Review Article

Comprehensive Review on Selective Siddha Medicines in the Management of Alcoholic Liver Disease

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ABSTRACT

Alcoholic liver disease (ALD) is a major global health burden, ranging from fatty liver to cirrhosis and end-stage liver failure. In Siddha medicine, these conditions are correlate with Kalleral Noi attributed to Azhal derangement, leading to impaired digestion and metabolic dysfunction. Conventional management has limitations including adverse effects and limited long-term hepatoprotection highlighting need for safer holistic alternatives. Siddha medicine offers integrative approaches using Herbal and Herbo-Mineral formulations with dietary and lifestyle regulation. This review evaluates the Siddha formulations Seenthil Chooranam, Inji Rasayanam, and Mandurathi Kudineer Chooranam for management of ALD. These formulations exhibit Hepatoprotective, Antioxidant, Anti-inflammatory, Immunomodulatory, Detoxifying and Hematinic effects targeting oxidative stress lipid accumulation and hepatic injury. Seenthil Chooranam reduces oxidative damage Inji Rasayanam improves digestion and lipid metabolism and Mandurathi Kudineer Chooranam supports liver regeneration and hematological balance. Collectively these formulations provide multi-targeted therapeutic effects in Kalleral Noi (ALD). Evidence from PubMed and Google Scholar indicates hepatoprotective potential with acceptable safety profiles but further experimental and clinical validation is required. This review suggests that Siddha formulations may serve as promising complementary therapeutics in alcoholic liver disease management supporting traditional knowledge with modern pharmacological evidence and emphasizing the need for standardized formulations mechanistic studies and well-designed clinical trials for broader clinical application in practice.

Keywords: Alcoholic Liver Disease (ALD), Kalleral Noi, Siddha Medicine, Seenthil Chooranam, Inji Rasayanam, Mandurathi Kudineer Chooranam.

INTRODUCTION

Alcohol consumption is widely prevalent across the world and has long been recognized as a major risk factor for liver disease. Alcoholic liver disease (ALD) is the third most common cause of chronic liver disease and contributes significantly global burden and mortality.[1] There are three histologic stages of alcoholic liver disease Alcoholic Fatty Liver or Steatosis - At this stage, fat accumulates in the liver parenchyma. Alcoholic Hepatitis - Inflammation of liver cells takes place at this stage, and the outcome depends on the severity of the damage. Alcoholic Cirrhosis - Liver damage at this stage is most advanced and irreversible that leads to complications of cirrhosis and portal hypertension". Clinical manifestations of ALD commonly include Nausea and vomiting, Abdominal pain or discomfort, Loss of appetite, altered body weight, increased thirst, yellowish discoloration of eyes, Weakness, Fever in alcoholic hepatitis, Confusion, Alteration of the sleep-wake cycle, Mood swings, Fainting.[2] Despite advances in conventional management, treatment options remain limited. Corticosteroids are currently preferred medication for severe alcoholic hepatitis; however, they have not demonstrated substantial improvement in six-month mortality, which is nearly 40% in severe cases.[3] In addition prolonged use of corticosteroids associated with adverse effects including immunosuppression, gastrointestinal complications, metabolic imbalance, and poor long-term compliance, those are highlighting the need for safer and integrative therapeutic options. In Siddha literature, liver disorders are classified under "Kalleral noigal" also referred to as Maandha katti, Valapaateeral noi and Yagudham. The etiological factors (Noi varum vazhi) described include excessive intake of food, taking unhealthy and heavy diets, long term intake of alcoholic beverages.[4] According to Siddha principles, Kalleral Noi primarily results from derangement of humoral balance, predominantly aggravated pitham, affecting hepatic function. Various Siddha formulations of polyherbal, herbo-mineral, and herbo-metallic origin, such as Chooranam, Kudineer, Ilagam, Mathirai, Nei, Chendhuram, Parpam, and Karpam, have been documented for the management of Kalleral noi. These formulations are traditionally intended to restore altered humoral equilibrium, enhance liver function, facilitate detoxification, and improve systemic health. Among them, Seenthil Chooranam, Inji Rasayanam, and Mandurathi Kudineer are widely used in clinical practice. Although Siddha medicine has long been used in the management of liver disorders, consolidated scientific evidence on Siddha formulations for Alcoholic Liver Disease (ALD) or Kalleral Noi remains limited. Existing studies mainly focus on individual formulations and pharmacological evaluations, with few comprehensive reviews integrating classical Siddha concepts and contemporary evidence. This

study aims to compile and summarise all available preclinical data on Seenthil Chooranam, Inji Rasayanam and Mandurathi Kudineer Chooranam in the treatment of ALD. It further evaluates the strength of evidence supporting its efficacy. The findings may highlight the potential of those Siddha formulation and provide a basis for future research in the management of ALD.

Table 1: Siddha Formulations and Their Therapeutic Indications

Medicines	Formulation	Anubanam	Indication
Seenthil Chooranam[5]	Herbo-Animal Formulation	Ghee	Megam (Diabetes Mellitus), Kavisai (Liver Disease), Eelai (Tuberculosis), Kasam (Cough), Elaippu (Bronchial Asthma), Andavaayu (Scrotal Swelling), Neerchurukku (Oliguria), Vadha Noi, Varatchi, Pitham and Thol Noigal (Skin Disease)
		Honey	Peenisam (Sinusitis), Naasi Pungal (Wound in the Nose) and Gunmam (Gastric Ulcer)
		Sugar	Puzhuvettu (Alopecia Areata), Mayir Vettu, Podugu(Dandruff), Suram (Fever) and Kan Thelivu(Improves Vision
Inji Rasayanam[6]	Herbal Formulation	Hot water	Vanthi (Vomiting), Udal erivu(Burning sensation of body), Mantham, Ajeeranam (Indigestion), Pitha noigal, Nenjerichal and Vayiru erichal.
Madurathi Kudineer Chooranam[7]	Herbo-Mineral Formulation	As decoction	Velluppu (Anaemia), Utal, Manjal Noi (Jaundice), Peruvayiru, Vayirril Katti(Mars in the Abdomen), Vikkam and Vayiru Porumal.

METHODS

Study design: Review

Research type: Literature Review

Data collection method:

The methodology for this study was designed to systematically gather and analyse information on selected siddha formulations, namely Seenthil Chooranam, Inji Rasayanam and Mandurathi Kudineer Chooranam used in the management of ALD. The data was collected from various Siddha literatures, and online platforms like PubMed, Cochrane, ScienceDirect, Medline, Scopus, and Google Scholar were systematically searched to identify relevant preclinical, clinical, and pharmacological studies. A structured search was conducted using keywords such as “Seenthil Chooranam,” “Inji Rasayanam,” “Mandurathi Kudineer,” “Siddha medicine,” and “Alcoholic Liver Disease,” with emphasis on pharmacological, ethnopharmacological, and hepatoprotective studies. Eligible studies comprised clinical trials, preclinical studies, pharmacological evaluations, and review articles with full-text availability. Duplicate studies, irrelevant articles, and those lacking sufficient methodological quality were excluded. Articles not addressing hepatic or therapeutic relevance were also omitted. A stepwise screening process involving title screening, abstract review, and full-text assessment was followed to ensure inclusion of relevant evidence.

The international classification of disease (ICD-10) recognizes several forms of alcoholic liver disease (ALD; ICD-10, K70), sometimes considered stages, that range from relatively mild and reversible alcoholic hepatic steatosis (fatty liver) (K70.0) and alcoholic hepatitis (K70.1), to alcoholic fibrosis and sclerosis of the liver (K70.2), and further to severe and irreversible stages of ALD, such as alcoholic liver cirrhosis (K70.3) and alcoholic hepatic failure (K70.4).[1]

Purification process:

1. Seenthil (Tinospora cordifolia): Peel off the outer skin of the stem and powdered, then washed it for 21 times in pure water and dried then sprinkled cow’s milk allow drying it.[8]

2. Karisalai (Eclipta prostrata Linn): Wash the whole plant and dry it in sunshade & powdered.[8]

3. Poonagam (Eudrilus eugeniae): Soaked Earth worm Butter milk for a while to spit out mud then sprinkled lime water over it to kill then dry and powdered.[9]

4. Inji (Zingiber officinale): Wash thoroughly, remove the outer skin and inner fibrous vein, and wipe clean before use.[8]

5. Seeragam (Cuminum cyminum):

- Removing dust particle and soil from the raw drug and dry it in the sunlight.[8]
- Soak the Cuminum cyminum in lime stone water for 3 hours (1 Saamam) and dry it to get the purified form.[10]
- Dry the Cuminum cyminum in sunlight for 6 hours and roast it slightly.[11]

6. MANDOORAM (Ferroso ferric oxide):

- Mix the pulverised Kittam (1 part), Tamarind leaf (4 parts), and water (8 parts) together and boil this for 3 hours. On cooling, rinse it off well, dry it, and winnow away the tamarind leaf from it. Triturate the Kittam powder and burn it with 8 volumes of cow’s urine. Finally, rinse it off well once all the urine has evaporated.[12]

- Soak the Ayakitta powder in Grape fermented liquid (Thiraatchai Kaadi) for 2 weeks and then soak it in garlic (Allium sativum) extract for one week. Roast this with almond oil or cow's ghee and pulverize it to a fine powder to get the purified form.[9]

Table 2: Ingredients of the medicines with drug profile

S.NO	Drug	Botanical/ zoological name	Taste	Potency	Division	Action
1.Seenthil Chooranam	Seenthil Kodi	*Tinospora cordifolia*	Bitter	Hot	Pungent	Alterative, Anti-Periodic, Aphrodisiac, Demulcent, Stimulant (Hepatic), Stomachic, Tonic, Mild Diuretic[13]
	Karisalai Chooranam	*Eclipta prostrata Linn*	Bitter	Hot	Pungent	Cholagogue, Tonic, Alterative, Emetic, Purgative, Hepatic Tonic, Deobstruent[13]
	Suthitha Nakkupoochi Chooranam	*Eudrilus eugeniae*	Pungent	Hot	Pungent	Stomachic Stimulant[9]
2.Inji Rasayanam	Inji	*Zingiber officinale*	Pungent	Hot	Pungent	Carminative, Stomachic, Sialagogue, Digestive, Stimulant, Rubefacient[13]
	Seeragam	*Cuminum cyminum Linn*	Pungent, Sweet	Cold	Sweet	Astringent, Stomachic, Stimulant, Carminative[13]
	Sarkarai	*Sugar*	Sweet	Cold	Sweet	Antiseptic, Demulcent[14]
	Nei	*Ghee*	Sweet	Cold	Sweet	Nutritive, Stomachic Digestive[9]
3.Mandurathi Kudineer Chooranam	Mandooram	*Ferroso Ferric Oxide*	Astringent,Mild Sour, Bitter	Hot	Pungent	Nutritive, Stomachic, Alterative, Haemopoietic[9]
	Maavilai	*Mangifera indica Linn*	Astringent	Hot	Pungent	Astringent[13]
	Neermulli	*Hygrophila auriculata (K. Schum) Heine*	Sweet, Slight Bitter	Cold	Sweet	Demulcent, Diuretic, Tonic, Refrigerant[13]
	Seeragam	*Cuminum cyminum Linn*	Pungent, Sweet	Cold	Sweet	Astringent, Stomachic, Stimulant, Carminative[13]
	Karisalai	*Eclipta prostrata Linn*	Bitter	Hot	Pungent	Cholagogue, Tonic, Alterative, Emetic, Purgative, Hepatic Tonic, Deobstruent[13]
	Keezhanelli	*Phyllanthus amarus Lin. Schum. & Thonn*	Astringent, Bitter, Sour, Sweet	Cold	Sweet	Deobstruent, Coolent, Diuretic, Astringent[13]

STUDIES ON SEENTHIL CHOORANAM:

Standardisation Of Seenthil Chooranam:

Macroscopic evaluation of Seenthil Chooranam showed a yellowish-brown colour, aromatic odour with a slight rotten note, bitter taste, and fine powder passing through sieve No. 80, indicating uniform processing. Microscopic analysis revealed diagnostic plant tissue elements including stone cells with calcium oxalate crystals, cork cells, various vessel types, parenchyma, sclereids, abundant starch grains, trichomes, stomata, pollen grains, and vein islets, collectively confirming its botanical authenticity and proper composition.[14]

Physicochemical analysis of Seenthil Chooranam showed water-soluble ash (6.70±0.058), acid-insoluble ash (2.90±0.003), alcohol-soluble extractive (9.10±0.500), water-soluble extractive (10.20±0.500), and loss on drying (9.03±0.500). Phytochemical screening indicated the presence of saponins, terpenoids, and lipids, while biochemical analysis revealed calcium, starch, iron, tannic acid, reducing sugars, amino acids, and unsaturated compounds.

FTIR analysis further confirmed functional groups including alcohols, phenols, alkenes, nitriles, aromatics, amines, alkynes, and carboxylic acids, supporting the formulation's chemical richness and therapeutic relevance. Overall, the study provides a scientific basis for quality control and batch-to-batch consistency of Seenthil Chooranam, thereby supporting its safe and effective therapeutic use.[15]

Pharmacological Studies On Seenthil Chooranam:

Hepatoprotective Activity

The hepatoprotective activity of Seenthil Chooranam was evaluated in Wistar rats with liver damage induced by carbon tetrachloride (CCl_4). In the disease control group, a significant elevation in serum hepatic enzymes (SGOT, SGPT, and ALP) was observed, indicating liver injury. However, treatment with Seenthil Chooranam at doses of 200 and 400 mg/kg body weight resulted in a marked and statistically significant reduction ($P < 0.001$) in these enzyme levels compared to the toxic control group. The findings suggest that Seenthil Chooranam effectively attenuates CCl_4-induced hepatic damage and exhibits notable hepatoprotective potential.[16]

Anti-Diabetic Activity

The antidiabetic activity of the alcoholic extract of Seenthil Chooranam was evaluated in alloxan-induced diabetic rats. In this placebo-controlled open study, animals were divided into five groups and administered three different oral doses of the extract (100–300 mg/kg body weight). Blood glucose levels were monitored daily for five weeks. The results demonstrated a significant hypoglycemic effect in the treated groups. The activity was found to be comparable to the standard antidiabetic drug glibenclamide (10 mg/kg). The wide effective dose range showing glucose-lowering activity suggests potential antidiabetic properties, warranting further detailed investigations.[17]

Anti-Obesity and Anti- Oxidant Activity

The study evaluated the anti-lipase and antioxidant properties of the decoction of Seenthil Chooranam. Phytochemical screening was performed, and the formulation demonstrated strong free radical scavenging activity, showing higher antioxidant potential than the standard ascorbic acid. In addition, it exhibited significant pancreatic lipase inhibition, with a maximum inhibition of 82.3% and strong correlation values ($R^2 > 0.95$). The findings indicate that the formulation may possess potential anti-obesity and antioxidant effects, suggesting its usefulness as a plant-based therapeutic candidate for metabolic disorders.[18]

Toxicity study

A 90-day repeated oral toxicity study of Seenthil Chooranam in rats showed no mortality or significant adverse effects. Treated animals exhibited normal body weight gain and comparable food intake with controls. Haematological and biochemical parameters remained within normal limits, with a notable reduction in blood glucose levels in treated groups. Gross and histopathological examinations of vital organs revealed no abnormalities, confirming the safety of the formulation under the tested conditions.[19]

Studies On Individual Ingredients of Seenthil Chooranam:

Tinospora cordifolia

Chemical Constituents of *Tinospora cordifolia*

It contains a wide range of bioactive phytoconstituents classified into terpenoids, alkaloids, lignans, steroids, and other minor compounds. The terpenoid fraction includes compounds such as tinosporide, furanolactone- and clerodane-type diterpenes, furanoid diterpenes, tinocordiside derivatives, ecdysterone, makisterone, and several glycosidic compounds including cordifoliosides (A–E), tinocordioside, cordioside, and palmatosides. It also contains sesquiterpene glucosides such as tinocordifolioside and tinocordifolin. The alkaloid profile includes tinosporaine, magnoflorine, berberine, jatrorrhizine, palmatine, beberine, tembetarine, choline, and related pyrrolidine derivatives. Lignans such as 3-(4,4-dihydroxy-3-methoxybenzyl)-4-(4-hydroxy-3-methoxybenzyl)
compounds are also present. Steroidal constituents include β-sitosterol, giloinsterol, and 20α-hydroxy ecdysone. In addition, other important compounds such as giloin, tinosporan and tinosporal acetates, tinosporidine, heptacosanol, octacosanol, sinapic acid, tinospanone, and phytoecdysone-related immunologically active arabinogalactan compounds have been identified.[20]

Hepatoprotective Activity

Kavitha BT et al. demonstrated that *Tinospora cordifolia* exhibits significant hepatoprotective activity against CCl_4-induced liver damage in experimental rats. The extract reduced elevated serum liver enzymes (ALT, AST, ALP) and bilirubin levels, indicating restoration of hepatic function. Histopathological analysis showed reduced necrosis and improved liver architecture in treated groups compared to toxicant control. The study concluded that its hepatoprotective effect is mediated through antioxidant mechanisms and stabilization of hepatocellular membranes, thereby preventing CCl_4-induced oxidative injury and supporting its traditional use in liver disorders.[21]

Anti Diabetic Activity and Hypo Lipidemic Activity

Tinospora cordifolia contains several bioactive constituents, including flavonoids, saponins, alkaloids, tannins, steroids, and cardiac glycosides, which contribute to its antidiabetic potential. Experimental studies in alloxan-induced diabetic albino rats have demonstrated significant dose-dependent hypoglycemic activity, with higher doses (400 mg/kg) showing glucose-lowering effects comparable to the standard drug glibenclamide.[22] Similarly, A study by Lohitasu et al. reported that the ethanolic extract of *Tinospora cordifolia* produced a dose-dependent reduction in blood glucose levels along with improvement in lipid profiles, comparable to glibenclamide. These findings suggest its potential therapeutic role in managing diabetes by regulating both glucose and lipid levels.[23]

Immunomodulatory Activity

It is widely recognized for its immunomodulatory properties. A study by Gupta et al. investigated the polysaccharide G1-4A derived from *Tinospora cordifolia* in the management of *Mycobacterium tuberculosis* infection. The compound enhanced macrophage activity, promoted the release of pro-inflammatory cytokines such as TNF-α and IFN-γ, and stimulated nitric oxide production via the TLR4–MyD88 signaling pathway, thereby reducing intracellular bacterial survival. Additionally, when combined with isoniazid, G1-4A showed improved therapeutic efficacy, suggesting its potential as an adjunct in tuberculosis management.[24] It has demonstrated significant immunomodulatory activity through its aqueous and methanolic stem extracts. These extracts enhance immune responses by regulating cytokine production, nitric oxide levels, and macrophage function. Experimental studies have shown effectiveness against *Salmonella typhimurium*, viral infections, and other immune-related conditions. The immunostimulatory effects are attributed to bioactive constituents such as alkaloids, glycosides, and polysaccharides, which promote phagocytosis, lymphocyte proliferation, and cytokine secretion.[25]

Anti-Inflammatory Activity

Sheena Philip et al. investigated the anti-inflammatory activity of the chloroform extract of *Tinospora cordifolia* (CETC) using RAW264.7 macrophage cells and a carrageenan-induced rat paw oedema model. The extract significantly suppressed inflammatory mediators including COX-2, TNF-α, iNOS, IL-6, IL-1β, and PGE2 without affecting COX-1 expression. It also inhibited phosphorylation of p38 MAPK and prevented nuclear translocation of NF-κB, indicating inhibition of key inflammatory pathways. In vivo studies showed marked reduction in paw edema. Phytochemical analysis identified compounds such as stigmasterol and β-sitosterol, suggesting its potential as a safe anti-inflammatory agent with minimal COX-1 inhibition.[26]

Anti-Oxidant

Neha Upadhyay et al. evaluated the antioxidant activity of stem extracts of *Tinospora cordifolia* and reported significant free radical scavenging potential. The ethanolic extract showed higher antioxidant activity (56.35%) than the methanolic extract, which was associated with its higher phenolic content. The study suggests that phenolic compounds play a key role in its antioxidant effects, supporting its potential in managing oxidative stress–related disorders as a natural antioxidant agent.[27]

***Eclipta prostrata*:**

Chemical Constituents of *Eclipta prostrata*

Eclipta prostrata contains a wide range of phytochemicals distributed throughout the plant, including alkaloids (nicotine, ecliptine, verazine, ecliptalbine), coumarin, wedelolactone, stigmasterol, dimethylwedelolactone-7-glucoside, β-sitosterol, flavonoids, triterpenoids (α-amyrin, ursolic acid, oleanolic acid), triterpene saponins, glycosides, reducing sugars, resins, and eclalbactin. Different plant parts show specific compositions, with roots rich in thiophenes, sterols, and long-chain alcohols; stems mainly containing wedelolactone; leaves containing sterols and β-terthienylmethanol; twigs containing sterols and ecliptalbine; seeds containing alkaloids; and aerial parts enriched with amyrin and luteolin-7-O-glucoside.[28] In addition, it contains coumestans (wedelolactone, demethylwedelolactone, and their glucosides), triterpenoid glycosides (eclabasaponins and ecliptasaponins), sterols (stigmasterol, daucosterol), flavonoids (luteolin, apigenin, orobol), sesquiterpene lactones, volatile oils, phenolic acids (protocatechuic acid, 4-hydroxybenzoic acid), polyacetylenes, and substituted thiophenes, confirming its rich phytochemical diversity.[29]

Pharmacological Activity of *Eclipta prostrata*

Hepatoprotective Activity

Several studies have reported the hepatoprotective activity of *Eclipta prostrata* in carbon tetrachloride (CCl_4)-induced liver toxicity models. Aqueous leaf extract (250 mg/kg) significantly reduced elevated serum transaminases and bilirubin levels in rats. Chloroform root and methanolic leaf extracts showed marked protection by reducing lysosomal enzyme activity by 47–73%, while isolated fractions such as triterpenoids, alkaloids, saponins, and coumestans exhibited up to 78% inhibitory effects. Ethanolic whole-plant extract also normalized altered biochemical parameters and restored hepatic enzyme functions after CCl_4 exposure. Additionally, compounds such as echinocystic acid and eclabasaponin II demonstrated antiproliferative activity on hepatic stellate cells, supporting the hepatoprotective potential of the plant.[30]

Anti-Diabetic Activity

Ampa Raoul et al. reported that leaf extracts of *Eclipta prostrata* exhibit significant antidiabetic and wound-healing activities. In Wistar rat models, the aqueous extract produced a dose-dependent reduction in blood glucose levels, including in streptozotocin-induced type II diabetes. Additionally, aqueous and hydroethanolic topical formulations promoted wound healing, achieving complete wound closure by day 14.[31] Rahman et al. reported that the methanolic extract of Eclipta prostrata and its compound eclalbasaponin II significantly reduced blood glucose levels in alloxan-induced diabetic rats. The treatment (300 mg/kg extract and 10 mg/kg compound) also improved body weight and normalized elevated liver enzyme levels without causing hepatotoxicity. These findings support its traditional use in diabetes management and suggest its antidiabetic potential.[32]

Anti-inflammatory Activity

Arunachalam et al. reported that the methanolic extract of Eclipta prostrata significantly reduced carrageenan- and egg white–induced paw oedema in albino Wistar rats in a dose-dependent manner (100 and 200 mg/kg). Its anti-

inflammatory effect was comparable to standard drugs like indomethacin and cyproheptadine, supporting its traditional use in inflammatory disorders.[33]

Anti-oxidant Activity

Yang reported that the ethyl acetate extract of Eclipta prostrata showed strong antioxidant activity due to its high phenolic and flavonoid content. It also exhibited antiproliferative effects against AGS, A549, and HT-29 cancer cell lines by inducing apoptosis. These findings highlight its potential as a natural antioxidant and anticancer agent.[34]

Toxicity Study

Earlier acute toxicity studies reported that the median lethal dose (LD_{50}) of the AEA was approximately 1,264 mg/kg for intraperitoneal administration and 3,807 mg/kg for oral administration.[35]

Earthworm

Chemical Constituents of Earthworm

Earthworms contain a wide range of bioactive compounds, including purine and pyrimidine derivatives such as lumbrofebrine, lumbritin, hypoxanthine, choline, and guanidine. Their lipid fraction includes fatty acids like palmitic, stearic, oleic, lauric, myristic, along with other long-chain and branched fatty acids, phospholipids, cholesterol, and other lipids. Species such as *Lumbricus terrestris* also contain carbohydrates, proteins, amino acids, and pigments in chloragogenous tissues, with pigments believed to be related to riboflavin. Earthworm tissues from species such as *Pheretima*, *Allolobophora*, *Eisenia foetida*, and *E. rosea* are rich in proteins, fats, minerals (Zn, Fe, Ca, Mn, Cr, Mo), and other nutrients. Their blood and body fluids contain small amounts of glucose and significant lipid fractions, including neutral fats, glycolipids, and phosphatides rich in unsaturated fatty acids. Earthworms contain biologically active enzymes such as catalase, peroxidase, phosphatases, and fibrinolytic enzymes capable of dissolving fibrin. These enzymes have been studied for therapeutic use in thrombosis and myocardial infarction. They also produce antimicrobial peptides and collagen-degrading enzymes, highlighting their pharmacological and biomedical importance.[36]

Pharmacological Activity of Earth Worm

Anti-inflammatory Activity

The anti-inflammatory potential of earthworm extract was evaluated using carrageenan-induced paw oedema and cotton pellet-induced granuloma models in rats. The extract significantly inhibited both acute and chronic inflammatory responses. It also reduced oxidative stress markers such as GSH, TBARS, SOD, and catalase, while modulating cytokine levels by decreasing TNF-α and increasing IL-10. Overall, the findings indicate that the earthworm extract exhibits strong anti-inflammatory and antioxidant effects comparable to indomethacin.[37]

Anti-oxidant

A comparative study evaluated the anti-ulcerative and antioxidant effects of indigenous earthworm paste against ranitidine in Wistar albino rats. Aspirin administration increased gastric juice secretion, total acidity, ulcer index, and altered pH, along with a reduction in antioxidant levels. Treatment with earthworm paste improved gastric pH, reduced gastric juice volume, and lowered ulcer index. These effects were more pronounced at a dose of 160 mg/kg, indicating significant anti-ulcer and antioxidant activity.[38]

STUDIES ON INJI RASAYANAM

Standardisation of Inji Rasayanam

Inji Rasayanam is a brown to dark brown formulation with a pleasant ginger aroma, pungent-sweet taste, and slightly oily smooth texture due to ghee and sugar. It appears as a semi-solid or coarse powder with uniform consistency, indicating proper blending and homogeneity. Microscopic evaluation showed characteristic powder features of **Zingiber officinale** and **Cuminum cyminum**, including cork cells, starch grains, spiral vessels, sclereids, endosperm cells, mesocarp cells, and calcium oxalate crystals. Pharmacognostic standardization and HPTLC fingerprinting established reliable macroscopic, microscopic, and chromatographic profiles for quality assurance and authentication of Inji Rasayanam. The distinct HPTLC fingerprint ensures batch-to-batch consistency, proper identification, and differentiation from adulterants, supporting the quality control, safety, reproducibility, and scientific validation of Inji Rasayanam in Siddha medicine.[39]

Clinical Studies on Inji Rasayanam

The study evaluated Siddha management of Alcohol Withdrawal Syndrome using formulations such as Inji Rasayanam, Brahmi Nei, and Amukkara Chooranam. A significant reduction in CIWA-Ar scores was observed, indicating improvement in anxiety, tremors, irritability, and sleep disturbances compared to baseline. The findings suggest that Siddha formulations effectively reduce withdrawal severity and show promising anxiolytic and neuroprotective effects in Alcohol Withdrawal Syndrome.[40]

Studies On Individual Ingredients of Inji Rasayanam:

INJI (*Zingiber officinale)*

Chemical Constituent of Ginger

Ginger is rich in bioactive constituents, particularly phenolic and terpene compounds. The major phenolic components include gingerols, shogaols, and paradols. In fresh ginger, gingerols such as 6-gingerol, 8-gingerol, and 10-gingerol are predominant, which may convert into shogaols during heat processing or prolonged storage, and further transform into paradols upon hydrogenation. In addition, ginger contains other important phenolic compounds including quercetin, zingerone, gingerenone-A, and 6-dehydrogingerdione. It is also a rich source of terpene constituents such as β-bisabolene, α-curcumene, zingiberene, α-farnesene, and β-

sesquiphellandrene, which form the primary components of its essential oil. Furthermore, ginger also contains polysaccharides, lipids, organic acids, and dietary fiber contributing to its overall pharmacological properties.[41]

Hepatoprotective activity

In mice fed an alcohol-containing liquid diet, ginger essential oil ameliorated alcoholic fatty liver disease by reducing AST, ALT, TG, and TC levels and increasing antioxidant enzymes such as catalase and SOD. The study demonstrated its protective role through modulation of lipid accumulation, oxidative stress, and energy metabolism, supporting ginger essential oil as a potential natural therapeutic agent for alcoholic fatty liver disease with hepatoprotective, antioxidant, and lipid-regulating properties.[42]

Antioxidant Activity

In experimental rats, ginger supplementation significantly reduced lipid peroxidation and enhanced antioxidant enzymes including superoxide dismutase (SOD), catalase, glutathione (GSH), glutathione reductase, glutathione peroxidase, and glutathione-S-transferase. Pre-ischemic ginger administration improved total antioxidant capacity, normalized glutathione peroxidase and superoxide dismutase levels, and reduced oxidative stress markers such as malondialdehyde (MDA), nitric oxide (NO), and protein carbonyl content. Dietary ginger at 5% also showed protective effects against ischemia-induced renal oxidative damage.[43]

Anti-Nausea Effect

Historically, ginger has been used to relieve nausea and vomiting. It acts as an antiemetic and carminative by reducing and expelling intestinal gas. Studies show that ginger is as effective as vitamin B6 in reducing nausea and vomiting frequency during pregnancy.[44]

Anti-Inflammatory Activity

Ginger is an ancient medicinal herb traditionally used to support immunity and reduce inflammation, swelling, and related discomfort. It is widely consumed for its immune-boosting effects. However, studies on osteoarthritis show mixed results, though some report that ginger extract can significantly relieve its symptoms.[45] Bioactive compounds such as 6-shogaol show strong anti-inflammatory and antioxidant effects and may help in managing gout, a rheumatic joint disease.[46] Similarly, 6-gingerol extracted from dried ginger has been reported to possess notable analgesic and anti-inflammatory effects.[47]

Anti-Cancer Activity

Ginger is recognized as a chemo preventive spice, and several studies have highlighted its bioactive compounds for their potential cancer-preventive and therapeutic roles.[48] Key constituents such as 6-gingerol, 6-shogaol, 6-paradol, and zerumbone have demonstrated notable anti-inflammatory and anti-tumorigenic properties. The anticancer potential of ginger has been investigated across multiple cancer types, including lymphoma, hepatoma, colorectal, breast, skin, liver, and bladder cancers, showing promising effects in inhibiting cancer development and progression.[49]

Anti-Diabetic Effect and Hypo Lipidemic activity

Research from the University of Sydney, Australia, reported that ginger improves glycemic control in individuals with type 2 diabetes. It has been shown that ginger extracts enhance glucose uptake in muscle cells independently of insulin, thereby aiding in blood glucose regulation. In a clinical trial, diabetic patients consuming 3 g of dried ginger daily for 30 days showed significant reductions in blood glucose, triglycerides, total cholesterol, and LDL cholesterol levels.[50,51]

Anti-obesity activity

Obesity is a major risk factor for diabetes, hypertension, and cardiovascular diseases. Studies show ginger may help in its prevention and management. In 3T3-L1 preadipocyte cells, gingerenone A inhibits adipocyte differentiation and lipid accumulation more effectively than gingerols and 6-shogaol, and regulates fatty acid metabolism via AMPK activation, reducing diet-induced obesity. In skeletal muscle myotubes, 6-shogaol and 6-gingerol enhance PPARδ-mediated gene expression, increasing fatty acid oxidation and catabolism.[52]

Toxicity Study

Ginger is generally considered non-toxic, with oral LD50 values of ginger oil exceeding 5 g/kg in various animals. In vitro studies have shown both mutagenic and antimutagenic effects of its isolated compounds. Its adverse reaction profile is mild, consistent with its common use as a spice and food (Chen et al., 2007).[53]

SEERAGAM (*Cuminum cyminum*)

Chemical Constituents of Seeragam

The review on *Cuminum cyminum* L. (cumin) concludes that it is a widely used dietary spice with extensive traditional applications and a rich phytochemical profile supporting diverse pharmacological activities. The plant contains bioactive constituents such as cuminlaldehyde, p-cymene, cuminal, α pinene, and α, β-dihydroxy ethylbenzene along with potassium (K), calcium (Ca), iron (Fe), sodium (Na), magnesium (Mg), zinc (Zn), Copper (Cu).[54]

Hepatoprotective And Nephroprotective Activity

Cuminum cyminum seed powder reduces serum ALT and AST levels and enhances antioxidant enzymes such as catalase (CAT) and peroxidase (POX) in acetaminophen-induced hepatotoxicity models, with the strongest effect at 400 mg/kg. Studies also highlight cumin and ginger as potent natural antioxidants, and comparative research shows their hepatoprotective effects, along with mustard, after prolonged pre-treatment against drug-induced liver injury.[55]

Antioxidant Activity

Cuminum cyminum shows significant antioxidant activity through DPPH radical scavenging, protection of lipids and DNA, and inhibition of protein oxidation. Methanolic and aqueous extracts exhibit stronger antioxidant effects than non-polar extracts due to higher phenolic content. Although its fruits contain 2.5–4% essential oil rich in cuminol, methanolic extracts show greater antioxidant activity than the essential oil, indicating its potential as a natural antioxidant source for food and therapeutic applications.[54]

Anti-Inflammatory Activity

The aqueous extract of *Cuminum cyminum* exhibited significant, dose-dependent anti-inflammatory activity in both acute and chronic models, with maximum inhibition at 200 mg/kg in the acute phase and 1000 mg/kg in the chronic phase, indicating strong anti-inflammatory potential influenced by dose and duration.[56]

Toxicity Study

Previous acute toxicity studies on *Cuminum cyminum* showed that its extract was well tolerated in experimental models and safe even at doses up to 2 g/kg, indicating a wide safety margin.[57]

MANDURATHI KUDINEER CHOORANAM

Studies On Individual Ingredients of Mandurathi Kudineer Chooranam

MANGIFERA INDICA

Chemical constituents of Mangifera indica

The review on *Mangifera indica* (mango) leaves reports that they are rich in bioactive phytochemicals with strong nutritional and therapeutic potential, showing antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, and antimicrobial activities. These effects are mainly due to compounds such as mangiferin, gallic acid, catechin, epicatechin, chlorogenic acid, protocatechuic acid, flavonoids (quercetin, kaempferol, isoquercitrin, rutin), tannins (gallotannins, ellagitannins), terpenoids and sterols (lupeol, β-sitosterol, ursolic acid), along with other phenolic acids, carotenoids, fatty acids, and minerals including K, P, N, Ca, Fe, Na, Mg, B, Zn, Mn, and vitamins A, B, E, and C, supporting their use in nutraceutical and pharmaceutical applications.[58]

Hepatoprotective Activity

The chemo preventive effect of mango pulp extract (MPE) and lupeol was evaluated against 7,12-dimethylbenz(a)anthracene (DMBA)-induced liver changes in albino Swiss mice. Both MPE and lupeol showed hepatoprotective effects by modulating cell growth regulators and reducing oxidative stress–mediated cellular damage.[59]

Anti-Inflammatory Activity

Mango-derived polyphenols, particularly gallic acid and gallotannins, showed significant anti-inflammatory effects in experimental colitis models by reducing inflammatory cytokines (TNF-α, IL-6, IL-1β) and suppressing COX-2, iNOS, and HIF-1α via the PI3K/AKT-mTOR pathway. Mango juice also reduced colon inflammation and cell proliferation in DSS-induced colitis. In addition, aqueous leaf extract demonstrated dose-dependent anti-inflammatory activity in carrageenan-induced paw oedema and cotton pellet granuloma models, showing moderate inhibition compared to indomethacin, with higher doses approaching standard drug efficacy.[60]

Anti–Anaemic Activity

Haemolytic anaemia induced in rats using PHZ led to reduced haematological parameters. Treatment with ethanolic extract of *Mangifera indica* leaves (200 mg and 400 mg) significantly improved haemoglobin levels and inhibited reactive oxygen species (ROS) production, indicating antioxidant activity. These findings suggest potential anti-anaemic effects, though further studies are needed to clarify the mechanisms.[61]

Antioxidant Activity

Extracts of *Mangifera indica* 'Irwin', particularly from flowers and mature dark green leaves, show strong antioxidant activity through DPPH radical scavenging and SOD-like effects. Pruned mature leaves, often discarded, may serve as a potential source for health supplements and cosmetics, though further studies are needed to confirm safety and identify the active compounds responsible.[62]

HYGROPHILA AURICULATA

Chemical Constituents of *Hygrophila auriculata*

The study on *Hygrophila auriculata* leaves concludes that the plant is a rich source of bioactive phytochemicals and essential minerals contributing to its significant antioxidant and antimicrobial activities. The presence of compounds Lupeol, Betulin, Leutolin, Apigenin 7 O-glucoside, Apigenin, 7-O glucuronide, Stimagsterol, 25-Oxo hentriacontyl acetate, Methyl 8-n-hexyltetracosanoate along with vital minerals like vitamin A, E, C, B1, B2, B5, B6, B7 and B9, Potassium, calcium, magnesium, phosphorus, iron, copper, zinc and manganese.[63]

Hepatoprotective Activity

In in vitro studies, rat hepatocytes isolated by the modified Seglen method were exposed to CCl_4 (1%) with or without alkaloid fraction (40–80 µg/ml), and hepatocellular damage was assessed by serum markers including AST, ALT, ALP, LDH, and triglycerides. The alkaloid fraction significantly normalized these biochemical parameters. Hepatoprotective activity was also confirmed in HepG2 cell lines, showing dose-dependent improvement in cell viability after CCl_4 exposure. In vivo studies in Wistar albino rats (150–200 g) demonstrated that the alkaloid fraction at 80 mg/kg provided hepatoprotection comparable to silymarin (250 mg/kg), supported by histopathological findings, indicating strong hepatoprotective potential.[64]

Antioxidant Activity

The antioxidant activity of the extract was evaluated using ferric thiocyanate (FTC) and thiobarbituric acid (TBA) assays. Another study reported that aqueous root extract of *Hygrophila spinosa* (200 mg/kg, oral) showed hepatoprotective effects in carbon tetrachloride (CCl_4)-induced liver injury in rats, assessed through enzymatic and non-enzymatic antioxidant parameters and histopathological analysis, confirming its hepatoprotective potential.[65]

Anti-Inflammatory Activity

The ethanolic and aqueous extracts showed significant anti-inflammatory activity, while petroleum ether and ethanolic extracts exhibited notable analgesic effects in albino rats and mice at 400 mg/kg oral dose. The results were statistically significant compared to controls and comparable to standard drugs such as diclofenac sodium and analgin.[65]

Hemopoetic Activity

The petroleum ether extract of *Hygrophila auriculata* significantly increased white blood cell count, while a combined petroleum ether and chloroform leaf extract markedly raised erythrocyte count, leukocyte count, and haemoglobin levels, indicating potential hematinic activity.[65]

PHYLLANTHUS AMARUS

Chemical Constituents of *Phyllanthus amarus*

The study on *Phyllanthus amarus* leaves concludes that it is a nutritionally and pharmacologically valuable medicinal species due to its rich phytochemical and mineral composition. The leaves contain bioactive constituents such as alkaloids, flavonoids, hydrolysable tannins (ellagitannins), lignans (phyllanthin, hypophyllanthin, nirurin, niranthin, phyltetralin, nirtetralin), polyphenols, triterpenes, sterols, and volatile oil, along with minerals including Ca, Na, Mg, K, Cu, Zn, Mn, Fe, Cr, Mo, Se, Ag, Pb, Hg, Ni, and Cd..[66]

Hepatoprotective Activity

Research on *Phyllanthus amarus* has demonstrated strong antiviral activity against hepatitis B virus (HBV). In vitro studies using HepG2/C3A cells showed that its ethanol extract inhibits HBV-infected cell growth, indicating suppression of viral proliferation. Further studies in HepG2-NTCP cells reported reduced HBsAg levels, suggesting inhibition of viral entry and replication, supporting its potential in anti-HBV drug development. A clinical study in patients with mild to moderate alcoholic hepatitis also showed therapeutic benefits after four weeks of treatment, indicating translational relevance. Additionally, *Phyllanthus amarus* exhibits hepatoprotective and anti-HCV potential by enhancing antioxidant activity, reducing lipid peroxidation, and protecting against oxidative liver damage. In vitro and molecular docking studies identified key lignans with anti-HCV activity, while structure-based analyses showed that phyllanthin derivatives inhibit HCV NS3 protease, an essential enzyme for viral replication, highlighting its promise as a source for novel antiviral therapies against HCV.[67]

Antioxidant Activity

Phyllanthus amarus has shown significant antioxidant activity in both in vitro and in vivo studies, including free radical scavenging, inhibition of lipid peroxidation, and enhancement of endogenous antioxidant enzymes. These effects are mainly due to bioactive constituents such as ellagitannins, flavonoids, and gallic acid derivatives. It also exhibits protective effects against oxidative stress–related disorders like liver injury, diabetes, obesity, and toxicity, supporting its use in nutraceutical and therapeutic applications.[67]

Anti-Inflammatory Activity

Research has demonstrated the anti-inflammatory potential of *Phyllanthus amarus* in benzene-induced leukemia models. The extract significantly reduced TGF-β levels, indicating modulation of immune responses, reduced fibrosis, and enhanced tissue repair, while inflammatory markers such as CRP, IL-8, and TNF-α remained unchanged, suggesting no adverse inflammatory effects. Overall, these findings highlight its therapeutic potential in managing benzene-related inflammation and as an adjunct in leukemia treatment, though further mechanistic and clinical studies are needed.[68]

Effect On Haematological Parameters

In benzene-induced leukemia models, *Phyllanthus amarus* extracts showed significant haematological effects. The methanolic extract improved red blood cell indices, indicating anti-anaemic potential, while the ethanolic extract affected white blood cell counts, suggesting immunomodulatory activity. However, all extracts prolonged clotting time, indicating a possible risk of bleeding tendency.[67]

Toxicity Study

Toxicological studies on *Phyllanthus amarus* showed that oral administration of 1000, 1500, and 2000 mg/kg for two weeks in albino rats was safe, with no toxicity signs, changes in body or organ weights, renal function, or histopathological abnormalities. It also enhanced antioxidant status and reduced malondialdehyde levels, supporting its non-toxic nature and therapeutic potential.[69] A sub-chronic toxicity study of *Phyllanthus amarus* showed that the LD_{50} of its crude ethanolic leaf extract is >5000 mg/kg, while the ED_{50} is 200 mg/kg, giving a therapeutic index of 25. These results indicate a wide safety margin and strong pharmacological efficacy, with no toxicity observed at therapeutic doses, confirming its safety and non-toxicity in experimental animals.[69,70]

DISCUSSION

Alcoholic liver disease (ALD) remains a major global health challenge, characterized by a progressive spectrum ranging from steatosis to alcoholic hepatitis, cirrhosis, and end-

stage liver failure. Its pathogenesis is multifactorial, involving oxidative stress, inflammatory cascades, lipid dysregulation, mitochondrial dysfunction, and hepatocellular injury. Despite advances in conventional management, current therapeutic options—particularly corticosteroids in severe alcoholic hepatitis—offer limited survival benefit and are frequently associated with significant adverse effects. This underscores the urgent need for safer, multi-targeted, and complementary therapeutic strategies.

In Siddha medicine, ALD correlates with Kalleral Noi, attributed primarily to derangement of Pitham, leading to impaired digestive and metabolic homeostasis. The present review systematically evaluates three classical Siddha formulations—Seenthil Chooranam, Inji Rasayanam, and Mandurathi Kudineer Chooranam—for their therapeutic relevance in ALD based on available experimental, pharmacological, and limited clinical evidence.

Seenthil Chooranam demonstrated consistent hepatoprotective activity in preclinical models, evidenced by significant reductions in serum hepatic enzymes (SGOT, SGPT, ALP) and preservation of hepatic architecture. Its pharmacological profile is further strengthened by antioxidant, antidiabetic, and anti-obesity activities, indicating broader metabolic regulation relevant to ALD pathophysiology. These effects are plausibly attributed to key bioactive constituents such as *Tinospora cordifolia* and *Eclipta prostrata*, which are known to modulate oxidative stress, inflammatory mediators, and hepatocellular regeneration.

Inji Rasayanam, primarily composed of *Zingiber officinale* and *Cuminum cyminum*, demonstrates clinically relevant effects in alcohol withdrawal syndrome, particularly in reducing CIWA-Ar scores and improving neurovegetative symptoms. Mechanistically, ginger-derived bioactives have shown hepatoprotective effects against alcohol-induced hepatic steatosis through modulation of lipid metabolism, antioxidant defense systems, and inflammatory signaling pathways, suggesting its dual role in both withdrawal management and hepatic protection.

Mandurathi Kudineer Chooranam, traditionally indicated for jaundice, anemia, and hepatomegaly, lacks extensive formulation-specific clinical validation; however, its individual constituents—including *Phyllanthus amarus*, *Hygrophila auriculata*, *Mangifera indica*, and *Cuminum cyminum*—exhibit well-documented hepatoprotective, antioxidant, anti-inflammatory, and hematinic properties. Collectively, these activities target key pathological mechanisms in ALD, including oxidative injury, impaired haematopoiesis, and inflammatory progression.

Oxidative stress is a central driver in ALD progression, and notably, all evaluated formulations and their constituent herbs demonstrate strong free radical scavenging potential, inhibition of lipid peroxidation, and enhancement of endogenous antioxidant enzyme systems. This multi-target antioxidant action represents a plausible mechanistic basis for their hepatoprotective effects.

Toxicological data across most ingredients suggest a favourable safety profile, with high therapeutic indices and minimal adverse effects in preclinical studies. However, variability in purification methods, formulation standardization, and dosage regimens remains a significant limitation, affecting reproducibility and translational applicability.

Overall, the evidence suggests that these Siddha formulations exert synergistic hepatoprotective, antioxidant, anti-inflammatory, and metabolic regulatory effects, thereby addressing multiple pathological pathways involved in ALD. Nevertheless, the current body of evidence is predominantly preclinical, with limited controlled clinical trials and insufficient alcohol-specific experimental models.

Therefore, rigorous standardization, mechanistic investigations, pharmacokinetic profiling, and well-designed randomized clinical trials are essential to establish their efficacy, safety, and clinical utility in evidence-based management of alcoholic liver disease.

CONCLUSION

This review indicates that Seenthil Chooranam, Inji Rasayanam, and Mandurathi Kudineer Chooranam possess promising multi-target hepatoprotective potential in alcoholic liver disease (ALD), primarily through antioxidant, anti-inflammatory, lipid-lowering, and hematinic mechanisms. Collectively, these formulations may help counter key pathological processes in ALD and reflect the synergistic therapeutic approach of Siddha medicine in Kalleral Noi. However, the evidence is largely preclinical, with limited formulation-specific clinical validation. Further standardization, mechanistic studies, and well-designed clinical trials are essential to confirm their safety, efficacy, and translational relevance in evidence-based ALD management.

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CONFLICT OF INTEREST

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