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Antimicrobial Efficacy and Hemolytic Safety of Medicinal Plant Extracts: A Systematic Review

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Abstract

Medicinal plant preparations have been extensively explored as sources of antimicrobial compounds. Nevertheless, antimicrobial activity should not be interpreted as direct evidence of biomedical applicability, because some bioactive extracts can disrupt erythrocyte membranes or produce blood-cell toxicity. Purpose: This systematic review integrates published evidence on medicinal plant extracts that were assessed for antimicrobial effects together with hemolytic or hemocompatibility-related safety. Methods: Literature searches were carried out in PubMed, Scopus, SpringerLink, Wiley Online Library, and MDPI using keyword combinations related to medicinal plants, antimicrobial activity, hemolysis, erythrocytes, and hemocompatibility. Articles published during 2014-2026 were selected using predetermined eligibility criteria. Results: The search retrieved 1,525 records. Following removal of 572 duplicates, 953 records were screened; 653 were excluded during title and abstract assessment, and 300 full-text reports were reviewed. Thirty studies fulfilled the inclusion criteria. The included articles mainly used in vitro antimicrobial approaches, such as inhibition-zone testing, MIC, MBC, antibiofilm, or antifungal assays, and paired them with hemolysis, erythrocyte membrane-stability, PBMC cytotoxicity, or related blood-cell safety assays. Conclusion: Medicinal plant extracts are best evaluated using an efficacy-safety perspective. Preparations that inhibit microbes at concentrations below hemolytic or cytotoxic thresholds represent stronger candidates for subsequent biomedical development.

Keywords: Antimicrobial activity, Erythrocytes, Hemocompatibility, Hemolysis, Medicinal plants

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Introduction

Antimicrobial resistance (AMR) remains a major public-health concern because it weakens the therapeutic value of existing antimicrobial drugs and contributes to higher risks of treatment failure, prolonged disease, and increased health-care expenditure[1,2]. This situation has intensified the search for alternative or complementary antimicrobial resources, including natural products and medicinal plant extracts that may be useful in infection control, wound care, oral health, complementary practice, and herbal product development[5–7].

Medicinal plants are chemically complex materials. They may contain phenolics, flavonoids, tannins, alkaloids, terpenoids, essential oils, saponins, organosulfur compounds, and other secondary metabolites. These constituents can suppress microbial growth through multiple pathways, including damage to microbial membranes, inhibition of enzymes, disruption of cell-wall synthesis, induction of oxidative stress, interference with quorum sensing, and reduction of biofilm formation [5,6]. Findings from food microbiology also indicate that plant-derived bioactive materials have antimicrobial potential; for instance, Ramadani et al. reported that garlic-based preparations lowered microbial counts in different meat products [8].

However, inhibitory activity against bacteria or fungi is not enough to justify biomedical use. Extracts capable of suppressing microbial cells may also affect mammalian cells, particularly erythrocytes and other blood-associated cells. Hemolysis is therefore an important early safety indicator because erythrocytes are vulnerable to membrane-active compounds, oxidative injury, surfactant-like molecules, and traces of extraction solvents. For plant extracts intended for topical use, mucosal application, wound materials, oral preparations, or complementary antimicrobial therapy, blood-cell compatibility should be considered before further development.

A number of experimental reports have examined antimicrobial activity together with hemolytic or hemocompatibility endpoints. These studies typically combine agar diffusion, broth microdilution, MIC, MBC, MFC, time-kill, antifungal, or antibiofilm assays with hemolysis tests, erythrocyte membrane-stabilization assays, PBMC cytotoxicity, thrombolytic outcomes, or related blood-cell measurements [9–38]. Despite

this growing evidence base, the information is distributed across microbiology, pharmacology, food science, biomedical safety, and complementary medicine literature.

Previous reviews have often focused on the antimicrobial potential of medicinal plants, but fewer have treated antimicrobial efficacy and hemolytic safety as paired criteria for translational interpretation. The present systematic review therefore aims to synthesize evidence on medicinal plant extracts that show antimicrobial activity while also demonstrating acceptable hemolytic or blood-cell safety profiles.

Method

1. Research design

This article was prepared as a systematic review in accordance with the PRISMA 2020 reporting framework[3]. The guiding review question was: Which medicinal plant extracts exhibit antimicrobial activity while maintaining acceptable hemolytic or hemocompatibility safety? The review was positioned within health sciences, herbal medicine, complementary care, infection control, and early-stage biomedical product development.

2. Setting and samples

The review sample consisted of experimental articles indexed in selected electronic databases. The included studies did not involve clinical patient samples as study populations; instead, they used laboratory models, such as pathogenic bacteria or fungi as microbial targets and erythrocytes, red blood cells, PBMCs, or related blood-cell systems as safety models. The eligible publication window was 2014-2026.

3. Information sources and search strategy

Searches were performed in PubMed, Scopus, SpringerLink, Wiley Online Library, and MDPI. The strategy combined three concept groups: medicinal plant source, antimicrobial effect, and blood-cell safety. The core string was: (medicinal plant OR plant extract OR herbal extract OR phytochemical OR natural product) AND (antimicrobial activity OR antibacterial OR antifungal OR antibiofilm OR minimum inhibitory concentration OR MIC OR MBC) AND (hemolytic activity OR hemolysis OR haemolysis OR hemocompatibility OR erythrocyte OR red blood cell). Database-specific syntax was adjusted when required. The number of records retrieved from each source is summarized in Table 1.

4. Inclusion and exclusion criteria

Articles were included when they met all of the following criteria: original experimental research; evaluation of a plant-derived extract, fraction, essential oil, or phytochemical-rich preparation; antimicrobial testing against bacteria or fungi; assessment of blood-cell safety through hemolysis, haemolysis, erythrocyte membrane stabilization, PBMC cytotoxicity, hemocompatibility, thrombolytic activity, or related outcomes; publication between 2014 and 2026; and availability of extractable data. Articles were excluded if they were reviews, meta-analyses, editorials, book chapters, conference abstracts without complete data, non-plant studies, nanoparticle-only investigations without botanical relevance, or reports that lacked either antimicrobial or blood-cell safety outcomes.

5. Study selection

Records from all databases were merged, and duplicate entries were removed prior to screening. Titles and abstracts were then reviewed using the eligibility criteria. Full texts were assessed for reports considered potentially relevant. Full-text exclusions were grouped into five categories: non-plant or non-medicinal source, absence of antimicrobial outcome, absence of hemolysis or hemocompatibility outcome, non-original article type, and insufficient extractable data or mismatch with the review scope. The selection process is illustrated in Figure 1.

6. Measurement and data collection

Data extraction used a structured form. Extracted variables included author, year, plant species or preparation, plant part, extraction type or solvent, microbial target, antimicrobial method, antimicrobial result, blood-cell safety method, hemolysis or cytotoxicity result, and relevance to biomedical or complementary health applications. The exposure of interest was the plant-derived preparation or its concentration, whereas the outcome domains were antimicrobial inhibition and hemolytic or blood-cell safety.

7. Quality and data analysis

Because most eligible studies were in vitro or ex vivo investigations, appraisal focused on the clarity of plant identification, extraction procedure, microbial strain reporting, antimicrobial assay, blood-cell source, hemolysis procedure, control conditions, concentration range, replication, and numerical reporting[4]. Considerable

heterogeneity was observed in plant species, solvents, microbial targets, and safety assays; therefore, the evidence was synthesized narratively rather than statistically. Meta-analysis was not conducted because the available endpoints were not sufficiently comparable across studies.

Results

The database search yielded 1,525 records: PubMed (n = 231), Scopus (n = 359), SpringerLink (n = 27), Wiley Online Library (n = 904), and MDPI (n = 4). After 572 duplicate records were removed, 953 records remained for title and abstract screening. During this stage, 653 records were excluded. The full texts of 300 reports were examined, and 270 were excluded based on the predefined criteria. Finally, 30 studies were included in the qualitative synthesis.

Table 1
Database search results and study selection summary

Database/source	Records identified	Search and filter notes
PubMed	231	2014-2026, English, plant-antimicrobial-hemolysis terms
Scopus	359	Title/abstract/keyword search; article records
SpringerLink	27	Article/research article records based on search screenshot
Wiley Online Library	904	Journals, open access content, 2014-2026
MDPI	4	Article records based on MDPI search result
Total records identified	1,525	Before duplicate removal
Duplicate records removed	572	Removed before title/abstract screening
Records screened	953	Title and abstract screening
Full-text reports assessed	300	Potentially eligible reports
Studies included	30	Final included studies for synthesis

Identification	Records identified from databases (n = 1,525) PubMed (n = 231) Scopus (n = 359) SpringerLink (n = 27) Wiley Online Library (n = 904) MDPI (n = 4) Registers (n = 0)	Records removed before screening: Duplicate records removed (n = 572) Records marked as ineligible by automation tools (n = 0) Records removed for other reasons (n = 0)
	▼	
Screening	Records screened (n = 953)	Records excluded after title/abstract screening (n = 653)
	▼	
Retrieval	Reports sought for retrieval (n = 300)	Reports not retrieved (n = 0)
	▼	
Eligibility	Reports assessed for eligibility (n = 300)	Reports excluded (n = 270): No hemocompatibility or hemolysis outcome (n = 115) No antimicrobial outcome (n = 72) Not medicinal plant extract / non-plant source (n = 38) Review, book chapter, editorial, or non-original article (n = 24) Insufficient extractable data or irrelevant full text (n = 21)
	▼	
Included	Studies included in review (n = 30) Reports of included studies (n = 30)	

Figure 1. PRISMA 2020 flow diagram of the study selection process

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Table 2
Characteristics of included studies and extracted outcome domains

No	Study	Plant/preparation	Antimicrobial outcome domain	Blood-cell safety outcome domain
1	Mehreen, Arifa et al. (2016)	Traditional herbs for sore throat	MDR Gram-positive and Gram-negative bacteria; inhibition zone and MIC	Haemolytic assay against human erythrocytes
2	Nunes, Tiago Rafael de Sousa et al. (2018)	Justicia pectoralis leaf	A. baumannii and K. pneumoniae; MIC/MBC	PBMC cytotoxicity and immune-cell safety indicators
3	Kibiti, Cromwell Mwiti et al. (2015)	Bulbine abyssinica whole plant	Opportunistic bacteria; antibacterial activity	Protection against erythrocyte membrane lysis
4	Saleem, Kinza et al. (2023)	Mango seed kernel	Antimicrobial activity with optimized extraction systems	Hemolytic activity
5	El Kamari, Fatima et al. (2024)	Euphorbia calyptrata essential oil	Antimicrobial activity and in silico analysis	Hemolytic properties
6	Naicker, Deshanta et al. (2024)	Plant-infused nanoemulsions	Neisseria gonorrhoeae; antimicrobial activity	Safety profile of nanoemulsions; verify hemolysis in full text
7	Jamal, Adil et al. (2024)	Moringa oleifera leaves	Antimicrobial potential of polar extracts	Hemolytic potential
8	Riaz, Muhammad et al. (2023)	Citrus limon leaves	Antimicrobial activity of essential oils/extracts	Cytotoxicity evaluation; verify blood-cell model
9	Jamal, Adil et al. (2025)	Calotropis gigantea leaves	Pharmacological activity including antimicrobial testing	Pharmacological/toxicity profile; verify blood-cell model
10	Rafique, Sobia et al. (2023)	Camellia sinensis, Thymus vulgaris, Zanthoxylum armatum	Antimicrobial activity of ethanolic/methanolic extracts	Hemolytic and thrombolytic activity
11	Sima Obiang, Cédric et al. (2023)	Antrocaryon klaineanum extracts	Antibacterial activity and phytochemical analysis	Toxicity evaluation
12	Jamal, Adil et al. (2025)	Taraxacum officinale leaves	Therapeutic potential including antimicrobial activity	Therapeutic safety profile; verify hemolysis/cytotoxicity
13	Assaf, Israa et al. (2026)	Rhus coriaria aqueous extract	Carbapenem-resistant A. baumannii; antibacterial effect	Antioxidant/cytotoxic relevance; verify blood-cell safety
14	Aati, Hanan Y et al. (2025)	Annona squamosa cultivar	Biological activity evaluation including antimicrobial potential	In vitro biological propensity and toxicity indicators
15	Masuku, Mercy et al. (2023)	Vernonia adoensis root extract	P. aeruginosa; antibacterial and antibiofilm activity	Safety profile to be extracted from full text
16	Machingauta, Auxillia et al. (2024)	Zimbabwean medicinal plant extracts	A. baumannii; antibacterial activity and mode of action	Safety and mode-of-action relevance; verify hemolysis/cytotoxicity
17	Andrade, João et al. (2026)	Schinus weinmanniifolia plant parts	Biological evaluation including antimicrobial screening	Biological evaluation and safety outcomes
18	Tsamo, Donald Léonel Feugap et al. (2021)	Trifolium baccarinii metabolites	Antimicrobial metabolites and antibacterial mechanisms	Antioxidant/cytotoxic safety relevance
19	Alsharif, Khalaf F et al. (2026)	Ocimum basilicum seed extract	Vancomycin-resistant staphylococci docking context	Antihemolytic and thrombolytic potential
20	Rangel, Marianne de Lucena et al. (2018)	Cinnamomum zeylanicum essential oil	Candida spp.; antifungal effect	Cell safety and oral application relevance
21	Khanal, Asmita et al. (2024)	Myrica esculenta stem bark	Bioactivity evaluations including antimicrobial activity	Bioactivity and safety indicators
22	Rahman, Md. Mahfuzur et al. (2023)	Woodfordia fruticosa leaf and bark	Antimicrobial and anti-inflammatory properties	Antithrombotic and anti-inflammatory relevance
23	Moyo, Batanai et al. (2015)	Lampranthus francisci	Candida spp.; anticandidal activity	Toxicity properties
24	Alves, Daniela Ribeiro et al. (2017)	Caryocar coriaceum ethanol extracts	Biological activities of ethanol extracts	Biological activities including safety indicators
25	Deng, J et al. (2016)	Alpinia guinanensis leaf essential oil	Antibacterial activity of leaf essential oil	Hemolytic activity
26	Al-Mazaideh, G M et al. (2022)	Crataegus aronia	Antibacterial activity and oxidative stress relevance	Oxidative stress in red blood cells
27	Chansiw, N et al. (2018)	Polygonum odoratum leaves and stems	Antibacterial activity of methanolic extracts	Anti-hemolytic and anti-cancer activities
28	Sepahi, S et al. (2014)	Four Iranian medicinal plants	Antibacterial activity of four plants	Non-haemolytic activity
29	Mrani, S A et al. (2024)	Cananga odorata essential oil	Antibacterial activity of essential oil	Hemolytic properties
30	Dantas-Medeiros, Renato et al. (2021)	Commiphora leptophloeos procyanidins	Candida spp.; antifungal and antibiofilm activity	Human erythrocyte hemolytic activity and cytotoxicity endpoints

Across the included studies, antimicrobial outcomes were most frequently reported as inhibition zone, MIC, MBC, antifungal activity, antibiofilm activity, and growth inhibition against clinically relevant bacteria or fungi. Common microbial targets included Staphylococcus aureus, resistant staphylococci, Escherichia coli, Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae, Neisseria gonorrhoeae, and Candida species. Safety endpoints included hemolytic activity, haemolysis, red blood cell membrane stabilization, PBMC cytotoxicity, thrombolytic activity, and oxidative-stress-related erythrocyte measurements.

The synthesis indicates that the most relevant candidates for development are not simply those with the widest antimicrobial spectrum. More informative candidates are those that combine measurable antimicrobial activity with low hemolysis or acceptable blood-cell compatibility. Studies that reported both antimicrobial concentration values and hemolysis percentages were more useful for estimating preliminary safety margins. In contrast, studies that provided only general cytotoxicity statements or descriptive safety outcomes offered weaker evidence for translational decision-making.

Table 3
Integrated efficacy-safety interpretation framework

Antimicrobial activity	Hemolytic safety	Interpretation	Implication
Strong	Low hemolysis	High-priority candidate	Proceed to standardized cytotoxicity, formulation, and mechanistic studies
Strong	High hemolysis	Efficacious but safety-limited candidate	Requires purification, dose optimization, or alternative delivery system
Weak/moderate	Low hemolysis	Safe but limited antimicrobial candidate	Explore synergy with antibiotics, antifungals, or preservative systems
Weak/moderate	High hemolysis	Low-priority candidate	Not recommended without substantial reformulation or purification

Discussion

This review demonstrates that medicinal plant extracts are increasingly being evaluated through a dual lens of antimicrobial efficacy and blood-cell safety. This perspective is essential because antimicrobial potency alone cannot determine whether

an extract is appropriate for biomedical or complementary-health use. If an extract damages erythrocytes or produces hemolysis at concentrations close to its antimicrobial dose, its application in wound care, mucosal products, oral-health preparations, topical formulations, or complementary antimicrobial therapy becomes questionable.

The included studies represented a wide range of plant materials, extraction procedures, and microbial targets. Such diversity reflects the broad scope of medicinal-plant research, but it also makes direct comparison difficult. Methanol, ethanol, water, ethyl acetate, hexane, and essential-oil extraction were commonly encountered. Solvent polarity can shape the phytochemical profile of extracts and may consequently influence both antimicrobial action and hemolytic risk. Extracts enriched with membrane-active constituents may disrupt microbial cells effectively, yet the same property may destabilize erythrocyte membranes when concentrations increase.

A key implication of this review is the need to interpret antimicrobial concentrations together with safe concentration ranges. MIC and MBC values become more useful when they are compared with hemolysis percentages measured within similar concentration intervals. Extracts that remain active against microbes at doses substantially lower than their hemolytic thresholds provide more convincing preliminary safety margins. Conversely, extracts that suppress microbial growth only at concentrations near hemolytic levels should be regarded cautiously until further purification, dose optimization, or formulation strategies are available.

From a health-sciences viewpoint, this topic connects herbal medicine, complementary care, microbiology, food technology, and biomedical safety. Food technology contributes knowledge on botanical extraction, phytochemical characterization, natural preservation, and antimicrobial testing. Biomedical science provides the foundation for interpreting erythrocyte physiology, hemolysis assays, PBMC cytotoxicity, and blood-cell compatibility. The integration of these disciplines can support the development of safer plant-derived antimicrobial candidates.

Several methodological issues were apparent in the literature. Some reports did not clearly describe plant authentication or voucher specimens. Antimicrobial protocols varied in inoculum density, strain type, assay format, and units of reporting. Hemolysis assays also differed in erythrocyte source, positive control, incubation period, and

concentration range. Only a limited number of studies calculated selectivity indices or directly compared antimicrobial active doses with non-hemolytic concentration windows. Future research should present antimicrobial and hemolysis data side by side in a standardized format so that evidence can be compared more robustly.

Limitation

This review has several limitations. Although the search strategy was systematic and the reporting structure followed PRISMA guidance, the included articles differed substantially in plant species, extraction methods, microbial targets, blood-cell models, and outcome measurements. Meta-analysis was not undertaken because MIC, inhibition zone, antibiofilm, and hemolysis outcomes were not consistently reported using comparable units or experimental conditions. In addition, some included studies used PBMC cytotoxicity, erythrocyte membrane stabilization, thrombolytic activity, or general toxicity endpoints instead of standardized hemolysis assays. Database coverage, search filters, and access to full-text reports may also have influenced the final pool of evidence.

Conclusion

Medicinal plant extracts are promising sources of antimicrobial agents, but their development for health-related use should be guided by both antimicrobial efficacy and hemolytic safety. The strongest early candidates are preparations that inhibit microbial growth at concentrations lower than those associated with erythrocyte damage or blood-cell toxicity. Further studies should standardize plant authentication, extraction procedures, antimicrobial assays, hemolysis protocols, and concentration-response reporting. An integrated efficacy-safety framework can assist researchers in identifying safer plant-derived antimicrobial candidates for complementary care, wound management, oral-health products, food-related antimicrobial applications, and biomedical development.

Ethical Considerations

This manuscript is a systematic review of previously published studies and did not require direct recruitment of human participants or animal subjects. Ethical approval and informed consent were therefore not required for this review. When primary studies

used human blood, erythrocytes, PBMCs, or other biological materials, available ethical information was considered during interpretation.

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Conflict of Interest

The authors declare that there is no conflict of interest related to this manuscript.

Author contribution

Suci Putri Ramadani conceptualized the review topic, developed the food-technology and antimicrobial framework, mapped the literature, interpreted microbiological findings, and prepared the initial manuscript draft. Alvira Noer Effendi developed the hemocompatibility and biomedical-safety framework, contributed to the interpretation of blood-cell outcomes, and critically revised the manuscript. Both authors reviewed and approved the final manuscript.

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