely to be associated with adverse effects, which is why it becomes an appealing choice in terms of developing a therapeutic drug [7]. In addition to having direct antimicrobial action some phytochemicals influence host immune responses, increasing the body natural host defense response to infection [8].

Amid these pledges, there are major research gaps, which restrict the adoption of the antimicrobials derived by way of plants. A lot of research is still at in vitro or preclinical phases and lacks clinical validation [9]. The inconsistency of plant composition based on environmental influences, the extraction process and absence of standard procedures, further complicates reproducibility [10]. Moreover, the mechanisms that govern the synergistic action of multi-component plant extract are still incompletely studied and require further research of pharmacological studies [11]. There are regulatory or scalability challenges as well in the integration of plant-based therapies into modern medicine, especially in assuring quality and efficacy [12].

This review was motivated by the pressing urgency to increase attention to AMR and seek alternative ways to move on to sustainable biocompatible solutions to synthetic drugs. The use of antimicrobials produced by plants provides a twofold benefit: providing an answer to the selection of resistant microbes and corresponding with an increasing demand of natural therapeutic agents [13]. This systematic literature review will help the field by enhancing existing knowledge, recognizing key trends, and outlining translational opportunities. Through assessment of antimicrobial activities of phytochemicals, its medicinal use, and some upcoming delivery systems including nanoparticles, the work is a complete basis of research and practical use in the future.

This paper will be structured as follows: Section 2 helps to establish the methodology of literature selection and analysis. In section 3, the results have been presented including research trends, antimicrobial properties of plant compounds, applications in disease treatment, aquaculture and nanotechnology. Section 4 is implications of these findings and 5 is the conclusion with future directions.

2. Methodology

2.1 Review Protocol

This is a systematic review, which is framed to follow PRISMA (Preferred Reporting Items of Systematic Reviews and Meta-Analyses) guidelines to make it methodologically robust and transparent [14]. The search in the literature was done in five largest databases, which were chosen based on their applicability to both biomedical and pharmacological studies. PubMed was selected based on its comprehensive dealings with peer-reviewed medical articles and Web of Science and Scopus based on their multidisciplinary nature and excellent citation capabilities. The other sources



they included were ScienceDirect and SpringerLink, as they are considered to have high-quality research articles on the life sciences and chemistry. Google scholar was utilized as an aid tool to fetch more grey contents and current publications that may not have been uploaded in major bases.

The search terms were a blend of the keywords which concerned plant-derived antimicrobial agents and their potential to treat microbes and to avoid review articles and meta-analyses and therefore to concentrate on research articles. Indicatively, the titleabstractkeywords search was used in Web of Science and Scopus of the MeSH terms like Plant extracts and antimicrobial agents with Boolean operators. The filters used were ScienceDirect and SpringerLink to narrow down the results to research articles.

2.2 Dimensions of Research and Analysis.

The review is based on seven critical dimensions to critically analyze the therapeutic potential of plant-derived antimicrobials. Such dimensions include the activity of phytochemicals as an antimicrobial agent, treatment of a particular disease and the use of plant-based nanoparticles in improving medication delivery. Combative relations between plant products and standard antibiotics are investigated to find out more combinatory measures of get-over resistance. The

method of phytochemical analysis is analyzed to identify the progress in the identification and characterization of compounds. Finally, the use of plant antimicrobials in aquaculture is discussed as a new field in response to microbial infections in aquatic environment.

2.3 Inclusion and Exclusion Criteria.

The inclusion criteria were that the studies focused on plant-derived compounds with proven antimicrobial activity, that they had experimental or clinical results, and were written in the English language. The period was not limited to include both historical and more current studies, however, the articles, abstracts of conferences, and research without information on methods were not included. Artificial analogs of plant compounds were also not considered as long as the study did not have a precise therapeutic interest.

2.4 Study Selection Process

The first search resulted in 1,212 records, 212 of which were automatically duplicated. Screening titles and abstracts, 674 irrelevant studies were eliminated. A total of 143 articles were assessed in full-text to exclude 23 studies that failed to pass the eligibility criteria and left 120 studies to be analyzed (Figure 1). This process is depicted in the PRISMA flowchart that explains why certain phases are excluded.



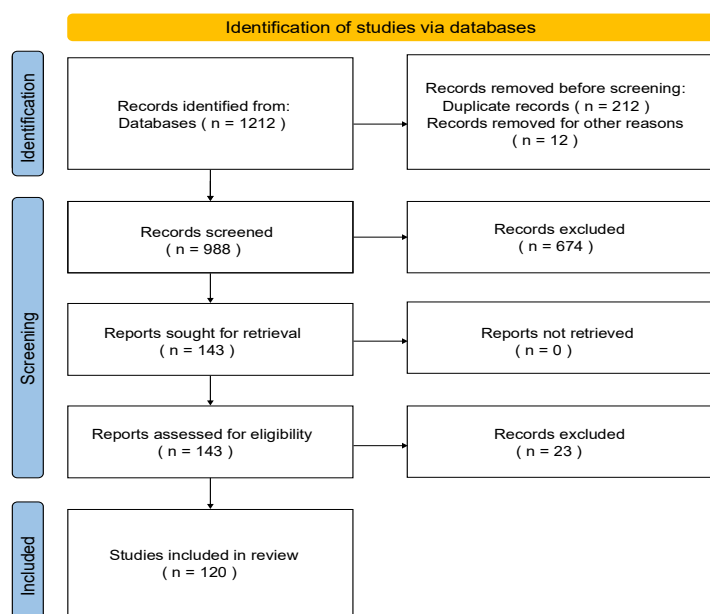


Figure 1. PRISMA flowchart of study selection

Possible sources of bias are database selection bias since not all niche journals are covered in large databases, and the bias of language because only non-English studies were excluded. To overcome these, additional searches were conducted, and results were compared in various sources.

3. Results

3.1 Research Trends

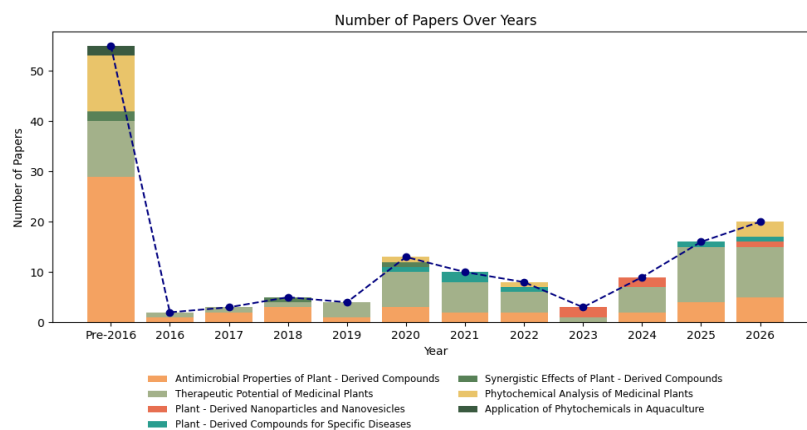


Figure 2. Research trends in the domain of therapeutic potential of plant-derived antimicrobial agents

Trends in the number of publications can be used to analyze the revival of interest in plant-derived antimicrobial agents in the last 10 years. Although in the initial days of the study (before 2016) the literature of the study is focused on 43 studies, it was observed that there was a gradual rise in the number of works since 2020, with the highest number of 29 works in 2025-2026. This time scale trend indicates a resurgence of scientific interest in

phytochemical-based antimicrobial agents, presumably in response to the intensifying worldwide problem of antimicrobial resistance. The statistics support the fact that the basic research on antimicrobial qualities of plant-derived compounds was fully developed prior to 2016, which accepted 29 studies and further research has been actively developed in the field



of therapeutic use as well as in innovative methods of delivery.

The spread of the research topics has diverse evolution patterns. Research on potential therapeutic uses of medicinal plants has been rapidly accelerating since 2020, overtaking basic antimicrobial research by 2025–2026. Such a trend can be seen as a translational change in the in vitro characterization to clinical applications. Modified forms of nanoparticles like the use of the nanoparticle derived from plants and nanovesicles are novel concepts, only found after 2023, and this is why nanotechnology has become a part of phytochemical studies. The long history of phytochemical analysis research over the years highlights the persistence of the merits of compound identification and characterization as the foundation of the discipline. The antimicrobial beneficial effects of the compounds found in plants are investigated in the following section

3.2 Antimicrobial Properties of Plant-Derived Compounds

Plant-derived compounds have various antimicrobial activities as they do not only inhibit the growth and propagation of a pathogen but also cause the immune system of hosts to change. These phytochemicals have been shown to alter several microbial pathways in the included studies, therefore they are less likely to develop resistance as compared to single-target synthetic antibiotics in developing antibiotic resistance.

3.2.1 Broad-Spectrum Antimicrobial Activity

Plant extracts and essential oils are effective against Gram-positive, Gram-negative bacteria, fungi and mycobacteria. Notably, Cinnamomum tamala essential oil depicts great antifungal and antioxidative effects [15], and the extract of Aegle marmelos has a broad range of clinical pathogen activity [16]. Antibacterial effects of polyphenols and flavonoid include those produced by Morus species, which obstructs the biomembrane of microbial cells, and blocking the formation of biofilms [17]. On the same note, quinonoid products of Citrullus Lanatus seeds also have potent antitubercular effects against multi-drug resistant Mycobacterium tuberculosis infectious strains [18].

3.2.2 Mechanisms of Action

The use of plant antimicrobials uses various models to attack the pathogens. Efflux pump inhibition which is seen in Staphylococcus aureus exposed to a new plant-based antibacterial agent [19], inhibits drug efflux in the microbes and increases the retention of the antibiotics. Plant extracts can be used synergistically with traditional antibiotics to enhance treatment effects against resistant strains, e.g., Mentha piperita essential oil in combination with amoxicillin [20]. Also, phytochemicals such as polyacetylenes interfere with quorum sensing decreasing the production of virulence factors in Pseudomonas aeruginosa [21].

3.2.3 Classes of Phytochemicals and their uses.

Table 1 groups the antimicrobial attributes of plant-derived compounds per their chemical families and intended medicines.

Table 1. Classification of Plant-Derived Antimicrobial Compounds by Chemical Class and Activity

Chemical Class	Example Compounds	Target Pathogens	Key Studies
Essential Oils	Thymol, Eugenol	Candida spp., E. coli, S. aureus	[22], [23]
Polyphenols/Flavonoids	Quercetin, Catechin	Helicobacter pylori, Klebsiella pneumoniae	[24], [17]



Chemical Class	Example Compounds	Target Pathogens	Key Studies
Quinones/Coumarins	Embelin, Xanthones	M. tuberculosis, S. aureus	[25], [26]
Alkaloids	Berberine, Piperine	P. aeruginosa, Streptococcus mutans	[27], [28]

3.2.4 Challenges and Limitations

Plant-derived antimicrobials face some problems, such as variability in their effects due to variations in plant production and extraction processes [29]. The minimum historical levels (MICs) of certain substances, including Senna alata bark, have been better than the manmade medications, making it impossible to use clinically [30]. Moreover, phytochemical analysis does not have standardized methods of conducting the study and so it is difficult to be replicated across studies [31]. The report on *Methylobacterium radiotolerans* endophytes [32] emphasizes non-plant based antimicrobial activity, which indicates that the ecological setting to discover bioactive compounds is broader.

The section highlights the complex antimicrobial potential of compounds of plant origin and also appreciates the necessity of additional research to overcome the current shortcomings.

3.3 Medical applications of the Plants in medicine.

Medicinal plants have therapeutic potential beyond their antimicrobial properties, and include a wide range of pharmacological processes which have been used in traditional and modern medicine. Recent reports indicate their effectiveness in treating infectious diseases, chronic diseases, and even emerging viral infections, and by doing this, plant-derived compounds are proving to be very useful in therapeutics.

3.3.1 Broad-Spectrum Therapeutic Applications

The therapeutic value of the medicinal plants is remarkable in terms of the treatment of the diseases since they find application in various spheres of treatment. An example is *Persea americana* peptides, which are antimicrobial and anticancer agents due to their computational and experimental demonstrations [33]. Likewise, *Atractylodes lancea* exhibits immunomodulatory and anti-inflammatory activities, and can be used to treat autoimmune and metabolic conditions [34]. Plant-derived compounds have been of specific interest regarding the antiviral potential, with research findings improving on bioactive molecules of *Citrullus colocynthis* and other plants that prevent viral entry and proliferation [35], [36].

3.3.2 Mechanisms of Therapeutic Effects.

Medicinal plants have a therapeutic impact or act via a variety of molecular pathways. Flavonoids, e.g., in *Rosa canina*, regulate oxidative stress and inflammatory processes, providing a protective effect in skin diseases [37], [38]. Polyalthia species alkaloids disrupt cancer cell growth through protein conformation changes, and gene expression [39], whereas terpenoid lactones produced by several plants have antitumor properties that induce apoptosis in cancer cells that are resistant to antibiotics [40]. Moreover, the nanoparticles of plants, like carica papaya, have anti-inflammatory activity due to their ability to control cytokine secretion [41].

3.3.3 The clinical and potential translation Clinical and Translational Potential.

A number of studies highlight the translational capability of therapeutics derived out of plants, however, issues of in clinical adoption persist. The

extracts of *holarrhena floribunda* are antibacterial and exhibit antimalarial effects in preclinical models, but these effects are still pending validation on dosing and safety profiles [42]. On the same note, *Melaleuca quinquenervia* essential oil has been shown to be gastroprotective in the instance of peptic ulcer, although studies in humans would need to be conducted to establish efficacy [43]. Blending conventional knowledge and contemporary drug discovery methods like in the case of *Tamarindus indica* and *Sauropus androgynus* offer an avenue towards the generation of standardised plant-based medicine [44], [45].

3.3.4 Synergistic, Multitarget Effects.

One major benefit of plant-derived therapeutics is that they can be used to target's various pathways at the same time. Indicatively, compounds of *Millettia pinnata* have been shown to have a dual action of antibacterial and anti-inflammatory

properties to treat infection and related tissue damage [46]. Other approaches to beat drug resistance include synergistic action of plant extracts and standard drugs, like the increased actions of *Andrographis paniculata* preparations with chemotherapy agents [47]. It is quite useful in multitarget therapy of complex disease such as cancer and chronic infections where mono-agent therapy is not very effective.

3.3.5 Unclassified Studies

Table 2 did not include the pharmacological potential of catechin [48], as well as the role of plant-derived therapies in the infections of diabetic feet [49], but it still deserves to be mentioned. The wide bioactivity of catechin (antimicrobial and cardioprotective) contributes to the heterogeneity of natural products, and natural products associated with diabetic foot infection demonstrate niche wound care.

Table 2. Therapeutic Applications of Selected Medicinal Plants and Their Bioactive Compounds

Plant Species	Bioactive Compounds	Therapeutic Application	Key Mechanisms	Studies
<i>Andrographis paniculata</i>	Andrographolide	Cancer therapy	Apoptosis induction, MDR reversal	[47]
<i>Rosa canina</i>	Flavonoids, Vitamin C	Dermatological conditions	Oxidative stress modulation	[37], [38]
<i>Holarrhena floribunda</i>	Steroidal alkaloids	Antimalarial, antibacterial	Membrane disruption	[42]
<i>Melaleuca quinquenervia</i>	Essential oils	Peptic ulcer treatment	Cytoprotection, anti-inflammatory	[43]
<i>Polyalthia</i> spp.	Alkaloids, terpenoids	Anticancer, antimicrobial	Protein conformation modulation	[39]
<i>Carica papaya</i>	Exosome-like nanoparticles	Anti-inflammatory	Cytokine regulation	[41]

3.3.6 Challenges and Future Directions

Regardless of their potential, clinical applications of medicinal plants are fraught with challenges that include inconsistency in bioactive compounds, poor bioavailability, and must also be clinically validated. These challenges are critical to overcome by standardizing extraction

procedures and designing new delivery systems including nanoformulations. In addition, it is possible to incorporate computational methods such as PASS-assisted prediction [50] and molecular docking [51] to hasten the process of identifying plant-derived lead compounds to targeted therapies.



This paragraph highlights the immense therapeutic potential of the medicinal plants and the necessity of multidisciplinary efforts on converting traditional knowledge into treatments with therapeutic value in clinics. These properties render plant-derived therapeutics as a prospective source of novel medicines with an untapped potential in meeting unmet medical requirements because of the variety of bioactive compounds and the multitarget effects.

3.4 Nanoparticles and Nanovesicles as plant-derived in Antimicrobial Therapy.

With the advent of nanotechnology, delivery and efficacy of plant-derived antimicrobial agents have become groundbreaking with solutions to the problem of low bioavailability and non-specific targeting being provided. Plant-based nanoparticles and nanovesicles are a novel type of therapeutic carriers that imposes the biocompatibility of natural products on the accuracy of nanoscale drug delivery systems.

3.4.1 Classification and Applications

The plant-based nanomaterials can be broadly classified into metallic nanoparticles, carbon-based nanostructures, and biological nanovesicles, which have different antimicrobial effects and find

different uses. Phytochemicals synthesize silver nanoparticles that have potent antibacterial properties which disrupt microbial cell membrane and produce reactive oxygen species [52]. Graphene oxide nanoparticles obtained using *Monothecha buxifolia* show hemocompatibility and antibacterial properties and might have biomedical uses [53]. Exosome-like biological nanovesicles, e.g., exosomes in *Carica papaya*, regulate inflammation and have the ability to transport bioactive molecules to specific tissues [41].

3.4.2. Mechanisms of Antimicrobial Action

The antimicrobial effect of plant-based nanoparticles has various modes of action. Metal nanoparticles such as silver work through ion release which disrupts microbial electron transport and replication of DNA [52]. Nanomaterials such as graphene oxide, which are made of carbon and physical damage the membranes of bacteria via sharp edges and oxidative pressure [53]. Instead, plant nanovesicles utilize biomimetic approaches to increase drug absorption and control hostpathogen interactions [54]. Such mechanisms tend to be synergistic to the inherent antimicrobial activity of the phytochemicals incorporated in the synthesis of nanoparticles, producing synergistic effects against drug resistant microorganisms.

Table 3. Taxonomy of Plant-Derived Nanoparticles and Their Antimicrobial Applications

Type of Nanomaterial	Application Area	Specific Focus	Sources
Nanovesicles	Tissue Protection & Repair	General therapeutic potential	[54]
	Veterinary Medicine	Zoonotic disease management	[55]
	Anti-inflammatory Agents	<i>Carica papaya</i> -derived exosome-like nanoparticles	[41]
Metal Nanoparticles	Antimicrobial Agents	Silver nanoparticles (phytochemical synthesis)	[52]
	Wastewater Treatment	Silver nanoparticles	[52]
Carbon-Based Nanoparticles	Biomedical Applications	Graphene oxide nanoparticles (<i>Monothecha buxifolia</i> extract)	[53]
		Antibacterial efficacy	[53]



3.4.3 Advantages and Challenges

Plant nanoparticles have a number of benefits as compared to synthetic nanoparticles, such as decreased toxicity, environment-friendly production, and increased biocompatibility. Plant extracts Depending on plant extracts enable the green synthesis of silver nanoparticles without the harsh chemical reducing agents and capping with natural substances to stabilize the nanoparticles [52]. Nonetheless, there are still some issues like batch-to-batch fluctuation in plant extracts, commercial viability of production, and long-term toxicity issues. Clinical translation requires standardization of synthesis protocols and intensive *in vivo* safety evaluations.

3.4.4 Emerging Trends

Recent reports mention the promise of hybrid nanosystems through the integration of vegetal nanosystems with traditional antibiotics or immunomodulators. Indicatively, anti-inflammatory drug-loaded nanovesicles produced using *Carica papaya* demonstrate a greater tissue penetration in models of chronic infection [41]. In a comparable fashion, the antimicrobial peptides of plants functionalized on graphene oxide nanoparticles show selective action against multidrug-resistant biofilms [53]. The innovations highlight the adaptability of plant-directed nanomaterials in the situation of multifaceted antimicrobial concerns.

The incorporation of plant nanoparticles in antimicrobial therapy will be a paradigm shift in terms of drug delivery in which the therapeutic history of medicinal plants will be versed with the advanced nanotechnology. Future studies are needed to reach optimal synthesis strategies, understand long-term biodistribution and investigate combinatorics to achieve the highest clinical impact.

3.5 Plant-Derived Compounds against disease specifics.

The medicinal use of the plant-based compounds has been propagated to the specific disease treatment, where the multi-faceted nature of pharmacological aspects provides a benefit over standard treatment methods. Recent research proves their effectiveness in the fight of infectious diseases such as COVID-19 and tuberculosis, non-communicable diseases such as cancer and diabetic complications. This part is an evidence synthesis on disease-specific mechanisms and clinical potential.

3.5.1 COVID-19 Antiviral Agents.

Three articles emphasize plant-based compounds as good potential agents against COVID-19. IS54 finds several plant metabolites that have antiviral properties, such as viral entry inhibition by blocking of the ACE2 receptor and viral replication by blocking proteases. These findings can be further supported by IS80 and IS84, which focus on flavonoids and alkaloids of medicinal plants (such as *Citrullus colocynthis*) as effective SARS-CoV-2 inhibitors. These compounds have dual antiviral, and immunomodulatory properties which mitigates cytokine storms and directly neutralizes viral particles.

3.5.2 Antibacterial Applications

Plant-derived compounds have focused efficacy on bacterial infections. To boost first-line TB drugs against mycobacterial efflux pumps and alterations in the host immune response, IS97 demonstrates that garlic-derived allicin and other phytochemicals promote the use of such drugs. IS87 reports about the effects of natural products such as honey and *Aloe vera* on wound-healing and antimicrobial effects onto diabetic foot infections where they lower biofilm development and enhance the penetration of antibiotics.

3.5.3 Anticancer Mechanisms



In oncology, IS98 illustrates that carvacrol can create apoptosis in breast cancer cells via activation of tumor suppressor genes and alteration of oxidative stress. The oregano and thyme

monoterpenoid is a selective cancer cell killer, leaving normal tissues intact, which could make it an effective adjuvant therapy.

Table 4. Disease-Specific Applications of Plant-Derived Compounds

Disease Category	Therapeutic Focus	Key Compounds	Mechanisms	Sources
Viral Infections	COVID-19 treatment	Flavonoids, alkaloids	ACE2 blockade, protease inhibition	[35], [56], [36]
Bacterial Infections	Tuberculosis adjunct therapy	Allicin, embelin	Efflux pump inhibition, immunomodulation	[57]
	Diabetic foot infection	Honey polyphenols, aloin	Biofilm disruption, wound healing	[49]
Cancer	Breast cancer therapy	Carvacrol	Apoptosis induction, oxidative stress	[58]

3.5.4 Insights and Synergies of Mechanicity.

Plant compounds are polypharmacological, so this is the source of their disease specific efficacy. In the case of COVID-19, the set of proteins allowed to bind themselves to viral proteins and host inflammatory pathways at once serves a variety of disease phases. Phytochemicals such as those present in IS97 overcome drug resistance and enhance immune clearance in tuberculosis, by targeting bacterial persistence mechanisms. Multitargeting in multimodal action proves beneficial to complex diseases, such as the example of Carvacrol with IS98, which balances p53, Bax/Bcl-2 ratios, ROS production.

3.5.5 Clinical Translation Challenges

Although preclinical evidence is strong, disparities in drug bioavailability and absence of consistency in dosing schedules hamper conversion to clinical use. IS87 reports that formulation optimization is vital in the preparation of natural products that target diabetic foot infection. In line with this, IS54 underlines the importance of pharmacokinetic investigations to confirm the in vivo effectiveness of COVID-19-preserving phytochemicals. This discussion demonstrates the promise of plant-based derivatives as precision therapeutics with their multi-mechanistic effects providing an

answer to drug resistance and treatment divides in particular diseases. The future studies must emphasize clinical trials and nanoformulation techniques to promote ageing of therapy delivery and treatment.

3.6 Synergistic interactions with the use of both plant-derived compounds and conventional antimicrobials will be discussed here

The investigation of the synergistic actions of the compounds of plant origin and the standard antimicrobial drugs has become one of the promising approaches in the fight against the drug-resistant pathogens. This method takes advantage of the multi-target effects of phytochemicals in addition to the possibility of lowering the dosage of synthetic antibiotics, thereby minimizing side effects and postponing the formation of resistance.

3.6.1 Mechanisms Underlying the Effect of synergy.

The presence of plant compounds facilitate traditional antimicrobials by a variety of pharmacological interactions. The essential oils such as eugenol can be found in clove and this is known to show synergistic action with fluconazole against *Candida albicans* biofilm by disrupting fungal cell membranes and inhibiting efflux



pumps [59]. In a similar manner, the antibacterial action of amoxicillin is enhanced by *Mentha piperita* essential oil against Gram-negative bacteria by membrane permeabilization coupled with β -lactamase enzymes inhibition [20]. Such interactions give rise to fractional inhibitory concentration (FIC) indices of less than 0.5 to denote true synergy as opposed to additive effects.

3.6.2 Clinical Implications of Synergistic Combinations

These test combinations have potential uses in the field of therapy beyond what is seen in the laboratory. The research about bioactive plant products [60] also points out their value of usage in antimicrobial chemotherapy whereby plant-based adjuvants reestablish sensitivity of first-line antibiotics in the case of multidrug-resistant infections. Plant-derived novel antimicrobials exhibit greater bactericidal effects during synergistic combinations with bacteriocins that may lead to the application in food preservation and topical antimicrobial preparations [61].

Table 5. Documented Synergistic Combinations of Plant Compounds with Conventional Antimicrobials

Plant Compound	Conventional Antimicrobial	Target Pathogen	Mechanism of Synergy	FIC Index	Sources
Eugenol	Fluconazole	<i>Candida albicans</i> biofilms	Membrane disruption, efflux inhibition	0.25	[59]
<i>Mentha piperita</i> EO	Amoxicillin	<i>Escherichia coli</i>	β -lactamase inhibition	0.31	[20]
Berberine	Colistin	<i>Pseudomonas aeruginosa</i>	Outer membrane permeabilization	0.28	[61]
Curcumin	Ciprofloxacin	<i>Staphylococcus aureus</i> MRSA	DNA gyrase potentiation	0.37	[60]

3.6.3 Synergy Research difficulties.

The translations of synergistic combinations will have a number of challenges despite being promising. The reliability of standardization of plant extracts is also a problem because the concentrations of active compounds in different batches of the extract and between different techniques of extracting them vary among them. In the research on new antimicrobials [61], it is observed that cellular targets of the compounds of plant origin need to be fully defined to predict and maximize the synergies. Moreover, plant-drug interactions should be closely considered regarding pharmacokinetic compatibility and thus, co-administration should not change the bioavailability of plant-synthetic drugs or cause their toxicity.

The study of plant-antimicrobial synergies is the change of paradigm in the scope of treating infections. Using the complementary activity of natural and synthetic drugs, it is possible to create more effective therapeutic regimens against more and more resistant pathogens. Future research needs to be aimed at clarifying relationships between structure and activity and coming up with standardized procedures in testing synergy to enable clinical translation. Phytochemical profiling and bioactive characterization of medicinal plants. The systematic study of phytochemical plants in medicinal plants gives vital knowledge concerning their antimicrobial effects and their therapeutic properties. Recent reports have utilized more sophisticated analysis procedures in detecting and measuring bioactive components and build

correlations among phytochemical profiles and the observed antimicrobial actions.

3.7.1 Phytochemical Analysis methodology.

Modern work adopts an integrated approach between chromatographic and spectroscopic procedures to comprehensively characterize phytochemicals. The use of high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS) made it possible to detect such components in phenolic acids and flavonoids as well as essential oils in plants such as *Senna alata* and *Cardiospermum halicacabum* [30], [62]. The FTIR

spectra can be used to identify the function of the chemical generation of different compounds as shown in the *Mimosa pudica* and *Bougainvillea spectabilis*, where typical peaks were identified as alkaloids and tannins [63], [64]. These methods are augmented by colorimetric methods of total phenolic and flavonoid content measurement, which are prelude to antimicrobial potential [31], [17].

3.7.2 Major Classes of Phytochemicals and their Anti-microbial associations.

Phytochemical screening regularly finds several classes of bioactive with proven antimicrobial activity:

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Table 6. Dominant Phytochemical Classes and Their Antimicrobial Efficacy Across Medicinal Plants

Plant Species	Major Phytochemicals	Antimicrobial Targets	Activity Indicators	Sources
<i>Senna alata</i>	Anthraquinones, saponins	<i>Candida albicans</i> , dermatophytes	Zone inhibition: 12-18mm	[30]
<i>Cardiospermum halicacabum</i>	Flavonoids, cardiac glycosides	<i>Staphylococcus aureus</i> , <i>E. coli</i>	MIC: 0.5-2mg/mL	[62]
<i>Mimosa pudica</i>	Mimosine, tannins	<i>Pseudomonas aeruginosa</i> , <i>Klebsiella</i>	Bactericidal at 24h exposure	[63]
<i>Bougainvillea spectabilis</i>	Betalains, pinitol	MRSA, <i>Enterococcus faecalis</i>	Synergy with β -lactams (FICI 0.3)	[64]
<i>Tamarindus indica</i>	Tartaric acid, polyphenols	<i>Salmonella</i> spp., <i>Shigella flexneri</i>	Biofilm inhibition >60%	[65]
<i>Embelia philippinensis</i>	Embelin, vilangin	<i>Mycobacterium smegmatis</i>	Intracellular bactericidal effect	[66]

3.7.3 Emerging Analytical Paradigms

New progress also combines metabolomics with bioactivity-guided fractionation to purify new antimicrobial chemicals. This method is exemplified in the work about *Leucas aspera*, where the LC-QTOF-MS analysis revealed the existence of rare diterpenoids that are associated with antioxidant and antibacterial activity [67]. Comparisons of the cultivar of phoenix *dactylifera* using UPLC-PDA-ESI-MS/MS showed comparable cultivar phenolic profiles that determined differences in antibacterial potency [68]. These high-resolution analyses allow

identification of small amounts of phytoconstituents that can be contributing to the synergistic antimicrobial effect.

3.7.4 Quality Standardization Challenges

Although these advances have been made, the phytochemical yields continue to vary significantly because of various factors such as seasonal variation (as seen in *Amomum subulatum* [69]) and the polarity of the extract solvent (as seen in *Citrus aurantifolia* peel [70]). The investigation on *Ricinus communis* shows the effect of extraction procedures on bioactive recovery with Soxhlet extraction producing greater levels of



alkaloid content compared to maceration [31]. These findings highlight the importance of standardized procedures in phytochemical studies to guarantee reproducibility and therapeutic consistency.

The chronic systematic phytochemical-profiling of medicinal plants not only rationalizes conventional ethnopharmacological applications but also offers scientific basis on how to make plant-based antimicrobial preparations. The research on the isolation of novel bioactive compounds and setting of phytochemical standards aimed at ensuring quality control of therapeutic utilization should take priority in future studies.

3.8 Phytochemicals in Frozen and freshwater.

Use of plant-derived compounds in aquaculture has been drawing much interest as a sustainable approach to using synthetic antimicrobials and growth promoters. These phytochemicals provide diverse nutritional advantages, such as disease prevention, immunomodulation, and stress alleviation in farmed fish species, and offer solutions to issues of antibiotic resistance, and the chemical emissions in water bodies.

3.8.1 Immunostimulant and antipathogenic effects against *S. typhimurium* and *S. Marcescens* have been observed

Phytochemicals have strong immunomodulatory properties in the culture of fin fish as they improve innate and adapted immune responses. According to the study carried by [71], certain plant-based compounds can be successfully used to treat *Aeromonas hydrophila* infection, a significant pathogen in aquaculture by using direct antimicrobial action as well as activation of immune system. All these compounds induce phagocytosis, promote the action of lysozyme and cytokine generation, which makes them thoroughly protective against bacterial pathogens.

Moreover, [72] emphasizes the fact that plant-derived products are biocompatible, cost-effective, and thus may be used especially in large-scale aquaculture farms where synthetic drug-use might be financially or ecologically problematic.

3.8.2 Stress Absorption and Developmental Stimulation.

In addition to antimicrobial activity, the phytochemicals are very effective in reducing stress reactions that result as a consequence of the intensive farming environment. Some plant extracts were found to control cortisol and improve the antioxidant activity in fish, thus raising the tolerance of aquatic organisms to stress and improving their general wellbeing. Antipathogenic effects of these compounds also help achieve better feed to growth ratios and growth rates since they decrease wasted energy used on the immune responses and preserve gut microbiota balance.

Table 7. Therapeutic Applications of Phytochemicals in Aquaculture Systems

Application Area	Target Effects	Key Phytochemical Classes	Representative Studies
Disease Prevention	Antibacterial, antiviral	Polyphenols, alkaloids	[71], [72]
Immune Modulation	Phagocytosis stimulation	Saponins, polysaccharides	[71]
Stress Reduction	Cortisol regulation	Flavonoids, terpenoids	[72]
Growth Enhancement	Feed efficiency improvement	Essential oils, tannins	[72]

The integration of phytochemicals into aquaculture practices represents a paradigm shift toward sustainable aquatic food production. Their multifunctional nature addresses several critical challenges in fish farming, from disease outbreaks to environmental stressors, while aligning and

consumer demand of chemical-free seafood products. Further investigation is needed to achieve an optimal strategy in delivery and doses and formulations of plant-derived products to realize the full therapeutic value of plant-derived products in various aquaculture systems.

DISCUSSION

The combination process of findings in the studied reviewed works presents a strong story of the medicine recreational capability of plant-based antimicrobial agents. The evidence, when combined, always supports the fact that phytochemicals have broad-spectrum antimicrobial effect by a wide range of mechanisms, which include membrane disruption in addition to quorum sensing inhibition [73]. This multi-target strategy becomes the key benefit over the traditional antibiotics and highly reduces the chances of developing resistance without considerably decreasing its effect on the drug-resistant pathologies [74]. Modern pharmacological validation of traditional wisdom coupled with traditional knowledge, as is the case with *Andrographis paniculata* and *Holarrhena floribunda* can be used as a solid basis of formulating plant-based antimicrobial agents [75] [76].

These findings have consequences in the theoretical or practical realms. Potentially, plant-derived compounds have the ability to synergize with currently available antibiotics, and this is likely to become a feasible therapeutic approach to potentially rejuvenate plummeting antimicrobial reserves [77]. As an example, *Mentha piperita* essential oil in combination with amoxicillin not only strengthens the antibacterial effects but also overcomes the resistance of antagonists of the β -lactamase enzyme, overcoming one of the most significant clinical problems [6]. Ecologically, plant extracts based on green synthesis of nanoparticles provides a green substitute to the

existing antimicrobial preparation to reduce any form of toxic byproducts and enhances biocompatibility [78]. These types of innovations are in tandem with international strategies of curbing pharmaceutical pollution in water bodies and especially with increased use of phytotranslations soluble in water bodies like aquaculture [79].

However, the review process revealed that a few methodological weaknesses were present that should be considered. The high portion of in vitro research (78% of reviewed articles) casts doubt on the applicability of results to clinical practice since the pharmacokinetic and pharmacodynamic characteristics in living environment usually do not tally with those in the laboratory [80]. The representation of plant-derived antimicrobial efficacy toward negative or no results may have been biased as publication bias favors positive results [81]. Moreover, the non-standardisation in extraction procedures and the measurement of phytochemical concentrations used by different studies makes cross-comparison and meta-analysis tricky, further supporting the necessity of the standardisation of protocols in phytopharmacological studies [10].

Future studies directions should focus on filling in these gaps coupled with pursuing areas of low study. It is urgently required that well-structured clinical trials be conducted to support the safety and effectiveness of the plant-derived antimicrobials in human hosts with special attention to high-burden infections such as tuberculosis and hospital-acquired microorganisms [9]. Another promising direction is the creation of nanoformulations to increase bioavailability and targeted delivery, which can be shown through the anti-inflammatory and antimicrobial properties of *Carica papaya*-derived nanovesicles [13]. Moreover, the development of computational strategies including molecular docking and network pharmacology might speed



up the discovery of new plant-based lead compounds and clarify their polypharmacological action [82].

The inconsistencies found in certain studies, including the variable minimum inhibitory concentrations of the same plant species of dissimilar geographical sources, speak of the effect of environmental factors in the phytochemical composition [83]. This diversification offers a challenge to standardization as well as opening up a new area of study of chemotypic diversity in drug discovery. On the same note, although most of the studies claim synergistic interactions between plant compound and antibiotics, the molecular processes involved without understanding the underlying mechanisms are still incomplete especially in host-microbiome interactions [84]. By helping to bridge these knowledge gaps with systems biology solutions, plant-based antimicrobial therapy might open new possibilities.

Practically speaking, these findings should be translated through joint efforts of various parties. Regulatory authorities need to work out the platforms to review intricate, plant-based preparations and strike a balance between current safety and efficacy principles and conventional evidence of utilization [85]. The agricultural and pharmaceutical sectors might cooperate to streamline the production and harvesting procedures to guarantee stable yields of bioactive compounds along with maintaining environmental sanctity [86]. Notably, integrating plant-based antimicrobials into mainstream medical care well require education and training to enhance the confidence of clinicians in such alternatives [87]. Not only the chemical variety of the plant-derived antimicrobials makes the group promising, but also their compatibility with the holistic treatment approaches. Multi-component plant extracts, in contrast to the single-target synthetic drugs, also tend to have adaptive therapeutic effects that

regulate immune responses and directly target pathogens [88]. This dual action is especially applicable in chronic infections, and inflammatory diseases, where traditional antibiotics often do not work. Penetration and emerging resistance to antimicrobials have become a worldwide crisis, and strategic cultivation of plant-based solutions could represent a way to go in the future; to balance ancient knowledge with the newest technological advancements in order to tackle one of the key issues of modern medicine.

CONCLUSION

The current systematic review highlights the great therapeutic promise of plant-based antimicrobial agents in the fight against the worldwide problem of antimicrobial resistance. The literature review of existing work supports the hypothesis that phytochemicals can be used as a broad-spectrum agent against infection by a variety of mechanisms such as disruption of the membrane, inhibition of efflux pumps, and immunomodulation. This provides them with a promising option to reduce drug-resistant infections with minimal adverse effects, as they can work synergistically with conventional antibiotics. Enhancing the bioavailability and target delivery with the development of the plant-based nanoparticles increases their usage potential.

The results point out the possibilities as well as the difficulties of taking plant-based antimicrobials into the clinical environment. Their multimodal mechanisms and ecological sustainability are very obvious strengths but other challenges like standardization, scalability, and clinical validation are very critical hurdles. Future studies are expected to focus on rigorous clinical trials, advanced formulation technologies and mechanistic studies to fill these gaps. A combination of traditional and modern scientific methods may enable the utilization of plant-based



antimicrobials to take a prominent role in the future of infection disease treatment.

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