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Traditional Siddha Medicine and Emerging Microbial Infections A Review

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Abstract:

Background:
Urinary tract infections (UTIs) and infection-induced renal stone disease represent a significant clinical burden worldwide, particularly due to rising antimicrobial resistance (AMR). *Proteus mirabilis* is a key uropathogen implicated in struvite stone formation through urease-mediated urinary alkalinization and biofilm development, leading to recurrent infection and obstructive uropathy.

Objective:
This review aims to evaluate the role of traditional Siddha medicine in the management of *Proteus*-associated urinary tract infections and renal stone disease, with special emphasis on single herbal drugs, polyherbal formulations, and the herbo-mineral preparation Nandukkal Paspam, and to assess their antimicrobial and anti-lithogenic potential based on available scientific evidence.

Methods:
A comprehensive literature review was conducted using databases including PubMed, Scopus, Web of Science, ScienceDirect, SpringerLink, Google Scholar, and AYUSH Research Portal for studies published between 2000 and 2025. Relevant classical Siddha texts, experimental studies, in vitro and in vivo research, phytochemical analyses, and molecular docking studies were included. Data were extracted and analyzed focusing on antimicrobial activity, anti-urease effects, anti-biofilm activity, and anti-urolithiatic potential.

Results:
Evidence indicates that Siddha single herbal drugs such as *Phyllanthus emblica*, *Tribulus terrestris*, and *Aerva lanata* exhibit antimicrobial, diuretic, and anti-urolithiatic properties. Polyherbal formulations including Kabasura Kudineer and Nilavembu Kudineer demonstrate broad-spectrum antimicrobial and immunomodulatory effects. The herbo-mineral formulation Nandukkal Paspam shows potential litholytic and antimicrobial activity, particularly against urease-producing organisms such as *Proteus spp.*, with possible inhibition of biofilm formation and crystal aggregation.

Conclusion:
Siddha medicinal interventions, particularly Nandukkal Paspam along with selected herbal and polyherbal formulations, may offer promising complementary strategies for managing *Proteus*-associated renal stone disease and UTIs. However, further pharmacological validation, toxicity assessment, and well-designed clinical trials are required to establish their safety, efficacy, and translational potential in modern healthcare.

Keywords: Siddha medicine; Proteus mirabilis; renal stones; urinary tract infection; Nandukkal Paspam; anti-urolithiatic; antimicrobial resistance; biofilm inhibition.

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Introduction:

Emerging microbial infections and antimicrobial resistance (AMR) have become major global health challenges, significantly increasing morbidity, mortality, and healthcare burden worldwide (1,2). Among uropathogens, *Proteus mirabilis* is particularly important due to its strong urease activity, which leads to urinary alkalinization and the formation of infection-induced renal calculi (struvite stones), often associated with recurrent urinary tract infections, biofilm formation, and obstructive uropathy (3,4). Conventional antimicrobial therapy alone is frequently insufficient to prevent recurrence because of persistent bacterial colonization and crystal–biofilm interactions within the urinary tract (5). This has created an urgent need to explore complementary therapeutic approaches, including traditional medical systems.

Siddha medicine, one of the oldest traditional medical systems practiced in South India, provides a wide range of therapeutic interventions, including single-herbal drugs, polyherbal formulations, and herbo-mineral preparations for the management of infectious and urological disorders (6,7). Single herbal drugs such as *Phyllanthus emblica* (Nellikai), *Tribulus terrestris* (Nerunjil), and *Aerva lanata* (Sirupilai) are traditionally used in urinary tract disorders due to their diuretic, antimicrobial, and anti-urolithiatic properties, which may help in flushing urinary pathogens and reducing stone formation risk (8,9). Polyherbal Siddha formulations such as Kabasura Kudineer and Nilavembu Kudineer are widely recognized for their broad-spectrum antimicrobial, antiviral, and immunomodulatory activities, making them useful supportive therapies in infectious disease conditions (10,11).

In the context of *Proteus*-associated urinary tract infection and renal stone disease, Siddha literature highlights the use of **Nandukkal Paspam**, a classical herbo-mineral formulation traditionally indicated for urinary calculi and obstructive uropathies. It is believed to exert litholytic, antimicrobial, and urinary system–cleansing effects, thereby targeting both infection and stone formation processes associated with *Proteus mirabilis* (12,13). Experimental observations suggest that such formulations may inhibit bacterial growth, reduce biofilm formation, and interfere with crystal aggregation and nucleation, although systematic clinical validation is still limited (14).

Recent advances in pharmacological screening, phytochemical analysis, and molecular docking studies have provided scientific support for several Siddha formulations by identifying bioactive compounds with antimicrobial and anti-urolithiatic potential (15,16). These studies suggest possible mechanisms including disruption of bacterial cell membranes, inhibition of urease activity, suppression of biofilm formation, antioxidant effects, and modulation of urinary biochemical parameters (17). However, most evidence remains preclinical, and well-designed clinical trials are required to establish safety, efficacy, and standardized dosing regimens (18).

Integration of Siddha medical knowledge with modern biomedical research may offer a promising strategy for addressing infection-induced renal stone disease and emerging microbial infections, particularly in the context of rising antimicrobial resistance and limited therapeutic options (19,20).

Therefore, this review aims to evaluate the role of Siddha medicine, including single herbal drugs, polyherbal formulations, and particularly Nandukkal Paspam, in the management of *Proteus*-associated renal stone disease and emerging microbial infections, and to critically assess the available scientific evidence supporting their antimicrobial and anti-lithogenic potential for future therapeutic applications.

Materials and Methods:

This review was conducted to systematically analyze and summarize the available scientific and traditional evidence on Siddha medicinal approaches used in the management of *Proteus*-associated urinary tract infections and infection-induced renal stone disease, with special emphasis on Nandukkal Paspam along with selected single-herbal and polyherbal Siddha formulations.

A comprehensive literature search was performed using multiple electronic databases including PubMed, Scopus, Web of Science, ScienceDirect, SpringerLink, Google Scholar, and the AYUSH Research Portal for studies published between 2000 and 2025 (21,22). Classical Siddha literature, pharmacopoeias, monographs, and reports from recognized institutions were also reviewed to collect traditional knowledge regarding urinary disorders and litholytic formulations (23).

The search strategy included combinations of keywords such as “Siddha medicine,” “Nandukkal Paspam,” “Proteus mirabilis,” “renal stone,” “struvite stone,” “infection-induced calculi,” “urease activity,” “urinary tract infection,” “anti-urolithiatic,” “biofilm inhibition,” “single herbal Siddha drugs,” and “polyherbal Siddha formulations” using Boolean operators (AND, OR) to ensure comprehensive retrieval of relevant literature (24).

Studies were included if they reported antimicrobial activity, anti-urolithiatic effects, anti-biofilm activity, urease inhibition, phytochemical analysis, pharmacological evaluation, molecular docking studies, in vivo or in vitro experiments, or clinical relevance related to Siddha formulations used in urinary tract disorders. Both experimental and review articles published in English were considered eligible (25). Studies lacking methodological clarity, duplicate reports, and articles not relevant to urinary

infections or renal stone pathology were excluded from analysis (26).

Data extraction was performed systematically, focusing on the composition of Siddha formulations, traditional indications, phytochemical constituents, antimicrobial spectrum, anti-lithogenic mechanisms, and reported effects against *Proteus mirabilis* and other uropathogens. Special attention was given to mechanisms related to urease inhibition, crystal aggregation prevention, and biofilm disruption (27).

The collected data were analyzed qualitatively and synthesized narratively to present an integrated overview of the role of Siddha medicine in infection-related renal stone disease. The findings were organized to highlight single-herbal drugs, polyherbal formulations, and herbo-mineral preparations such as Nandukkal Paspam for their potential therapeutic relevance in modern biomedical contexts (28).

Results:

The literature review revealed a growing body of evidence supporting the role of Siddha medicine in the management of urinary tract infections (UTIs) and infection-induced renal stone disease, particularly those associated with *Proteus mirabilis*. The findings highlight that Siddha interventions, including single herbal drugs, polyherbal formulations, and herbo-mineral preparations such as Nandukkal Paspam, may exert antimicrobial, anti-biofilm, anti-urease, and anti-lithogenic effects (29,30).

Single herbal drugs traditionally used in Siddha medicine demonstrated significant relevance in urinary disorders due to their diuretic, antimicrobial, and anti-calculi properties. These herbs are commonly used to support urinary flow, reduce bacterial load, and prevent crystal aggregation in the urinary tract (31,32).

Polyherbal Siddha formulations showed broader pharmacological effects, particularly in reducing infection severity and enhancing host immunity. These formulations are widely used in respiratory and systemic infections and are increasingly being explored for their secondary benefits in urinary tract infections (33,34).

Herbo-mineral formulations, especially Nandukkal Paspam, were identified as key interventions in Siddha literature for the management of renal calculi associated with infection. Reported evidence suggests potential litholytic activity along with antimicrobial effects against urease-producing organisms such as *Proteus spp.*, which play a major role in struvite stone formation (35,36).

Table 1. Single Herbal Siddha Drugs Used in Urinary Tract Infections and Renal Stones

Herb (Siddha Name)	**Botanical Name**	**Traditional Use**	**Reported Activities**	**References**
Nellikai	*Phyllanthus emblica*	Urinary infections, general detoxification	Antioxidant, antimicrobial, anti-inflammatory, mild diuretic	(31)
Nerunjil	*Tribulus terrestris*	Renal stones, urinary obstruction	Anti-urolithiatic, diuretic, anti-crystallization	(32)
Sirupilai	*Aerva lanata*	Kidney stones, urinary infections	Litholytic, diuretic, anti-inflammatory	(32)

Table 2. Polyherbal Siddha Formulations in Infections and Urological Disorders

Formulation	**Indications**	**Pharmacological Actions**	**Potential Relevance in UTI/Stone Disease**	**References**
Kabasura Kudineer	Febrile illnesses, infections	Antiviral, antibacterial, immunomodulatory	Supports infection control and immune response	(33)
Nilavembu Kudineer	Viral fevers, systemic infections	Antipyretic, antimicrobial	Reduces systemic infection burden	(34)

Table 3. Herbo-Mineral Siddha Formulations for Infection-Induced Renal Stones

Formulation	**Traditional Indication**	**Proposed Mechanism**	**Activity Against *Proteus*-Related Stone Formation**	**References**
Nandukkal Paspam	Renal stones, urinary obstruction	Litholytic, antimicrobial, anti-inflammatory	Inhibits urease activity, reduces crystal aggregation, anti-biofilm potential	(35,36)

Table 4. Mechanisms of Siddha Medicines in Proteus-Associated Renal Stone Disease

Mechanism	Description	Therapeutic Effect	References
Urease inhibition	Reduces ammonia production by *Proteus mirabilis*	Prevents urine alkalization and struvite stone formation	(35)
Anti-biofilm activity	Disrupts bacterial biofilm on urinary epithelium	Reduces recurrent infection	(36)
Anti-crystallization	Inhibits crystal nucleation and aggregation	Prevents stone growth	(36)
Diuretic action	Increases urine flow	Promotes microbial and crystal clearance	(31,32)

Discussion

The present review highlights the growing relevance of Siddha medicine in the management of urinary tract infections (UTIs) and infection-induced renal stone disease, particularly those associated with *Proteus mirabilis*. The increasing prevalence of antimicrobial resistance (AMR) and recurrent urolithiasis has created a therapeutic gap that conventional antibiotics alone are often unable to address effectively (37,38). In this context, Siddha formulations such as single herbal drugs, polyherbal preparations, and herbo-mineral medicines like Nandukkal Paspam may provide complementary therapeutic benefits through multi-target pharmacological actions.

Single herbal Siddha drugs such as *Phyllanthus emblica*, *Tribulus terrestris*, and *Aerva lanata* demonstrate diuretic, antimicrobial, antioxidant, and anti-urolithiatic properties, which are relevant in both infection control and prevention of stone formation (31,32). These actions may help reduce bacterial colonization in the urinary tract, enhance urine flow, and inhibit crystal nucleation, thereby interrupting the pathological cycle of infection and calculi formation (39,40). Such multi-mechanistic activity is particularly important in *Proteus*-associated stones, where urease-mediated alkalinization plays a central role in struvite crystallization (41).

Polyherbal formulations like Kabasura Kudineer and Nilavembu Kudineer are widely recognized for their broad-spectrum antimicrobial and immunomodulatory effects (33,34). Although primarily used for respiratory and systemic infections, their potential secondary benefits in urinary infections may be attributed to systemic immune enhancement and reduction of microbial load (42). The synergistic interaction of multiple phytoconstituents in these formulations may also contribute to biofilm inhibition and suppression of microbial virulence factors, which are critical in chronic and recurrent UTIs (43).

Nandukkal Paspam, a classical Siddha herbo-mineral formulation, occupies a central role in the management of renal calculi associated with infection. Traditional Siddha texts describe its use in urinary obstruction and stone dissolution, which aligns with its proposed litholytic and antimicrobial properties (35,36). Experimental evidence suggests that such formulations may inhibit urease activity of *Proteus mirabilis*, thereby reducing ammonia production and preventing urine alkalinization, a key step in struvite stone formation (44). Additionally, its potential anti-biofilm activity may disrupt bacterial persistence on the urinary epithelium and stone surfaces, reducing recurrence rates (45).

Recent pharmacological and phytochemical studies further support the role of Siddha medicines in modulating multiple biological pathways involved in infection-induced nephrolithiasis (46). Bioactive compounds present in these formulations may exert antioxidant effects, reduce oxidative stress in renal tissues, and interfere with calcium oxalate and struvite crystal aggregation processes (47). Molecular docking and in silico studies have also identified potential interactions between phytoconstituents and microbial enzymes, including urease and quorum sensing regulators, supporting their mechanistic plausibility (48).

Despite these promising findings, most evidence remains preclinical, with limited clinical validation available. Standardization of formulations, quality control of herbo-mineral preparations, and comprehensive toxicological assessments are essential before wider clinical application (49). Furthermore, variability in preparation methods and lack of dose standardization pose challenges for reproducibility and translational research (50).

Future research should focus on controlled clinical trials, mechanistic studies, and advanced molecular investigations to validate the safety and efficacy of Siddha formulations in *Proteus*-associated renal stone disease and recurrent UTIs. Integrating traditional Siddha knowledge with modern biomedical approaches may offer a promising strategy for addressing infection-related urolithiasis and the broader challenge of antimicrobial resistance (51,52).

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