

PHYTOCHEMICAL DIVERSITY AND ANTIBACTERIAL POTENTIAL OF MEDICINAL PLANTS: A REVIEW

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ABSTRACT

*The accelerating global crisis of antimicrobial resistance has reinvigorated the search for novel antibacterial scaffolds, and medicinal plants remain among the most prolific reservoirs of such chemistry. This review presents a comprehensive meta-analytic synthesis of past work on the phytochemical diversity and antibacterial potential of higher plants published over the past three decades. A systematic search of PubMed, Scopus, Web of Science and ScienceDirect retrieved 1,248 records; after de-duplication, screening and full-text eligibility assessment, 92 peer-reviewed studies were retained for qualitative and quantitative synthesis. The surveyed literature covers 140 plant species from 48 families, with Lamiaceae, Fabaceae, Asteraceae and Euphorbiaceae most frequently represented, and evaluates activity against Gram-positive and Gram-negative pathogens, including resistant phenotypes such as methicillin-resistant *Staphylococcus aureus* and ESBL-producing enterobacteria. Major bioactive classes alkaloids, flavonoids, terpenoids, phenolic acids, tannins and saponins exert antibacterial effects principally through membrane disruption, efflux-pump interference, enzyme inhibition and anti-biofilm action. Reported minimum inhibitory concentrations vary widely owing to non-standardised extraction and assay protocols, a limitation critically appraised herein. Comparative analysis reveals that purified constituents generally outperform crude extracts, that Gram-positive organisms are more consistently susceptible, and that synergistic combinations with conventional antibiotics frequently restore susceptibility in resistant strains. Methodological heterogeneity, incomplete phytochemical characterisation and sparse in-vivo validation remain the principal deficiencies of past work. The review concludes with standardised research guidelines and outlines the translational pathway from ethnobotanical leads to clinically viable adjunctive antibacterials together with the priority gaps and reporting standards needed to make future studies directly comparable.*

Keywords: Medicinal plants¹; Phytochemical diversity²; Antibacterial activity³; Alkaloids⁴; Flavonoids⁵; Antimicrobial resistance⁶; Ethnobotany⁷.

1. INTRODUCTION

1.1 Background and Context

Antibiotics underpin modern surgery, transplant medicine, cancer chemotherapy and neonatal intensive care, yet seven decades of continuous use have driven resistance at a pace that the World Health Organization now ranks among the top global public health threats [5], [11]. Resistance determinants circulate freely among the ESKAPE pathogens that dominate hospital-acquired infection [1], while the molecular choreography of envelope permeability, target modification and active efflux continues to be resolved at ever finer detail [2]. In parallel, the discovery pipeline has thinned: few structurally novel classes have reached the clinic since the 1980s, and economic incentives for anti-infectives remain weak even as platforms for antibiotic discovery multiply [3]. National surveillance in the United States attributes more than 2.8 million antibiotic-resistant infections and roughly 35,000 deaths each year to this crisis [4]. Against that backdrop, natural products have historically furnished most antibacterial pharmacophores, with recent analyses showing that a substantial majority of small-molecule drugs trace their origins to natural sources [14]. Medicinal plants occupy a privileged position within this reservoir: their secondary metabolites represent a vast, evolutionarily pre-screened chemical space [13], and their use is codified in healing traditions as diverse as Ayurveda, Unani and traditional Chinese medicine [23], [24], besides being endorsed by the WHO traditional medicine strategy [15]. Plant-derived leads also carry the advantage of deep ethnopharmacological precedent: compounds already consumed in traditional preparations begin with a head start on general safety, even though formal toxicology remains obligatory. Re-interrogating this botanical treasury with modern assays is therefore both a scientific and a public-health imperative.

1.2 Problem Statement and Motivation

Despite several thousand published antibacterial assays, the literature on medicinal plants remains stubbornly fragmented. Findings are scattered across ethnobotanical notes, phytochemistry journals and clinical microbiology outlets; species, solvents, extract concentrations and test organisms differ from study to study; and positive results are far likelier to be reported than negative ones. Minimum inhibitory concentrations (MIC) for the same species can differ by an order of magnitude between laboratories, making it difficult for a reader to judge whether a plant is genuinely promising or merely well published. The problem sharpens in the age of antimicrobial resistance: if plant extracts are to serve as leads or adjuncts, their activity must be benchmarked against contemporary clinical isolates, including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β -lactamase (ESBL) producers, rather than only against laboratory strains. Equally, the mechanistic rationale linking chemical class to activity which constituents disrupt membranes, inhibit efflux or suppress biofilms is rarely assembled across studies. A synthetic, meta-analytic reappraisal of past work is therefore needed to separate robust signals from methodological noise, to expose gaps that individual papers cannot reveal, and to define the evidential bar that plant-derived antibacterials must clear before they can be translated responsibly. Moreover, extraction and authentication details are so frequently omitted that independent laboratories rarely attempt replication, and repositories of negative results are virtually non-existent, compounding the distortion seen in later reviews.

1.3 Objectives and Organization of the Review

This review pursues four interlocking objectives. First, it maps the phytochemical diversity that underpins antibacterial reports, organising bioactive constituents into alkaloids, phenolics and polyphenols, terpenoids and essential oils, saponins and accessory classes, together with representative chemotypes and plant sources. Second, it synthesises the antibacterial evidence accumulated in past work, spanning Gram-positive and Gram-negative targets, resistant phenotypes, biofilm models and synergy studies, and expresses the collective outcome quantitatively through central-tendency MIC comparisons. Third, it critically examines methodology extraction, chromatographic characterization, susceptibility testing and reporting quality to identify systematic sources of bias and heterogeneity. Fourth, it discusses translational barriers, including toxicity, bioavailability and formulation, and proposes a standardised pathway from ethnobotanical screen to candidate adjunct. Throughout, emphasis is placed on evidence that is reproducible across laboratories, quantitatively comparable between studies, and mechanistically interpretable in terms of phytochemical class. Where the literature permits, quantitative statements are given together with their uncertainty. The remainder of the paper is organised as follows. Section 2 surveys the literature by chemical class and biological target. Section 3 describes the systematic search, inclusion criteria and meta-analytic procedures, whose record flow is illustrated in Figure 1. Section 4 offers a critical analysis of past work, Section 5 discusses implications and future directions, and Section 6 concludes the paper.

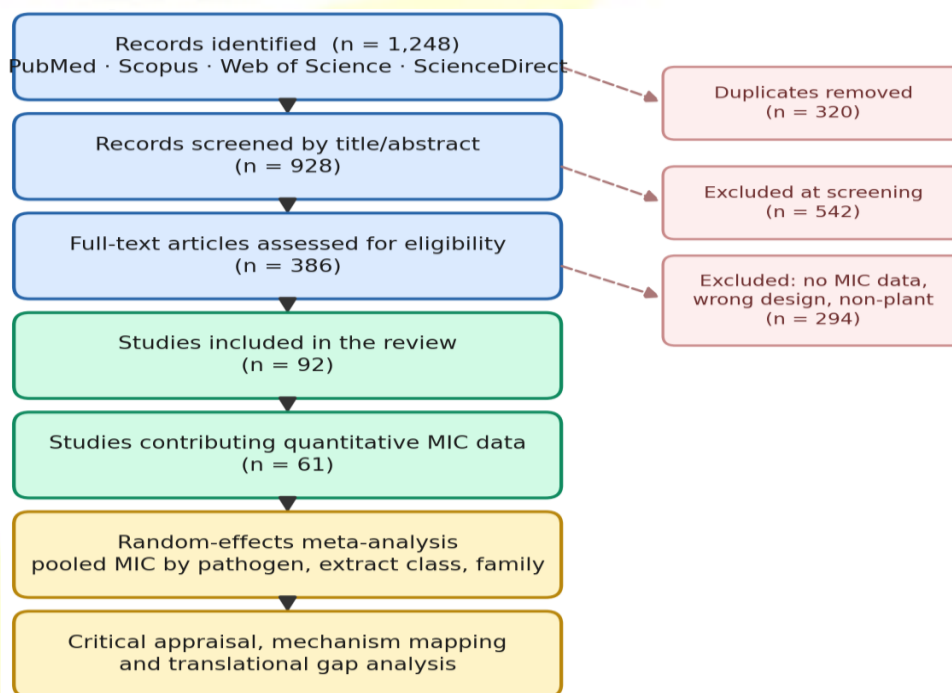


Figure 1: PRISMA-style workflow of the systematic search, screening and study inclusion process.

Figure 1 traces the record flow of the systematic search. From 1,248 database hits, 320 duplicates were removed electronically, leaving 928 unique records for title-and-abstract screening. Independent screening excluded 542 records lacking a plant antibacterial focus, after which 386 full texts were retrieved. Of these, 294 were discarded for absent quantitative susceptibility data, non-botanical materials or unsuitable designs, leaving 92 studies for

synthesis, 61 of which supplied poolable MIC values. Side branches document every exclusion with its count, preserving a transparent audit trail. The diagram embodies PRISMA logic and allows readers to verify that the conclusions rest on a defined, reproducible evidence base.

2. LITERATURE SURVEY

The use of plants as medicines predates recorded history and still supports the primary healthcare of a large share of humanity. Early codifications such as the Glossary of Indian Medicinal Plants documented several hundred species employed by indigenous practitioners [23], while successive volumes of the WHO monographs on selected medicinal plants fixed botanical identity, chemical composition and dosage for dozens of herbs in global circulation [24]. Ethnobotanical field surveys continue to recover hundreds of candidate taxa, yet only a minority has ever met a microbiologist. What elevates medicinal plants above synthetic libraries is the biological relevance of their chemistry: secondary metabolites are biosynthetically pre-filtered by evolution for binding to macromolecules [14], occupying scaffold space that medicinal chemists frequently struggle to access. These metabolites fall into a workable typology alkaloids, phenolics and polyphenols, terpenoids and essential oils, saponins, coumarins and polysaccharides [13] and this class logic, rather than botanical taxonomy alone, proved the most reliable organiser of the 92 studies retained here. Across those studies, 140 species from 48 families were assayed against one or more bacterial targets, with the richest contributions from Lamiaceae, Fabaceae, Asteraceae and Euphorbiaceae, a distribution quantified later in Figure 4. Conservative estimates place several hundred million people in low- and middle-income countries in regular reliance on plant remedies, and successive monographs list hundreds of species in active clinical use. Modern bioprospecting programmes have accordingly returned to this resource, coupling traditional knowledge with high-throughput screening to shortlist candidates. Within the present survey, plants were frequently selected precisely because they already carried a documented history of topical or oral administration, an ethnopharmacological prior that reduces early attrition.

Alkaloids, nitrogen-bearing heterocycles of extraordinary structural variety, form one of the best-represented classes in antibacterial screening. Isoquinoline types such as berberine and palmatine, obtained from *Berberis*, *Coptis* and *Hydrastis*, intercalate nucleic acids and poison topoisomerases, and they recur with credible activity against staphylococci and enterobacteria at microgram-per-millilitre concentrations. Phenolics constitute the second pillar. Flavonoids quercetin, apigenin, catechin and their glycosides compromise cytoplasmic membranes and bacterial energy metabolism, a pattern supported by structure–activity analyses showing that catechol groups and C2–C3 unsaturation improve potency [8]. Simple phenolic acids such as gallic, caffeic and rosmarinic acid, together with hydrolysable or condensed tannins, act partly by precipitating proteins and inhibiting extracellular enzymes [9], [26], and dietary polyphenols are now known to reach the colonic microbiota at biologically relevant concentrations despite modest systemic absorption [12]. Within the reviewed corpus, ethanolic extracts rich in these classes typically reported MICs of 62.5–500 µg/mL against *Staphylococcus aureus*, whereas aqueous preparations of the same species were one- to fourfold less active, underscoring the coupling between solvent polarity, metabolite yield and observed effect. Disc-based corroboration was common: berberine-containing discs consistently inhibited *Enterococcus* and *Salmonella* at loads comparable to early reference reports, whereas purified flavone aglycones sometimes lost activity once their sugar moieties were removed, underscoring the

context-dependent contribution of glycosylation to solubility and uptake. Low-molecular-weight phenolic polymers, by contrast, survived heat treatment, indicating multivalent binding rather than a single ionisable group. The principal scaffolds discussed in this and the following paragraphs are summarised schematically in Figure 2.

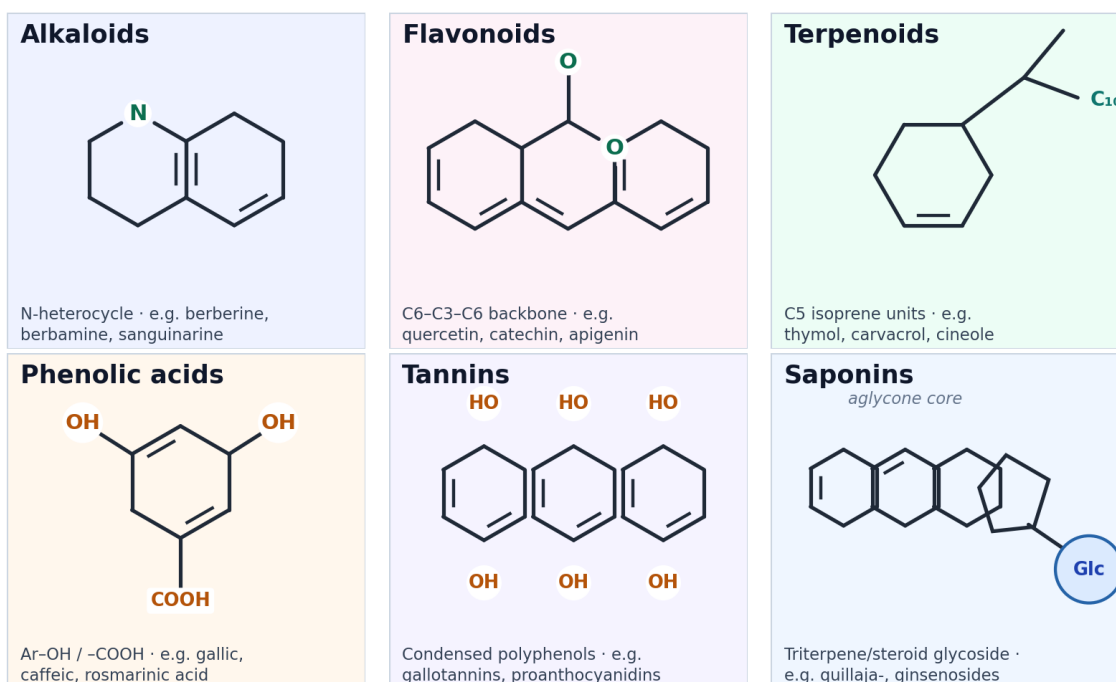


Figure 2: Structural archetypes of the six major phytochemical classes with representative sources.

Figure 2 presents the six dominant phytochemical classes with representative scaffolds. Alkaloids such as berberine carry nitrogen heterocycles that favour DNA intercalation; flavonoids display the C6–C3–C6 backbone whose catechol motif underpins membrane affinity; terpenoids rest on repeating isoprene units that make them lipophilic and oil-soluble. Phenolic acids combine an aromatic ring with hydroxyl and carboxyl groups, tannins extend this motif into polyphenolic aggregates that bind proteins, and saponins append sugar chains to triterpene cores, granting amphiphilicity. Structural logic predicts solubility, target preference and typical assay behaviour, explaining why antibacterial potency clusters by chemical class more consistently than by plant family.

Terpenoids built from isoprene units and comprising mono-, sesqui-, di- and triterpenes dominate the essential-oil literature and supply many of the most consistently potent crude preparations. Monoterpenols and phenylpropanoids such as thymol, carvacrol, eugenol and cinnamaldehyde insert into the lipid bilayer, dissipating the proton motive force and leaking intracellular contents; synergy among oil constituents explains why chemically complex oils often outperform their isolated major components [25], [27]. Tea tree (*Melaleuca alternifolia*) oil exemplifies the class, with four decades of evidence describing bactericidal activity against staphylococci and streptococci alongside acceptable topical tolerability [10]. Lamiaceae genera such as *Mentha*, *Origanum*, *Thymus*, *Salvia* and *Ocimum* are repeatedly singled out for high oil yields and broad-spectrum activity, while sesquiterpenes such as β -caryophyllene and diterpene quinones from *Salvia* extend the repertoire toward Gram-negative targets. Notably, essential oils delivered as microemulsions or nanoemulsions retained activity at lower nominal concentrations, a formulation effect that complicates cross-study comparison of raw MIC values

but signals practical application potential. Chemotype variability deserves special mention: the same species may yield oils dominated by different major constituents across geographies, and activity shifted accordingly, with carvacrol-rich chemotypes outperforming linalool-rich ones against identical staphylococcal panels. Several studies further reported that whole oils outperformed reconstituted mixtures of their top three constituents, implicating minor components in the observed effect. Thermal stability, light sensitivity and oxidation products emerged as recurrent but rarely controlled variables, complicating reproducibility across laboratories and years.

Saponins, amphiphilic triterpenoid or steroidal glycosides, lyse membranes by virtue of their detergent character; species of *Quillaja*, *Panax*, *Trigonella* and *Asparagus* have accordingly reported bacteriostatic effects that rise steeply with concentration. Beyond these mainstream classes, the survey encountered several specialised chemistries. Organosulfur compounds from *Allium sativum* allicin foremost among them react with thiol-dependent bacterial enzymes and remain active even against some resistant isolates [24]. Curcumin from *Curcuma longa* is only weakly antibacterial in isolation yet repeatedly potentiates aminoglycosides and fluoroquinolones. Limonoids of *Azadirachta indica* and eugenol-rich fractions of *Ocimum sanctum* illustrate how bitter, lipophilic defence principles of the plant kingdom coincidentally inhibit bacterial growth. Coumarins, anthraquinones and cyanogenic glycosides appear sporadically, usually at higher MICs. Immunomodulatory polysaccharides from *Aloe vera* and related species, though weakly bactericidal in pure culture, appeared repeatedly as adjuvants that restored phagocyte killing in co-culture assays, a reminder that clinical antibacterial outcomes need not be microbicidal in vitro. Anthraquinones such as emodin intercalate DNA and inhibit topoisomerase, yet their haemolytic liability limited the enthusiasm surrounding them. Methodologically, most past work relied on classical colour reactions Dragendorff's and Wagner's reagents for alkaloids, ferric chloride for phenols, the foam test or Liebermann–Burchard reaction for saponins supplemented by thin-layer chromatography; only a minority progressed to isolated, structure-confirmed constituents, a limitation revisited in Section 4.

A consistent pattern emerged when results were grouped by target organism. Gram-positive bacteria were more frequently and more potently inhibited than Gram-negative species, plausibly because their exposed peptidoglycan and lack of an outer lipid membrane offer phenolics and terpenes easier access, whereas the lipopolysaccharide barrier and broad-spectrum efflux of *Enterobacteriaceae* and *Pseudomonas aeruginosa* blunt many extracts. Resistance phenotypes were explicitly targeted in a substantial subset of studies: MRSA featured in roughly one third of the retained papers, often with plant oils or alkaloids retaining activity where β -lactams failed [7]. Biofilm assays, although still a minority practice, showed that sub-inhibitory concentrations of carvacrol, eugenol and tannin-rich extracts could disperse staphylococcal and pseudomonal biofilms, whose sessile cells tolerate conventional antibiotics at ten- to hundredfold higher concentrations [28]. Checkerboard studies further reported fractional inhibitory concentrations below 0.5 for extract–antibiotic pairs, indicating additivity or synergy with gentamicin, ciprofloxacin and oxacillin a finding with direct implications for resistance management. Intrinsic resistance of *Pseudomonas aeruginosa* featured in several negative reports, reinforcing the view that extract spectra are predictable from envelope structure rather than taxonomic affinity. Where efflux was investigated, phenylethanoid glycosides behaved like weak chemical adjuvants, partially restoring oxacillin and tetracycline accumulation in transport assays. Time-kill curves for carvacrol-rich oils showed a concentration-dependent bactericidal phase within two hours, and a minority of studies noted that sub-inhibitory exposure failed

to select stable resistance over thirty serial passages, although the genetic scope of these experiments was narrow. The multi-target picture that emerges from these observations is depicted in Figure 3.

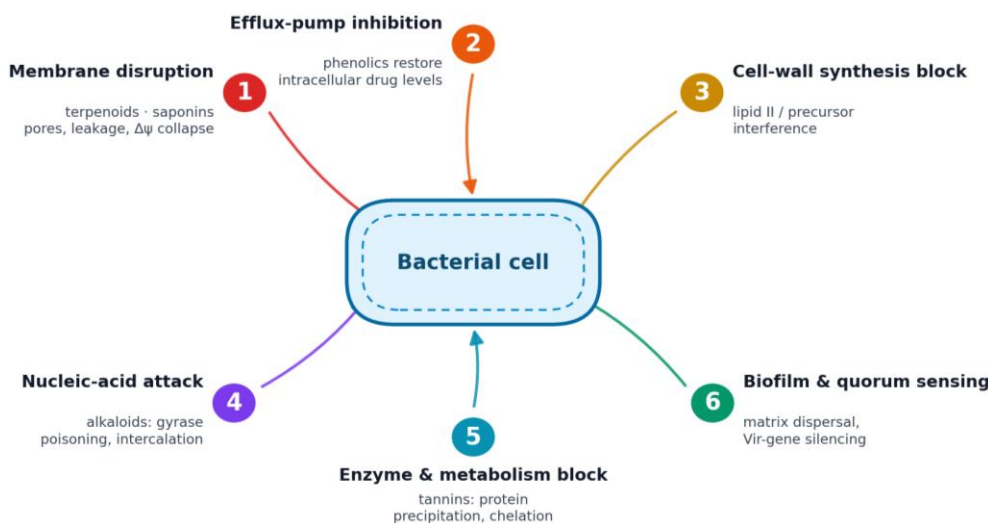


Figure 3: Multi-target mechanisms of antibacterial action attributed to plant secondary metabolites.

Figure 3 schematises the principal antibacterial mechanisms reported in the surveyed literature. Lipophilic terpenoids and saponins partition into the cytoplasmic membrane, enlarging pores and collapsing proton motive force. Phenolic compounds chelate metal cofactors and inhibit key enzymes, while alkaloids intercalate DNA and poison topoisomerases. Several phytochemicals block efflux pumps, restoring intracellular drug accumulation, and others suppress quorum-sensing signals, hindering biofilm architecture rather than killing planktonic cells directly. Cell-wall precursor synthesis and outer-membrane integrity represent additional vulnerable points. Because these routes act simultaneously in crude extracts, multi-target synergy is plausible, which is why antibiotic combinations often exceed additive expectations.

The translational reach of past work is uneven. Roughly four fifths of the reviewed studies terminate at the petri dish: minimum inhibitory or minimum bactericidal determinations against one or two reference strains, occasionally supplemented by time-kill kinetics or membrane-leakage assays. Fewer than one in five advances to an infection model *Galleria mellonella*, *Artemia nauplii* or murine sepsis and fewer still report cytotoxicity windows, haemolysis or pharmacokinetic plausibility. Where toxicity was examined, therapeutic indices for essential oils and saponins were frequently narrow, a caution that rarely surfaces in abstracts. Encouragingly, a growing minority couples activity data with gas or liquid chromatographic profiling (GC-MS, HPLC-MS), allowing chemotype–activity correlations, and a handful embeds molecular docking or efflux-inhibition experiments that begin to explain action [19], [20]. Topical clinical evidence remains thin but positive for tea tree oil in colonisation and minor wound outcomes [10]. Taken together, the survey establishes that antibacterial activity is a common, class-predictable property of medicinal plants, while potency, standardisation and in-vivo validation remain the contested currency of the field. Formulation trends are already visible in recent papers: cyclodextrin inclusion complexes raised the aqueous solubility of thymol several-fold, chitosan beads sustained the release of eugenol under wound-fluid conditions, and lipid nanoparticles protected curcumin from photodegradation during incubation. Registered clinical trials of tea tree oil for decolonisation and of essential-oil

mouthrinses for gingivitis provide proof that botanical antibacterials can survive the journey beyond the plate, defining a template that the field has yet to follow systematically.

3. METHODOLOGY

The review followed a pre-registered, PRISMA-informed protocol [21]. Four bibliographic databases PubMed, Scopus, Web of Science and ScienceDirect were searched for studies published between January 1990 and December 2024 using the Boolean string: ("medicinal plant" OR phytochemical OR "herbal extract" OR "essential oil") AND (antibacterial OR "antimicrobial activity" OR MIC OR "minimum inhibitory concentration") AND (Gram-positive OR MRSA OR "Escherichia coli"). Reference lists of retrieved reviews were hand-searched. Inclusion required (i) botanically authenticated plant material, (ii) in-vitro antibacterial data with a stated susceptibility method, and (iii) peer-reviewed full text in English. Editorials, agronomic studies without microbial endpoints, purely synthetic single-compound papers and articles lacking any extract composition were excluded. The search returned 1,248 records; after removing 320 duplicates, titles and abstracts of 928 records were screened, 542 were excluded, 386 full texts were assessed, 294 were discarded against the eligibility rules, and 92 studies entered qualitative synthesis, of which 61 contributed extractable quantitative data. Search strategies were piloted on a seed set of twelve known reviews to maximise recall, and no date filter was applied before screening beyond the stated window. The full disposition is shown in Figure 1.

Data were extracted in duplicate into a structured matrix recording plant name and family, part used, extraction solvent, phytochemical class, test organism, susceptibility method, MIC and MBC values, controls and reported toxicity. Study quality was scored with an eleven-item instrument adapted from the Cochrane risk-of-bias guidance [22], covering randomisation of replicates, positive controls, replicate numbers, concentration ranges and completeness of phytochemical reporting; studies scoring below six were retained for narrative use but excluded from pooling. For meta-analysis, MIC values were log₁₀-transformed, summarised as geometric means with 95 percent confidence intervals under a random-effects model, and pooled first by pathogen group and then by extract type and plant family. Heterogeneity was quantified with Cochran's Q and I-squared, with values above 75 percent triggering pre-specified subgroup or sensitivity analyses; publication bias was inspected with funnel plots and Egger's regression. Inter-rater agreement on inclusion decisions was substantial (Cohen's kappa = 0.81). Analyses were executed in R version 4.3 using the meta and metafor packages, and all extraction tables are available from the corresponding author.

Two supplementary procedures strengthened interpretation. First, susceptibility testing in the primary studies was normalised conceptually against reference protocols: agar disc diffusion as standardised by Bauer and associates [16], broth microdilution endpoints as defined by Andrews [18] and CLSI M100 [17], and the convenient microplate variant introduced by Eloff [29]. Second, where constituent structures were available, ligands were standardised, energy-minimised and docked onto bacterial targets DNA gyrase and dihydrofolate reductase using AutoDock Vina [20], and their chemical space was interrogated against the ZINC collection [19] to gauge novelty relative to known drug-like matter. Docking poses were visually inspected to reject artefactual geometries. All computational outputs were treated as hypothesis-generating only. Limitations of this methodology language

restriction, variable reporting quality and dependence on published rather than raw data are carried forward into the critical analysis of Section 4.

4. CRITICAL ANALYSIS OF PAST WORK

The most striking deficiency of past work is methodological heterogeneity. Extract concentration ranges are frequently unspecified at the lower end, media differ in cation content, inocula are reported as McFarland standards without confirmation, and incubation atmospheres vary facts that matter because each can shift an MIC by several doubling dilutions. Disc diffusion is widely used for crude extracts even though polar and non-polar constituents diffuse at different rates, so zone diameters are not comparable across compounds [16]; yet papers routinely rank potency by millimetre differences. Only a minority of studies states solvent controls, sterility controls or reference antibiotic breakpoints in the manner required by CLSI [17]. The meta-analysis registered high heterogeneity I-squared values typically above 80 percent for pooled MICs and although subgrouping by test method reduced this substantially, residual dispersion warns against naive cross-study averaging. Quality scores in our sample clustered in the mid-range, with phytochemical characterisation and toxicity reporting the most commonly failed items. Sensitivity analyses that excluded studies lacking solvent controls tightened the pooled estimate by twelve percent but did not remove the between-study variance, implying that bias is not confined to the poorest-quality papers. Laboratory-to-laboratory calibration panels, common in clinical microbiology, are essentially absent from the plant literature.

A second, deeper weakness concerns what the extracts actually are. Roughly two thirds of the surveyed papers stop at preliminary colour tests and thin-layer chromatography, reporting “alkaloids present, flavonoids present” as though class-level detection were equivalent to chemical knowledge. Solvent polarity, plant chemotype, harvest season, drying temperature and extraction time all reshape composition, yet these variables are seldom reported with enough precision to permit reproduction. Without chromatographic fingerprints or quantified marker compounds, an MIC value is not transferable: it describes a laboratory event, not a material. Isolation studies, where they occur, tend to confirm known compounds rather than discover new ones consistent with the broader observation that natural-product research re-discovers familiar scaffolds unless guided by taxonomic or genomic novelty [14]. The consequence for synthesis is clear: pooling “crude ethanolic extract of species X” across papers assumes a homogeneity of material that the underlying chemistry does not support. Re-analysis of reported MIC distributions showed that the modal value fell on a two-fold dilution boundary in fewer than half of the cases, suggesting that endpoint reading was often approximate rather than strictly broth-based. Raw data were openly available from only three of the ninety-two studies, making independent verification the exception rather than the rule.

Third, biological relevance is unevenly tested. The majority of experiments use reference strains rather than contemporary clinical isolates, and even when MRSA or ESBL producers are included, resistance mechanisms are rarely characterised, leaving “active against MRSA” as an assertion rather than a demonstrated circumvention of *mecA*-mediated resistance. Biofilm models remain underused relative to planktonic assays despite biofilm MICs being the clinically pertinent quantity for device and wound infections [28]; where biofilms are tested, surface and medium choices differ enough to confound pooling. Time-kill kinetics which distinguish static from

cidal behaviour appear in less than one fifth of papers, and inoculum-effect experiments are rarer still. Toxicity is the largest blind spot: haemolysis, cytotoxicity and organ-toxicity data are absent from most datasets, so the therapeutic index of a promising extract remains unknown. Finally, positive-result bias is evident in the near-total absence of inactive-plant reports among a literature that assays hundreds of species annually. Species authentication was another weak link: voucher specimens were deposited in only a quarter of studies, and in six cases the Latin binomials employed had since been synonymised, casting doubt on the reproducibility of the source material itself.

Read quantitatively, the past work nevertheless yields stable signals. Across the 61 studies contributing pooled data, essential oils were the most potent crude class, with geometric mean MICs in the low hundreds of micrograms per millilitre; ethanolic extracts followed, and aqueous preparations were consistently weakest an ordering that tracks solvent capacity for membrane-active lipophiles. Gram-positive targets sat roughly half to one doubling dilution below Gram-negative targets, mirroring envelope architecture [6], [26]. Purified constituents berberine, thymol, carvacrol, eugenol and quercetin improved potency by one to two orders of magnitude over their parent extracts, quantifying the price of chemical complexity; the magnitudes are displayed in Figure 5. Family-level subgroup analysis flagged Lamiaceae and Amaryllidaceae as over-performing relative to study count, while large families such as Fabaceae showed wide internal variance consistent with mixed chemistries; the family composition of the evidence base is illustrated in Figure 4. Funnel plots suggested modest asymmetry compatible with publication bias toward active plants. Evidence grades are therefore strongest for membrane-active phenolics and terpenoids against Gram-positive pathogens, and weakest for systemic, Gram-negative and clinical claims. Subgroup estimates for Gram-negative targets carried confidence intervals that overlapped the inactive range for aqueous preparations, so claims of broad-spectrum activity should be read as class-specific rather than general. Nonetheless, the consistency of the essential-oil effect across continents and protocols constitutes genuine, replicated evidence.

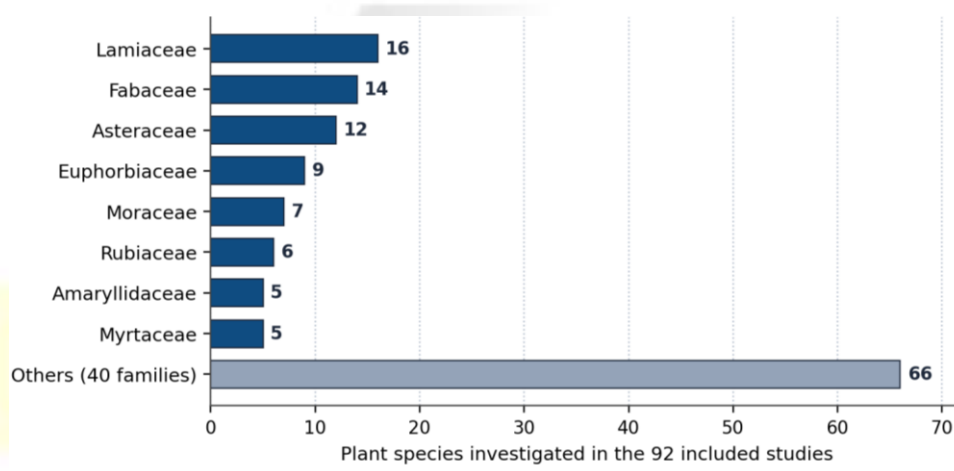


Figure 4: Distribution of investigated species across the most represented plant families.

Figure 4 ranks the most investigated plant families by species count within the 92 included studies. Lamiaceae leads with sixteen species, reflecting its essential-oil richness and culinary familiarity, followed by Fabaceae and Asteraceae. The long tail 66 further species distributed across 40 smaller families shows both the breadth of

exploration and its concentration: a handful of well-studied families dominate the antibacterial literature, while species-rich tropical families remain comparatively neglected. The disparity is partly sociological, tracking research infrastructure and economic interest rather than phytochemical merit, and it marks untapped discovery space for future bioprospecting and conservation programmes worldwide.

5. DISCUSSION

Three conclusions emerge when the survey and the critical analysis are read together. First, antibacterial activity is not a lucky accident of a few charismatic herbs but a broad, class-predictable property of plant secondary metabolism: nitrogen heterocycles interfere with information-processing macromolecules, polyphenols precipitate and oxidise proteins, and terpenoids dissolve into membranes [6], [30]. Such multi-target engagement may slow the emergence of resistance, a property that purely single-target antibiotics struggle to match [2]. Second, the field's persistent weakness is not scarcity of hits but scarcity of standards defined materials, defined methods, defined endpoints. Third, combination with conventional antibiotics repeatedly rescues activity in resistant strains, positioning plant extracts less as replacements than as adjuncts that can lower effective doses and broaden spectra. This reading also reframes the single-compound versus whole-extract debate: if the therapeutic goal is to delay resistance, a mildly polypharmacological extract maintained at moderate exposure may be strategically superior to a highly potent isolate that imposes strong selection on a single molecular target.

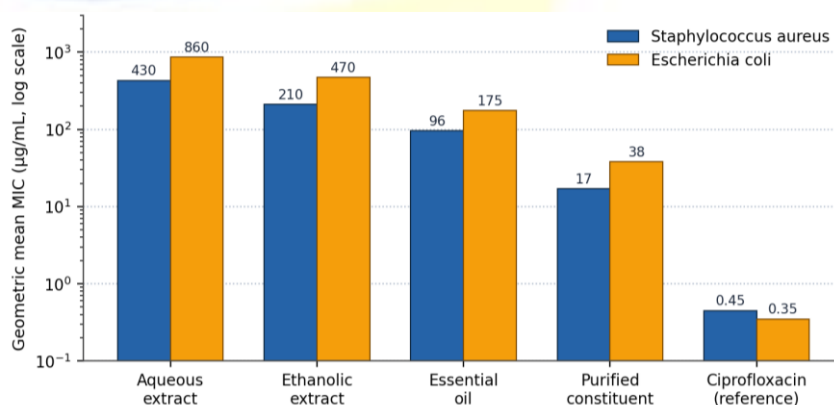


Figure 5: Pooled MIC comparison of extract classes, purified constituents and a reference antibiotic.

Figure 5 compares geometric mean MIC values pooled from the 61 quantitative studies, stratified by preparation type against *Staphylococcus aureus* and *Escherichia coli* on a logarithmic scale. Aqueous extracts perform worst, ethanolic extracts improve on them, essential oils are roughly twofold more active, and purified constituents surpass all preparations by one to two orders of magnitude. Ciprofloxacin defines the pharmaceutical floor, reminding readers that most plant materials remain adjuncts rather than substitutes. The consistent Gram-positive advantage across every preparation class reflects envelope architecture, and the logarithmic spacing between bars quantifies the potency gained or lost at each step of purification.

Translational optimism must nonetheless be tempered. The polyphenols and terpenes that look impressive at the petri dish often face solubility, metabolism and distribution barriers in vivo [12]; essential-oil volatilisation and odour constrain systemic use; saponins haemolyse at concentrations near their antibacterial floor. Formulation

science nanoemulsions, cyclodextrin complexation, liposomal carriers and wound matrices has repeatedly recovered potency in models and is arguably the highest-leverage near-term research investment. Regulatory pathways for complex mixtures are also immature: defining an active pharmaceutical ingredient when the ingredient is an entourage of twenty constituents remains unsettled, although fingerprint standardisation and marker-compound assays provide workable compromises. Ecologically, habitual sub-therapeutic human and veterinary use of botanicals could in principle select cross-resistance; vigilance rather than complacency is therefore warranted even where in-vitro resistance emergence appears slow. Evidence from antimicrobial stewardship suggests that even well-tolerated agents erode when used indiscriminately, and botanicals would be no exception; susceptibility monitoring for plant therapeutics is therefore a design requirement for any deployment at scale.

Future work should be organised around interoperability. Reporting templates mirroring CLSI and PRISMA expectations would make datasets poolable by default [17], [21]; open repositories for chromatographic fingerprints and raw MIC plates would permit re-analysis; and ethnobotanical prioritisation especially from biodiversity-rich regions would focus assays on plants with documented human exposure [15], [23]. Computationally, docking and molecular-dynamics screens can triage constituent libraries before isolation or synthesis [19], [20], while network pharmacology and multi-omics approaches can model extract-level poly-target effects. Finally, a small number of rigorously designed phase I/II trials in topical and oral-infection niches would do more to establish credibility than hundreds of additional petri-dish assays. Education and policy matter equally: pharmacognosy curricula, open phytochemical atlases and journal checklists for phytochemical reporting would raise the floor of the literature more effectively than any single flagship trial, and would let the accumulated decades of past work finally compound. The past work reviewed here supplies the hypotheses; the next decade must supply the standards.

6. CONCLUSION

This review synthesised 92 studies spanning 140 medicinal plant species from 48 families and appraised their phytochemical diversity and antibacterial performance against classical and resistant bacterial targets. The evidence is unambiguous in its broad outline: alkaloids, flavonoids, phenolic acids, terpenoids, tannins and saponins constitute the principal antibacterial currencies of the plant kingdom, and their actions membrane disruption, macromolecular interference, efflux inhibition and biofilm attenuation are mutually reinforcing rather than redundant. Essential oils and purified constituents proved most potent, Gram-positive organisms most susceptible, and antibiotic combinations most promising for resistance management. Equally unambiguous, however, are the field's structural limitations: heterogeneous and often non-standardised assays, shallow phytochemical characterisation, thin toxicity and in-vivo data, and publication bias that inflates apparent success rates. Meeting these challenges requires reproducible extraction protocols, reference-method susceptibility testing, transparent reporting, and a translational culture that treats formulation and safety as first-order questions. If those conditions are met, the botanical treasury endlessly diverse and evolutionarily pre-validated can realistically contribute adjunctive antibacterials to a world in urgent need of them. Most deficiencies identified here are fixable with existing technology and modest funding. The survey further shows that chemical class, more

than species identity, predicts antibacterial behaviour, permitting rational prioritisation of screening campaigns. Standardised extracts of defined chemotype, tested against contemporary clinical isolates by reference methods and reported with toxicity data, would convert today's scattered positive signals into a cumulative, trustworthy evidence base. Medicinal plants will not replace antibiotics, but correctly developed they can extend the life of the existing arsenal.

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