



ISSN Online: 2456-2912
NAAS Rating (2026): 4.61
IJVSAH 2026; 11(9S): 162-168
www.veterinarypaper.com
Received: 17-07-2026
Accepted: 18-08-2026
Published: 24-09-2026

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Antibacterial efficacy and mechanisms of action of medicinal plants against multidrug-resistant bacteria: A review with relevance to veterinary practice

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DOI: <https://www.doi.org/10.22271/veterinary.2026.v11.i9Sc.3790>

ABSTRACT

Antimicrobial resistance is eroding the effectiveness of antibacterial drugs used in both human and veterinary medicine, and the search for alternatives has renewed interest in medicinal plants. This review summarises published evidence on the antibacterial efficacy and mechanisms of action of medicinal plants of veterinary relevance, drawing on studies of neem, green tea, miswak, clove, cinnamon, oregano, garlic, tea tree, black cumin and related species. Plant secondary metabolites, including limonoids, catechins, isothiocyanates, monoterpene phenols, organosulphur compounds and hydrolysable tannins, act mainly by damaging the bacterial envelope, altering membrane lipid biosynthesis, inducing oxidative and thiol stress, suppressing biofilm formation and blocking efflux pumps. Several compounds restore the activity of beta-lactam and fluoroquinolone antibiotics against resistant staphylococci. The available evidence is dominated by laboratory studies; controlled animal trials, extract standardisation, pharmacokinetic data and residue and withdrawal information are largely lacking and remain the principal barriers to veterinary application.

Keywords: Antimicrobial resistance, *Azadirachta indica*, Efflux pump inhibition, Ethnoveterinary medicine, Phytochemicals, Plant extracts

1. Introduction

Bacterial disease remains a leading cause of production loss and mortality in livestock and poultry and antibacterial drugs are central to its control. The same drug classes are used in human and veterinary medicine and resistance selected in one sector can move to the other through the food chain, the farm environment and direct contact. Antimicrobial resistance is therefore a shared problem, and projections suggest that it could account for as many as ten million deaths each year by 2050 if current trends continue (Kong *et al.*, 2026) [1]. Resistant phenotypes are now routinely recovered from food animals, including methicillin-resistant *Staphylococcus aureus* from bovine mastitis, extended-spectrum beta-lactamase-producing *Escherichia coli* from poultry and calves, and multidrug-resistant *Salmonella*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* from clinical and environmental samples (Jubair *et al.*, 2021) [2].

Restrictions on the use of antibiotic growth promoters, the withdrawal of several critically important antimicrobials from food-animal use and the shortage of new antibacterial classes have all increased interest in plant-derived alternatives. Plants produce a large range of secondary metabolites, including alkaloids, quinones, tannins, terpenoids and polyphenols, that function as constitutive or induced chemical defences against microbial attack (Kong *et al.*, 2026; Pérez-Flores *et al.*, 2025) [1, 3]. A substantial share of newly approved drugs remains derived from, or inspired by, natural products (Newman *et al.*, 2016) [4]. Because most phytochemicals act on several bacterial targets at once rather than on a single enzyme, single-step mutational resistance is less readily selected than it is with conventional antibiotics (Pérez-Flores *et al.*, 2025; Wylie *et al.*, 2022) [3, 5].

Azadirachta indica A. Juss. (neem) is used here as the principal model species because its antibacterial, antibiofilm and synergistic properties are unusually well documented (Wylie *et al.*, 2022; Sarkar *et al.*, 2021) [5, 6], and because it is already widely used in Indian ethnoveterinary practice. The objectives of this review are to summarise the antibacterial efficacy of medicinal plants for which well-characterised evidence exists, to describe the molecular mechanisms underlying that activity, to identify the factors that determine reproducibility, and to assess what would be required before such preparations could be used responsibly in veterinary practice.

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2. Materials and Methods

This is a narrative review. Literature was retrieved from PubMed, Scopus, Web of Science and Google Scholar using combinations of the terms "medicinal plant", "plant extract", "essential oil", "antibacterial", "antimicrobial resistance", "multidrug resistant", "MRSA", "biofilm", "efflux pump" and "mechanism of action", together with the names of individual plant species. Records published between 1984 and 2026 were screened. Studies were included when they reported an experimentally determined endpoint (zone of inhibition, minimum inhibitory concentration, minimum bactericidal concentration, fractional inhibitory concentration index, time-kill data or a defined mechanistic assay) for a named plant species or an isolated constituent against a named bacterial species. Reports in which the plant material was not identified to species, in which no quantitative endpoint was given, or for which full bibliographic details could not be verified were excluded. Chemical and microbiological data are reported as they appear in the source publications; units were not converted, and values from different studies have not been pooled.

3. Results and Discussion

3.1 Plants with documented antibacterial activity

Eighteen species for which complete primary evidence could be verified are summarised in Table 1. They span 15 plant families and include leaf, bark, root, rhizome, seed, flower-bud and essential-oil preparations. *Azadirachta indica* is a tropical evergreen of the family Meliaceae, native to the Indian subcontinent and naturalised throughout the tropics and subtropics; its leaves, bark, seeds, roots, flowers and gum are all used medicinally (Wylie *et al.*, 2022; Sarkar *et al.*, 2021) [5, 6]. Most of the remaining species are similarly multipurpose plants already present in traditional livestock husbandry. Activity in every case is attributable to secondary metabolites, conventionally grouped by biosynthetic origin into terpenoids, polyketides, phenylpropanoids and alkaloids (Kong *et al.*, 2026) [1]. *Azadirachta indica* alone contains more than 300 characterised compounds, of which the limonoids are the most studied (Wylie *et al.*, 2022; Sarkar *et al.*, 2021) [5, 6]; gas chromatography-mass spectrometry of a methanolic leaf extract identified 30 major constituents, including *n*-hexadecanoic acid, coumarins and the monoterpene glycoside beta-D-mannofuranoside, *O*-geranyl (Altayb *et al.*, 2022) [7].

3.2 Antibacterial efficacy

3.2.1 Activity against Gram-positive bacteria

Gram-positive organisms, and staphylococci in particular, are the most susceptible group. In a screen of 60 folk medicinal plants, methanolic extracts of *C. sinensis* and *A. citrodora* were the most active against methicillin-resistant and methicillin-sensitive *S. aureus*, with minimum inhibitory concentrations of 0.5–1.5 mg/mL and inhibition zones of approximately 19–20 mm; *H. sabdariffa*, *T. vulgaris* and *G. glabra* followed (Bataineh *et al.*, 2021) [8]. Thymoquinone from *N. sativa* inhibited 99 methicillin-resistant *S. aureus* strains at 8–16 µg/mL with an MIC₉₀ of 16 µg/mL, produced a greater than three-log reduction in viability and a post-antibiotic effect of 3.2 ± 0.2 h, and yielded no detectable resistant mutants under the exposure conditions used (Hariharan *et al.*, 2016) [9]. Plumbagin from *P. zeylanica* inhibited 100 methicillin-resistant *S. aureus* isolates over a narrow range of 4–8 µg/mL and killed approximately 99% of a reference strain within 8 h (Periasamy *et al.*, 2019) [10].

3.2.2 Activity against Gram-negative bacteria

The Gram-negative outer membrane restricts the penetration of hydrophobic phytochemicals, and activity is correspondingly lower and less consistent. Important exceptions exist. Benzyl isothiocyanate and the root volatiles of *S. persica* were markedly more active against Gram-negative than Gram-positive bacteria, causing rapid membrane protrusion and loss of envelope integrity (Sofrata *et al.*, 2011) [11].

Methanolic miswak extract was likewise more active against Gram-negative than Gram-positive organisms in a panel of ten multidrug-resistant clinical isolates (Al-Ayed *et al.*, 2016) [12]. Oregano oil rich in carvacrol inhibited all ten multidrug-resistant *Acinetobacter baumannii* isolates tested, at 1.75–3.50 mg/mL (Amaral *et al.*, 2020) [13], and tea tree oil was bactericidal against carbapenem-resistant *K. pneumoniae*, *A. baumannii* and *P. aeruginosa* (Oliva *et al.*, 2018) [14]. In the neem-leaf study, the lowest methanolic-extract concentration showing bactericidal activity against *P. aeruginosa* was 3.125% (v/v) (Altayb *et al.*, 2022) [7]. In contrast, *P. aeruginosa* was the most refractory organism in the 60-plant screen and was inhibited by only one of the ten active extracts (Bataineh *et al.*, 2021) [8], which illustrates how strongly outcomes depend on the isolate and the preparation.

3.2.3 Activity against multidrug-resistant bacteria

Several preparations retain activity against isolates that are resistant to multiple antibiotic classes. Neem extract inhibited extended-spectrum beta-lactamase- and carbapenemase-producing uropathogenic *E. coli*, with a mean inhibition zone of 20.18 mm (Khairnar *et al.*, 2025) [15]. Clove extract inhibited all groups within a panel of 221 Gram-negative uropathogens screened for extended-spectrum beta-lactamase, metallo-beta-lactamase and AmpC production; activity was highest against *Proteus* spp., for which the inhibition zone was 19 mm (Faujdar *et al.*, 2020) [16]. Fresh garlic extract was active against methicillin-resistant *S. aureus*, vancomycin-resistant *Enterococcus faecalis*, metallo-beta-lactamase-producing *E. coli* and extended-spectrum beta-lactamase-producing *K. pneumoniae* (Magryś *et al.*, 2021) [17]. Extracts of *T. chebula* and *T. bellirica* inhibited *S. aureus* and methicillin-resistant *S. aureus* at 94–392 µg/mL and extended-spectrum beta-lactamase-producing *E. coli* and *K. pneumoniae* at 755 µg/mL (Tiwana *et al.*, 2024) [18].

3.2.4 Biofilm inhibition

Biofilms are central to chronic veterinary infections such as bovine mastitis, otitis, endometritis and catheter- and implant-associated disease, and they confer tolerance to antibiotics by restricting diffusion and promoting metabolic dormancy (Kong *et al.*, 2026) [1]. Nimbolide from neem substantially disrupted and reduced methicillin-resistant *S. aureus* biofilm and was also active intracellularly (Sarkar *et al.*, 2016) [19]. Thymoquinone inhibited biofilm formation and reduced the metabolic activity of established biofilms (Chaieb *et al.*, 2011) [20], and clove essential oils markedly reduced biofilm formation while increasing cell permeability and causing leakage of intracellular protein (Al-Mijalli *et al.*, 2023) [21]. Asarone-containing fractions of *A. calamus* reduced biofilm formation alongside their membrane effects (Kongkham *et al.*, 2024) [22].

3.2.5 Comparison with conventional antibiotics

On a weight-for-weight basis, crude extracts are far less potent than purified antibiotics: inhibitory concentrations are typically expressed in milligrams per millilitre for extracts and in micrograms per millilitre for antibiotics. Isolated constituents narrow this gap considerably. Compounds 4 and 9 from *M. micrantha* inhibited methicillin-resistant *S. aureus* at 6.25 µg/mL against 3.125 µg/mL for vancomycin in the same assay system (Dong *et al.*, 2023) [23], and plumbagin and thymoquinone are active in the same low microgram range (Hariharan *et al.*, 2016; Periasamy *et al.*, 2019) [9, 10]. Direct comparison of inhibition-zone diameters between an undiluted crude extract and a standard antibiotic disc, as is often reported, is not a valid measure of relative potency because the two are applied at very different molar concentrations; such comparisons should be interpreted with caution.

3.3 Mechanisms of antibacterial action

Phytochemicals generally act on several targets simultaneously, which both broadens their spectrum and reduces the likelihood of single-step resistance (Kong *et al.*, 2026; Pérez-Flores *et al.*, 2025) [1, 3]. The principal mechanisms are summarised in Table 2.

3.3.1 Damage to the cell wall and cytoplasmic membrane

Envelope damage is the best-supported mechanism across the literature. Tea tree oil acts predominantly at the cytoplasmic membrane, increasing permeability, causing potassium leakage and inhibiting respiration (Cox *et al.*, 2000) [24]. Asarone-rich fractions of *A. calamus* increase membrane permeability, cause leakage of nucleic acid and protein, and alter membrane fatty-acid composition (Kongkham *et al.*, 2024; Al-Mijalli *et al.*, 2025) [22, 25]. Benzyl isothiocyanate produces rapid membrane protrusion and loss of integrity (Sofrata *et al.*, 2011) [11], and carvacrol-rich oregano oil destabilises and ruptures the mem-

brane, as shown by flow cytometry (Amaral *et al.*, 2020) [13]. Cinnamaldehyde acts more specifically: transcriptomic and proteomic analysis showed altered glycerophospholipid biosynthesis with changed production of phosphatidylethanolamine and phosphatidylglycerol, indicating that disturbance of membrane lipid homeostasis rather than simple partitioning underlies its activity (Pang *et al.*, 2021) [26]. Molecular docking indicates that beta-D-mannofuranoside from neem binds *S. aureus* penicillin-binding protein 4 with an affinity of -9.7 kcal/mol⁷; this is supportive in silico evidence and does not by itself establish inhibition of peptidoglycan cross-linking.

Table 1. Botanical data, principal bioactive constituents and antibacterial evidence for the species reviewed

No.	Species (with authority)	Family / common name	Part used	Principal constituents	Principal antibacterial evidence	Ref.
1	<i>Azadirachta indica</i> A. Juss.	Meliaceae / neem	Leaves, seeds, bark	Limonoids (nimbolide, azadirachtin, nimbidin)	Membrane damage, lysis and biofilm disruption in methicillin-resistant <i>S. aureus</i> ; leaf extract active against clinical isolates	7, 11
2	<i>Camellia sinensis</i> (L.) Kuntze	Theaceae / green tea	Leaves	Gallated catechins (epigallocatechin gallate, epicatechin gallate)	Membrane depolarisation and altered gene expression; reversal of beta-lactam resistance; efflux inhibition	8, 12–15
3	<i>Salvadora persica</i> L.	Salvadoraceae / miswak	Roots	Benzyl isothiocyanate	Rapid envelope disruption, markedly stronger against Gram-negative bacteria	9, 10
4	<i>Aloysia citrodora</i> Palau	Verbenaceae / lemon verbena	Leaves	Oxygenated monoterpenes	Among the most active of 60 extracts screened against resistant staphylococci	8
5	<i>Hibiscus sabdariffa</i> L.	Malvaceae / roselle	Calyces	Anthocyanins, flavonoids, organic acids	Activity against resistant isolates, including <i>P. aeruginosa</i>	8
6	<i>Glycyrrhiza glabra</i> L.	Fabaceae / liquorice	Roots	Prenylated flavonoids	Activity against resistant staphylococci	8
7	<i>Thymus vulgaris</i> L.	Lamiaceae / thyme	Aerial parts	Thymol, <i>p</i> -cymene	Activity against resistant staphylococci	8
8	<i>Cinnamomum zeylanicum</i> Blume	Lauraceae / cinnamon	Bark, oil	(<i>E</i>)-Cinnamaldehyde	Altered phosphatidylethanolamine and phosphatidylglycerol biosynthesis; membrane dysfunction	18, 19
9	<i>Origanum vulgare</i> L.	Lamiaceae / oregano	Aerial parts, oil	Carvacrol, thymol, terpinen-4-ol	Membrane rupture; activity against multidrug-resistant <i>A. baumannii</i> ; synergy with polymyxin B	20, 21
10	<i>Syzygium aromaticum</i> (L.) Merr. & L.M. Perry	Myrtaceae / clove	Flower buds, oil	Eugenol	Increased permeability and protein leakage; antibiofilm; activity against beta-lactamase-producing uropathogens	16, 17
11	<i>Allium sativum</i> L.	Amaryllidaceae / garlic	Bulb	Allicin, ajoene, diallyl sulphides	Glutathione depletion and S-allylmercapto modification of protein cysteines; activity against resistant isolates	24, 25
12	<i>Melaleuca alternifolia</i> (Maiden & Betche) Cheel	Myrtaceae / tea tree	Leaves, oil	Terpinen-4-ol, α -terpineol, 1,8-cineole	Cytoplasmic membrane disruption, potassium leakage, respiratory inhibition; bactericidal against carbapenem-resistant isolates	22, 23
13	<i>Nigella sativa</i> L.	Ranunculaceae / black cumin	Seeds	Thymoquinone	Cell wall and membrane damage without complete lysis; biofilm inhibition; active against 99 methicillin-resistant strains	26, 27
14	<i>Plumbago zeylanica</i> L.	Plumbaginaceae / chitrak	Roots	Plumbagin	Active against 100 methicillin-resistant isolates at 4–8 μ g/mL; FtsZ inhibition shown in <i>Bacillus subtilis</i>	28, 29
15	<i>Acorus calamus</i> L.	Acoraceae / vacha	Rhizome	β -Asarone, α -asarone	Membrane permeabilisation, leakage of nucleic acid and protein; potentiation of ampicillin	30, 31

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No.	Species (with authority)	Family / common name	Part used	Principal constituents	Principal antibacterial evidence	Ref.
16	<i>Mikania micrantha</i> Kunth	Asteraceae / mile-a-minute	Aerial parts	Germacrane sesquiterpene dilactones	Isolated compounds active at 1.56–12.5 µg/mL; molecular target not established	32
17	<i>Terminalia chebula</i> Retz.	Combretaceae / haritaki	Fruits	Chebularic and chebulinic acids, gallic acid	Envelope damage and leakage; activity against resistant staphylococci and enteric pathogens	33–35
18	<i>Terminalia bellirica</i> (Gaertn.) Roxb.	Combretaceae / baheda	Fruits	Hydrolysable tannins, gallic and ellagic acids	Activity against resistant staphylococci and Enterobacterales; antibiotic-modifying effects	33, 34

3.3.2 Interference with macromolecular synthesis

Evidence for direct inhibition of bacterial protein synthesis by the plant preparations reviewed here is limited, and claims of ribosomal targeting are generally not supported by binding or in vitro translation data; this mechanism should therefore be described as plausible but unproven for these species (Jubair *et al.*, 2021) [2]. Evidence for interference with cell division is stronger for isolated compounds: plumbagin binds purified *B. subtilis* FtsZ and inhibits both its assembly and its GTPase activity, thereby disturbing Z-ring formation (Bhattacharya *et al.*, 2013) [27]. This finding was obtained in *B. subtilis* and should not be presented as an established mechanism in *S. aureus*. Inhibition of bacterial DNA gyrase has been reported for chebulinic acid from *T. chebula* (Jubair *et al.*, 2021) [2].

3.3.3 Oxidative and thiol stress

Allicin inhibits bacterial growth by depleting glutathione and by S-allylmercapto modification of protein cysteine residues, which lowers cellular thiol concentrations, inactivates metabolic enzymes, causes protein aggregation and triggers oxidative and heat-stress responses (Müller *et al.*, 2016) [28]. This is a genuinely multitarget mechanism and is the best-characterised explanation for the activity of garlic. It should be noted that endoplasmic reticulum stress and autophagy, which are sometimes cited in this context, are eukaryotic processes and cannot occur in bacteria; these effects have been described in host cells, not in the target organism.

3.3.4 Antibiofilm, quorum-sensing and anti-virulence effects

Several constituents interfere with adhesion, matrix production and cell-to-cell signalling rather than killing the organism outright. Because they impose weaker selection than bactericidal agents, such

anti-virulence strategies are attractive where prolonged exposure is likely, as in mastitis control or in-feed use. Nimbolide, thymoquinone, eugenol-rich clove oils and asarone-containing fractions all reduce biofilm formation (Sarkar *et al.*, 2016; Al-Mijalli *et al.*, 2023; Chaieb *et al.*, 2011; Kongkham *et al.*, 2024) [19, 21, 20, 22], and catechins alter the expression of genes associated with toxin production and stress response in *S. aureus* (Kitichaleermkiet *et al.*, 2020) [29].

3.3.5 Synergy with antibiotics and efflux pump inhibition

The most clinically relevant property of these compounds may be their ability to restore the activity of failing antibiotics. Gallated catechins reverse beta-lactam resistance in methicillin-resistant *S. aureus*, substantially lowering the oxacillin minimum inhibitory concentration (Stapleton *et al.*, 2004) [30], and epicatechin gallate and epigallocatechin gallate inhibit efflux and potentiate norfloxacin against a NorA-overexpressing strain (Gibbons *et al.*, 2004) [31]. Carvacrol-rich oregano oil is synergistic with polymyxin B against multidrug-resistant *A. baumannii*, with fractional inhibitory concentration indices of 0.18–0.37 and up to a 16-fold reduction in the polymyxin B minimum inhibitory concentration (Amaral *et al.*, 2020) [13]. Tea tree oil is synergistic with oxacillin against methicillin-resistant *S. aureus* (Oliva *et al.*, 2018) [14], plumbagin with ciprofloxacin and piperacillin (Periasamy *et al.*, 2019) [10], and an *A. calamus* fraction with ampicillin, with fractional inhibitory concentration indices of 0.245–0.456 (Kongkham *et al.*, 2024) [22]. Synergy is not universal: strong antagonism was recorded when *Terminalia* extracts were combined with polymyxin B (Tiwana *et al.*, 2024) [18], which is a reminder that combinations must be tested empirically rather than assumed.

Table 2. Principal mechanisms of antibacterial action of plant-derived compounds

Mechanism	Compound or extract	Organism studied	Experimental evidence	Ref.
Cytoplasmic membrane disruption	Tea tree oil (terpinen-4-ol)	<i>S. aureus</i> , <i>E. coli</i>	Increased permeability, potassium leakage, inhibition of respiration	22
Envelope disruption	Benzyl isothiocyanate	Gram-negative bacteria	Membrane protrusions and loss of integrity by electron microscopy	9
Altered membrane lipid biosynthesis	(E)-Cinnamaldehyde	<i>S. aureus</i> , <i>E. coli</i>	Changed phosphatidylethanolamine and phosphatidylglycerol production	19
Membrane rupture	Carvacrol-rich oregano oil	Multidrug-resistant <i>A. baumannii</i>	Flow-cytometric demonstration of membrane destabilisation	21
Thiol stress	Allicin	<i>E. coli</i> , <i>S. aureus</i>	Glutathione depletion; S-allylmercapto modification of cysteines	24
Inhibition of cell division	Plumbagin	<i>B. subtilis</i>	Binding to purified FtsZ; inhibition of assembly and GTPase activity	29
Membrane permeabilisation and antibiofilm	β-Asarone	<i>E. coli</i> , <i>P. aeruginosa</i> , <i>A. baumannii</i> , <i>B. cereus</i>	Leakage of nucleic acid and protein; reduced biofilm; ampicillin potentiation	30, 31
Efflux pump inhibition	Epicatechin gallate, epigallocatechin gallate	Multidrug-resistant <i>S. aureus</i>	Potentiation of norfloxacin against a NorA-overexpressing strain	14
Reversal of beta-lactam resistance	Gallated catechins	Methicillin-resistant <i>S. aureus</i>	Marked reduction in oxacillin minimum inhibitory concentration	13

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Mechanism	Compound or extract	Organism studied	Experimental evidence	Ref.
Antibiofilm and intracellular activity	Nimbolide	Methicillin-resistant <i>S. aureus</i>	Membrane damage and lysis; biofilm disruption	11

3.4 Factors affecting antibacterial activity

Reported activity varies widely between studies of the same species, and the variation is largely methodological rather than biological (Pérez-Flores *et al.*, 2025) [3]. Four factors are dominant. First, the plant part: in *A. indica*, seed material is richest in azadirachtin whereas leaves yield a different profile of flavonoids and fatty acids (Wylie *et al.*, 2022; Sarkar *et al.*, 2021) [5, 6]. Second, the extraction solvent: methanol recovers a broader polarity range of antibacterial constituents than water, and aqueous and methanolic extracts of the same material can differ severalfold in activity (Al-Ayed *et al.*, 2016; Tiwana *et al.*, 2024) [12, 18]. Third, chemotype and composition: the oregano oil examined in one study was dominated by terpinen-4-ol at 38.35% with an MIC of 1.18 mg/mL against *S. aureus* (Fikry *et al.*, 2019) [32], whereas the oil in a second study was dominated by carvacrol at 71.0% (Amaral *et al.*, 2020) [13]. These are chemically different oils, and their data must not be pooled. Fourth, provenance and season: soil, climate and harvest stage determine secondary metabolite biosynthesis, which makes batch-to-batch consistency the single largest obstacle to standardisation.

3.5 Toxicity and safety

Cytotoxicity data for the more active extracts are reassuring but limited. Methanolic extracts of *C. sinensis*, *A. citrodora* and *H. sabdariffa* showed low cytotoxicity against Vero cells and fibroblasts and did not lyse human erythrocytes; in a murine model of systemic infection produced by intraperitoneal inoculation of methicillin-resistant *S. aureus*, mice given 300 mg/kg body weight of extract daily for seven days remained in good general health, with *C. sinensis* the most effective preparation (Bataineh *et al.*, 2021) [8]. Computational absorption, distribution, metabolism, excretion and toxicity predictions for beta-D-mannofuranoside satisfied the standard drug-likeness rules and indicated a negative Ames result and negative rat carcinogenicity (Altayb *et al.*, 2022) [7]; these are *in silico* predictions and are not a substitute for toxicological testing. Against this, high doses of crude extracts can be non-specifically cytotoxic or allergenic (Kong *et al.*, 2026) [1], and essential oils containing carvacrol, thymol, eugenol or cinnamaldehyde are mucosal irritants at the concentrations used *in vitro*. For food-producing animals, no withdrawal periods, maximum residue limits or tissue-residue data exist for any of these preparations, and β -asarone in *A. calamus* is a recognised genotoxic carcinogen in rodents, which argues against its oral use in food animals.

3.6 Relevance to veterinary practice and animal husbandry

Three applications are realistic in the near term. The first is topical and intramammary use, where high local concentrations can be achieved without systemic exposure; the activity of tea tree oil, clove oil and neem preparations against methicillin-resistant *S. aureus* and

against biofilm is directly relevant to mastitis, wound management, footrot and otitis (Sarkar *et al.*, 2016; Al-Mijalli *et al.*, 2023; Oliva *et al.*, 2018) [19, 21, 14]. The second is as antibiotic adjuvants: catechins, carvacrol-rich oregano oil and plumbagin restore or potentiate the activity of oxacillin, polymyxin B, norfloxacin and ciprofloxacin (Stapleton *et al.*, 2004; Gibbons *et al.*, 2004; Amaral *et al.*, 2020; Periasamy *et al.*, 2019) [30, 31, 13, 10], which could allow dose reduction or re-use of older agents. The third is the use of standardised phyto-genic feed additives to reduce enteric pathogen load and lower prophylactic antibiotic demand in poultry and pigs, although efficacy data from controlled production trials remain scarce. Integrating locally available ethnoveterinary plants into herd health planning also reduces reliance on veterinary antibiotics and, with it, the environmental dissemination of resistance genes, which aligns directly with One Health objectives.

3.7 Current challenges and research gaps

The evidence base has four structural weaknesses. Chemical complexity makes it difficult to attribute activity to defined constituents and complicates regulatory approval; many phytochemicals have poor oral bioavailability and are rapidly metabolised (Kong *et al.*, 2026) [1]; *in vivo* veterinary efficacy data are almost entirely absent; and crude preparations are difficult to patent, which limits commercial investment in the trials that would be required. Specific gaps and the work needed to close them are listed in Table 3. Green synthesis of silver nanoparticles using plant extracts as reducing and capping agents, and other encapsulation approaches, offer a route to improved stability, targeted delivery and sustained release with lower host cytotoxicity (Wylie *et al.*, 2022) [5], but these formulations themselves require residue and safety evaluation before use in food animals.

4. Conclusion

Medicinal plants offer a chemically diverse and biologically plausible source of antibacterial agents at a time when resistance is limiting the usefulness of conventional drugs in both human and veterinary medicine. The strongest and most reproducible evidence concerns damage to the bacterial envelope, disturbance of membrane lipid homeostasis, thiol and oxidative stress, suppression of biofilm formation and inhibition of efflux, with several constituents restoring the activity of beta-lactam and fluoroquinolone antibiotics against resistant staphylococci. These properties are most immediately applicable in veterinary practice as topical and intramammary preparations and as adjuvants to existing antibiotics rather than as replacements for them. Progress now depends less on further *in vitro* screening than on chemically standardised preparations, properly controlled trials in target species and the pharmacokinetic and residue data without which no product can be used responsibly in food-producing animals.

Table 3. Research gaps and priorities for veterinary application

Research gap	Consequence	Priority action
Absence of controlled trials in target species	Efficacy inferred almost entirely from <i>in vitro</i> and rodent data	Randomised, blinded field trials in cattle, poultry and small ruminants with defined clinical endpoints
Undefined molecular targets for most extracts	Mechanistic claims outrun the evidence; resistance risk cannot be predicted	Target identification by resistant-mutant selection, proteomics and biophysical binding studies
No pharmacokinetic or residue data	Dose, route, withdrawal period and maximum residue limits cannot be set	Pharmacokinetic and tissue-depletion studies in food-producing species
Batch-to-batch variability	Prevents standardisation and regulatory registration	Chemically standardised extracts with marker-compound specification and stability testing
Inconsistent and non-comparable methodology	Results across studies cannot be pooled or compared	Adoption of standard broth microdilution with reference strains and reporting of full chemical composition

Acknowledgement

The authors sincerely acknowledge and thank all researchers whose valuable research articles and scientific contributions provided the foundation and supporting evidence for this review.

Conflict of interest

The authors declare that they have no conflict of interest.

Author contributions

Coauthor contributed to the conception of the review, the literature search and the drafting of the manuscript and both read and approved the final version.

Funding

This review received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

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How to cite this article: Warhade GM, Warhade RM, Hangarkar MD, Vaghela SS, Jadhav MM, Sabale SC, et al. Antibacterial efficacy and mechanisms of action of medicinal plants against multidrug-resistant bacteria: A review with relevance to veterinary practice. *International Journal of Veterinary Sciences and Animal Husbandry*. 2026;11(9S):162-168. doi: <https://www.doi.org/10.22271/veterinary.2026.v11.i9Sc.3790>

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