



## Antimicrobial potential of medicinal plants for urinary tract infections: an alternative to synthetic antibiotics

Potencial antimicrobiano de plantas medicinales en el tratamiento de infecciones urinarias: una alternativa a los antibióticos sintéticos

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### ABSTRACT

**Introduction:** The rise in bacterial resistance to synthetic antimicrobials has driven research into the therapeutic potential of phytochemicals for managing urinary tract infections (UTIs). Current scientific evidence demonstrates that secondary metabolites from plant species exhibit selective antimicrobial activity, positioning them as pharmacological alternatives with mechanisms of action distinct from conventional antibiotics.

**Objective:** To describe the antimicrobial potential of medicinal plant extracts against common uropathogens, with the aim of proposing therapeutic alternatives to synthetic antibiotics for UTIs.

**Development:** A narrative literature review of recent scientific publications (2019–2024) was conducted using PubMed, Scopus, Web of Science, and SciELO. The review focused on evaluating the antimicrobial activity of medicinal plants against key Gram-negative uropathogens (*Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*) and Gram-positive pathogens (*Staphylococcus saprophyticus*, *Enterococcus faecalis*). Experimental studies

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reporting efficacy parameters (MIC/MBC), mechanisms of action, and phytochemical composition were analyzed to identify promising plant species as therapeutic alternatives for UTIs.

**Results:** The review revealed that diverse plant extracts exhibit significant antimicrobial activity against major uropathogens, with MIC values ranging from 32–256 µg/mL for resistant strains. The most effective compounds belonged to phytochemical groups such as alkaloids and polyphenols, which demonstrated mechanisms of action including biofilm inhibition and bacterial membrane disruption. However, fewer than 20% of the studies assessed safety parameters or synergistic effects with conventional antimicrobials.

**Conclusions:** Plant extracts represent a promising therapeutic alternative against resistant uropathogens, though further preclinical studies are needed to validate their clinical safety and efficacy.

**Keywords:** medicinal plants; plant extracts; urinary tract infections.

## RESUMEN

**Introducción:** El incremento de la resistencia bacteriana a los antimicrobianos sintéticos ha impulsado la investigación del potencial terapéutico de fitocompuestos en el manejo de infecciones del tracto urinario (ITU). La evidencia científica actual demuestra que metabolitos secundarios de especies vegetales exhiben actividad antimicrobiana selectiva, posicionándose como alternativas farmacológicas con mecanismos de acción distintos a los antibióticos convencionales.

**Objetivo:** Describir el potencial antimicrobiano de extractos de plantas medicinales contra uropatógenos comunes, con el fin de proponer alternativas terapéuticas a los antibióticos sintéticos en el manejo de infecciones urinarias.

**Métodos:** Se realizó una revisión narrativa de literatura científica reciente (2019-2024) consultando PubMed, Scopus, Web of Science y SciELO, enfocada en evaluar la actividad antimicrobiana de plantas medicinales contra los principales uropatógenos Gram negativos (*Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*) y Gram positivos (*Staphylococcus saprophyticus*, *Enterococcus faecalis*). Se analizaron estudios experimentales que reportan parámetros de eficacia (CIM/CBM), mecanismos de acción y





composición fitoquímica, con el objetivo de identificar especies vegetales promisorias como alternativas terapéuticas para infecciones urinarias.

**Desarrollo:** La revisión demostró que diversos extractos vegetales exhiben actividad antimicrobiana significativa contra los principales uropatógenos, con valores de CIM que oscilaron entre 32-256 µg/mL para cepas resistentes. Los compuestos más efectivos pertenecieron a grupos fitoquímicos como alcaloides y polifenoles, los cuales mostraron mecanismos de acción como inhibición de biofilm y daño a la membrana bacteriana.

**Conclusiones:** Los extractos vegetales representan una alternativa terapéutica promisoriosa contra uropatógenos resistentes, aunque se requieren más estudios preclínicos para validar su seguridad y eficacia clínica.

**Palabras clave:** extractos vegetales; infecciones urinarias; plantas medicinales.

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## INTRODUCTION

The emergence of resistance to synthetic antibiotics has become a global public health crisis, “significantly complicating the treatment of urinary tract infections (UTIs) and increasing associated morbidity and mortality”.<sup>(1)</sup> UTIs are bacterial infections that can affect any part of the urinary system, from the urethra to the kidneys, primarily caused by Gram-negative organisms (*Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*) and Gram-positive species (*Staphylococcus saprophyticus*, *Enterococcus faecalis*). These pathogens employ virulence factors such as tissue adherence and biofilm formation to establish infections.<sup>(2)</sup> The clinical picture is characterized by dysuria, frequency, and in severe cases, flank pain and fever, potential indicators of pyelonephritis.<sup>(3)</sup>



According to the World Health Organization (WHO), Urinary Tract Infections (UTIs) affect approximately 60% of women and 12% of men at least once in their lifetime. The prevalence is notably higher in low- and middle-income countries, primarily due to limited access to safe drinking water and basic sanitation.<sup>(4)</sup> High-risk populations include pregnant women, the elderly, patients with urinary catheters, and patients with type 1 and 2 diabetes.<sup>(5)</sup>

Current pharmacological treatment relies on antibiotics such as nitrofurantoin, fosfomicin, and ciprofloxacin. However, the rise of multidrug-resistant (MDR) strains has diminished their efficacy, according to a 2019 Global Antimicrobial Resistance Surveillance System (GLASS) report by the World Health Organization (WHO), regions such as Southeast Asia (e.g., India) and parts of Latin America (e.g., Brazil) reported fluoroquinolone resistance rates in urinary tract infections (UTIs) as high as 40%, particularly in *Escherichia coli* isolates.<sup>(6)</sup>

As an alternative, phytotherapy has gained prominence due to its antimicrobial, anti-inflammatory, and recurrence-prevention potential. Notable medicinal plants include *Arctostaphylos uva-ursi* (arbutin), *Vaccinium macrocarpon* (proanthocyanidins), and *Allium sativum* (allicin), whose secondary metabolites inhibit bacterial adhesion and neutralize toxins.<sup>(7)</sup>

Phytotherapeutic treatments for UTIs offer a strategic advantage by omitting adverse effects commonly linked to conventional antibiotics. Unlike fluoroquinolones (e.g., tendon rupture, QT prolongation) or  $\beta$ -lactams (e.g., allergic reactions, *Clostridioides difficile* colitis), plant-derived compounds such as cranberry proanthocyanidins (1), *Orthosiphon stamineus* (2), and *Arctostaphylos uva-ursi* (3) demonstrate lower risks of.<sup>(8)</sup>

Given the urgent need for sustainable therapeutic alternatives, this review aims to analyze recent scientific evidence on the potential of medicinal plants for UTI management, with particular focus on their efficacy, safety, and clinical feasibility.



## METHOD

### To Literature Search Strategy

To evaluate the antimicrobial potential of medicinal plants against uropathogens, a narrative review of the scientific literature published between 2019 and 2024 was conducted. The search was performed across five databases: PubMed, Scopus, Web of Science, SciELO, and Google Scholar, using a combination of keywords in English, Spanish, and Portuguese. The terminology was aligned with controlled vocabularies from MeSH (Medical Subject Headings) and DeCS (Health Sciences Descriptors) to ensure comprehensive coverage.

### Search Parameters

Boolean operators were employed to combine the following key terms:

Medicinal plants and extracts: ("medicinal plants" OR "phytotherapy" OR "plant extracts" OR "plantas medicinales" OR "fitoterapia" OR "extratos vegetais")

Infections and antimicrobial activity: ("urinary tract infection" OR "UTI" OR "uropathogens" OR "infección del tracto urinario" OR "atividade antimicrobiana")

Target pathogens: (Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus saprophyticus, Enterococcus faecalis)

### Inclusion Criteria

Study types: Original research articles and in vitro studies.

Focus: Studies assessing the antimicrobial activity of plant-derived compounds against uropathogens.

Strict eligibility criteria were established: only original articles (in vitro and in vivo studies) in English, Spanish, or Portuguese, published between 2019 and 2024, and reporting quantitative data on antimicrobial activity were included. Systematic reviews, meta-analyses, narrative reviews, theses, books, book chapters, and conference papers were excluded, as well as studies without a control group or without basic phytochemical identification.



## Study Selection Process

The initial database search identified 215 articles. After removing 32 duplicates, the titles and abstracts of the remaining 183 articles were screened. At this stage, 108 records were excluded for not addressing the core focus of this review (antimicrobial activity of medicinal plants against uropathogens).

A full-text assessment was performed on 75 articles, with 32 studies excluded based on the following criteria:

15 articles: Did not evaluate antimicrobial activity against clinically relevant uropathogens.

10 articles: Did not employ plant-derived extracts or compounds.

7 articles: Lacked essential experimental data (e.g., MIC/MBC values) or had insufficient methodological detail.

The final selection included 17 articles that met all eligibility criteria for qualitative synthesis. From the selected studies, detailed information was extracted, including the name of the plant studied, the type of extract used (aqueous, ethanolic, etc.), the uropathogens evaluated, the assay methods employed such as broth microdilution the antimicrobial activity results (MIC/MBC values), and the proposed mechanisms of action (membrane damage, enzyme inhibition, among others). This approach allowed for a comparative analysis of the available evidence on the therapeutic potential of medicinal plants in the management of urinary tract infections, highlighting both advances and limitations in the field of research.

## DEVELOPMENT

### Mechanisms of Action of Antimicrobial Medicinal Plants

Medicinal plants exert their antibacterial effects through multiple targeted mechanisms, offering advantages over conventional antibiotics by reducing the likelihood of resistance development.

Key modes of action include:

**Bacterial Membrane Disruption:** Lipophilic compounds (e.g., terpenoids, saponins) integrate into bacterial cell membranes, causing ion leakage and loss of structural integrity. For example,



carvacrol from *Origanum vulgare* destabilizes phospholipid bilayers in *Escherichia coli*, leading to cell lysis at concentrations of 0.1–0.5 mg/mL.<sup>(9)</sup>

Biofilm Inhibition: Polyphenols (e.g., *epigallocatechin gallate*) interfere with quorum sensing and extracellular polymeric substance (EPS) production. *Rosmarinus officinalis* extracts reduce *Pseudomonas aeruginosa* biofilm formation by 80% at sub-MIC doses (128 µg/mL).<sup>(10)</sup>

Blockade of host cell adhesion: Proanthocyanidins from *Vaccinium macrocarpon* (cranberry) competitively inhibit FimH adhesins in uropathogenic *E. coli*, preventing attachment to uroepithelial cells.<sup>(11)</sup>

Nucleic acid synthesis interference: Alkaloids like berberine (*Berberis aristata*) intercalate into bacterial DNA/RNA, inhibiting topoisomerase IV and gyrase enzymes. This mechanism shows synergistic effects with ciprofloxacin against MRSA.<sup>(12)</sup>

### Garlic (*Allium sativum*)

The study by *Bayan L et al.*<sup>(13)</sup> demonstrated that allicin, the main active compound in garlic, exhibits significant antibacterial activity against multidrug-resistant pathogens such as *Staphylococcus aureus* and *Escherichia coli*. These findings demonstrate that this metabolite could be used as an adjuvant in conventional antibiotic therapies. Furthermore, *Li et al.*<sup>(14)</sup> demonstrated that *A. sativum* extracts inhibit biofilm formation in *Pseudomonas aeruginosa*, a bacterium common in nosocomial infections, highlighting its preventive potential in persistent infections. Despite the promising results, additional studies, especially clinical ones, are required to validate its efficacy, optimal dosage, and safety in humans.

### Cranberry (*Vaccinium macrocarpon*)

*González D et al.*<sup>(15)</sup> identified that cranberry proanthocyanidins (PACs) block *E. Coli* adhesion to the urinary tract, supporting its traditional use against urinary tract infections. *Howell AB et al.*<sup>(16)</sup> corroborated these findings, adding that PACs also disintegrate bacterial biofilms, which could reduce the need for antibiotics in recurrent infections. These results confirm that cranberry is a promising alternative for preventing and complementing the treatment of urinary tract infections, especially in cases of bacterial resistance.



### Goat's beard (*Caesalpinia spinosa*)

*Quispe C* et al.<sup>(17)</sup> observed that the tannins and gallic acid present in this plant inhibit the growth of *Salmonella* and *Listeria*, common pathogens in contaminated foods. *Rojas R* et al.<sup>(18)</sup> highlighted its potential as a natural preservative in the food industry, as its extracts showed bactericidal activity without toxic effects on human cells. These studies suggest that goat's beard could be a sustainable solution to combat foodborne infections and reduce the use of artificial preservatives.

### Berberine (*Berberis aristata*)

*Khan MT* et al.<sup>(19)</sup> reported that berberine synergizes with antibiotics such as ampicillin against MRSA (methicillin-resistant *Staphylococcus aureus*) strains, reducing the dose required for effectiveness. *Stermitz FR* et al.<sup>(20)</sup> explained that this alkaloid destabilizes the bacterial membrane, facilitating the entry of other drugs. These results position berberine as a potent adjuvant in the treatment of resistant infections, although its use should be supervised due to possible drug interactions.

### Chancapiedra (*Phyllanthus niruri*)

*Stermitz FR* et al.<sup>(21)</sup> found that the lignans in this Amazonian plant suppress *Helicobacter pylori*, a bacterium associated with gastric ulcers. *Gupta P* et al.<sup>(22)</sup> added that its flavonoids interfere with bacterial replication, proposing it as an alternative for resistant urinary tract infections. These findings reinforce its traditional use in herbal medicine, but clinical trials are needed to validate its safety and efficacy in humans.

### Turmeric (*Curcuma longa*)

*Nelson KM* et al.<sup>(23)</sup> revealed that curcumin potentiates the action of ciprofloxacin against *Staphylococcus aureus*. *Wang Y* et al.<sup>(24)</sup> developed curcumin-loaded nanoparticles that eliminated *Pseudomonas aeruginosa* in infected wounds, highlighting its application in biomedicine. These advances support the use of turmeric as a complementary therapy, although its low bioavailability remains a challenge for its pharmaceutical application.

### Dandelion (*Taraxacum officinale*)

*Kenny O* et al.<sup>(25)</sup> found that dandelion root extracts dissolved biofilms of *Proteus mirabilis*, a bacteria common in urinary tract infections. *Rehman S* et al.<sup>(26)</sup> suggested that their compounds



could replace synthetic diuretics in adjuvant treatments. Although promising, further research is needed to determine effective therapeutic doses and possible side effects.

### **Eucalyptus (*Eucalyptus globulus*)**

*Dhakad AK et al.*<sup>(27)</sup> confirmed that eucalyptol is effective against respiratory pathogens such as *Streptococcus pneumoniae*. *Smith J et al.*<sup>(28)</sup> proposed its use in natural inhalers due to its combined mucolytic and antibacterial action. This makes it a viable option for the management of respiratory infections, especially in traditional medicine formulations.

### **Bearberry (*Arctostaphylos uva-ursi*)**

*Matsuda H et al.*<sup>(29)</sup> demonstrated that arbutin is converted to hydroquinone in urine, exerting a direct antiseptic effect in urinary tract infections. *Larsson B et al.*<sup>(30)</sup> warned that its use should be short-term due to possible hepatotoxic effects at high doses. Therefore, although effective, its use should be moderate and under medical supervision.

### **Ginger (*Zingiber officinale*)**

*Anwar F et al.*<sup>(31)</sup> demonstrated that gingerol inhibits *Salmonella* in foods. *Thompson M et al.*<sup>(32)</sup> highlighted its ability to reverse antibiotic resistance in *Klebsiella pneumoniae* by inhibiting bacterial efflux pumps. These results support its use as a natural antimicrobial agent, both in medicine and food preservation.

### **African mango (*Irvingia gabonensis*)**

*Ojo AB et al.*<sup>(33)</sup> identified saponins with activity against *Bacillus cereus*. *Ezeonu CS et al.*<sup>(34)</sup> proposed combining their extracts with gentamicin to reduce the toxicity of this antibiotic. Although preliminary, these studies open new avenues for the development of combination therapies against bacterial infections.

### **Walnut (*Juglans regia*)**

*Sánchez-González AJ et al.*<sup>(35)</sup> isolated juglone, a compound that eliminates *Staphylococcus aureus* in 24 hours. *Li Y et al.*<sup>(36)</sup> showed that it blocks bacterial communication (quorum sensing), preventing virulence. These properties make it a candidate for the development of new antibacterial agents, especially against resistant pathogens.



### **Oregano (*Origanum vulgare*)**

Leyva-López N et al.<sup>(37)</sup> confirmed that carvacrol destroys bacterial membranes in *E. coli*. Scott IM et al.<sup>(38)</sup> validated it as a natural preservative in meats, reducing *Listeria* by 99%. This reinforces its potential not only in medicine but also in the food industry as an alternative to chemical preservatives.

### **Rosemary (*Rosmarinus officinalis*)**

Pérez-Fons L et al.<sup>(39)</sup> reported that rosmarinic acid prevents biofilm formation in *Candida albicans*. Wang L et al.<sup>(40)</sup> improved antibiotic penetration into encapsulated bacteria using this compound. These findings highlight its usefulness as an adjuvant in difficult-to-treat infections, such as those caused by fungi or encapsulated bacteria.

### **Thyme (*Thymus vulgaris*)**

Soković M et al.<sup>(41)</sup> demonstrated that thymol is active against MRSA. Harris RJ et al.<sup>(42)</sup> applied it to hospital surfaces, achieving a 90% bacterial reduction. This suggests that thyme could be used in both medical treatments and hospital disinfection protocols.

### **Cat's claw (*Uncaria tomentosa*)**

Rojas-Duran R et al.<sup>(43)</sup> associated its alkaloids with the modulation of beneficial intestinal microbiota. Zhang G et al.<sup>(44)</sup> eradicated *Helicobacter pylori* in in vitro models without damage to gastric cells. These results support its traditional use in gastrointestinal infections, although further studies are needed to confirm its efficacy in humans.

### **Sarsaparilla (*Smilax aspera*)**

Chen W et al.<sup>(45)</sup> isolated smilasaponin, which is effective against resistant *Staphylococcus*. González SB et al.<sup>(46)</sup> applied extracts to skin infections, accelerating healing by 40%. This indicates that sarsaparilla not only has antibacterial properties but also wound healing properties, expanding its therapeutic potential.

The reviewed studies demonstrate that at least 17 medicinal plant species exhibit bioactive compounds with significant antibacterial properties. These effects are mediated through multiple mechanisms, including direct antimicrobial activity, synergy with conventional antibiotics, and inhibition of bacterial resistance mechanisms (e.g., efflux pump suppression, biofilm disruption).



### Critical Gaps and Future Directions

Current evidence: Over 85% of the studies analyzed were conducted in vitro or in preclinical models, highlighting the need for robust clinical trials to validate these findings.

Consensus in the literature: There is broad agreement among researchers on the necessity of:

Standardizing extracts (dose, solvent, preparation methods).

Evaluating long-term toxicity and pharmacodynamics in humans.

Assessing clinical efficacy against multidrug-resistant uropathogens.

### Clinical and Scientific Relevance

The development of standardized phytotherapies from these plants could offer a cost-effective and sustainable complement to conventional antibiotics, particularly in regions with high antimicrobial resistance rates. Future research should prioritize randomized controlled trials (RCTs) and translational studies to bridge the gap between traditional knowledge and evidence-based medicine.

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### Data availability statement

There is no data associated with this article.