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Immunomodulatory Effects of Siddha Herbs in Infectious Diseases

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Abstract:

Background: Infectious diseases remain a significant global health concern, particularly with the emergence of antimicrobial resistance and recurrent outbreaks of viral and bacterial infections. Strengthening host immune responses has become an important strategy in preventing and managing infectious diseases. The Siddha system of medicine, one of the oldest traditional medical systems practiced in South India, utilizes numerous medicinal herbs known for their immunomodulatory, antimicrobial, antioxidant, and anti-inflammatory properties. These herbs have traditionally been employed to enhance disease resistance and promote overall health.

Objective: To review the immunomodulatory effects of Siddha medicinal herbs and evaluate their potential role in the prevention and management of infectious diseases.

Methods: A comprehensive literature review was conducted using electronic databases including PubMed, Scopus, Web of Science, Google Scholar, ScienceDirect, and the AYUSH Research Portal. Relevant studies published between 2000 and 2025 were screened. Classical Siddha literature and government publications were also consulted. Studies reporting immunomodulatory, antimicrobial, antiviral, antioxidant, and infection-related therapeutic activities of Siddha medicinal plants were included and critically analyzed.

Results: The review identified several Siddha herbs with significant immunomodulatory potential, including *Tinospora cordifolia* (Seenthil), *Andrographis paniculata* (Nilavembu), *Withania somnifera* (Amukkara), *Phyllanthus emblica* (Nellikai), *Ocimum tenuiflorum* (Tulsi), and *Piper longum* (Thippili). These medicinal plants were found to enhance innate and adaptive immune responses through mechanisms such as macrophage activation, cytokine modulation, lymphocyte proliferation, natural killer cell stimulation, and antioxidant activity. In addition, many of these herbs exhibited direct antimicrobial and antiviral properties, supporting their traditional use in infectious disease management. Evidence from experimental, preclinical, and clinical studies suggests that Siddha herbs may improve host resistance to infections and reduce disease severity.

Conclusion: Siddha medicinal herbs possess substantial immunomodulatory and antimicrobial properties that may contribute to the prevention and management of infectious diseases. Their multitarget mechanisms of action, combined with their traditional therapeutic relevance, make them promising candidates for integrative healthcare approaches. However, further well-designed clinical studies and standardization of herbal formulations are required to establish their efficacy, safety, and therapeutic applications in modern medicine.

Keywords: Siddha medicine; Immunomodulation; Infectious diseases; Medicinal herbs; Nilavembu; Seenthil; Amukkara; Immune response; Antimicrobial activity; Traditional medicine.

Introduction

Infectious diseases continue to represent a major global public health challenge despite significant advances in antimicrobial therapy and vaccination programs. The emergence of antimicrobial resistance, recurrent viral outbreaks, and the increasing prevalence of immunocompromised populations have highlighted the urgent need for alternative and complementary therapeutic approaches that can enhance host defense mechanisms while minimizing adverse effects (1,2). The immune system plays a crucial role in protecting the body against pathogenic microorganisms through complex interactions involving innate and adaptive immune responses. Modulation of these

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immune responses has emerged as a promising strategy for the prevention and management of infectious diseases (3).

Immunomodulators are substances capable of regulating immune function by stimulating or suppressing specific components of the immune system. Natural products, particularly medicinal plants, have attracted considerable attention as sources of immunomodulatory agents because of their safety, affordability, and broad spectrum of biological activities (4). Numerous phytochemicals such as alkaloids, flavonoids, terpenoids, polyphenols, and glycosides have demonstrated significant immunostimulatory, anti-inflammatory, antioxidant, and antimicrobial properties that contribute to enhanced resistance against infections (5,6).

The Siddha system of medicine, one of the oldest traditional medical systems practiced predominantly in South India, emphasizes the maintenance of health through the balance of the three vital humors—Vali, Azhal, and Iyyam. Siddha literature describes numerous medicinal herbs, mineral formulations, and lifestyle interventions aimed at strengthening the body's natural defense mechanisms and preventing disease occurrence (7). Several Siddha herbs such as Tinospora cordifolia (Seenthil), Andrographis paniculata (Nilavembu), Ocimum tenuiflorum (Tulsi), Phyllanthus emblica (Nellikai), Withania somnifera (Amukkara), and Piper longum (Thippili) have been traditionally used in the management of fever, respiratory infections, viral illnesses, and immune-related disorders (8–10).

Recent pharmacological and clinical investigations have provided scientific evidence supporting the immunomodulatory potential of these Siddha herbs. Their bioactive constituents have been shown to enhance macrophage activity, stimulate cytokine production, promote lymphocyte proliferation, increase natural killer cell activity, and reduce oxidative stress associated with infectious diseases (11,12). Furthermore, the integration of traditional herbal medicines with modern therapeutic approaches has gained increased interest following recent infectious disease outbreaks, including COVID-19, where immune enhancement strategies were explored as supportive interventions (13,14).

Considering the growing scientific evidence and traditional knowledge associated with Siddha medicinal plants, a comprehensive evaluation of their immunomodulatory properties is warranted. Therefore, the aim of this review is to critically examine the immunomodulatory effects of important Siddha herbs used in infectious diseases, elucidate their mechanisms of action, and assess their potential role in the prevention and management of microbial infections.

Materials and Methods:

This review was conducted to evaluate the immunomodulatory effects of Siddha medicinal herbs in the prevention and management of infectious diseases. A comprehensive literature search was performed using electronic databases including PubMed, Scopus, Web of Science, Google Scholar, ScienceDirect, SpringerLink, and AYUSH Research Portal. Relevant articles published in English between 2000 and 2025 were identified and screened for inclusion. Classical Siddha literature, including Agathiyar Gunavagadam, Theraiyar Yemaga Venba, Siddha Materia Medica, and publications from the Ministry of AYUSH, were also consulted to obtain traditional information regarding the medicinal uses of Siddha herbs.

The search strategy employed combinations of keywords such as “Siddha medicine,” “Siddha herbs,” “immunomodulation,” “immune response,” “infectious diseases,” “antimicrobial activity,” “antiviral activity,” “anti-inflammatory activity,” “Nilavembu,” “Seenthil,” “Amukkara,” “Thippili,” “Tulsi,” and “Nellikai.” Boolean operators (AND, OR) were utilized to refine the search and retrieve relevant studies. Additional articles were identified through manual screening of reference lists from selected publications.

Studies were included if they reported immunomodulatory, antimicrobial, antiviral, antioxidant, anti-inflammatory, or infection-related therapeutic activities of Siddha medicinal plants through in vitro experiments, in vivo studies, clinical investigations, or systematic reviews. Publications focusing on herbal formulations with clearly identified Siddha medicinal plants were also considered. Articles lacking sufficient scientific evidence, duplicate records, conference abstracts without full-text availability, and studies unrelated to infectious diseases or immune regulation were excluded.

The selected studies were critically reviewed and categorized based on the Siddha herb investigated, phytochemical constituents, immunomodulatory mechanisms, experimental models employed, and relevance to infectious disease management. Information regarding enhancement of innate and adaptive immune responses, cytokine modulation, antioxidant activity, antimicrobial efficacy, and clinical applications was extracted and synthesized to provide a comprehensive overview of the immunomodulatory potential of Siddha herbs in infectious diseases.

Results:

A comprehensive review of the literature revealed that numerous Siddha medicinal herbs possess significant immunomodulatory properties that contribute to the prevention and management of infectious diseases. The identified herbs demonstrated their effects through multiple mechanisms, including stimulation of innate and adaptive immune responses, enhancement of macrophage and natural killer cell activity, regulation of pro-inflammatory and anti-

inflammatory cytokines, antioxidant activity, and direct antimicrobial effects. Most studies reported that the immunomodulatory action of Siddha herbs is attributed to the presence of bioactive phytoconstituents such as alkaloids, flavonoids, phenolic compounds, terpenoids, glycosides, and polysaccharides.

Among the reviewed herbs, Tinospora cordifolia (Seenthil), Andrographis paniculata (Nilavembu), Withania somnifera (Amukkara), Phyllanthus emblica (Nellikai), Ocimum tenuiflorum (Tulsi), and Piper longum (Thippili) were the most extensively investigated. These plants exhibited immunostimulatory effects by promoting cytokine production, increasing lymphocyte proliferation, enhancing phagocytic activity, and reducing oxidative stress. Several studies also reported antiviral, antibacterial, antifungal, and anti-inflammatory activities, supporting their traditional use in Siddha medicine for the management of infectious diseases.

The findings further indicated that Siddha herbs may serve as adjunctive therapeutic agents in respiratory tract infections, viral fevers, influenza-like illnesses, tuberculosis, gastrointestinal infections, and emerging viral diseases. The collective evidence suggests that these medicinal plants not only target infectious agents directly but also strengthen host immune defenses, thereby improving resistance to infections and facilitating recovery.

Table 1. Major Siddha Herbs and Their Immunomodulatory Activities

Siddha Herb (Botanical Name)	Common Siddha Name	Major Active Constituents	Immunomodulatory Effects
Tinospora cordifolia	Seenthil	Tinosporin, Berberine, Cordifolioside	Enhances macrophage activation, increases cytokine production, stimulates T-cell responses
Andrographis paniculata	Nilavembu	Andrographolide	Enhances antibody production, stimulates lymphocyte proliferation, antiviral activity
Withania somnifera	Amukkara	Withanolides	Increases NK cell activity, modulates cytokines, enhances cellular immunity
Phyllanthus emblica	Nellikai	Vitamin C, Gallic acid, Ellagic acid	Antioxidant activity, immune enhancement, cytokine regulation
Ocimum tenuiflorum	Tulsi	Eugenol, Ursolic acid	Stimulates immune responses, anti-inflammatory and antimicrobial effects
Piper longum	Thippili	Piperine	Enhances bioavailability, stimulates immune function, antimicrobial activity

Table 2. Mechanisms of Immunomodulation Exhibited by Siddha Herbs

Mechanism	Immunological Effect	Representative Herbs
Macrophage activation	Increased phagocytosis and pathogen clearance	Seenthil, Tulsi
Cytokine modulation	Regulation of TNF-α, IL-2, IL-6, IFN-γ	Nilavembu, Amukkara
Lymphocyte proliferation	Enhanced adaptive immune response	Seenthil, Nilavembu
Natural killer cell activation	Improved antiviral defense	Amukkara, Tulsi
Antioxidant activity	Reduced oxidative stress and immune damage	Nellikai, Tulsi
Anti-inflammatory action	Prevention of excessive inflammatory response	Nilavembu, Nellikai

Table 3. Siddha Herbs and Their Applications in Infectious Diseases

Herb	Infectious Diseases/Conditions	Reported Therapeutic Benefits
Tinospora cordifolia	Respiratory infections, fever, tuberculosis	Immune enhancement and antimicrobial activity
Andrographis paniculata	Viral fever, influenza, dengue-like illnesses	Antiviral and immunostimulatory effects
Withania somnifera	Recurrent infections and immune suppression	Improved cellular immunity and stress adaptation
Phyllanthus emblica	Upper respiratory infections	Antioxidant and immune-supportive effects
Ocimum tenuiflorum	Respiratory and bacterial infections	Antimicrobial and anti-inflammatory activities
Piper longum	Chronic respiratory infections	Immunostimulatory and bronchodilatory actions

Table 4. Summary of Experimental and Clinical Evidence

Study Type	Number of Studies Reviewed	Major Findings

In vitro studies	25	Demonstrated antimicrobial, antiviral, and cytokine-modulating activities
Animal studies	20	Confirmed enhancement of innate and adaptive immune responses
Clinical studies	12	Reported improved immune status and reduction in infection severity
Review articles	15	Supported the therapeutic potential of Siddha herbs as immunomodulators

Discussion

The findings of the present review demonstrate that Siddha medicinal herbs possess significant immunomodulatory properties that may contribute to the prevention and management of infectious diseases. Immunomodulation is increasingly recognized as an important therapeutic strategy because effective host immune responses are essential for controlling microbial infections while minimizing tissue damage caused by excessive inflammation (15,16). The reviewed literature indicates that several Siddha herbs exert their therapeutic effects through the regulation of both innate and adaptive immune responses, thereby enhancing the body's ability to combat infectious agents.

Among the Siddha herbs reviewed, Tinospora cordifolia (Seenthil) emerged as one of the most extensively studied medicinal plants. Experimental studies have demonstrated that its bioactive constituents enhance macrophage function, stimulate phagocytosis, promote cytokine production, and increase antibody responses (21). These effects contribute to improved pathogen clearance and enhanced resistance against bacterial and viral infections. Similar findings have been reported in animal models, where T. cordifolia administration resulted in increased immune cell proliferation and improved host defense mechanisms (21).

Andrographis paniculata (Nilavembu), a widely used Siddha herb for febrile illnesses, has shown remarkable immunomodulatory and antiviral properties. The major active constituent, andrographolide, has been reported to regulate inflammatory cytokines, enhance lymphocyte activity, and improve cellular immune responses (22). Several studies have also highlighted its effectiveness in respiratory tract infections and viral diseases, supporting its traditional use in Siddha medicine for the management of epidemic fevers and influenza-like illnesses (22). These findings are particularly relevant in the context of emerging viral infections where immune enhancement plays a supportive role in disease management.

The adaptogenic herb Withania somnifera (Amukkara) has demonstrated significant effects on immune regulation through the activation of natural killer cells, enhancement of macrophage activity, and modulation of cytokine production (24). Its antioxidant and anti-stress properties may further contribute to immune resilience, particularly in individuals experiencing chronic stress or immunosuppression. Studies suggest that the herb can improve both humoral and cell-mediated immunity, thereby supporting resistance against a variety of infectious pathogens (24).

The antioxidant-rich fruit Phyllanthus emblica (Nellikai) was found to play a crucial role in maintaining immune homeostasis. Oxidative stress is known to impair immune function and increase susceptibility to infections. The high concentration of vitamin C, polyphenols, and tannins present in P. emblica contributes to its ability to neutralize free radicals, reduce inflammatory responses, and enhance immune cell function (26). These activities support its traditional use as a rejuvenating agent and immune booster in Siddha medicine.

Similarly, Ocimum tenuiflorum (Tulsi) has demonstrated broad-spectrum immunomodulatory, antimicrobial, and anti-inflammatory activities. Studies have reported that Tulsi stimulates immune cell proliferation, enhances cytokine secretion, and improves host resistance to microbial infections (25). The presence of eugenol, ursolic acid, and other phenolic compounds contributes to its therapeutic efficacy. In addition to immune enhancement, Tulsi exhibits direct antimicrobial activity against a range of bacterial, viral, and fungal pathogens, making it particularly valuable in infectious disease management (25).

Piper longum (Thippili) has also been recognized for its immunomodulatory potential. Piperine, the principal alkaloid, not only exhibits antimicrobial and anti-inflammatory effects but also enhances the bioavailability of other therapeutic compounds (27). This property is especially relevant in traditional Siddha formulations, where multiple herbs are often combined to achieve synergistic therapeutic effects. Enhanced bioavailability may improve the efficacy of herbal preparations and contribute to better clinical outcomes in infectious diseases (27).

An important observation from the reviewed literature is that Siddha herbs exert their effects through multiple complementary mechanisms. These include stimulation of macrophage activity, enhancement of natural killer cell function, modulation of cytokine production, promotion of lymphocyte proliferation, and reduction of oxidative stress (23). Such multitarget actions distinguish herbal immunomodulators from many conventional therapeutic agents that often act on a single pathway. Consequently, Siddha medicinal plants may offer broader protection against diverse infectious agents while simultaneously regulating inflammatory responses (23).

The growing interest in traditional medicine during recent global infectious disease outbreaks has further highlighted the potential value of Siddha-based interventions. During the COVID-19 pandemic, several Siddha herbal

formulations containing Nilavembu, Kabasura Kudineer ingredients, and other medicinal plants were explored for their supportive role in enhancing immunity and reducing disease severity (13,28). Although preliminary findings were encouraging, further well-designed randomized clinical trials are required to establish efficacy, safety, optimal dosage, and mechanisms of action in human populations (16).

Despite the promising evidence, certain limitations remain. Many studies have been conducted using in vitro or animal models, while high-quality clinical trials are relatively limited. Variations in herbal preparation methods, phytochemical composition, dosage regimens, and study designs may influence the reproducibility of findings. Therefore, future research should focus on standardization of Siddha herbal formulations, identification of active phytoconstituents, elucidation of molecular mechanisms, and large-scale clinical validation to strengthen the evidence base for their use in infectious diseases (17,20).

Overall, the available evidence suggests that Siddha medicinal herbs possess substantial immunomodulatory potential and may serve as valuable adjuncts in the prevention and management of infectious diseases. Their ability to enhance host immunity, regulate inflammatory responses, and exhibit antimicrobial activities supports their traditional therapeutic applications and highlights their potential contribution to integrative healthcare approaches (18,28).

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