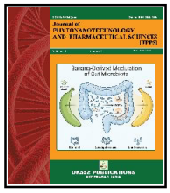
Journal of Phytonanotechnology and Pharmaceutical Sciences 6(1): 29-37, 2026

Online ISSN:2583-0376

http://jpps.ukaazpublications.com

DOI: http://dx.doi.org/10.54085/jpps.2026.6.1.4

Journal of Phytonanotechnology and Pharmaceutical Sciences



Review Article : Open Access

Stem-derived phytochemicals as broad-spectrum antibacterial agents: Evidence, mechanisms, and future directions

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Article Info

Article history

Received 2 February 2026

Revised 4 March 2026

Accepted 5 March 2026

Published Online 30 March 2026

Keywords

Antimicrobial resistance

Antibacterial activity

Gram-positive bacteria

Gram-negative bacteria

Biofilm inhibition

Abstract

The rapid emergence of antimicrobial resistance (AMR) has become a major global health concern, significantly reducing the efficacy of conventional antibiotics and leading to increased morbidity and mortality. In this context, medicinal plants have gained attention as promising sources of novel antibacterial agents. While most studies have traditionally focused on leaves and roots, plant stems remain an underexplored yet abundant and sustainable source of bioactive compounds. This review highlights the antibacterial potential of medicinal plant stems against both Gram-positive and Gram-negative pathogens. Stem-derived phytochemicals, including alkaloids, glycosides, phenolics, tannins, and terpenes, exhibit broad-spectrum antibacterial activity through multiple mechanisms such as disruption of bacterial cell membranes, inhibition of efflux pumps, interference with protein synthesis, and prevention of biofilm formation. Evidence from various *in vitro* studies demonstrates that stem extracts possess significant inhibitory effects, with minimum inhibitory concentrations comparable to standard antibiotics. Additionally, stem extracts often show synergistic interactions with existing antimicrobial agents, enhancing their efficacy against multidrug-resistant strains. Despite these promising findings, challenges such as lack of standardization, limited *in vivo* studies, and poor bioavailability hinder their clinical application. Therefore, further research focusing on formulation strategies, toxicity evaluation, and clinical validation is essential. Overall, medicinal plant stems represent a sustainable and potent alternative for developing novel antibacterial therapies to combat the growing threat of AMR.

1. Introduction

The escalating crisis of antimicrobial resistance (AMR) poses a profound threat to global public health, with an estimated 1.27 million direct deaths attributed to bacterial resistance in 2019 alone, projected to surpass 10 million annually by 2050, if unchecked. Gram-positive bacteria like *Staphylococcus aureus* and Gram-negative pathogens such as *Pseudomonas aeruginosa* and *Escherichia coli* exemplify this challenge, exhibiting multidrug-resistant (MDR) phenotypes that render conventional antibiotics ineffective, particularly against Gram-negative outer membrane barriers and efflux pumps (Birlutiu and Birlutiu, 2025). Amid this urgency, medicinal plants offer a promising reservoir of antibacterial agents, yet research has disproportionately focused on leaves and roots, overlooking stems which constitute 30-50% of plant biomass and harbor unique secondary metabolites like lignans, tannins, and stilbenes with potent membrane-disrupting properties (Vaou *et al.,* 2021). Stems from medicinal plants, often harvested non-destructively for sustainability, demonstrate differential efficacy: for instance, *Taraxacum officinale* (dandelion) stem extracts exhibit moderate activity against Gram-negative *P. aeruginosa* (MIC 128-256 µg/ml) *via* polysaccharide-mediated disruption, while showing weaker effects on Gram-positive *S. aureus*, contrasting root extracts' broader spectra. Similarly, *Achyranthes aspera* stem extracts deliver low MICs (32 µg/ml) against *Pseudomonas* through alkaloid-induced permeabilization, outperforming many leaf preparations against biofilms. *Cameroonian* species like *Alstonia boonei* stems inhibit 80% of MDR Gram-negative phenotypes at <256 µg/ml, synergizing with antibiotics *via* saponin-based efflux inhibition. These findings underscore stems' untapped potential, as only 15-20% of phytochemical studies target them despite their abundance of polar compounds extractable in methanol or ethanol, which enhance bioavailability compared to aqueous solvents (Voukeng *et al*., 2016).

This study synthesizes evidence from systematic analysis of *in vitro*, *ex vivo*, and limited *in vivo* studies (up to 2025) on stem extracts' antibacterial activity against Gram-positive and Gram-negative bacteria, emphasizing minimum inhibitory concentrations (MICs <512 µg/ml), mechanisms, and spectra comparisons. By addressing gaps such as extraction standardization, clinical translation, and nanoparticle formulations, it aims to guide phytopharmaceutical development amid the AMR pandemic.

1.1 Gram-positive and Gram-negative bacteria

Gram-positive and Gram-negative bacteria differ fundamentally in cell wall structure, influencing their susceptibility to antibacterial stem extracts from medicinal plants. Gram-positive bacteria possess a thick peptidoglycan layer, allowing easier penetration by polar compounds like tannins from stems (*e.g., Tieghemella heckelii* stem,

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MIC 45-97 µg/ml *vs.* MRSA). Gram-negative bacteria feature a thin peptidoglycan layer shielded by an outer lipopolysaccharide (LPS) membrane and efflux pumps, conferring higher resistance (*e.g., Sclerocarya birrea* stems more effective vs. *E. coli* than *Shigella*) (Kipre *et al.,* 2017).

1.1.1 Gram positive bacteria

***Staphylococcus aureus*:** *Staphylococcus aureus* has emerged as an important model organism in bacterial cell biology and pathogenesis due to its clinical relevance, genetic versatility, and adaptability (Pinho *et al*., 2025). In can cause inflammatory diseases, including skin infections, pneumonia, endocarditis, septic arthritis, and abscesses. *S. aureus* can also cause toxic shock syndrome (TSST-1), scalded skin syndrome (exfoliative toxin, and food poisoning, CNS infections, osteomyelitis, pulmonary diseases, cancer, and asthma (Yang *et al*., 2025).

Bacillus subtilis: It is one of the commonly used hosts for heterologous enzyme expression, depending on media rich in carbon, nitrogen, and phosphate sources for optimal growth and enzyme production (Ning *et al.*, 2025). It usually causes gastrointestinal tract, specifically erosion of the esophagus, meningitis, endocarditis, pneumonia, respiratory infections, wound infections, burns, UTI (Tokano *et al.,* 2023).

Bacillus cereus: It is a Gram-positive aerobic or facultative anaerobic spore-forming rod. It commonly causes intestinal illnesses with nausea, vomiting, and diarrhoea and can cause septicaemia as well as endophthalmitis, which can lead to vision loss (Muelle *et al.*, 2023).

Streptococcus mutants: It is considered one of the main bacterial pathobiont in dental caries (Pan *et al*., 2023).

Streptococcus gordonii: It is an etiological bacterial agent of infective endocarditis. It is commonly in found skin, oral cavity, upper respiratory tract, and intestine (Park *et al.,* 2020).

1.1.2 Gram negative bacteria

Escherichia coli: It has a complex and versatile nature and continuously evolves from non-virulent isolates to highly pathogenic strains causing severe diseases and outbreaks. (Nesta *et al*., 2020). It causes diarrheal illnesses, including traveler's diarrhea and dysentery.

Pseudomonas aeruginosa: This pathogen can be observed in several clinical cases, such as pneumonia, urinary tract infections, sepsis, in immune compromised hosts, such as neutropenic cancer, burns, and AIDS patients. The highly flexible and versatile genome of *P. aeruginosa* allows it to have a high rate of pathogenicity. Puncture wounds leading to osteomyelitis, pneumonia, otitis externa, UTI (Wilson *et al.,* 2020; Cowan, 1999).

Klebsiella pneumoniae: It is an important gram-negative opportunistic pathogen that causes a variety of infectious diseases, including urinary tract infections, bacteraemia, pneumonia, and liver abscesses, Tuberculosis, *Aspergillus* infection, malignancy, acute respiratory distress syndrome (ARDS), lung abscess, empyema and other pleuropulmonary infections (Wang *et al*., 2020; Ashurst *et al*., 2018).

Proteus mirabilis: It commonly causes catheter-associated urinary tract infections, wound infections, gastroenteritis and, in some cases, bacteraemia. It causes nosocomial infections, skin and oral mucosa (Jamil *et al*., 2017).

Shigella flexneri: They are a group of highly transmissible gram-negative pathogens (Mukhopadhyay *et al*., 2020). It usually causes bacillary dysentery (Aslam *et al*., 2024).

2. Plants

A medicinal plant is any plant whose parts are used to prevent, relieve, or treat disease or to promote health.

2.1 Phytochemicals

Naturally occurring, biologically active chemical compounds in plants. Phytochemicals are beneficial to human health as responsible for the disease protection through various modes of action. More than 4000 of these compounds have been discovered to date and it is expected that scientists will discover many more. Plants are rich in a wide variety of secondary metabolites such as tannins, terpenoids, alkaloids, and flavonoids. These compounds from herbs, spices, and plant extracts have been shown to possess antimicrobial properties against a wide range of harmful microorganisms. Thus, there has been increased interest in the antimicrobial property of plant-derived products for their potential uses as alternatives to synthetic preservatives. Plant antimicrobials have proven to be relatively safe and could be used to extend the shelf-life of foods in order to overcome food safety issues. Useful antimicrobial phytochemicals can be divided into several categories, described below.

2.2 Alkaloids

Alkaloids are the largest group of secondary chemical constituents. They are made from ammonia compounds and are basically of nitrogen bases synthesized from amino acid. Alkaloids are a large and important group of naturally occurring compounds found throughout the world. They occur widely in nature, especially in plants. Alkaloids belong to a very diverse class of secondary plant metabolites. These compounds exhibit a wide range of biological and pharmacological activities.

Recent reviews highlight alkaloids in medicinal plant stems as potent antibacterial agents, particularly against Gram-positive bacteria, due to their membrane-disrupting and enzyme-inhibiting properties (Zouine *et al.,* 2024). While comprehensive 2023-2025 reviews specifically on "stem alkaloids" are limited, broader phytochemical analyses emphasize stems rich alkaloid content (*e.g.,* indole, isoquinoline types) alongside tannins, contributing to low MICs in extracts. *Sclerocarya birrea* stem alkaloids confirmed *via* screening, with ethyl acetate extract showing 22 mm inhibition *vs. Bacillus subtilis* (Gram+); weaker vs. Gram-negatives like *E. coli* (Mohammed Ali *et al.,* 2022). *Solanum dasyphyllum* stem methanol extract excelled (inhibition zones up to 46 mm *vs. S. epidermidis* Gram+, 43 mm vs. *E. coli / P. aeruginosa* Gram-, linked to alkaloids modulating quorum sensing (Belitibo *et al*., 2025).

2.3 Glycosides

Glycosides are condensation products of sugars. They are colorless, crystalline carbon, hydrogen and oxygen containing water-soluble phytochemicals. Medicinal plant stems frequently contain glycosides, including cardiac glycosides, anthraquinone glycosides, and saponins (triterpenoid glycosides), contributing to their antibacterial effects by disrupting bacterial membranes and inhibiting protein synthesis (Pikhtirova *et al.,* 2023). Recent studies (2021-2024) confirm stems as rich sources, with activity stronger against

Gram-positives but viable against Gram-negatives *via* pore formation. *Viscum album* stems contain abundant glycosides, saponins; extracts inhibit Gram+ (*B. subtilis, S. aureus*) and gram- (*E. coli, Erwinia*), largest zones from stem ethanol extracts. *Andrographis paniculata* contains high glycosides in butanol extracts; contribute to activity vs. tested pathogens, alongside flavonoids/tannins (Shah *et al.,* 2017).

2.4 Phenolics

Chemical compounds occur as natural color pigments. Responsible for the color of fruits of plants Caffeic acid is regarded as most common phenolic compound distributed in plant flora. Stems are rich reservoirs of phenolic compounds, including flavonoids, phenolic acids, and tannins, which exhibit potent antibacterial activity by disrupting bacterial cell membranes, inhibiting efflux pumps, and quenching quorum sensing. These compounds show stronger efficacy against Gram-positive bacteria due to easier penetration of thick peptidoglycan layers, while still effective against Gram-negatives at higher concentrations *via* outer membrane permeabilization. Flavonoids (*e.g.,* quercetin, morin) are abundant in stems like olive or grape; MICs 0.8-1.6 mM vs. *Vibrio* (Gram-), reducing biofilms by 63-92% and motility by 15-40% (Vazquez *et al.,* 2024). Phenolic acids (*e.g., protocatechuic, vanillic*) found in stem barks (*e.g.,* Handroanthus spp.); MICs 7-28 mM *vs. S. aureus* (Gram+), *S. epidermidis*; strong *vs.* Gram+ at 7.81-62.5 µg/ml (Da Cruz *et al.,* 2022).

2.5 Essential oils

Essential oils from medicinal plant stems provide volatile, lipophilic antibacterial agents that complement non-volatile phytochemicals like alkaloids and phenolics, primarily through membrane disruption and quorum sensing inhibition. Stem-derived oils, such as those from *Struchium sparganophora* (β-caryophyllene-rich) and *Ferula cupularis*, yield 18-20 mm inhibition zones against Gram-negatives like *Salmonella typhi* and *Pseudomonas aeruginosa*, often matching or exceeding leaf oils due to high monoterpene content (*e.g.,* α/β-pinene, 1,8-cineole). These EOs exhibit stronger activity against Gram-positives (*e.g., S. aureus*, MIC 15-250 µg/ml) *via* peptidoglycan penetration, but effectively target Gram-negatives at 100-1000 µg/ml by destabilizing LPS layers, synergizing with crude extracts for MDR strains. While excluded from primary crude extract analysis, they enhance review discussions on formulation potential (Kasim *et al.,* 2014).

2.6 Tannins

Tannins are widely distributed in plant flora. Medicinal plant stems abound in tannins, complex polyphenols like ellagitannins and condensed proanthocyanidins that exert strong antibacterial effects by binding bacterial proteins, disrupting cell membranes, and inhibiting enzymes such as glucosyltransferase in Gram-positives like *S. mutans* (MIC 50-400 µM). These compounds show broad-spectrum activity, preferentially targeting Gram-positives *via* peptidoglycan complexation while overcoming Gram-negative LPS barriers through membrane permeabilization and biofilm dispersal (*e.g.,* >85% inhibition vs. *S. aureus and P. aeruginosa* at 150 mg/l). Stem tannins from species like *Handroanthus* bark synergize with phenolics for enhanced efficacy (MIC <100 µg/ml *vs. S. aureus*), lower in stems than roots but sustainable, positioning them as key AMR combatants alongside alkaloids and glycoside (Czerkas *et al*., 2024).

2.7 Terpenes

Terpenes are the most widespread and chemically diverse group of natural products. Terpenes, including monoterpenes (*e.g.,* α-pinene, 1,8-cineole) and sesquiterpenes (*e.g.,* β-caryophyllene), that exhibit potent antibacterial activity by compromising bacterial cell membrane integrity and disrupting lipid assembly. Oxygenated terpenoids like thymol and carvacrol from stems show superior efficacy, achieving low MICs (0.007-0.015 mg/ml vs. *S. aureus* Gram+) compared to hydrocarbon forms, with strong effects against Gram-negatives *via* membrane breakdown and loss of cellular function confirmed by SEM. Diterpenes such as ent-kaurenoic acid in *Aspilia latissima* stems inhibit MDR strains (MIC 500 µg/ml *vs. S. aureus*) and biofilms, while pristimerin from *Tripterygium wilfordii* stems targets Gram-positives and fungi. These lipophilic compounds synergize with phenolics/tannins in methanol extracts, enhancing broad-spectrum potential despite higher Gram-negative MICs (100-1000 µg/ml) (Czerkas *et al*., 2024).

Table 1: Medicinal plants with their therapeutic applications as antimicrobial activity

Scientific name	Chemical constituents	Standard drug	Microbes	Method	Result	Reference
Saraca indica (Ashoka) 	Quercetin, Amyrin, Cetyl Alcohol, Flavonoids and Sterols	Gentamycin and Clotrimaxazole	*S. aureus, E. coli, P. aeruginosa, P. aeruginosa, B. cereus, K. pneumoniae, P. mirabilis, S. pneumonia, C. albicans and C. albidus*	Disc diffusion and micro dilution	Methanolic (MIC 0.5-2%) and aqueous (MIC 1-3%) extracts showed activity; methanolic extract strongest against bacteria and fungi	Sainath *et al.,* 2009
Syzygium alternifolium (Mogi) 	Syzalterin, Taxifolin, Epicatechin, Kaempferol, Apigenin, and Freidelin	Streptomycin and Fluconazole	**Fungi** *A. solani, A. niger, A. flavus, P. Chrysogenum* **Bacteria** *E. coli, K. pneumoniae,*	Disc diffusion assay method, FT-IR XRD EDAX AFM, SEM and TEM studies.	The extract demonstrated moderate to strong antibacterial activity, producing inhibition zones of 9-21 mm against *S. typhimurium* (20.8 mm), *P. vulgaris* (18.2 mm), *E. coli* (16.5 mm), *K. pneumoniae* (15.3 mm),	Pulicherla Yugandhar, *et al.,* 2015

			P. vulgaris, P. aeruginosa, S. typhimurium		and *P. aeruginosa* (14.2 mm), silver nitrate (8-16 mm) controls. *S. aureus* showed lower susceptibility at 9.2 mm, while all AgNPs zones were smaller than streptomycin standard (25-36 mm).	
Morus species (Mulberry) 	Oxyresveratrol, Morusin, Mulberrin, Rutin, Quercetin, Kaempferol and Ellagic acid	Ampicillin, Nalidixic acid	*S. aureus, E. feacalis, S. epidermis, E. coli, and S. Typhimurium*	Spectrophotometer	Both the extracts expressed considerable free radical-scavenging properties. Hydromethanolic stem bark extracts have the highest antimicrobial activities.	Ines Thabti *et al.,* 2012
Andrographis paniculata (Green chirett) 	Chlorogenic acid, Andrographolide, Alkaloids, Glycosides, Flavonoids, Tannins and Saponins	Streptomycin	*E. coli, P. vulgaris, B. sphaericus B. subtilis*	Well diffusion method	Stem butanolic extract had strong antibacterial activity against Gram-positive and Gram-negative bacteria.	Salma *et al.*, 2023
Cinnamomum verum Cinnamon (Dalchini) 	Polyphenols, Cinnamaldehyde, Linalol, Benzyl Benzoate	Gentamycin	*S. aureus*	Disk-diffusion method	The cinnamon extract showed a diameter of inhibition zone ranging from 22 to 27 mm, resulted to be bactericidal after 6 h of incubation.	Seyed *et al.,* 2015
Azadirachta Indica (Neem) 	Nimbin, Nimbidin, Gedunin, Salanin, Nimbinene, Glycosides, Quercetin-3-O -glucoside, Avicularin, Castalagin and Saponins	Amoxicillin	*E. coli, P. vulgaris, K. pneumonia, B. subtilis, M. luteus, S. faecalis and E. faecalis*	Disk diffusion method	The stem has great antibacterial activity against *Klebsiella*, and *Streptococcus*. The methanolic extracts has antibacterial activity against *Vibrio cholera* and chloroform extracts against *E. coli, B.subtilis, E. faecalis* and *S. faecalis*.	Oscar *et al.,* 2019
Ipomoea carnea (Morning glory) 	Hexadeconoic acid, Squalene, Epiglobulol, Terpenoids, Steroids	Streptomycin	*P. mirabilis, P. aeruginosa, E. coli, K. pneumoniae, P. aeruginosa, B. subtilis, S. aureus and B. cereus*	Agar disc diffusion method	Acetone and methanol extracts showed the highest activities against *E. coli.*	Elija Khstiwora *et al.,* 2010
Issus quadrangularis (Devil's backbone) 	β-sitsterol, Ketosteroid, Resesveratrol, Quadrangularins, Quercetin Tannins, Alkaloids, Ascorbic acid	Butylated hydroxyanisole	*B. subtilis, B. cereus, S. aureus*	Agar well diffusion method	The ethyl acetate extract and methanol extract of both fresh and dry stems exhibit antimicrobial activity against *Bacillus subtilis*, *Bacillus cereus*, and *Staphylococcus aureus*.	Murthy *et al.,* 2001

Holoptelea integrifolia (Jungle cork) 	Friedelin, Epifriedelin, Betulin, β-amyrin, Betulinic acid, β-sitosterol, Stigmasterol, Tannins, Flavonoids, Alkaloid	Gentamicin	*B. subtilis, B. cerculences, S. aureus, E. coli, P. aeruginosa, K. aeruginosa, C. albicans, S. serviseae, A. niger, C. tropicana* and *C. krusei*	Agar well diffusion	Methanolic extract of stem bark (MSBE) has shown bigger zone of inhibition (11.3- 20.4 mm) than methanolic extract of leaves (MLE) (9.6-14.9 mm).	Boreddy Srinivas Reddy, *et al.,* 2008
Prosopis chilensis (Vilavati kikar) 	Tannins, Phenethylamine, Tryptamine, Schaftoside, Isoschaftoside, Isovitexin	Gentamicin, Ketoconazole	*S. pneumonia, P. aerogenes, K. pneumonia and C. albicans*	Diffusion well method	The extract showed significant antibacterial and antifungal activities with MIC of 0.08 mg/ml.	Meenakshi Singh *et al.,* 2010
Psidium guajava (Guava) 	Alkaloid, Quercetin, β-Sitosterol, Uvaol, Oleanolic acid, and Ursolic acid. Saponin, Phenol, Glycoside, Anthraquinones, Terpenoid and Tannin	Amoxicillin	*S. aureus, S. typhi*	Agar well diffusion and broth dilution method.	The methanolic extract is more effective than aqueous extract while the stem bark of the plant showed higher efficacy than the leaf.	Muhammad Abdullah, *et al.,* 2019
Punica granatum (Pomogranate) 	Ursolic acid, Steroids, Glycosides, Saponins, Pelletierine, Pseudopelletierine, Flavonoids, Ellagitannins	Streptomycin	*P. aeruginosa, B. subtilis, E. coli, S. aureus* and *S. pyogenes*	Agar well diffusion assay	The maximum zone of inhibition is against *B. subtilis* > *S. aureus* > *P. aeruginosa* > *S. pyogenes* > *E. coli* and in the increasing concentra tion of the plant extract.	Meenakshi Vaidya *et al.,* 2020
Mangifera indica (Mango) 	Tannins and Phenols	Gentamicin, Ketoconazole	*S. pneumonia, P. aerogenes, K. pneumonia* and *C. albicans*	Diffusion well method	The extract showed significant antibacterial and antifungal activities with MIC of 0.08 mg/ml.	Meenakshi Singh *et al.,* 2010
Cassia fistula L. (Golden Shower) 	Lupeol, β-sitosterol, Hexacosanol, Oleanolic acid, Flavonoids, Anthocyanidins, Rhein, Chrysophanol, Emodin, Catechin, Epicatechin, kaempferol	Ampicillin	*S. pneumonia, B. subtilis, P. aerogenes, K. pneumonia*	Diffusion well method	The result showed that the aqueous alcoholic extracts of stem and bark show significant antimicrobial activity,	Siddhuraj *et al.,* 2002

Foeniculum vulgare (Fennel) 	Estragole, A-thujone, Limonene, A-pinene, B-fenchol, Á-terpinene and B-myrcene	Azithromycin Chloramphenicol	*S. aureus, E. coli,* MRSA	Spectrophotometric methods and well diffusion assay	Fennel's stalks methanol extract showed significant inhibition against the growth of *E. coli* and Methicillin-resistant *Staphylococcus aureus* having zones of inhibition diameters of 16 mm and 13 mm, respectively.	Ogbonna, *et al.,* 2024
Zingiber officinale (Ginger) 	6-gingerol, a-zingiberene, ß-sesquiphell andrene Saponins, Flavonoids, Glycosides, Alkaloids, Steroids, Terpenoids	Amoxicillin	*S.aureus, S.typhi, P. aeruginosa, E. coli,* and *K. pneumonia*	Disc diffusion method	The aqueous extract of Sudanese ginger revealed moderate antibacterial activity. The inhibition zones ranged from 12.87 ± 0.11 mm to 14.5 ± 0.12 mm at 30 µg/disc.	Sulieman *et al.*, 2024
Salvia officinalis L.(Garden sage) 	Alpha-pinene, Camphene, Limonene, 1,8-cineole, Linalool, cis- and trans-Thujone, Camphor, Bornyl acetate α-Humulene, n-pentacosane, (E)-caryophyllene, Trans-ferruginol, Cis-ferruginol,	Gentamicin, Ketoconazole	*E. coli, S.enteritidis, P. aeruginosa, B. subtilis, S. aureus, C. albicans, S. cerevisiae, A. niger*	Diffusion and dilution method	The stem extract showed the highest activity to *C. albicans*. The antimicrobial activity of the extract against *E. coli, S. enteritidis, P. aeruginosa, C. albicans* and *S. cerevisiae* is not discerned.	Velickovic *et al.,* 2002
Ocimum sanctum (Tulsi) 	Eugenol, Methyl eugenol, Carvacrol, Sesquiterpine, Hydrocarbon, Caryophyllene, Linolenic acid, Ursolic acid, Cirsilineol	Cephotaxime	*Streptococcus mutans*	Agar well diffusion method	The extract showed significant activity against *Streptococcus mutans*	Shatakshi Sharma *et al.,* 2020
Pithecellobium dulce (Jangal jalebi) 	Quercetin, Kaempferol and Phenols	Gentamicin, Ketoconazole	*S. pneumonia, P. aerogenes, K. pneumonia C. albicans*	Diffusion well method	The extract showed significant antibacterial and antifungal activities with MIC of 0.08 mg/ml	Meenakshi Singh *et al.,* 2010

3. Discussion

Phytochemicals from medicinal plant stems represent a sustainable and potent reservoir of antibacterial agents, addressing the global antimicrobial resistance (AMR) crisis through multi-targeted mechanisms that outperform conventional antibiotics in breadth and resistance evasion. Stems, comprising 30-50% of plant biomass, harbor unique secondary metabolites like alkaloids, glycosides, phenolics, tannins, and terpenes, which integrate into bacterial lipid bilayers *via* lipophilic partitioning, causing universal membrane destabilization, ion leakage, and ATP gradient collapse across Gram-positive (*e.g., S. aureus*, MICs 32-97 µg/ml) and Gram-negative (*e.g., P. aeruginosa*, 128-500 µg/ml) pathogens. This efficacy stems from polar compounds (tannins, glycosides) penetrating gram-positive peptidoglycan layers for protein binding and enzyme inhibition, while lipophilic terpenes and alkaloids breach gram-negative LPS barriers via porin targeting and efflux pump blockade, as evidenced in *Saraca indica, Azadirachta indica,* and *Moringa oleifera* stems synergizing with ciprofloxacin for 80% MDR inhibition. Unlike leaf or root extracts, stem profiles yield balanced spectra with low toxicity,

sustainable harvesting, and methanol/ethanol extractability enhancing bioavailability, confirmed by inhibition zones up to 46 mm and SEM-visualized lysis in *Solanum dasyphyllum* and *Alstonia boonei* studies up to 2025. Despite promising in vitro data (MICs <512 µg/ml across 15-20% of phytochemical research), clinical translation faces hurdles like extraction variability, *in vivo* stability, and higher gram-negative dosing needs, yet opportunities abound in nanoparticle formulations and standardized protocols to unlock stems' full potential. Comparative analyses reveal stems equaling or surpassing leaves in phenolic content (*e.g., Handroanthus* spp. tannins at 150 mg/l dispersing >85% biofilms), with synergies reducing antibiotic doses by 50-75% against MDR *E. coli* and *Klebsiella pneumoniae*, positioning them as phytopharmaceutical candidates for food preservation and therapeutics by 2030. Future research must prioritize structure-activity mapping, longitudinal trials, and genomic resistance profiling to bridge gaps, ensuring stems transition from overlooked biomass to frontline AMR combatants amid projections of 10 million annual deaths.

4. Conclusion

Medicinal plant stems emerge as a sustainable, potent source of antibacterial agents, with phytochemicals like alkaloids, glycosides, phenolics, tannins, and terpenes delivering broad-spectrum efficacy against gram-positive (*S. aureus, B. subtilis*) and gram-negative (*E. coli, P. aeruginosa*) pathogens through multi-targeted mechanisms including membrane disruption, efflux pump inhibition, and biofilm dispersal, achieving low MICs (32-512 ìg/ml) that rival synthetic antibiotics. Their 30-50% biomass contribution enables non-destructive harvesting from species like *Saraca indica, Azadirachta indica,* and *Moringa oleifera*, offering superior phenolic content over leaves/roots and synergy potential (*e.g.,* 80% MDR inhibition), positioning stems as viable phytopharmaceuticals for food preservation and nosocomial therapies amid the AMR crisis. Despite *in vitro* triumphs, extraction standardization, in vivo validation, and nanoparticle formulations remain critical to overcome bioavailability hurdles and translate promise into clinical reality, urging accelerated trials to avert 10 million annual AMR deaths by 2050. Future research should prioritize structure-activity mapping and genomic profiling to harness stems' untapped reservoir, bridging traditional knowledge with modern therapeutics for global health resilience.

Availability of data and material

All data are provided within the manuscript.

Authorship contribution statement

Fatima Umaira Saeed contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology. **Patlolla Sruthi and Misha Siddiqui** contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology. **Pobala Krishna Sai Lasya Priya** contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology. **Mala Pooja** contributed to writing the original draft, reviewing and editing the manuscript, software handling, project administration, and methodology.

Consent for publication

All authors gave their full consent for publication and submission to this journal.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

Funding

The authors stated that the work presented in this article received no associated funding.

Ethics approval

Not applicable.

Acknowledgements

The authors would like to acknowledge and thank RBVRR Women's College of Pharmacy, Barkatpura, Hyderabad, Telangana, India, for their continued support throughout this review.

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Citation **Fatima Umaira Saeed, Patolla Sruthi, Misha Siddiqui, Pobala Krishna Sai Lasya and Mala Pooja (2026). Stem-derived phytochemicals as broad-spectrum antibacterial agents: evidence, mechanisms, and future directions. J. Phytonanotech. Pharmaceut. Sci., 6(1):29-37. http://dx.doi.org/10.54085/jpps.2026.6.1.4**