OPEN ACCESS
World Journal of Applied Medical Sciences
ISSN: 3049-0200 (Online) | Vol. 2, No. 12, 2025
Website: https://wasrpublication.com/index.php/wjams/

Modern Microbiological Validation of the Antiviral Potential of Siddha Formulation Santha Santhrothaiya Tablet Against Hepatitis B Virus: A Review

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Received: 05/10/2025 | Accepted: 16/11/2025 | Published: 01/12/2025

Abstract:

Background: Hepatitis B virus (HBV) infection remains a major global health concern, contributing significantly to chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. Despite effective vaccines and antiviral agents, complete viral eradication remains challenging due to viral persistence, drug resistance, and limited therapeutic options. This has increased interest in alternative and complementary therapies derived from traditional medical systems.

Objective: This review aims to evaluate the antiviral potential of the Siddha formulation **Santha Santhrothaiya Tablet** against HBV through modern microbiological validation approaches and to explore its relevance in contemporary antiviral drug discovery.

Materials and Methods: An evidence-based narrative review was conducted using databases such as PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, and AYUSH Research Portal. Classical Siddha texts and official pharmacopeias were also reviewed. Studies published between 2000 and 2025 related to antiviral activity, hepatoprotective effects, phytochemical analysis, molecular docking, and microbiological validation of Siddha-relevant herbs were included. Data were extracted and synthesized qualitatively.

Results: The review identified that Siddha formulation Santha Santhrothaiya Tablet contains bioactive phytochemicals with reported antiviral, immunomodulatory, and hepatoprotective properties. Key constituents such as flavonoids, alkaloids, tannins, terpenoids, and polyphenols demonstrated potential to inhibit HBV replication, suppress viral enzymes, and modulate host immune responses. In silico studies indicated strong binding affinity of plant-derived compounds to HBV polymerase and related viral targets. Additionally, antioxidant and anti-inflammatory effects contribute to hepatocyte protection. However, direct experimental validation of the complete formulation against HBV remains limited.

Conclusion: Siddha-based formulation Santha Santhrothaiya Tablet shows promising antiviral potential against HBV through multi-target mechanisms. Further standardized preclinical and clinical studies are required to validate its efficacy and support its integration into modern antiviral therapeutic strategies.

Keywords: Hepatitis B virus; Siddha medicine; Santha Santhrothaiya tablet; antiviral activity; herbal medicine; phytochemicals; molecular docking; hepatoprotection; traditional medicine.

Introduction:

Hepatitis B virus (HBV) infection remains a significant global health burden, affecting hundreds of millions of people worldwide and contributing to serious complications such as chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma (1,2). Despite the availability of effective vaccines and antiviral agents, HBV continues to persist as a major clinical challenge due to incomplete viral eradication, long-term drug dependence, emergence of resistant viral strains, and limited accessibility of advanced therapies in resource-constrained settings (3,4). These limitations have intensified the need for alternative and complementary therapeutic approaches with improved safety, affordability, and long-term efficacy.

Natural products derived from traditional medical systems have gained increasing attention in antiviral drug discovery due to their structural diversity and multi-target biological activities (5). Plant-based compounds have demonstrated significant antiviral effects against DNA and RNA viruses through mechanisms such as inhibition of viral entry, suppression of replication enzymes, modulation of host immune responses, and protection of host cells from oxidative damage (6,7). In this context, traditional systems of medicine such as Siddha provide a valuable source of therapeutic knowledge and bioactive formulations that may contribute to the development of novel antiviral agents.

Siddha medicine, one of the ancient systems of South India, has long been used for the management of liver disorders

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and infectious diseases described under clinical conditions resembling jaundice and hepatic dysfunction (8). Siddha formulations are typically composed of herbal and herbo-mineral ingredients that are believed to exert hepatoprotective, detoxifying, and immune-enhancing effects. Among these, **Santha Santhrothaiya Tablet** is traditionally referenced in Siddha practice for liver-related ailments and systemic disorders, suggesting its potential relevance in the management of viral hepatitis, including HBV infection.

Recent advances in modern microbiology and pharmacology have enabled the scientific validation of traditional medicines through techniques such as in vitro antiviral assays, molecular docking studies, cell culture-based viral inhibition models, and computational biology approaches (9,10). These methodologies provide a robust framework for evaluating the antiviral efficacy, safety, and mechanistic pathways of traditional formulations. Integration of Siddha knowledge with modern experimental validation can therefore facilitate evidence-based drug development and translational research.

Furthermore, contemporary research emphasizes the importance of multi-target antiviral strategies for chronic viral infections such as HBV, where single-target drugs often fail to achieve complete viral clearance due to viral persistence mechanisms such as covalently closed circular DNA (cccDNA) formation (11). Herbal formulations with multiple bioactive compounds may offer synergistic effects by targeting different stages of the viral life cycle while simultaneously enhancing host immune responses.

Despite the traditional use of Siddha formulations for liver disorders, scientific evidence specifically validating the antiviral potential of Santha Santhrothaiya Tablet against HBV remains limited. Issues such as standardization of herbal-mineral composition, lack of mechanistic studies, and insufficient clinical validation further highlight the need for systematic investigation (12,13). Addressing these gaps is essential for translating traditional Siddha formulations into scientifically validated antiviral therapeutics.

Therefore, the aim of this review is to evaluate the antiviral potential of the Siddha formulation **Santha Santhrothaiya Tablet** against Hepatitis B virus through modern microbiological validation approaches and to explore its relevance in contemporary antiviral drug discovery and translational medicine.

Materials and Methods:

This review was conducted to evaluate the antiviral potential of the Siddha formulation **Santha Santhrothaiya Tablet** against Hepatitis B virus (HBV) through modern microbiological validation approaches. The study followed an evidence-based narrative review design integrating classical Siddha literature with contemporary scientific research in microbiology, virology, pharmacology, and computational biology.

A comprehensive literature search was performed using electronic databases including PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, MEDLINE, SpringerLink, and the AYUSH Research Portal. In addition, classical Siddha texts, the Siddha Formulary of India, and publications from the National Institute of Siddha and Ministry of AYUSH were reviewed to identify traditional descriptions and therapeutic indications of Santha Santhrothaiya Tablet. The search period was restricted to studies published between 2000 and 2025 to include recent advances in antiviral research and validation techniques.

The search strategy used combinations of keywords such as “Santha Santhrothaiya tablet,” “Siddha antiviral formulations,” “Hepatitis B virus natural products,” “herbal antiviral activity,” “hepatoprotective Siddha medicine,” “in vitro HBV inhibition,” “molecular docking HBV,” “cccDNA inhibition natural compounds,” and “traditional medicine antiviral validation,” combined using Boolean operators (AND, OR) to refine results.

Studies were included if they reported antiviral, hepatoprotective, immunomodulatory, or microbiological validation of Siddha or Siddha-relevant herbal formulations, or if they investigated individual herbal constituents of Santha Santhrothaiya Tablet for activity against HBV or related viral models. Experimental studies (in vitro, in vivo), computational studies (molecular docking, network pharmacology), clinical observations, and review articles were considered. Studies lacking relevance to antiviral activity or without sufficient methodological detail were excluded.

Data extraction was performed systematically using a structured format to collect information on formulation composition, traditional Siddha indications, phytochemical constituents, antiviral activity, mechanism of action, experimental model used (cell culture, in vitro enzyme assays, computational docking), and reported outcomes related to HBV or similar viral systems. Special emphasis was placed on identifying bioactive compounds with activity against viral replication pathways, including reverse transcription, viral entry, and cccDNA maintenance.

The collected data were analyzed qualitatively and synthesized thematically under key domains: (i) traditional Siddha therapeutic relevance of Santha Santhrothaiya Tablet, (ii) antiviral potential of constituent herbs and minerals, (iii) modern microbiological validation techniques applicable to HBV research, and (iv) mechanistic insights from computational and experimental studies. The synthesis aimed to correlate traditional Siddha claims with modern scientific evidence to assess the translational potential of the formulation in antiviral drug development.

Results:

The review findings indicate that the Siddha formulation **Santha Santhrothaiya Tablet** has strong ethnopharmacological relevance in the management of liver disorders and infectious conditions, and its constituent herbal-mineral components demonstrate promising antiviral and hepatoprotective potential relevant to Hepatitis B virus (HBV) infection. The synthesis of available literature suggests that the formulation may exert its therapeutic effects through multiple complementary mechanisms involving antiviral, immunomodulatory, antioxidant, and hepatoprotective pathways.

The analysis revealed that several individual herbal ingredients commonly used in Siddha liver formulations contain bioactive phytochemicals with documented activity against HBV and related viral models. Compounds such as flavonoids, alkaloids, polyphenols, tannins, and terpenoids were frequently reported to inhibit viral replication, interfere with viral entry, and suppress reverse transcriptase activity. These compounds also demonstrated the ability to modulate host immune responses, thereby enhancing antiviral defense mechanisms.

Modern microbiological and virological studies on Siddha-relevant herbs indicate that plant extracts can reduce viral antigen expression, inhibit HBV DNA replication, and downregulate viral gene transcription in experimental models. In addition, several constituents exhibit hepatoprotective effects by reducing oxidative stress, stabilizing hepatocyte membranes, and enhancing detoxification enzyme activity, which is particularly important in chronic HBV-induced liver damage.

Computational studies such as molecular docking and network pharmacology analyses further support the antiviral potential of Siddha medicinal components. These studies suggest strong binding affinity of plant-derived phytochemicals with key HBV targets such as viral polymerase, surface antigens, and core proteins, indicating possible inhibition of viral replication cycles. Network analysis also highlights multi-target interactions involving immune signaling pathways, inflammation regulation, and apoptosis modulation.

The review also identified that modern microbiological validation approaches—including in vitro cell culture assays, polymerase inhibition studies, and gene expression analysis—are increasingly being applied to evaluate traditional formulations. However, direct experimental studies specifically validating **Santha Santhrothaiya Tablet against HBV** remain limited, indicating a significant research gap.

Overall, the results suggest that Santha Santhrothaiya Tablet, through its polyherbal and herbo-mineral composition, has potential antiviral relevance against HBV. Its therapeutic action is likely mediated through a synergistic combination of viral suppression, immune enhancement, and hepatocyte protection. Nevertheless, the lack of standardized experimental validation and clinical evidence highlights the need for further rigorous microbiological and pharmacological studies to confirm its efficacy and safety.

Discussion:

The present review highlights that the Siddha formulation **Santha Santhrothaiya Tablet** may possess significant antiviral and hepatoprotective potential against Hepatitis B virus (HBV), primarily through the combined actions of its herbal and herbo-mineral constituents. The findings from this review align with recent advances in antiviral pharmacology, which emphasize multi-target therapeutic strategies for chronic viral infections such as HBV, where single-target drugs often fail to eliminate covalently closed circular DNA (cccDNA) and achieve complete viral clearance (14,15).

Recent studies in natural product antiviral research have demonstrated that plant-derived bioactive compounds exhibit broad-spectrum antiviral effects by targeting multiple stages of the viral life cycle, including viral entry, replication, transcription, and protein synthesis (16,17). This multi-target mechanism is particularly relevant in HBV infection, where viral persistence and immune evasion mechanisms complicate treatment outcomes. In this context, Siddha formulations like Santha Santhrothaiya Tablet, which contain multiple phytochemical constituents, may provide synergistic antiviral effects through diverse biochemical pathways (18).

Table 1 - Mechanistic Comparison of Siddha Formulation with Recent Antiviral Studies

Aspect	Siddha Formulation (Santha Santhrothaiya Tablet)	Recent Scientific Evidence	Interpretation
Antiviral strategy	Multi-component herbal-mineral synergy	Multi-target antiviral approach	Strong correlation
Viral inhibition	Traditional liver detoxification and viral suppression	HBV DNA replication inhibition reported in natural products	Partial experimental support
Immune modulation	Enhancement of host resistance	Cytokine regulation and immune activation	Strong agreement
Hepatoprotection	Liver detoxification and regeneration	Antioxidant-mediated hepatocyte protection	Strong agreement
Resistance risk	Low (polyherbal complexity)	Reduced resistance with phytochemicals	Supported

The phytochemical constituents of Siddha medicinal plants, including flavonoids, alkaloids, tannins, terpenoids, and polyphenols, have been widely reported to exert antiviral effects through multiple molecular mechanisms. These include inhibition of viral polymerase activity, suppression of reverse transcription, blocking of viral entry receptors, and interference with viral protein assembly (19,20). Such mechanisms are particularly relevant for HBV, which relies heavily on reverse transcription and stable nuclear cccDNA formation for persistence.

Table 2 - Mode of Action of Siddha Antiviral Constituents Against HBV

Mechanism	Biological Effect	Relevance to HBV
Viral entry inhibition	Blocks attachment and penetration into hepatocytes	Prevents initial infection
Polymerase inhibition	Suppresses HBV reverse transcription	Reduces viral replication
cccDNA modulation	Interferes with viral persistence reservoir	Potential long-term control
Immunomodulation	Enhances T-cell and macrophage response	Improves viral clearance
Antioxidant activity	Reduces oxidative liver damage	Protects hepatocytes
Anti-inflammatory action	Suppresses cytokine-mediated damage	Prevents liver fibrosis

Recent molecular docking and network pharmacology studies further support the interaction of plant-derived compounds with key HBV targets such as viral polymerase, surface antigen proteins, and core proteins (21). These computational findings suggest that multi-constituent herbal formulations may exert synergistic inhibition across multiple viral pathways, which is consistent with the traditional Siddha therapeutic philosophy.

However, despite promising in silico and in vitro evidence, direct experimental validation of **Santha Santhrothaiya Tablet** against HBV remains limited. Most available data are derived from studies on individual plant constituents rather than the complete formulation. This creates a translational gap between traditional usage and modern clinical application (22,23). Additionally, variability in preparation methods, lack of standardization, and absence of pharmacokinetic profiling further limit clinical translation.

Another important consideration is safety and toxicity evaluation. While herbal constituents generally show favorable safety profiles, the presence of herbo-mineral components in Siddha formulations necessitates rigorous toxicological assessment to ensure long-term safety, especially in chronic conditions such as HBV infection (24). Recent WHO guidelines emphasize the importance of standardized quality control and evidence-based validation for traditional medicines before clinical integration (25).

Overall, the comparative analysis suggests that Santha Santhrothaiya Tablet aligns well with modern antiviral strategies that emphasize multi-target, immune-enhancing, and hepatoprotective approaches. However, further preclinical and clinical studies are essential to validate its efficacy against HBV and to establish standardized therapeutic protocols for its use in modern healthcare systems.

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