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Evidence-Based Siddha Antimicrobial Research (Kunmakudori Mezhugu) for Translational Medicine

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Abstract:

Background: *Helicobacter pylori* infection is one of the most common chronic bacterial infections worldwide and is strongly associated with chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric cancer. The increasing prevalence of antibiotic-resistant *H. pylori* strains has reduced the effectiveness of conventional eradication therapies, necessitating the exploration of alternative and complementary antimicrobial strategies. Siddha medicine, a traditional medical system practiced in South India, offers a rich repository of herbal and herbo-mineral formulations for the management of gastrointestinal disorders. Among these, **Kunmakudori Mezhugu** has traditionally been used for conditions resembling chronic gastritis, gastric ulceration, and digestive disturbances, making it a potential candidate for antimicrobial drug research and translational medicine applications.

Objective: To review the available evidence regarding the antimicrobial potential of Kunmakudori Mezhugu and its constituent ingredients against *Helicobacter pylori*, and to evaluate its relevance in translational medicine and antimicrobial drug development.

Materials and Methods: A comprehensive literature review was conducted using electronic databases including PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, SpringerLink, MEDLINE, and the AYUSH Research Portal. Classical Siddha texts, pharmacological studies, microbiological investigations, phytochemical analyses, molecular docking studies, and translational medicine reports published between 2000 and 2025 were systematically reviewed. Information related to phytochemical composition, antimicrobial activity, anti-*H. pylori* effects, urease inhibition, anti-biofilm properties, antioxidant activity, anti-inflammatory effects, and gastroprotective mechanisms was extracted and synthesized.

Results: The reviewed evidence demonstrated that the medicinal ingredients associated with Kunmakudori Mezhugu contain diverse bioactive compounds including flavonoids, tannins, alkaloids, terpenoids, phenolic compounds, glycosides, and saponins. These phytochemicals exhibited antimicrobial activity through multiple mechanisms, including inhibition of bacterial growth, suppression of urease activity, disruption of biofilm formation, interference with bacterial adhesion, and modulation of virulence factors. In addition to direct antimicrobial effects, the formulation's constituent ingredients demonstrated significant antioxidant, anti-inflammatory, immunomodulatory, and gastroprotective properties that may contribute to the management of *H. pylori*-associated gastric disorders. Molecular docking studies further supported the interaction of plant-derived compounds with key *H. pylori* targets such as urease, DNA gyrase, and adhesins, highlighting their potential as lead molecules for antimicrobial drug development.

Keywords: Siddha medicine; Kunmakudori Mezhugu; *Helicobacter pylori*; Antimicrobial activity; Translational medicine; Gastroprotection; Urease inhibition; Phytochemicals; Drug discovery; Peptic ulcer disease.

Introduction:

Helicobacter pylori infection remains one of the most prevalent chronic bacterial infections worldwide, affecting nearly half of the global population and serving as a major etiological factor for chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric carcinoma (1,2). Despite the widespread use of standard eradication regimens consisting of proton pump inhibitors and multiple antibiotics, treatment success rates have declined substantially due to increasing antimicrobial resistance, poor patient compliance, adverse drug reactions, and recurrence of infection (3,4). The emergence of clarithromycin-resistant, metronidazole-resistant, and levofloxacin-resistant *H. pylori* strains has become a significant challenge, emphasizing the urgent need for novel antimicrobial agents and alternative therapeutic strategies (5).

Translational medicine seeks to bridge the gap between traditional knowledge, laboratory research, and clinical practice by transforming promising therapeutic discoveries into evidence-based healthcare interventions (6). Natural

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products and traditional medical systems have historically contributed significantly to antimicrobial drug discovery, with many modern pharmaceuticals originating from plant-derived compounds and indigenous medical knowledge (7). Consequently, there is growing interest in exploring traditional Siddha formulations as potential sources of novel antimicrobial agents capable of addressing the limitations of current therapies.

The Siddha system of medicine, one of the oldest traditional medical systems practiced in South India, contains extensive descriptions of gastrointestinal disorders and their management through herbal, mineral, and herbo-mineral formulations (8). In Siddha literature, conditions resembling chronic gastritis, peptic ulceration, indigestion, abdominal pain, and gastric disturbances are described under various disease categories, including *Kunmam*. Siddha physicians have traditionally employed several formulations to restore digestive health, alleviate gastric symptoms, and improve gastrointestinal function (9).

Among these formulations, **Kunmakudori Mezhugu** is a classical Siddha preparation widely used in the management of gastric and duodenal disorders associated with *Kunmam*. The formulation contains multiple medicinal ingredients possessing antimicrobial, anti-inflammatory, antioxidant, gastroprotective, and digestive properties. Traditional Siddha practitioners have long prescribed Kunmakudori Mezhugu for chronic gastric complaints characterized by abdominal discomfort, indigestion, bloating, hyperacidity, and ulcerative conditions (10). Recent scientific interest has focused on investigating whether the therapeutic benefits of this formulation may be related to activity against *H. pylori*, the primary microbial pathogen implicated in many chronic gastric diseases.

Several medicinal ingredients present in Siddha formulations have demonstrated antimicrobial activity against gastrointestinal pathogens. Phytochemicals such as alkaloids, flavonoids, phenolic compounds, tannins, terpenoids, and essential oils have been reported to inhibit bacterial adhesion, disrupt microbial cell membranes, suppress urease activity, reduce biofilm formation, and modulate inflammatory responses associated with *H. pylori* infection (11,12). These mechanisms are particularly relevant because *H. pylori* persistence within the gastric mucosa depends upon urease production, biofilm formation, immune evasion, and chronic inflammation.

Advances in microbiology, pharmacology, phytochemistry, molecular docking, metabolomics, and translational medicine have enabled systematic evaluation of traditional Siddha formulations and their bioactive constituents (13). Such interdisciplinary approaches provide opportunities to scientifically validate traditional therapeutic claims, identify novel antimicrobial compounds, and develop evidence-based interventions for infectious diseases. The investigation of Kunmakudori Mezhugu within a translational medicine framework may contribute to the development of alternative or adjunctive therapies for *H. pylori* infection, particularly in regions where antimicrobial resistance continues to compromise conventional treatment outcomes (14).

Given the increasing prevalence of antibiotic-resistant *H. pylori* strains and the growing demand for evidence-based traditional therapeutics, systematic scientific evaluation of Siddha formulations is essential. Therefore, the aim of this review is to critically examine the available evidence regarding the antimicrobial potential of Kunmakudori Mezhugu against *Helicobacter pylori*, explore its phytochemical and pharmacological basis, and evaluate its translational relevance as a Siddha antimicrobial drug candidate for future clinical applications.

Materials and Methods:

This review was undertaken to critically evaluate the evidence supporting the antimicrobial potential of **Kunmakudori Mezhugu**, a classical Siddha formulation, against *Helicobacter pylori* infection and to examine its translational relevance in antimicrobial drug development. An evidence-based literature review methodology was adopted by integrating information from classical Siddha texts, microbiological investigations, phytochemical studies, pharmacological research, molecular docking analyses, and translational medicine literature. A comprehensive search of electronic databases, including PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, SpringerLink, MEDLINE, and the AYUSH Research Portal, was conducted to identify relevant publications published between January 2000 and June 2025. Additional information was obtained from authoritative Siddha sources such as the *Siddha Formulary of India*, *Siddha Materia Medica*, publications of the Ministry of AYUSH, and the National Institute of Siddha (15–20).

The literature search was performed using combinations of keywords and Medical Subject Headings (MeSH) terms including “Kunmakudori Mezhugu,” “Siddha medicine,” “Helicobacter pylori,” “gastritis,” “peptic ulcer disease,” “antimicrobial activity,” “anti-H. pylori activity,” “phytochemicals,” “translational medicine,” “natural products,” “drug discovery,” “molecular docking,” “gastric pathogens,” “biofilm inhibition,” “urease inhibition,” and “traditional medicine.” Boolean operators such as AND and OR were applied to refine and optimize the search process. Studies were included if they investigated Kunmakudori Mezhugu or its constituent ingredients, evaluated antimicrobial activity against *H. pylori* or related gastrointestinal pathogens, reported phytochemical, pharmacological, microbiological, molecular, or clinical findings relevant to gastric infections, and were available as full-text articles in English. Eligible study designs included in vitro investigations, animal experiments, clinical studies, molecular docking analyses, systematic reviews, and narrative review articles. Conference abstracts lacking full-

text availability, duplicate publications, studies unrelated to antimicrobial activity, and articles with insufficient methodological information were excluded from the review (15–17).

Data extraction was performed systematically using a standardized approach. Information regarding study design, formulation composition, phytochemical constituents, antimicrobial targets, anti-*H. pylori* activity, urease inhibitory effects, anti-biofilm activity, antioxidant and anti-inflammatory properties, molecular mechanisms, pharmacological actions, and translational applications was collected and organized. The methodological quality and scientific relevance of the selected studies were assessed based on study design, analytical techniques employed, reproducibility of findings, sample size, and clinical applicability. Greater emphasis was placed on peer-reviewed publications, systematic reviews, and studies employing validated microbiological and pharmacological methodologies (21,22).

The extracted information was subsequently synthesized into thematic categories including traditional Siddha perspectives on *Kunmam* and gastric disorders, phytochemical composition of Kunmakudori Mezhugu ingredients, antimicrobial activity against *H. pylori*, mechanisms of antimicrobial action, gastroprotective and anti-inflammatory effects, molecular docking and bioinformatics findings, and translational medicine applications. The findings were narratively analyzed to provide a comprehensive overview of the current evidence supporting Kunmakudori Mezhugu as a potential Siddha antimicrobial drug candidate for the management of *Helicobacter pylori* infection and its future development within translational medicine frameworks (23,24).

Results:

The literature review identified substantial evidence supporting the antimicrobial and gastroprotective potential of **Kunmakudori Mezhugu** and its constituent ingredients against *Helicobacter pylori* and other gastrointestinal pathogens. The selected studies included phytochemical investigations, in vitro antimicrobial assays, anti-ulcer studies, molecular docking analyses, pharmacological evaluations, and translational medicine reports. Collectively, the findings demonstrated that the ingredients present in Kunmakudori Mezhugu contain multiple bioactive compounds capable of exerting antimicrobial, anti-inflammatory, antioxidant, anti-ulcer, and immunomodulatory effects relevant to the management of *H. pylori*-associated gastric disorders.

Analysis of the phytochemical profile revealed the presence of several biologically active compounds, including alkaloids, flavonoids, tannins, phenolic compounds, terpenoids, glycosides, saponins, and essential oils. These phytochemicals have been reported to possess antimicrobial activities against a wide range of pathogenic microorganisms. Several studies demonstrated that plant-derived phenolics and flavonoids inhibit bacterial growth by disrupting microbial cell membranes, interfering with protein synthesis, and suppressing bacterial adhesion to host tissues. Such mechanisms are particularly important in *H. pylori* infection because successful colonization of the gastric mucosa depends on bacterial adherence and persistence within the gastric environment.

The reviewed evidence further indicated that several ingredients traditionally incorporated into Siddha anti-ulcer formulations possess direct anti-*H. pylori* activity. Experimental studies reported inhibition of bacterial growth, reduction in urease enzyme activity, suppression of bacterial motility, and disruption of biofilm formation. Urease inhibition is considered particularly significant because the survival of *H. pylori* within the acidic gastric environment relies heavily on urease-mediated neutralization of gastric acid. Phytochemicals capable of inhibiting urease may therefore reduce bacterial colonization and enhance therapeutic outcomes.

Several investigations also demonstrated potent anti-inflammatory and antioxidant activities among the medicinal ingredients of Kunmakudori Mezhugu. Chronic *H. pylori* infection is characterized by persistent gastric inflammation, oxidative stress, and mucosal damage, which contribute to gastritis, ulcer formation, and gastric carcinogenesis. The antioxidant constituents identified in Siddha medicinal plants were found to reduce reactive oxygen species production, stabilize cellular membranes, and protect gastric mucosal tissues from oxidative injury. Simultaneously, anti-inflammatory compounds modulated cytokine production and reduced inflammatory responses within the gastric mucosa.

Molecular docking and computational studies provided additional support for the antimicrobial potential of Siddha phytochemicals. Several bioactive compounds demonstrated favorable binding affinities toward important *H. pylori* targets, including urease, DNA gyrase, adhesins, and other virulence-associated proteins. These findings suggest that Siddha-derived phytochemicals may interfere with multiple bacterial survival pathways and could serve as promising lead molecules for antimicrobial drug development.

The review also identified evidence supporting the gastroprotective properties of Siddha medicinal ingredients. Experimental animal studies demonstrated reductions in gastric ulcer indices, enhancement of mucosal defense mechanisms, increased mucus secretion, and accelerated healing of gastric lesions. Such effects are particularly relevant because successful management of *H. pylori*-associated diseases requires not only bacterial eradication but also restoration of gastric mucosal integrity.

From a translational medicine perspective, the reviewed studies highlighted the potential of Kunmakudori Mezhugu as a multi-target therapeutic intervention. Unlike conventional antibiotic therapies that primarily focus on bacterial eradication, Siddha formulations appear to combine antimicrobial, anti-inflammatory, antioxidant, immunomodulatory, and tissue-protective effects within a single therapeutic framework. This integrated mechanism may offer advantages in reducing disease recurrence, improving patient outcomes, and addressing challenges associated with antimicrobial resistance.

Overall, the findings suggest that Kunmakudori Mezhugu possesses significant potential as a Siddha antimicrobial drug candidate for *Helicobacter pylori*-associated gastric disorders. However, further standardization of the formulation, phytochemical characterization, microbiological validation, molecular investigations, toxicological studies, and well-designed clinical trials are required to establish its efficacy and safety for evidence-based translational applications.

Table 1. Biological Activities Relevant to *Helicobacter pylori* Management

Biological Activity	**Reported Effect**
Antimicrobial activity	Inhibition of *H. pylori* growth
Urease inhibition	Reduced bacterial survival in acidic environment
Anti-biofilm activity	Prevention of bacterial colonization
Anti-inflammatory activity	Reduction of gastric inflammation
Antioxidant activity	Protection against oxidative stress
Gastroprotective activity	Enhancement of mucosal defense
Immunomodulatory activity	Support of host immune response

Table 2. Major Phytochemical Groups Identified in Siddha Anti-Ulcer Ingredients

Phytochemical Class	**Pharmacological Significance**
Alkaloids	Antimicrobial and anti-inflammatory actions
Flavonoids	Antioxidant and anti-*H. pylori* activity
Tannins	Mucosal protection and bacterial inhibition
Phenolic compounds	Antioxidant and antimicrobial effects
Terpenoids	Anti-inflammatory and antimicrobial properties
Saponins	Gastroprotective and immunomodulatory effects
Glycosides	Cytoprotective and therapeutic activities

Table 3. Potential Molecular Targets of Siddha Phytochemicals Against *H. pylori*

Molecular Target	**Biological Role**	**Potential Outcome of Inhibition**
Urease	Acid neutralization and survival	Reduced bacterial colonization
DNA gyrase	DNA replication	Inhibition of bacterial proliferation
Adhesins	Gastric mucosal attachment	Reduced bacterial adherence
Virulence proteins	Pathogenicity	Attenuation of infection severity
Biofilm-associated proteins	Biofilm formation	Improved bacterial eradication

Table 4. Translational Relevance of Kunmakudori Mezhugu

Translational Aspect	Potential Benefit
Natural antimicrobial source	Alternative to conventional antibiotics
Multi-target therapeutic action	Reduced resistance development
Anti-inflammatory effects	Improved gastric healing
Gastroprotective activity	Prevention of ulcer progression
Immunomodulatory effects	Enhanced host defense
Drug discovery potential	Identification of novel lead compounds

Table 5. Summary of Evidence Supporting Kunmakudori Mezhugu Research

Study Category	Major Findings
Phytochemical studies	Presence of antimicrobial bioactive compounds
In vitro antimicrobial studies	Activity against gastric pathogens
Anti-ulcer studies	Protection of gastric mucosa
Molecular docking studies	Interaction with *H. pylori* targets
Pharmacological investigations	Anti-inflammatory and antioxidant effects
Translational research reports	Potential for antimicrobial drug development

Discussion:

The present review highlights the potential of **Kunmakudori Mezhugu**, a classical Siddha formulation, as a promising candidate for translational antimicrobial research targeting *Helicobacter pylori* infection. The increasing prevalence of antibiotic-resistant *H. pylori* strains has significantly reduced the efficacy of conventional eradication therapies, creating an urgent need for alternative and complementary treatment strategies (15,16). The findings of this review suggest that Kunmakudori Mezhugu possesses multiple pharmacological properties that may contribute to the management of *H. pylori*-associated gastric disorders through antimicrobial, anti-inflammatory, antioxidant, gastroprotective, and immunomodulatory mechanisms.

One of the most important observations from the reviewed literature is the presence of diverse phytochemical constituents within Siddha medicinal ingredients. Bioactive compounds such as flavonoids, tannins, alkaloids, phenolic compounds, terpenoids, and glycosides have been reported to exert broad-spectrum antimicrobial activities against numerous pathogenic microorganisms, including *H. pylori* (25–28). These compounds may inhibit bacterial growth through disruption of microbial membranes, interference with essential metabolic pathways, inhibition of nucleic acid synthesis, and suppression of bacterial virulence factors. Such multitarget mechanisms are particularly advantageous in the context of antimicrobial resistance because they reduce the likelihood of resistance development compared with single-target antibiotics (29,30).

A notable finding is the potential anti-*H. pylori* activity of medicinal plants commonly incorporated into Siddha gastrointestinal formulations. Several studies have demonstrated that plant-derived compounds inhibit bacterial adhesion, impair motility, suppress biofilm formation, and interfere with urease activity (25–28). Urease plays a critical role in the survival of *H. pylori* within the acidic environment of the stomach by hydrolyzing urea and generating ammonia, which neutralizes gastric acid. Therefore, inhibition of urease represents an important therapeutic target. The reported ability of phytochemicals to interfere with this enzyme suggests that Siddha formulations may directly affect bacterial colonization and persistence within the gastric mucosa (27,28).

The anti-inflammatory properties observed among the ingredients of Kunmakudori Mezhugu are also highly relevant to the pathogenesis of *H. pylori*-associated diseases. Chronic infection induces persistent inflammation characterized by infiltration of inflammatory cells, release of cytokines, oxidative stress, and progressive mucosal damage (3,4). The reviewed studies indicate that Siddha medicinal plants can modulate inflammatory pathways, reduce pro-inflammatory cytokine production, and attenuate tissue injury through antioxidant mechanisms (29,30). These actions may contribute to symptom relief and prevention of long-term complications such as peptic ulcer disease and gastric malignancy.

Oxidative stress is another critical factor involved in the progression of chronic gastritis and gastric ulceration. Reactive oxygen species generated during *H. pylori*

infection can damage gastric epithelial cells and exacerbate inflammation (31). Many phytochemicals identified in Siddha medicinal ingredients possess potent antioxidant activities capable of scavenging free radicals, stabilizing cellular membranes, and protecting gastric tissues from oxidative injury (31,32). This dual antimicrobial and antioxidant effect may offer significant therapeutic advantages by simultaneously addressing both microbial infection and host tissue damage.

The gastroprotective effects reported in experimental studies further support the therapeutic potential of Kunmakudori Mezhugu. Successful management of *H. pylori*-associated disorders requires not only eradication of the pathogen but also restoration of gastric mucosal integrity. Animal studies evaluating Siddha medicinal ingredients have demonstrated increased mucus secretion, reduced ulcer indices, enhanced mucosal regeneration, and improved healing of gastric lesions (20,24). Such findings suggest that the formulation may facilitate recovery of the gastric mucosa while reducing disease recurrence.

Recent advances in molecular biology and computational pharmacology have provided additional insights into the translational potential of Siddha formulations. Molecular docking studies have identified significant interactions between plant-derived phytochemicals and important *H. pylori* targets, including urease, DNA gyrase, adhesins, and virulence-associated proteins (29,31). These findings provide mechanistic support for the traditional use of Siddha medicines and strengthen the rationale for further drug development efforts. Moreover, the ability of individual phytochemicals to act on multiple bacterial targets aligns well with contemporary strategies aimed at overcoming antimicrobial resistance.

From a translational medicine perspective, Kunmakudori Mezhugu represents an attractive therapeutic candidate because it embodies a multi-component, multi-target approach. Unlike conventional antibiotic regimens that focus primarily on bacterial eradication, Siddha formulations may simultaneously exert antimicrobial, anti-inflammatory, antioxidant, immunomodulatory, and tissue-healing effects (30). Such a holistic therapeutic profile may improve treatment outcomes, reduce adverse effects, and complement existing antimicrobial therapies. Furthermore, the identification of active phytochemicals from this formulation may contribute to the discovery of novel antimicrobial lead compounds for future pharmaceutical development (32).

Despite these promising findings, several limitations remain. Most available evidence is derived from studies investigating individual medicinal ingredients rather than the complete Kunmakudori Mezhugu formulation. Standardization of formulation composition, phytochemical characterization, and quality control measures remain essential prerequisites for scientific validation (18,21). Additionally, well-designed microbiological studies specifically evaluating the anti-*H. pylori* activity of Kunmakudori Mezhugu are limited. Further investigations involving in vitro susceptibility testing, animal models, pharmacokinetic analyses, toxicity assessments, and randomized controlled clinical trials are required to establish efficacy and safety for clinical application (17,21).

Future research should adopt an interdisciplinary approach involving Siddha physicians, microbiologists, pharmacologists, phytochemists, molecular biologists, and clinical researchers. Integration of modern analytical techniques such as metabolomics, proteomics, systems pharmacology, artificial intelligence-assisted drug discovery, and genomic analysis may facilitate identification of bioactive compounds and elucidation of molecular mechanisms underlying the therapeutic effects of Kunmakudori Mezhugu (23,29). Such collaborative efforts will be essential for translating traditional Siddha knowledge into evidence-based antimicrobial therapies.

Overall, the available evidence indicates that Kunmakudori Mezhugu possesses considerable potential as a Siddha antimicrobial drug candidate for the management of *Helicobacter pylori*-associated gastric disorders. Its multitarget pharmacological actions, gastroprotective properties, and translational relevance support further scientific investigation and clinical validation within the framework of evidence-based medicine (29–32).

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