

## Nature's Elixir: The Art of Siddha Herbs in Transforming Liver Disorders

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### Abstract

This review synthesizes research on "Liver disorder medicine herbs prevalence complication investigation into diet lifestyle modification" to address gaps in understanding the role of Siddha herbal therapies integrated with diet and lifestyle in liver disorder management. The review aimed to evaluate prevalence and complications of liver diseases treated with Siddha herbs, benchmark herbal formulations against dietary and lifestyle interventions, identify

phytochemical constituents and mechanisms, compare Siddha with other traditional systems, and assess safety profiles. Literature from clinical, ethnobotanical, pharmacological, and preclinical studies published primarily in India was systematically analyzed for therapeutic efficacy, phytochemical characterization, integration outcomes, and safety data. Findings indicate Siddha herbal formulations demonstrate hepatoprotective effects with improvements in liver function and symptom relief, often enhanced by concurrent diet and lifestyle modifications. Key bioactive compounds such as flavonoids and terpenoids mediate antioxidant and anti-inflammatory actions, though standardization and mechanistic clarity remain limited. Comparative insights reveal overlaps and distinctions between Siddha and Ayurveda, yet direct clinical comparisons are scarce. Safety profiles are generally favorable, but comprehensive toxicological evaluations are lacking. Overall, Siddha medicine shows promise for holistic liver disorder management, but robust randomized controlled trials and standardized methodologies are essential to substantiate efficacy and safety claims. These findings inform culturally relevant integrative approaches and highlight priorities for future research in traditional hepatotherapy.

## Introduction

Research on liver disorder Siddha medicine herbs prevalence complication investigation diet lifestyle modification has emerged as a critical area of inquiry due to the increasing global burden of liver diseases, including non-alcoholic fatty liver disease (NAFLD), hepatitis, and cirrhosis, which contribute significantly to morbidity and mortality worldwide (Pratap et al., 2023; Daniyal et al., 2019). Over the past decades, traditional medicinal systems such as Siddha, Ayurveda, and Unani have gained attention for their potential hepatoprotective effects, with evolving research documenting herbal formulations, dietary interventions, and lifestyle modifications as integral components of liver health management (Swathi & Revathy, 2024; Rathi et al., 2023; Orlova et al., 2024). The prevalence of NAFLD alone ranges from 9% to 37% in various populations, underscoring the urgent need for effective, accessible therapies (Gupta et al., 2023; Yadav et al., 2024). The social and clinical significance of this research lies in addressing the limitations of conventional treatments, which often involve high costs, adverse effects, and limited efficacy, thereby motivating exploration of traditional herbal remedies and lifestyle strategies (Patel et al., 2015; Mancak et al., 2024).

Despite the growing interest, the management of liver disorders through Siddha medicine herbs and associated lifestyle modifications faces challenges due to insufficient standardized clinical evidence and unclear mechanisms of action (-, 2023; Mancak et al., 2024; Sarkar et al., 2024). While several studies report promising outcomes with polyherbal formulations and dietary changes, controversies persist regarding optimal treatment protocols, dosage, and long-term safety (Panda & Kar, 2024; Yadav et al., 2024; Kantharia et al., 2023). Moreover, the integration of herbal therapies with conventional medicine remains debated, with concerns about herbal interactions and variability in herbal product quality (Prete et al., 2012; Mishra et al., 2014). The knowledge gap is further compounded by limited large-scale randomized controlled trials and systematic evaluations of Siddha-specific interventions, impeding their broader clinical acceptance (-, 2023; Darbar et al., 2024; Mancak et al., 2024). This gap has significant implications, as untreated or poorly managed liver disorders can progress to life-threatening complications such as cirrhosis, hepatic failure, and hepatocellular carcinoma (Patel

et al., 2015; Choudhary et al., 2023).

The conceptual framework for this review is grounded in the interrelationship between liver disorders, herbal medicinal interventions, and lifestyle modifications, emphasizing the hepatoprotective, anti-inflammatory, and metabolic regulatory roles of Siddha herbs within a holistic treatment paradigm (Khadse et al., 2024; Rajappa et al., 2024; Li et al., 2020). Key concepts include the pathophysiology of liver diseases, the pharmacological properties of herbal constituents, and the impact of diet and lifestyle on disease progression and management (Sivakrishnan, 2019; Orlova et al., 2024). This framework supports the investigation of Siddha medicine as a complementary approach that addresses both the biological and behavioral determinants of liver health (P et al., 2022; Bhavani, 2017).

The purpose of this systematic review is to critically evaluate the prevalence, complications, and therapeutic potential of Siddha medicinal herbs in liver disorders, alongside the role of diet and lifestyle modifications, to bridge existing knowledge gaps and inform evidence-based clinical practice (Pratap et al., 2023; -, 2023). By synthesizing current research, this review aims to provide a comprehensive understanding of Siddha interventions' efficacy, safety, and mechanisms, thereby contributing valuable insights for integrative liver disease management (Darbar et al., 2024; Sarkar et al., 2024).

This review employs a rigorous methodology involving systematic literature searches across multiple databases, inclusion of peer-reviewed clinical and preclinical studies, and thematic analysis of herbal formulations, dietary patterns, and lifestyle factors (-, 2023; Poo et al., 2024). Findings are organized to elucidate the prevalence and complications of liver disorders, the pharmacodynamics of Siddha herbs, and the impact of lifestyle interventions, facilitating a structured discourse on their clinical relevance and future research directions (Swathi & Revathy, 2024; Mancak et al., 2024).

## **Purpose and Scope of the Review**

### **Statement of Purpose**

The objective of this report is to examine the existing research on "Liver disorder Siddha medicine herbs prevalence complication investigation diet lifestyle modification" in order to provide a comprehensive synthesis of current knowledge regarding the use of Siddha herbal medicines in managing liver disorders. This review aims to elucidate the prevalence and complications associated with liver diseases, investigate the therapeutic potential of Siddha herbs, and assess the role of diet and lifestyle modifications in disease management. By integrating findings across clinical, ethnobotanical, and pharmacological studies, the report seeks to identify gaps in evidence and inform future research directions. Such an analysis is crucial for advancing holistic and culturally relevant approaches to liver health, optimizing treatment efficacy, and improving patient outcomes in populations relying on traditional medicine systems.

### **Specific Objectives:**

- To evaluate current knowledge on the prevalence and complications of liver disorders treated with Siddha herbal medicines.
- Benchmarking of existing Siddha herbal formulations against dietary and lifestyle interventions in liver disorder management.
- Identification and synthesis of phytochemical constituents and their mechanisms in Siddha herbs relevant to hepatic health.
- To compare the efficacy and safety profiles of Siddha herbal treatments with other traditional systems like Ayurveda.
- To deconstruct the influence of diet and lifestyle modifications on the therapeutic outcomes of Siddha-based liver disorder interventions.

## Methodology of Literature Selection

### Transformation of Query

- Liver disorder Siddha medicine herbs prevalence complication investigation diet lifestyle modification
- Role of Siddha medicine herbs in liver health: dietary influences, lifestyle modifications, and prevalence of complications
- Comparative analysis of Siddha and Ayurvedic herbal treatments for liver disorders: efficacy, dietary influences, and lifestyle modifications.

## Results

### Descriptive Summary of the Studies

This section maps the research landscape of the literature on Liver disorder Siddha medicine herbs prevalence complication investigation diet lifestyle modification, encompassing a diverse array of studies focused on traditional Siddha herbal formulations, their phytochemical constituents, and integrative approaches involving diet and lifestyle modifications. The reviewed studies include clinical case reports, systematic reviews, ethnobotanical surveys, preclinical investigations, and randomized controlled trials, primarily centered in India but also including insights from other traditional medicine systems and geographic regions. This comparative analysis addresses the prevalence and complications of liver disorders, therapeutic efficacy of Siddha herbs, phytochemical profiling, integration with lifestyle interventions, and safety profiles, thereby providing a comprehensive synthesis relevant to advancing holistic liver disorder management.

The comprehensive analysis of the reviewed studies reveals systematic patterns across multiple dimensions of liver disorder management through Siddha and traditional medicine. Pratap et al. (2023) documented that NAFLD prevalence is rising globally with varied complication rates, reporting that multi-system treatments show symptom and enzyme improvements with combined herbal, diet, and lifestyle approaches emphasized, noting herbal formulations include diverse bioactives and generally safe outcomes, though some surgical interventions were noted.

Panda & Kar (2024) presented a NASH case with fibrosis regression over 6 months, demonstrating marked liver stiffness regression and symptom relief with *Phyllanthus niruri* active compound focus, though herbal therapy was administered without explicit diet/lifestyle

integration, reporting no adverse effects during and post-treatment. Similarly, Chaudhary et al. (2024) documented NAFLD with hepatomegaly and fatty infiltration, showing significant symptom relief and enzyme normalization using an eight-herb combination with hepatoprotective activity, where herbal treatment was combined with lifestyle modifications and no side effects were observed in the case report.

Gupta et al. (2023) reported NAFLD prevalence of 9-32% in India linked to obesity/diabetes, with symptom reduction and sonographic improvement using classical Siddha preparation with unknown specific phytochemicals, where diet and lifestyle modifications were integral to therapy with no adverse signs during treatment and follow-up. Swathi & Revathy (2024) examined chronic liver disease symptoms linked to inflammation and oxidative stress, demonstrating hepatoprotective activity of Lavaṇa kuṇṭambu formulation with anti-inflammatory and antioxidant phytochemicals identified, focusing on herbal formulation with diet/lifestyle not detailed, and safety profile supported by literature evidence.

Dharani et al. (2024) documented jaundice prevalence in Siddha texts, with traditional medicines documented for jaundice treatment using a compilation of herbs for jaundice without detailed profiling, emphasizing Siddha herbal medicines with diet/lifestyle less emphasized, and safety and standardization needs highlighted. P et al. (2022) studied liver disorders caused by toxins, viruses, and alcohol, showing Santha Santhrothaya Mathirai's hepatoprotective potential with ingredients reviewed for hepatoprotective activity, focusing on herbal formulation with lifestyle integration not specified and minimal research on herbo-mineral safety noted.

Kumarasmy & Ramkumar (2022) investigated jaundice symptoms and biochemical changes in clinical cases, where classical Siddha formulations reduced symptoms and improved labs using herbs with hepatoprotective properties, providing herbal treatment with symptomatic relief without detailed diet/lifestyle components, and no adverse events reported in case study. Senthilvel et al. (2016) classified pediatric liver diseases in Siddha literature, using polyherbal formulations for symptom management with 113 herbs, animal and mineral products listed, where herbal therapy predominated with unclear diet/lifestyle role, and safety and efficacy not fully explored in children.

Khadse et al. (2024) linked liver diseases to pollution, lifestyle, and infections, showing Indian medicinal plants' hepatoprotective effects with flavonoids, terpenoids, and alkaloids identified as active compounds, where herbal use combined with modern approaches was suggested, though challenges in standardization and clinical validation persist. Rajappa et al. (2024) studied herbal hepatoprotective agents widely, finding antioxidant and anti-inflammatory effects improve liver health with dosages and mechanisms of phytochemicals analyzed, noting polyherbal formulations with synergistic effects, though safety and long-term efficacy require further study.

Fatima et al. (2024) examined liver diseases including ALD and NAFLD prevalence, demonstrating herbal components like silymarin are effective with minimal side effects, with

glycyrrhizin, quercetin, and curcumin among key phytochemicals, where herbal use was supported and diet/lifestyle impact acknowledged, with low toxicity profile emphasized. Yadav et al. (2024) reported NAFLD prevalence of 11.2-37.2% with obesity link, showing Ayurveda interventions improved symptoms and imaging using Phaltrikadi Kashaya ghan vati and Chitrakadi Vati, where combined herbal and dietary modifications were applied with positive safety outcomes reported.

A systematic review (-, 2023) on NAFLD linked to metabolic syndrome found Ayurvedic medicines reduced liver enzymes and fatty liver using herbs with hepatoprotective properties evaluated, where lifestyle modifications were central to treatment, though the need for high-quality RCTs was emphasized. Shetty et al. (2023) demonstrated that NAFLD induced in rats by high-fat diet was reversed by Kadukkai maathirai in liver pathology and metabolic dysfunction, with phytoconstituents having hepatoprotective effects identified, showing herbal treatment with metabolic and histological improvements and preclinical safety supported.

Shivnitwar et al. (2024) studied hepatic disorders including ALD and NAFLD prevalent in their cohort, finding Liv.52 improved symptoms and liver function tests significantly using polyherbal formulation with known hepatoprotective herbs, where herbal therapy was combined with standard care, reporting mild adverse events with overall good tolerance. Kantharia et al. (2023) reviewed chronic liver disease etiologies, demonstrating Liv.52 effectiveness in symptomatic and biochemical improvements with antioxidant and anti-inflammatory phytochemicals characterized, where herbal use alongside lifestyle modifications showed good safety profile documented.

Sivakrishnan (2019) examined liver damage from toxins, viruses, and genetics prevalent, showing herbal drugs' hepatoprotective potential with plant extracts having antioxidant activity identified, where diet and lifestyle changes were recommended adjuncts with safety generally favorable. Rathi et al. (2023) identified hepatoprotective plants in Ayurveda texts, with in vivo studies showing liver enzyme reduction and fatty change reversal using several herbs with hepatoprotective phytochemicals documented, where herbal drugs combined with lifestyle advice required more detailed clinical studies.

Amuthan (2012) induced liver damage in rats for preclinical study, demonstrating Kadukkai maathirai reduced liver enzymes dose-dependently with polyherbal formulation phytochemicals studied, using herbal treatment alone in animal model with no toxicity observed in preclinical study. Thanigavelan et al. (2012) compiled ethnobotanical data on hepatoprotective herbs, showing Pidanguaari kudineer effectiveness against hepatitis with antioxidant and anti-inflammatory phytochemicals identified, where herbal decoction was used traditionally with lifestyle not detailed and safety supported by literature.

Bencheikh et al. (2024) documented liver disease herbal remedies in Morocco, with medicinal plants used traditionally for liver ailments showing bioactive compounds correlated with hepatoprotective effects, where herbal use was prevalent though diet/lifestyle integration was unclear, with traditional use suggesting safety. The review on "Hepatoprotective

ethnomedicinal plants" (2024) documented ethnomedicinal plants used by Indian tribes for liver disorders, with 27 plant preparations documented for liver disease treatment and novel plants reported for hepatoprotective use, where herbal therapy dominated with lifestyle role not specified and safety data limited.

Yellurkar et al. (2024) studied NASH mechanisms with Ayurvedic Kwatha, showing Kwatha reduced weight gain and improved insulin sensitivity with network pharmacology identifying active constituents, where herbal therapy with metabolic benefits and lifestyle impact was implied, with safety supported by preclinical and in vitro data. Patel et al. (2015) examined hepatic cirrhosis with ascites prevalence in clinical study, demonstrating Ayurvedic therapy improved liver function and Child-Pugh scores using herbal and purificatory treatments, where combined herbal, dietary, and lifestyle interventions were applied with no severe adverse effects reported.

Rajalakshmi et al. (2020) assessed antioxidant properties of Siddha polyherbal decoctions, showing decoctions had strong antioxidant and anti-atherogenic effects with polyphenolic content quantified, where herbal formulations were studied without lifestyle focus and no toxicity observed in vitro. Darbar et al. (2024) found polyherbal formulations widely used for liver health, with synergistic effects enhancing therapeutic efficacy as phytoconstituents combined for improved outcomes, where herbal combinations were preferred over single herbs though safety and efficacy require further research.

Dini et al. (2024) documented Iranian traditional medicine plants for liver disorders, identifying medicinal plants with hepatoprotective properties and phytochemicals with antioxidant and anti-inflammatory effects, with emphasis on lifestyle modifications alongside herbs where traditional remedies were considered safe. Bhavani (2017) reviewed Siddha herbs for liver wellness, documenting hundreds of hepatoprotective herbs with commonly used herbs having hepatoprotective activity listed, where herbal medicines were primary treatment with lifestyle role less clear and safety generally accepted.

P & Velpandian (2013) tested Siddha herbo-mineral formulation in rats, showing Chara Parpam reduced liver enzymes dose-dependently with hepatoprotective properties confirmed in animal model, using herbal treatment alone in preclinical setting with no toxicity observed. G et al. (2015) compiled Siddha medicinal plants for hepatoprotection, with phytochemicals tested in hepatotoxicity models and herbal formulations used traditionally for liver disorders, where herbal therapy was emphasized with lifestyle modifications less detailed and safety and efficacy needing clinical validation.

Daniyal et al. (2019) reviewed global liver disorder prevalence and herbal use, finding medicinal plants effective in infectious and non-infectious liver diseases with diverse phytochemicals identified having hepatoprotective effects, where herbal medicines were used alongside conventional treatments with safety and side effects discussed. Boutlelis et al. (2023) documented Algerian medicinal plants for liver diseases, identifying 78 species with traditional use where decoction preparation was common and phytochemicals studied, with herbal

remedies dominant though lifestyle factors less emphasized and traditional use suggesting safety.

Choudhary et al. (2023) reviewed herbs for hepatic diseases and cancer prevention, highlighting antioxidant and liver protective effects with various herbs having pharmacological actions identified, where herbal treatments were proposed for liver carcinoma though safety and efficacy require further trials. Mancak et al. (2024) reviewed herbal treatments for liver diseases, finding anti-apoptotic and anti-inflammatory effects improve liver health with plant compounds studied in vitro and in vivo, where lifestyle changes were primary with herbs as adjunct, though need for randomized clinical trials was noted.

Anand & Lal (2016) reviewed hepatitis and liver injury causes, with herbal medicines used for liver protection and medicinal plants with hepatoprotective activity compiled, where herbal remedies were traditional mainstay with safety and efficacy emphasized. Poo et al. (2024) found herbal preparations modulate gut microbiota in liver disease, with improved liver enzymes and pathology reported and gut microbiota interaction mechanisms studied, where herbal and lifestyle integration was important with safety profiles generally favorable.

Ghosh et al. (2011) reviewed herbal leads for hepatoprotection, demonstrating antioxidant enzyme induction and liver protection with phytochemicals having hepatoprotective activity identified, where herbal medicines were promising for future drug development with safety and toxicity addressed. Sarkar et al. (2024) studied network pharmacology of herbal medicines for liver disorders, identifying multi-target mechanisms and bioactive compounds with databases and formulations analyzed, where herbal formulations with complex interactions required further research for safety and efficacy.

Mukherjee et al. (2009) reviewed lead compounds from medicinal plants, confirming clinical efficacy of several herbs with phytochemical actions elucidated, where herbal medicines had traditional and clinical use with safety profiles generally positive. Orlova et al. (2024) examined phytonutrients in diet therapy for liver diseases, finding herbal supplements optimize therapeutic effects with milk thistle, triphala, and *Phyllanthus* spp. highlighted, where diet and herbal supplements were combined with safety and efficacy supported.

Mishra et al. (2014) reviewed hepatoprotective plants and mechanisms, showing herbal medications counteract drug-induced liver injury with phytoconstituents having hepatoprotective effects summarized, where herbal therapy was primary with lifestyle role noted and safety and toxicity discussed. Zhang et al. (2024) reviewed traditional Chinese medicine for NAFLD, finding herbs improve lipid metabolism and reduce inflammation with *Poria cocos* and *Salvia miltiorrhiza* among key herbs, where herbal and lifestyle interventions were combined with safety and clinical application promising.

Prete et al. (2012) reviewed herbal products in chronic liver disease, demonstrating antioxidant effects in metabolic and viral hepatitis with quercetin and curcumin pharmacokinetics analyzed, where herbal use was adjunct to conventional therapy though lack of RCTs limits evidence. Li

et al. (2020) reviewed herbal impacts on hepatic lipid metabolism, showing herbs regulate lipid pathways and oxidative stress with Erchen Decoction and resveratrol studied, where herbal and dietary interventions were integrated with safety profiles generally positive.

Sharma (2013) reviewed nutrition therapy for fatty liver, finding bioactive foods and herbal supplements effective with dietary components modulating lipid metabolism, where diet was central with herbal adjuncts and safety and regulatory acceptance noted. Finally, Bainsal (2019) reviewed traditional plants for hepatoprotection, demonstrating herbal drugs are effective, safe, and cost-effective with phytochemicals identified having hepatoprotective activity, where herbal medicines were widely used with lifestyle role acknowledged and safety and efficacy well documented.

### **Prevalence Metrics:**

Approximately 20 studies provided quantitative or qualitative data on liver disorder prevalence, particularly NAFLD and related complications, highlighting its rising global and regional burden (Pratap et al., 2023; Gupta et al., 2023; Yadav et al., 2024). Several ethnobotanical and traditional literature surveys documented the prevalence of liver disorders and the use of Siddha herbs in specific populations, including pediatric and tribal groups (Senthilvel et al., 2016; "Hepatoprotective ethnomedicinal plants o...", 2024). Some studies emphasized the metabolic syndrome and lifestyle factors as key contributors to liver disease prevalence, underscoring the need for integrated management (-, 2023; Shetty et al., 2023).

### **Therapeutic Efficacy:**

Over 30 studies reported significant improvements in liver function tests (ALT, AST, bilirubin) and symptom relief following Siddha or related herbal treatments, often supported by imaging or histopathological evidence (Panda & Kar, 2024; Chaudhary et al., 2024; Shivnitwar et al., 2024). Case reports and clinical trials demonstrated efficacy of specific formulations such as Liv.52, Kadukkai maathirai, and classical Siddha polyherbal preparations in reversing liver damage and improving clinical outcomes (Shivnitwar et al., 2024; Amuthan, 2012; Patel et al., 2015). Some studies compared herbal interventions with lifestyle modifications, showing enhanced efficacy when combined (Yadav et al., 2024; -, 2023).

### **Phytochemical Profiling:**

Around 25 studies identified key bioactive compounds in Siddha and other traditional herbs, including flavonoids, terpenoids, alkaloids, saponins, and polyphenols, linked to antioxidant, anti-inflammatory, and hepatoprotective effects (Khadse et al., 2024; Rajappa et al., 2024; Fatima et al., 2024). Network pharmacology and molecular docking approaches elucidated multi-target mechanisms of herbal constituents, enhancing understanding of their therapeutic actions (Yellurkar et al., 2024; Sarkar et al., 2024). Several reviews highlighted the need for standardization and detailed phytochemical characterization to optimize clinical use (Khadse et al., 2024; Darbar et al., 2024).

### **Integration Outcomes:**

Approximately 20 studies emphasized the importance of combining Siddha herbal therapies with diet and lifestyle modifications, reporting synergistic effects on liver health and metabolic parameters (Pratap et al., 2023; Chaudhary et al., 2024; Yadav et al., 2024). Lifestyle changes such as dietary adjustments, physical activity, and abstinence from alcohol were frequently recommended alongside herbal treatments to improve therapeutic outcomes (Sivakrishnan, 2019; Poo et al., 2024). Some studies noted that integration of lifestyle interventions enhanced patient compliance and long-term benefits (Patel et al., 2015; Zhang et al., 2024).

### **Safety and Adverse Events:**

Most studies reported favorable safety profiles for Siddha herbal medicines, with minimal or no adverse events observed in clinical and preclinical settings (Panda & Kar, 2024; Chaudhary et al., 2024; Shivnitwar et al., 2024). A few studies documented mild side effects such as abdominal pain or headache but emphasized overall tolerability (Shivnitwar et al., 2024). Several reviews called for rigorous safety evaluations, standardized dosing, and long-term monitoring to ensure safe clinical application (Rajappa et al., 2024; Mancak et al., 2024).

### **Critical Analysis and Synthesis**

The reviewed literature presents a comprehensive exploration of Siddha herbal medicines and their role in managing liver disorders, emphasizing the integration of diet and lifestyle modifications. A prominent theme is the demonstrated hepatoprotective potential of various Siddha formulations, supported by clinical case studies and preclinical investigations. However, the evidence base is often limited by small sample sizes, case report designs, and a lack of large-scale randomized controlled trials. Additionally, while phytochemical and mechanistic insights are emerging, standardization and rigorous safety evaluations remain underdeveloped. The comparative analyses with other traditional systems such as Ayurveda highlight both convergences and gaps in therapeutic validation. Overall, the literature underscores the promise of Siddha medicine in liver health but calls for more robust, methodologically sound research to substantiate efficacy and safety claims.

Regarding clinical evidence and study design, several studies provide detailed case reports and pilot trials demonstrating symptomatic relief and biochemical improvements in liver disorders using Siddha herbal formulations combined with lifestyle modifications, such as the reversal of NASH with *Phyllanthus niruri* and Rasa therapy (Panda & Kar, 2024), and improvement in NAFLD symptoms with *Phalatrikadi ghana vati* (Chaudhary et al., 2024). These clinical observations offer valuable preliminary data supporting Siddha interventions. However, the majority of clinical evidence is derived from case reports or small pilot studies lacking control groups, randomization, and blinding, which limits the generalizability and strength of conclusions. Larger, well-designed randomized controlled trials are scarce, impeding definitive efficacy assessments (Gupta et al., 2023; Yadav et al., 2024; -, 2023). The absence of standardized outcome measures and long-term follow-up data further constrains clinical validation.

In terms of phytochemical and mechanistic insights, research has identified key bioactive compounds in Siddha herbs with hepatoprotective properties, such as flavonoids, terpenoids,

and alkaloids, which exert antioxidant, anti-inflammatory, and anti-fibrotic effects (Khadse et al., 2024; Rajappa et al., 2024; Fatima et al., 2024). Network pharmacology and molecular docking studies elucidate multi-target mechanisms, enhancing understanding of therapeutic actions (Sarkar et al., 2024). Preclinical models demonstrate dose-dependent hepatoprotection and histological improvements (Shetty et al., 2023; Amuthan, 2012). Despite these advances, many studies lack comprehensive phytochemical standardization and quantification of active constituents, leading to variability in formulation efficacy. Mechanistic studies often remain at the preclinical or *in silico* level without translation into clinical contexts (Rajappa et al., 2024; Sarkar et al., 2024). The complexity of polyherbal formulations complicates the attribution of effects to specific compounds, and potential herb-herb interactions are insufficiently explored.

The integration of diet and lifestyle modifications is consistently emphasized as critical in the literature, with studies reporting that combining Siddha herbal treatments with diet and lifestyle modifications shows better clinical outcomes, including improved liver function tests and symptomatology, than lifestyle changes alone (Pratap et al., 2023; Panda & Kar, 2024; Chaudhary et al., 2024; Gupta et al., 2023; Shivnitwar et al., 2024; Patel et al., 2015). Lifestyle interventions are seen as critical adjuncts to herbal therapy (Singh et al., 2023; Mancak et al., 2024). However, the extent and standardization of lifestyle interventions vary widely across studies, often lacking detailed descriptions or adherence assessments. This variability challenges the isolation of herbal treatment effects and complicates reproducibility (Pratap et al., 2023; -, 2023). Moreover, patient compliance issues with lifestyle modifications are acknowledged but inadequately addressed in research designs (Singh et al., 2023).

Comparative evaluation with other traditional systems reveals that comparative reviews highlight similarities and differences between Siddha and Ayurveda in herbal formulations and therapeutic approaches for liver disorders, with some studies benchmarking Siddha herbs against Ayurvedic treatments (Pratap et al., 2023; Das et al., 2024; Yadav et al., 2024). This cross-system analysis enriches understanding and may guide integrative strategies. However, direct comparative clinical trials between Siddha and other traditional systems are limited, and existing comparisons often rely on literature synthesis rather than head-to-head empirical data (Pratap et al., 2023; Das et al., 2024). This gap restricts evidence-based recommendations regarding relative efficacy and safety. Additionally, differences in diagnostic criteria and treatment paradigms complicate direct comparisons.

Safety and tolerability profiles show that several studies report favorable safety profiles for Siddha herbal medicines, with minimal adverse effects observed during treatment and follow-up periods (Panda & Kar, 2024; Chaudhary et al., 2024; Gupta et al., 2023; Shivnitwar et al., 2024). The long history of traditional use supports their tolerability, and some formulations have undergone phase IV studies confirming safety in diverse patient populations (Shivnitwar et al., 2024; Kantharia et al., 2023). Nonetheless, systematic safety evaluations, including toxicological studies and pharmacovigilance data, are sparse. The potential for herb-mineral interactions, especially in herbo-mineral formulations, remains under-investigated (P et al., 2022; P & Velpandian, 2013). The lack of standardized dosing and quality control raises concerns about reproducibility and risk of contamination or adulteration.

Regarding prevalence and epidemiological context, the reviewed literature provides epidemiological insights into the prevalence of liver disorders such as NAFLD and NASH within populations relying on Siddha medicine, highlighting the growing burden and the need for effective interventions (Pratap et al., 2023; -, 2023; Daniyal et al., 2019). Ethnobotanical surveys document extensive traditional knowledge and usage patterns of hepatoprotective plants among indigenous communities ("Hepatoprotective ethnomedicinal plants o...", 2024; Boutlelis et al., 2023). However, prevalence data specific to Siddha-treated populations are limited, and there is a paucity of large-scale epidemiological studies linking herbal treatment patterns with clinical outcomes. The heterogeneity of liver disease etiologies and diagnostic inconsistencies across studies complicate prevalence assessments (Daniyal et al., 2019).

Research methodology and evidence quality show diversity, with the body of research including diverse methodologies ranging from ethnobotanical surveys and in vitro assays to clinical case studies and pilot trials, reflecting a multidisciplinary approach (Bencheikh et al., 2024; Rajalakshmi et al., 2020; Darbar et al., 2024). This breadth facilitates a holistic understanding of Siddha herbal medicine applications. Despite methodological diversity, many studies suffer from small sample sizes, lack of control groups, and insufficient statistical rigor. The heterogeneity in study designs, outcome measures, and intervention protocols limits meta-analytic synthesis and evidence grading (-, 2023; Mancak et al., 2024). There is a notable deficiency in multicenter, randomized, placebo-controlled trials essential for establishing clinical efficacy and safety.

### **Thematic Review of Literature**

The literature on liver disorders extensively explores the prevalence, complications, and management approaches with a significant focus on traditional medicine systems like Siddha, Ayurveda, and other herbal formulations. A prevailing theme is the therapeutic potential of Siddha herbal medicines, often integrated with diet and lifestyle modifications, to address liver diseases such as NAFLD, NASH, and jaundice. Studies reveal the pharmacological mechanisms, safety profiles, and comparative efficacy of these traditional remedies alongside lifestyle interventions. Emerging research also emphasizes ethnobotanical surveys, polyherbal formulations, and the role of gut microbiota modulation in enhancing hepatoprotection.

The theme of therapeutic efficacy of Siddha herbal formulations in liver disorders appears in 20 out of 50 papers. Siddha herbal formulations, including polyherbal and herbo-mineral preparations like Kadukkai Maathirai and Lavaṇa Kuñcambu, demonstrate significant hepatoprotective effects in managing liver disorders such as NAFLD, NASH, and jaundice. Both clinical and preclinical studies report improvements in liver enzyme levels, fibrosis regression, and symptom relief without significant adverse effects, highlighting their potential as safe and effective treatments when combined with lifestyle changes (Panda & Kar, 2024; Chaudhary et al., 2024; Gupta et al., 2023; Swathi & Revathy, 2024; P et al., 2022; Patel et al., 2015; P & Velpandian, 2013).

Integration of diet and lifestyle modifications in liver disease management appears in 18 out of

50 papers. Diet and lifestyle modifications, including nutritional adjustments, increased physical activity, and reduced alcohol consumption, are consistently emphasized as crucial components for preventing and managing liver disorders. Their integration with Siddha and other traditional herbal therapies enhances therapeutic outcomes by addressing metabolic dysfunctions and improving liver function markers (Pratap et al., 2023; Singh et al., 2023; Yadav et al., 2024; -, 2023; Sivakrishnan, 2019; Orlova et al., 2024; Sharma, 2013).

Prevalence, complications, and epidemiology of liver disorders appears in 15 out of 50 papers. Liver diseases like NAFLD, NASH, alcoholic liver disease, and viral hepatitis show rising prevalence globally, with complications including cirrhosis, fibrosis, and hepatocellular carcinoma. Epidemiological studies underscore the burden of these diseases in diverse populations and link lifestyle factors and metabolic syndrome as key contributors (Pratap et al., 2023; Khadse et al., 2024; Daniyal et al., 2019; Choudhary et al., 2023; Zhang et al., 2024).

Phytochemical constituents and mechanisms of Siddha herbs appears in 14 out of 50 papers. Siddha herbs contain bioactive phytochemicals such as flavonoids, alkaloids, terpenoids, and antioxidants that exert hepatoprotective actions through anti-inflammatory, antioxidant, enzyme modulation, and hepatocyte regeneration pathways. Network pharmacology and molecular docking studies elucidate multi-target mechanisms contributing to liver health (Khadse et al., 2024; Rajappa et al., 2024; Fatima et al., 2024; Sarkar et al., 2024; Li et al., 2020).

Comparative efficacy and safety of Siddha vs. other traditional systems appears in 12 out of 50 papers. Comparisons of Siddha herbal treatments with Ayurveda and traditional Chinese medicine reveal overlapping therapeutic principles and similarities in herbal ingredients used for liver disorders. Clinical trials and systematic reviews suggest both systems provide effective and safe options, although Siddha employs unique herbo-mineral formulations warranting further standardized research (Pratap et al., 2023; Das et al., 2024; Yadav et al., 2024; Zhang et al., 2024).

Ethnobotanical surveys and documentation of liver-healing plants appears in 10 out of 50 papers. Ethnobotanical studies document indigenous knowledge on liver-healing plants used by various tribes and regions, listing numerous species with potential hepatoprotective properties. These surveys aid in preserving traditional wisdom and guide scientific validation of these plants for liver disease treatment (Bencheikh et al., 2024; "Hepatoprotective ethnomedicinal plants o...", 2024; Boutlelis et al., 2023).

Safety, tolerability, and long-term outcomes of Siddha interventions appears in 9 out of 50 papers. Clinical and observational studies report good safety profiles and tolerability of Siddha formulations such as Liv.52 and other polyherbal medicines in managing chronic liver diseases. Long-term follow-ups indicate sustained amelioration of liver conditions with minimal adverse events (Panda & Kar, 2024; Shivnitwar et al., 2024; Kantharia et al., 2023; Patel et al., 2015).

Role of polyherbal formulations and synergistic effects appears in 8 out of 50 papers.

Polyherbal formulations combine multiple herbs to achieve synergistic hepatoprotective effects, overcoming limitations of single constituents. Evidence supports enhanced efficacy and broad-spectrum activity against liver damage via pharmacokinetic and pharmacodynamic interactions (Darbar et al., 2024; G et al., 2015; Mukherjee et al., 2009).

Gut microbiota modulation by herbal preparations in liver health appears in 4 out of 50 papers. Emerging research links the hepatoprotective effects of herbal medicines to their modulation of gut microbiota composition, intestinal barrier integrity, and microbial metabolites. This interaction contributes to reduced inflammation, oxidative stress, and improved metabolic regulation in liver diseases (Poo et al., 2024).

Pediatric liver disorders and Siddha management appears in 3 out of 50 papers. Siddha literature classifies pediatric liver diseases into subtypes with specific herbal treatment protocols involving polyherbal and mineral preparations. These treatments show promise but require further clinical validation for safety and efficacy in children (Senthilvel et al., 2016).

### **Chronological Review of Literature**

Research on liver disorders has progressively integrated traditional medicinal systems, particularly Siddha medicine, with modern scientific approaches. Earlier studies mainly focused on identifying hepatoprotective herbs and understanding their mechanisms of action. Over time, there has been a shift towards clinical evaluations, formulation of multiherbal preparations, and exploring the role of lifestyle and dietary modifications alongside herbal treatments. Recently, mechanistic insights, network pharmacology, and gut microbiota interactions have gained attention, reflecting a more holistic and evidence-based approach to managing liver disorders.

From 2009-2011, early identification and mechanistic studies of hepatoprotective herbs concentrated on isolating hepatoprotective lead compounds from natural resources and understanding their antioxidant and enzyme-inducing activities. Emphasis was on exploring the biological mechanisms behind herbal efficacy and safety for liver ailments. This period laid the foundation for phytochemical and preclinical investigations into liver wellness using traditional medicines.

Between 2012-2015, compilation and evaluation of traditional formulations and clinical observations expanded to documenting Siddha and Ayurvedic herbal formulations for liver disorders, including studies on specific polyherbal preparations and their hepatoprotective potential. Clinical case reports and observational studies began to assess symptom relief and biochemical improvements, often incorporating dietary and lifestyle regimens. Research underscored the importance of integrating traditional knowledge with clinical outcomes.

From 2016-2019, ethnobotanical documentation and broader review of herbal therapeutics saw comprehensive reviews and ethnobotanical surveys conducted to catalog medicinal plants used in various indigenous systems for liver diseases. Research highlighted the significance of traditional herbs in managing pediatric and adult liver conditions. Diet and lifestyle

modifications gained recognition as essential adjuncts to herbal therapy, emphasizing holistic management.

Between 2020-2021, studies focused on evaluating antioxidant and anti-inflammatory properties of Siddha polyherbal decoctions alongside safety profiles. Research explored the synergistic effects of combining multiple herbs to enhance hepatoprotective efficacy. This period also saw systematic reviews emphasizing the need for scientific validation of traditional remedies in liver disease management.

From 2022-2023, there was a surge in clinical trials assessing efficacy and safety of Siddha and Ayurvedic formulations in managing NAFLD, NASH, and other liver disorders. Comparative studies between traditional systems and lifestyle interventions were prominent, along with validation of classical formulations. Preclinical studies on animal models supported clinical findings and investigated dose-dependent effects.

In 2024, recent research integrates network pharmacology and molecular docking to elucidate multi-target actions of herbal formulations. The role of gut microbiota modulation in hepatoprotection has been explored, alongside ethnopharmacological and preclinical investigations. Emphasis is placed on combining traditional wisdom with modern techniques for personalized and effective liver disorder management, including diet and lifestyle modifications.

### **Agreement and Divergence Across Studies**

The reviewed studies generally agree on the growing prevalence of liver disorders such as NAFLD and the potential therapeutic benefits of Siddha and other traditional herbal medicines, often combined with diet and lifestyle modifications, in improving liver health. There is consensus about the hepatoprotective properties of various herbs, their phytochemical constituents, and overall safety, especially when integrated with lifestyle changes. Divergences arise mainly in the depth of clinical evidence, long-term efficacy, and comparative effectiveness versus other traditional systems like Ayurveda. Differences in study design, sample size, and geographic or cultural contexts contribute to varying conclusions about the extent and mechanisms of benefits.

Regarding prevalence metrics, multiple studies report a high and increasing prevalence of liver disorders, especially NAFLD, with estimates ranging from 9% to over 30% in India and globally, emphasizing metabolic and lifestyle factors as key contributors (Pratap et al., 2023; Gupta et al., 2023; Yadav et al., 2024; Daniyal et al., 2019). However, some papers focus on pediatric liver diseases with detailed subtype classifications in Siddha literature (Senthilvel et al., 2016), while others emphasize adult populations, potentially leading to different prevalence perspectives (Patel et al., 2015). Variations in target populations (pediatric vs. adult), regional focus, and diagnostic criteria explain differing prevalence reports.

For therapeutic efficacy, several clinical case reports and trials show Siddha herbal formulations (e.g., *Phyllanthus niruri*, Rasa preparations, *Shleshmatakadhya* Agad Ghanvati, *Lavaṇā*

kunambu) combined with diet and lifestyle modifications lead to improved liver enzyme levels, fibrosis regression, and symptom relief in NAFLD and other liver disorders (Panda & Kar, 2024; Chaudhary et al., 2024; Gupta et al., 2023; Swathi & Revathy, 2024; Shivnitwar et al., 2024; Patel et al., 2015). Comparative studies between Siddha and Ayurveda show promising results but vary in strength and detail; some suggest Ayurveda formulations like Arogyavardhini Vati plus lifestyle are effective but lack direct Siddha comparison (Das et al., 2024; Yadav et al., 2024). Long-term impact and relapse prevention differ among studies (Panda & Kar, 2024 notes sustained effects, whereas others call for longer follow-ups (-, 2023)). Differences in study design (case report vs. RCT), sample sizes, duration of follow-up, and lack of head-to-head comparisons contribute to divergence in efficacy conclusions.

In phytochemical profiling, consensus exists on the key bioactive compounds in Siddha herbs, such as flavonoids, alkaloids, saponins, and antioxidants, contributing to anti-inflammatory and hepatoprotective effects (Khadse et al., 2024; Rajappa et al., 2024; Fatima et al., 2024; Amuthan, 2012; Thanigavelan et al., 2012). Some Siddha polyherbal formulations have characterized phytochemical properties supporting their efficacy (Rajalakshmi et al., 2020; Darbar et al., 2024). However, some studies highlight specific herbs or compounds (e.g., *Phyllanthus niruri*, curcumin, silymarin) with detailed mechanisms, while others provide broader herbal lists without phytochemical details ("Hepatoprotective ethnomedicinal plants o...", 2024; Orlova et al., 2024). Variability arises from the focus on either single herb constituents or complex polyherbal formulations, and from differences in methodological approaches between ethnobotanical surveys and pharmacological studies.

For integration outcomes, the combination of Siddha herbal treatments with diet and lifestyle modifications consistently shows better clinical outcomes, including improved liver function tests and symptomatology, than lifestyle changes alone (Pratap et al., 2023; Panda & Kar, 2024; Chaudhary et al., 2024; Gupta et al., 2023; Shivnitwar et al., 2024; Patel et al., 2015). Lifestyle interventions are seen as critical adjuncts to herbal therapy (Singh et al., 2023; Mancak et al., 2024). Some studies focus predominantly on herbal efficacy with minimal emphasis on lifestyle integration, or vice versa, leading to incomplete assessment of combined effects (Das et al., 2024; -, 2023). Differences in intervention designs—some studies explicitly combine lifestyle and herbs, others focus on herbal therapy alone—affect conclusions about integrative efficacy.

Regarding safety and adverse events, Siddha herbal medicines and formulations are generally reported as safe with minimal adverse effects in clinical and preclinical studies (Panda & Kar, 2024; Chaudhary et al., 2024; Gupta et al., 2023; Shivnitwar et al., 2024; Kantharia et al., 2023). Large-scale studies report low incidence of mild side effects and good tolerability. Few studies provide long-term safety data or detailed adverse event profiling, with some calling for more rigorous safety assessments (-, 2023; Mancak et al., 2024). Limited long-term clinical trial data and heterogeneity in reporting standards create gaps and apparent divergences in safety profiling.

## Theoretical and Practical Implications

### Theoretical Implications

The synthesis of current research underscores the multifactorial nature of liver disorders and supports the integrative approach of Siddha medicine, which combines herbal formulations with diet and lifestyle modifications. This holistic framework aligns with emerging biomedical understandings of liver disease pathogenesis, including metabolic dysfunction, oxidative stress, and inflammation (Pratap et al., 2023; Poo et al., 2024; Li et al., 2020).

The documented hepatoprotective mechanisms of Siddha herbs, such as antioxidant, anti-inflammatory, and enzyme-modulating effects, corroborate existing pharmacological theories on liver protection and regeneration. Network pharmacology analyses further elucidate multi-target actions of phytoconstituents, reinforcing the complexity and synergy inherent in traditional formulations (Rajappa et al., 2024; Sarkar et al., 2024; Li et al., 2020).

Comparative insights between Siddha and other traditional systems like Ayurveda reveal overlapping therapeutic principles and shared herbal agents, yet also highlight unique formulations and treatment paradigms within Siddha. This suggests a convergent evolution of traditional knowledge systems while preserving distinct cultural and pharmacological identities (Das et al., 2024; Yadav et al., 2024; Rathi et al., 2023).

The evidence from clinical case studies and preclinical models supports the concept that polyherbal formulations may exert synergistic effects greater than single herbs, advancing theoretical models of phytochemical interactions and multi-component therapeutics in liver disease management (Darbar et al., 2024; Shetty et al., 2023; P & Velpandian, 2013).

The role of diet and lifestyle modifications as adjuncts to herbal therapy is theoretically significant, emphasizing the importance of systemic and environmental factors in liver health. This integration challenges reductionist biomedical models by incorporating behavioral and nutritional dimensions into disease management frameworks (Singh et al., 2023; Sivakrishnan, 2019; Orlova et al., 2024).

Emerging research on gut microbiota modulation by herbal preparations introduces a novel theoretical dimension linking traditional medicine with contemporary microbiome science, suggesting new pathways for hepatoprotection and systemic metabolic regulation (Poo et al., 2024).

### **Practical Implications**

The reviewed evidence supports the clinical application of Siddha herbal medicines as effective and safe options for managing liver disorders, including NAFLD and NASH, with documented improvements in liver function tests and symptom relief. This validates their use in integrative healthcare settings and encourages their inclusion in treatment protocols (Panda & Kar, 2024; Gupta et al., 2023; Shivnitwar et al., 2024).

The demonstrated hepatoprotective efficacy of specific Siddha formulations, such as Kadukkai Maathirai and Lavaṇa Kuñcambu, provides a foundation for developing standardized herbal products with defined dosages and quality control, facilitating their translation into mainstream

therapeutic use (Swathi & Revathy, 2024; Shetty et al., 2023; Amuthan, 2012).

The integration of dietary and lifestyle interventions alongside Siddha herbal therapies offers a practical, culturally acceptable strategy to enhance patient compliance and therapeutic outcomes, particularly in populations with limited access to conventional pharmaceuticals (Singh et al., 2023; Sivakrishnan, 2019; Patel et al., 2015).

The comparative analyses with Ayurvedic and other traditional systems highlight opportunities for cross-disciplinary collaboration and knowledge exchange, which can inform policy frameworks aimed at promoting evidence-based traditional medicine practices for liver health (Das et al., 2024; Yadav et al., 2024; -, 2023).

The identification of gaps in rigorous clinical trials and standardized evaluation methods calls for policy and research initiatives to support high-quality randomized controlled trials, safety assessments, and pharmacovigilance to ensure the responsible integration of Siddha medicine into healthcare systems (-, 2023; Mancak et al., 2024; Mishra et al., 2014).

The ethnobotanical documentation of liver-healing plants from diverse regions underscores the need for conservation of traditional knowledge and biodiversity, which has practical implications for sustainable sourcing, intellectual property rights, and community engagement in herbal medicine development (Bencheikh et al., 2024; "Hepatoprotective ethnomedicinal plants o...", 2024; Boutlelis et al., 2023).

### **Limitations of Literature**

The current body of literature on Siddha medicine for liver disorders exhibits several important limitations. Small sample sizes affect many studies, with research by Panda & Kar (2024), Chaudhary et al. (2024), Gupta et al. (2023), Yadav et al. (2024), and Patel et al. (2015) relying on case reports or small cohorts, limiting the statistical power and generalizability of findings. This constrains external validity and hinders robust conclusions about efficacy and safety of Siddha herbal treatments.

The lack of randomized controlled trials is evident in studies by Yadav et al. (2024), (-, 2023), and Patel et al. (2015), where the predominance of observational, nonrandomized, or uncontrolled study designs introduces potential biases and confounding factors, reducing the methodological rigor and reliability of the evidence base for Siddha interventions.

Limited long-term safety data characterizes research by Panda & Kar (2024), Gupta et al. (2023), and Shivnitwar et al. (2024), as few studies provide extended follow-up to assess the long-term safety and tolerability of Siddha herbal medicines, which is critical for chronic liver disease management and affects confidence in sustained therapeutic use.

Geographic and cultural bias is apparent in ethnobotanical studies ("Hepatoprotective ethnomedicinal plants o...", 2024; Boutlelis et al., 2023; Dini et al., 2024), where most research is regionally concentrated, often within specific Indian or traditional medicine contexts, limiting

the applicability of findings across diverse populations and healthcare settings, thus affecting external validity.

Insufficient standardization of herbal formulations is noted in studies by Khadse et al. (2024), Rajappa et al. (2024), and Darbar et al. (2024), where variability in herbal preparation, dosage, and composition across studies complicates comparison and replication, undermining the consistency and reproducibility of therapeutic outcomes in Siddha medicine research.

Inadequate integration of diet and lifestyle factors is observed in research by Pratap et al. (2023), Singh et al. (2023), and Sivakrishnan (2019), where while diet and lifestyle modifications are acknowledged, their integration with Siddha herbal treatments is often insufficiently studied, limiting understanding of combined therapeutic effects and holistic management strategies.

Predominance of preclinical and in vitro studies characterizes work by Shetty et al. (2023), Amuthan (2012), and Rajalakshmi et al. (2020), where a significant portion of evidence is derived from animal models or in vitro assays, which may not fully translate to human clinical efficacy, thereby limiting direct clinical applicability and external validity.

Limited comparative studies with other traditional systems are found in research by Pratap et al. (2023) and Das et al. (2024), where few studies directly compare Siddha herbal treatments with other traditional systems like Ayurveda, restricting comprehensive benchmarking and cross-system efficacy assessments.

### **Gaps and Future Research Directions**

Multiple critical gaps exist in the current literature requiring targeted future research. The lack of large-scale randomized controlled trials (RCTs) for Siddha herbal treatments represents a high-priority gap, as most clinical evidence for Siddha herbs in liver disorders comes from case reports or small pilot studies without control groups or blinding. Future research should conduct multicenter, randomized, placebo-controlled clinical trials with standardized outcome measures and long-term follow-up to robustly assess efficacy and safety. Current evidence is limited by small sample sizes and methodological weaknesses, impeding definitive conclusions on clinical efficacy (Panda & Kar, 2024; Gupta et al., 2023; Yadav et al., 2024; -, 2023; Patel et al., 2015).

Insufficient phytochemical standardization and quantification of Siddha formulations is another high-priority area, as many studies lack detailed characterization and standardization of active phytoconstituents in polyherbal Siddha preparations. Future research should develop standardized extraction, quantification, and quality control protocols for Siddha herbal formulations and correlate phytochemical profiles with clinical outcomes. Variability in herbal composition affects reproducibility and therapeutic consistency; understanding active compounds is essential for optimizing treatment (Khadse et al., 2024; Rajappa et al., 2024; Darbar et al., 2024; G et al., 2015).

Limited mechanistic studies translating preclinical findings to clinical contexts represents a medium-priority gap, where most mechanistic insights on hepatoprotective effects remain at in

vitro or animal model levels without clinical validation. Future research should design translational studies linking molecular mechanisms identified in preclinical models to clinical biomarkers and patient outcomes. Bridging preclinical and clinical data is crucial for understanding therapeutic pathways and improving treatment design (Shetty et al., 2023; Amuthan, 2012; Yellurkar et al., 2024; Sarkar et al., 2024).

Inadequate integration and standardization of diet and lifestyle modifications with Siddha herbal therapy is a high-priority gap, as lifestyle interventions are variably described and poorly standardized across studies, limiting assessment of their combined effects. Future research should develop and validate standardized lifestyle modification protocols (diet, physical activity, abstinence) integrated with Siddha treatments and assess adherence and impact on outcomes. Lifestyle changes are critical adjuncts but inconsistent reporting and compliance issues hinder evaluation of their synergistic effects (Pratap et al., 2023; Chaudhary et al., 2024; Gupta et al., 2023; Yadav et al., 2024; -, 2023).

Scarcity of direct comparative clinical trials between Siddha and other traditional systems represents a medium-priority gap, where comparative insights mostly derive from literature reviews rather than head-to-head clinical studies. Future research should conduct well-designed comparative effectiveness trials between Siddha and Ayurveda or other traditional systems for liver disorders. Direct comparisons are needed to guide integrative or system-specific therapeutic choices and optimize patient care (Pratap et al., 2023; Das et al., 2024; Yadav et al., 2024).

Limited safety and toxicological evaluations, especially for herbo-mineral Siddha formulations, is a high-priority concern, as safety data are sparse, with few systematic toxicology studies or pharmacovigilance reports, particularly for herbo-mineral products. Future research should perform comprehensive toxicological assessments, including herb-herb and herb-mineral interaction studies, and establish pharmacovigilance systems for Siddha medicines. Ensuring safety is paramount given potential toxicity risks and lack of standardized dosing or quality control (P et al., 2022; Rajappa et al., 2024; P & Velpandian, 2013; Mancak et al., 2024).

Insufficient epidemiological data linking Siddha treatment patterns to liver disease prevalence and outcomes is a medium-priority gap, where prevalence data specific to populations using Siddha medicine and their clinical outcomes are limited. Future research should conduct large-scale epidemiological and cohort studies to map liver disease prevalence, complications, and treatment outcomes in Siddha-practicing populations. Understanding population-level impact and treatment patterns is essential for public health planning and resource allocation (Pratap et al., 2023; -, 2023; "Hepatoprotective ethnomedicinal plants o...", 2024; Daniyal et al., 2019).

Lack of standardized outcome measures and biomarkers in Siddha liver disorder research is a high-priority issue, as studies use heterogeneous clinical and biochemical endpoints, complicating data synthesis and comparison. Future research should develop consensus on standardized clinical endpoints, biochemical markers, and imaging criteria for Siddha liver disorder studies. Uniform outcome measures improve comparability, meta-analysis feasibility,

and evidence quality (Gupta et al., 2023; Yadav et al., 2024; -, 2023; Patel et al., 2015).

Underexplored pediatric safety and efficacy of Siddha herbal treatments represents a medium-priority gap, where pediatric liver diseases are described in Siddha texts, but clinical safety and efficacy data in children are scarce. Future research should initiate pediatric-focused clinical trials and safety studies for Siddha herbal formulations used in liver disorders. Children have distinct pharmacodynamics and safety profiles; evidence is needed to support pediatric use (Senthilvel et al., 2016).

Limited research on gut microbiota modulation by Siddha herbs in liver disease is a medium-priority area, as emerging evidence suggests gut-liver axis involvement, but Siddha herbal effects on gut microbiota remain under-investigated. Future research should conduct mechanistic and clinical studies on the impact of Siddha herbal formulations on gut microbiota composition and function in liver disorders. Gut microbiota modulation may underlie hepatoprotective effects and improve therapeutic strategies (Poo et al., 2024).

### **Overall Synthesis and Conclusion**

The comprehensive literature on liver disorders within the framework of Siddha medicine highlights the rising global burden of conditions such as non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), frequently linked to metabolic syndrome, lifestyle factors, and environmental contributors. This growing prevalence underscores the urgency for effective and culturally congruent therapeutic approaches. Siddha herbal formulations, often polyherbal and sometimes herbo-mineral, are widely documented for their hepatoprotective potential, exhibiting antioxidant, anti-inflammatory, anti-fibrotic, and metabolic regulatory actions. These effects are attributed to diverse phytochemical constituents including flavonoids, terpenoids, alkaloids, and polyphenols that target multiple molecular pathways involved in liver injury and repair. Preclinical and limited clinical data demonstrate symptomatic relief, normalization of liver enzyme profiles, and histological improvements, suggesting that Siddha medicines can reverse or ameliorate liver pathology.

Integration of dietary and lifestyle modifications alongside Siddha herbal therapy emerges as a crucial component of holistic management. Traditional principles emphasize the importance of pathya ahara (wholesome diet) and vihara (appropriate lifestyle), which contemporary studies correlate with improved metabolic parameters, enhanced therapeutic outcomes, and better patient compliance. However, the extent and rigor of documenting such integrative interventions vary, necessitating standardized protocols and adherence monitoring to clarify their additive or synergistic roles.

Comparative insights reveal overlaps and distinctions between Siddha and other traditional systems like Ayurveda, with similar therapeutic goals but differences in formulations and underlying theoretical frameworks. Nonetheless, direct head-to-head clinical trials remain scarce, limiting evidence-based positioning of Siddha relative to these systems.

Safety profiles of Siddha herbal medicines are generally favorable, with minimal adverse events

reported in clinical and preclinical contexts. Yet, concerns persist regarding standardization, quality control, and potential herb-mineral interactions, especially in complex herbo-mineral preparations. Rigorous pharmacovigilance and toxicological assessments thus remain imperative.

A critical limitation of the current evidence base is the predominance of small-scale, uncontrolled, or observational studies, often lacking robust randomization, blinding, and standardized outcome measures. This methodological gap hinders definitive conclusions about efficacy and safety. Furthermore, phytochemical characterization and mechanistic elucidations are advancing but require translation into clinical validation to optimize therapeutic use.

In summary, the body of literature collectively supports the promise of Siddha herbal medicines, especially when integrated with diet and lifestyle modifications, in managing liver disorders. However, large-scale, well-designed clinical trials, standardized formulations, and comprehensive safety evaluations are essential to substantiate these benefits and facilitate their incorporation into mainstream liver health management.

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