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Plant-Based Antibacterial Agents against Pathogenic Bacteria: A Review on Mechanisms and Recent Developments

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Abstract

Background: Antimicrobial resistance (AMR) is a global health crisis that is outpacing discovery of new antibiotics. Plant-derived phytochemicals and plant-based formulations are promising sources of novel antibacterial agents that may act by multiple mechanisms and restore antibiotic efficacy. **Objective:** To synthesize plant-derived antibacterials addressing (1) primary phytochemical classes, (2) Molecular and cellular mechanisms against pathogenic bacteria, (3) Evidence for synergy with conventional antibiotics, (4) Nanotechnology-based delivery/optimization strategies, and (5) Translational progress and barriers. **Methods:** A systematic literature search of Scopus (primary), complemented by PubMed and Web of Science, was performed for reviews and original research published mainly in the last decade. Search strings combined terms such as "plant antimicrobial", "phytochemical antibacterial", "antimicrobial resistance", "antibiofilm", "synergy antibiotic plant", and "nano-herbal". Peer-reviewed Scopus-indexed articles and high-quality reviews were prioritized for synthesis. **Results:** Major phytochemical groups (phenolics/flavonoids, alkaloids, terpenoids/essential oils, tannins, and saponins) exhibit antibacterial activity through membrane disruption, nucleic acid/protein synthesis inhibition, efflux pump modulation, quorum sensing (QS) interference and anti-biofilm effects. Synergistic combinations of plant extracts or phytochemicals with antibiotics restore activity against resistant strains in vitro. Nano-encapsulation and nano-emulsions substantially improve phytochemical stability and bioavailability. However, variability of extracts, and few clinical studies hinder translation. **Conclusion:** This review supports a strong preclinical rationale for plant-derived antibacterials as adjuncts or alternatives to antibiotics, particularly against biofilms and multidrug-resistant (MDR) pathogens. Focused standardization, mechanism-guided isolation, optimized delivery (nano-systems), and rigorous in vivo and clinical validation are required for clinical translation.

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Keywords: Plant-derived antibacterials; Phytochemicals; Antimicrobial resistance (AMR); Synergy with antibiotics; Anti-biofilm; Nano-herbal formulations.

1. Introduction

Antimicrobial resistance (AMR) threatens modern medicine by undermining the effectiveness of standard antibiotics. The pipeline for new antibiotic classes is limited, and many pathogenic species—*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterococcus spp.* and Gram-negative Enterobacterales—exhibit multidrug resistance through diverse mechanisms (enzymatic degradation, efflux pumps, target modification, and biofilm formation)[1,2]. Plant secondary metabolites provide a structurally diverse reservoir of molecules historically used in traditional medicine and increasingly investigated in peer-reviewed Scopus sources for antibacterial potential. Plant compounds frequently act on multiple bacterial targets, a property that may reduce the rate of resistance emergence and provide synergistic opportunities when combined with conventional antibiotics. Recent Scopus-indexed reviews emphasize both mechanistic diversity and advances in delivery (including nano-formulations) that improve therapeutic potential[2,3].

2. Methods

2.1 Search strategy: Primary searches were executed in publications from 2010–2025.

2.2 Review criteria:

- Reviews and original research articles reporting antibacterial activity, mechanisms, synergy with antibiotics, nano-formulation of plant extracts or phytochemicals, and translational/clinical data.
- Human-pathogen focus (clinical isolates or clinically relevant strains).
- English language[4].

2.3 Extraction & synthesis: Extracted information included plant species, active phytochemicals, extraction methods, bacterial targets, MIC/MBC when available, proposed mechanisms, synergy data (checkerboard/FICI), anti-biofilm assays, and any in vivo/clinical data. Thematic synthesis grouped findings into (i) phytochemical classes/mechanisms, (ii) anti-biofilm and anti-virulence actions, (iii) synergy and efflux pump modulation, (iv) nano-formulations, and (v) translational evidence[4,5].

3. Results

Detailed evaluations of multiple reviews: Extensive evaluation of plant-derived antibacterial agents over the past decade has revealed that multiple phytochemical classes contribute collectively to antimicrobial efficacy.

- Phenolics and flavonoids are among the most widely studied constituents, exhibiting strong activity against both Gram-positive and Gram-negative bacteria. These compounds primarily exert their effects through disruption of bacterial cell membranes, chelation of essential metal ions, and inhibition of key enzymes involved in nucleic acid and protein synthesis. Several in vitro investigations have demonstrated that flavonoids such as quercetin, kaempferol, and catechins increase membrane permeability, leading to leakage of intracellular contents and collapse of proton motive force. Additionally, phenolic acids have been reported to interfere with DNA gyrase and topoisomerase IV, thereby suppressing bacterial replication[6].
- Alkaloids represent another important class of antibacterial phytochemicals, acting mainly through intercalation into DNA and inhibition of RNA polymerase activity. Studies using isoquinoline and indole alkaloids have shown dose-dependent suppression of bacterial growth accompanied by morphological changes such as cell elongation and membrane distortion. Certain alkaloids also exhibit efflux pump inhibitory properties, which is particularly relevant in combating multidrug-resistant (MDR) strains. By blocking efflux transporters, these compounds increase intracellular accumulation of antibiotics, thereby restoring bacterial susceptibility[7].
- Terpenoids and essential oils demonstrate rapid bactericidal effects attri[7]buted largely to their lipophilic nature, enabling them to penetrate bacterial membranes and disrupt lipid bilayer integrity. Monoterpenes and sesquiterpenes have been shown to destabilize membrane proteins, impair ATP synthesis, and alter membrane fluidity. Essential oil components such as thymol, carvacrol, and eugenol additionally inhibit quorum sensing (QS) pathways, reducing bacterial virulence factor production and motility. This QS interference has been directly linked to diminished biofilm formation, a critical factor in persistent infections and antibiotic resistance.
- Tannins and saponins further contribute to antibacterial activity via distinct mechanisms. Tannins form irreversible complexes with bacterial cell wall proteins and extracellular enzymes, leading to growth inhibition and impaired nutrient uptake. Saponins, owing to their surfactant properties, interact with membrane sterols and phospholipids, resulting in pore formation and cytoplasmic leakage. Several

comparative studies indicate that crude extracts containing multiple phytochemical groups often display superior antibacterial activity compared to isolated constituents, suggesting additive or synergistic interactions among plant metabolites[8].

- A growing body of research highlights the capacity of plant extracts and purified phytochemicals to modulate bacterial resistance mechanisms. Anti-biofilm activity has been reported for numerous medicinal plants, with significant reductions observed in biofilm biomass, extracellular polymeric substance production, and surface adhesion. Microscopic analyses reveal disrupted biofilm architecture and increased susceptibility of embedded bacteria to conventional antibiotics. Moreover, phytochemicals targeting quorum sensing pathways effectively downregulate genes responsible for toxin production, adhesion, and biofilm maturation, offering a promising anti-virulence strategy that exerts less selective pressure for resistance development[9].
- Synergistic combinations of phytochemicals with standard antibiotics have emerged as a particularly impactful approach. Multiple in vitro checkerboard and time-kill assays demonstrate that plant-derived compounds significantly reduce the minimum inhibitory concentrations (MICs) of β-lactams, fluoroquinolones, aminoglycosides, and macrolides against resistant bacterial strains. Such combinations have been shown to reverse resistance phenotypes by enhancing membrane permeability, inhibiting efflux pumps, and suppressing resistance gene expression. These findings support the concept of phytochemical–antibiotic adjuvant therapy, wherein plant metabolites act as resistance-modifying agents rather than direct bactericidal drugs[10].
- Recent advances in nanotechnology have further amplified the therapeutic potential of plant-based antibacterials. Nano-encapsulation techniques, including polymeric nanoparticles, lipid-based carriers, and nano-emulsions, markedly improve the stability, solubility, and bioavailability of phytochemicals. Nano-formulated plant extracts demonstrate enhanced cellular uptake, sustained release profiles, and significantly lower MIC values compared to their conventional counterparts. Additionally, nanoparticle systems facilitate targeted delivery to infection sites and protect sensitive phytoconstituents from degradation. Several studies report superior anti-biofilm efficacy and prolonged antibacterial action using nano-herbal formulations, highlighting their relevance for chronic and resistant infections[10,11].

- Despite these encouraging results, substantial challenges remain in translating plant-based antibacterial agents from laboratory to clinic. Variability in phytochemical composition due to differences in plant species, geographical origin, harvesting conditions, and extraction methods leads to inconsistent biological activity. Lack of standardized extraction protocols and quality control measures further complicates reproducibility. Moreover, while numerous in vitro and limited in vivo studies validate antibacterial potential, well-designed clinical trials are scarce. Toxicological profiling, pharmacokinetic characterization, and regulatory frameworks for herbal and nano-herbal products also remain insufficiently developed[12].

Existing evidence underscores the multifaceted antibacterial mechanisms of plant-derived compounds, encompassing membrane disruption, inhibition of nucleic acid and protein synthesis, efflux pump modulation, quorum sensing interference, and anti-biofilm activity. The integration of phytochemicals with antibiotics and nanocarrier systems represents a promising strategy to overcome antimicrobial resistance. However, systematic standardization, mechanistic validation, and clinical evaluation are imperative to fully realize the translational potential of plant-based antibacterial therapeutics[9,12].

4. Discussion: The present synthesis highlights the substantial antibacterial potential of plant-derived phytochemicals against clinically relevant pathogens, particularly in the context of antimicrobial resistance (AMR). Unlike conventional antibiotics that typically act on a single molecular target, plant metabolites demonstrate multi-target activity involving membrane destabilization, inhibition of nucleic acid and protein synthesis, efflux pump modulation, quorum sensing suppression, and disruption of biofilm architecture. This mechanistic diversity provides a strong biological rationale for their effectiveness against multidrug-resistant (MDR) bacteria and supports their use as resistance-modifying agents[11].

- Phenolics, flavonoids, alkaloids, terpenoids, tannins, and saponins collectively contribute to antibacterial efficacy through complementary pathways. The ability of flavonoids and phenolic acids to interfere with DNA gyrase and topoisomerase IV mirrors the action of fluoroquinolones, while terpenoids and essential oils exert rapid bactericidal effects by compromising membrane integrity and cellular energetics. Importantly, several phytochemicals inhibit bacterial efflux pumps and quorum sensing systems, thereby attenuating virulence and restoring susceptibility to conventional antibiotics[8,11].

- A key finding across Scopus-indexed studies is the consistent observation of synergy between plant compounds and antibiotics. Checkerboard and time-kill assays reveal significant reductions in MIC values when phytochemicals are combined with β-lactams, aminoglycosides, fluoroquinolones, and macrolides. These interactions appear to arise from enhanced membrane permeability, inhibition of resistance determinants, and suppression of biofilm-associated tolerance. Such results support the emerging paradigm of phytochemical–antibiotic adjuvant therapy, where plant metabolites enhance antibiotic efficacy rather than replacing existing drugs[9].
- Biofilm inhibition represents another clinically relevant advantage of plant-derived antibacterials. Biofilms protect bacteria from host immunity and antimicrobial agents, contributing to chronic and recurrent infections.
- The reviewed evidence demonstrates that multiple plant extracts and isolated compounds significantly reduce biofilm biomass, disrupt extracellular polymeric substances, and downregulate quorum sensing–regulated virulence genes. These antivirulence effects offer a promising strategy for managing persistent infections while minimizing selective pressure for resistance[5,8].
- Recent advances in nano-formulation technologies further strengthen the translational potential of plant-based antibacterials. Nano-encapsulation and nano-emulsion systems improve phytochemical solubility, stability, and bioavailability while enabling sustained release and targeted delivery. Nano-herbal formulations consistently exhibit enhanced antibacterial and anti-biofilm activity compared with crude extracts, highlighting the importance of optimized delivery systems in overcoming pharmacokinetic limitations of natural compounds[13].

5. Future Perspectives and Scopes:

Future research should prioritize mechanism-guided isolation of active phytochemicals, followed by standardized extraction and formulation protocols. Synergistic phytochemical–antibiotic combinations warrant systematic evaluation using clinically relevant MDR isolates and validated in vivo infection models. Particular emphasis should be placed on anti-biofilm strategies and efflux pump inhibition, given their relevance to persistent infections[11].

Nano-enabled delivery platforms offer substantial promise but require further optimization for safety, scalability, and regulatory acceptance. Rigorous pharmacokinetic, toxicological, and clinical investigations are essential to bridge the gap between laboratory findings and

therapeutic application. Additionally, development of unified regulatory frameworks for plant-based and nano-herbal medicines will be critical for successful clinical translation[13].

Integration of computational modeling, systems biology, and artificial intelligence may further accelerate identification of lead phytochemicals and predict synergistic interactions. Ultimately, multidisciplinary collaboration among pharmacologists, microbiologists, formulation scientists, and clinicians will be central to advancing plant-derived antibacterials toward practical healthcare solutions.

6. Conclusion: This review provides comprehensive evidence that plant-derived antibacterial agents possess multifaceted mechanisms of action, including membrane disruption, inhibition of nucleic acid and protein synthesis, efflux pump modulation, quorum sensing interference, and anti-biofilm activity. Synergistic interactions with conventional antibiotics and advances in nano-formulation technologies substantially enhance their therapeutic potential, particularly against multidrug-resistant pathogens[14].

While current findings strongly support the preclinical promise of phytochemicals as adjuncts or alternatives to antibiotics, translation into clinical practice remains constrained by extract variability, limited in vivo validation, and scarcity of controlled clinical trials. Focused standardization, mechanism-driven development, optimized nano-delivery systems, and rigorous clinical evaluation are essential to fully realize the role of plant-based antibacterials in combating antimicrobial resistance[15].

7. References

1. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. *Pharm Ther.* 2015;40(4):277-283.
2. Cowan MM. Plant products as antimicrobial agents. *Clin Microbiol Rev.* 1999;12(4):564-582. doi:10.1128/CMR.12.4.564
3. Gibbons S. Phytochemicals for bacterial resistance—strengths, weaknesses and opportunities. *Planta Med.* 2008;74(6):594-602. doi:10.1055/s-2008-1074518.
4. Savoia D. Plant-derived antimicrobial compounds: alternatives to antibiotics. *Future Microbiol.* 2012;7(8):979–990. doi:10.2217/fmb.12.68
5. Hemaiswarya S, Kruthiventi AK, Doble M. Synergism between natural products and antibiotics against infectious diseases. *Phytomedicine.* 2008;15(8):639–652. doi:10.1016/j.phymed.2008.06.008
6. Cushnie TPT, Lamb AJ. Antimicrobial activity of flavonoids. *Int J Antimicrob Agents.* 2005;26(5):343–356. doi:10.1016/j.ijantimicag.2005.09.002

7. Daglia M. Polyphenols as antimicrobial agents. *Curr Opin Biotechnol.* 2012;23(2):174–181. doi:10.1016/j.copbio.2011.08.007
8. Cushnie TPT, Cushnie B, Lamb AJ. Alkaloids: an overview of their antibacterial activity. *Int J Antimicrob Agents.* 2014;44(5):377–386. doi:10.1016/j.ijantimicag.2014.06.001
9. Bharti K, Sharma M, Vyas GK, Sharma S. Phytochemical screening of alcoholic extract of Thuja occidentalis leaves for formulation and evaluation of wound healing ointment. Asian Journal of Pharmaceutical Research and Development. 2022 Apr 15;10(2):17-22.
10. Borges A, Simões M, Saavedra MJ, Simões LC. The action of selected phytochemicals on quorum sensing and biofilm formation. *Food Res Int.* 2014;62:806–817. doi:10.1016/j.foodres.2014.04.034
11. Abreu AC, McBain AJ, Simões M. Plants as sources of new antimicrobials and resistance-modifying agents. *Nat Prod Rep.* 2012;29(9):1007–1021. doi:10.1039/c2np20035j
12. Khan I, Saeed K, Khan I. Nanoparticles: properties, applications and toxicities. *Arab J Chem.* 2019;12(7):908–931. doi:10.1016/j.arabjc.2017.05.011.
13. Patra JK, Das G, Fraceto LF, et al. Nano based drug delivery systems: recent developments and future prospects. *J Nanobiotechnology.* 2018;16:71. doi:10.1186/s12951-018-0392-8
14. Rodrigues T, Reker D, Schneider P, Schneider G. Counting on natural products for drug design. *Nat Chem.* 2016;8(6):531–541. doi:10.1038/nchem.2479
15. World Health Organization. WHO guidelines on good agricultural and collection practices (GACP) for medicinal plants. *WHO Press.* 2003.