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A CRITICAL REVIEW ON THIRATCHAI KUDINEER -A SIDDHA DECOCTION FOR LIVER DISEASES

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ABSTRACT: Pollution and overgrowing populations cause many problems such as environmental degradation, climate change, disease, etc. Among all the problems, the disease is an important factor that may affect the normal day-to-day activities of human beings, and it may be fatal sometime. Hence many researchers, government and private sectors are involved in the process of formulating new drugs to the existing diseases. Western medicine is the widely accepted way of medical practice which is adopted by many countries. But unfortunately, sometimes Western medicine is not applicable for certain people due to their allergic nature, cost and unavailability, *etc.* Hence peoples search for alternate medicine to cure their ailments. Siddha System of Medicine (SSM) is one of the widely accepted ways of alternate medicine practiced in India's southern region. This Siddha medicine is widely used to treat various dangerous diseases like cancer, liver disease, viral diseases, *etc.* Liver disease is common in developing countries like India. The Thiratchai kudineer is a polyherbal formulation used to treat various liver diseases. Thus, this review is mainly focused on finding out the impact of Thiratchai kudineer on liver disease treatment and their other pharmacological activities in both Siddha and modern aspects.

INTRODUCTION: The Siddha System of Medicine (SSM) has been most prevalent in the ancient Tamil land and it is the prime system for all other medical systems that emerged in the world ¹. Tamil scholars hold that Siddha medicine has a tradition of more than 5000 years. This is one of the important primitive systems of medicine practiced from ancient days to cure human illness ².

Siddhars, who are considered to be Tamil Nadu spiritual scientists, who have researched the truth of nature. They also, through their yogic consciousness and experimental results, clarified the relationship between man and nature ³.

The principles of Siddha highlight the medicinal methodology of body, soul, and mind by applying the concepts of alchemy, treatment, yoga, and wisdom. According to the SSM, diet, and lifestyle are all together, helping to make the body healthy and disease-free. This concept is called pathya and apathya, which is basically a list of do's and don'ts for both medicine and disease ⁴. Siddha medicine system is known to be fine-tuned with several research and development achievements, which

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outstrips modern medicines in most of the medical domains. The only medicinal system which connects the concepts of nature into mankind is known as the Siddha medicine system. The basic principle of SSM describes the importance of five elements for everything, from the evolution of the galaxy to the evolution of humans⁵. Now, it's very common in present days for human beings to be prone to many diseases. It is very difficult to spot a human without disease and thereby to consume medicines to tackle the diseases. The main reason for the human susceptible to disease is the change in their lifestyle with which human genetic is subject to all kind of changes in food, pollution, and industrialization. Siddha medicinal system has its own pharmacology known as Gunapadam. It classifies raw drugs into three large categories based on their origins, such as plants, minerals, metals, and animals⁶. This medical system highlights that the first choice of drug for treatment should be planted. Plants play a significant role in the preparation of Siddha medicines with mineral, metallic, and animal sources. Herbs in Siddha medicine are used for purification and pulverization of mineral, metallic and animal drugs⁷. The SSM can cure various ailment which affects the human body.

2. Liver Disease: According to the World Health Organization, around 59% of death happens every year due to chronic diseases. Among the 59% of deaths, 12% of the world's individuals suffer from chronic liver diseases. Over the years, liver disease rates have gradually increased⁸. The liver is one of the human body's biggest internal organs. It is the main organ in the human body that controls homeostasis. Almost all biochemical pathways related to development, detoxification, disease resistance, nutrient supply and energy supply are involved in the liver^{8, 9}. Exposure to toxic chemicals, bacteria, metabolic disorders, and genetic defects are the causes of most liver diseases. There are different types of liver disease

that are there in the world they are; jaundice, hepatitis, cirrhosis, fatty liver, and cancer, *etc*. The liver diseases constitute the most prevalent chronic disease in India¹⁰. The common symptoms of liver disease are the loss of appetite, weight loss, dark color urine, abdominal pain, yellow skin or eye, pale color stool, *etc*.

The maintenance of a healthy liver is important for an individual's overall well-being¹¹. There is a long tradition of using herbal remedies for the treatment of liver disorders¹². One of the essential components of complementary and alternative medicine is the prevention and treatment of liver disease by a nutritional or herbal method¹³.

A Siddha classical text, Noykalukku Siddha parikaram highlights a polyherbal formulation Thiratchai kudineer for the management of Kamalai (liver diseases)¹⁴. In this article, the thiratchai kudineer (polyherbal decoction) and their composition and function in treating liver disease were discussed.

3. Ingredients of Thiratchaikudineer: The major herbal composition of Thiratchaikudineer are listed below

- 1 *Vitis vinifera* L. (Wine grape)
- 2 *Elettaria cardamomum* L. (Cardamom)
- 3 *Cuminum cyminum* L. (Cumin)
- 4 *Piper cubeba* L. (Cubeb)
- 5 *Rosa x damascena* Mill. (Rose)
- 6 *Phyllanthus amarus* (Gale of wind)

3.1 Siddha Aspect of Thiratchaikudineer: Pharmacological action of the ingredients of TK as per Siddha. The mode of action of a drug depends on its *suvai*, *gunam*, *veeriyam*, which is a unique concept in Siddha¹⁵.

TABLE 1: SIDDHA PHARMACOLOGICAL VIEW OF EACH INGREDIENT IN TK

S. no.	Plant name	Part used	Suvai (Taste)	Gunam (Character)	Veeriyam (Potency)	Seykai (Action) ¹⁶
1	<i>Vitis vinifera</i> L.	Seed	Inippu	Thatpam	Inippu	Malamilakki(Laxative) Kulirchiyundakki(Refrigerant) Siruneerperukki(Diuretic) Udaluramakki(Nutrient)
2	<i>Elettaria cardamomum</i> L.	Seed	Kaarppu	Veppam	Kaarppu	Veppamundakki(Stimulant)

3	<i>Cuminum cyminum</i> L.	Seed	Kaarppu, Inippu	Thatpam	Inippu	Akattuvayvakatri(Carminative) Pasitheethoondi(Stomachic) Akattuvayvakatri(Carminative) Veppamundakki(Stimulant) Pasitheethoondi(Stomachic) Thubarppi(Astringent)
4	<i>Piper cubeba</i> L.	Dried fruit	Kaarppu, viruvirup pu	Veppam	Kaarppu	Veppamundakki(Stimulant) Akattuvayvakatri(Carminative) Siruneerperukki(Diuretic) Kozhaiyagatri(Expectorant)
5	<i>Phyllanthus amarus</i>	Dried fruit	Thuarpu Kaippu Pulippu Inippu	Thatpam	Inippu	Veekamurukki (Deobstuent) Siruneerperukki (Diuretic) Kulirchiyundakki(Coolant) Thubarppi (Astringent)

4. Method of Preparation:

4.1 Purification: The raw drugs must be purified according to the reference in Siddha text, Sigicharathnadeepam¹⁷.

4.2 Preparation:

Rule of Decoction: Siddha literature describes decoction for many diseases.

It is used both internally and externally, internally advocated for fever, cough, phlegmatic affections and externally administered to wash wounds, gargling, vaginal and anal wash¹⁸.

a) Quantity of Water: The quantity of water to be used depends upon the weight of drugs of a particular formulation. It is a general rule to add water 16 times the weight of the raw drug.

b) Proportion of Condensation: The quantity of water used to prepare and to condense determines the efficacy and indication.

Generally, decoctions for internal administration are condensed to 1/4 or 1/8th of the original quantity¹⁹.

c) Methods: Decoction can be prepared by soaking the drugs in water for few hours or overnight in hot water or cold water.

This is named as "ooralkiyazham". Eg: Sandhanaooralkiyazham Decoction can also be prepared by boiling and reducing the water quantity. This is called "kodikiyazham". Eg: Nilavembu kudineer, Kaba sura kudineer

d) Shelf Life: The shelf life of herbal decoction (kudineer) is about three hours (90 min)²⁰.

5. Pharmacological Properties of Dried Grapes:

5.1. Flavonoids: The Flavonoids of (4.5%) comprises kaempferol-3-O-glucosides, quercetin-3-O-glucosides, quercetin and myricetin²¹.

5.2. Polyphenols: Grapes are rich in polyphenols, and in grape seeds, 60.70% of grape polyphenols are found. The polyphenols from grape seeds are flavan-3-ol derivatives. Catechins, epicatechin, epicatechin-3-O-gallate, procyanidins dimer (B1-B5), procyanidin C1 and procyanidin B5-32-gallate are the main compounds²².

5.3. Anthocyanins: The anthocyanins which are reported for *V. vinifera* includes 3-glucosides, 3-acetyl glucosides, 3-coumaroyl glucosides, 3-caffeoyl glucosides, 3,5-di-glucosides, 3-acetyl-5-di-glucosides, 3-coumaroyl-5-di-glucosides, and 3-caffeoyl-5-di-glucosides of cyanidin, delphinidin, peonidin, petunidin, and malvidin²².

5.4. Stilbene Derivatives: The compound Trans-Resveratrol (trans-3, 5, 40-trihydroxystilbene) is present in grapes²². Pre-exposure to grape seed extract (3 or 7 days, 100 mg/kg, p.o.) followed by hepatotoxic doses of acetaminophen (400 and 500 mg/kg, i.p.) has been shown to significantly attenuate acetaminophen-induced hepatic DNA damage, apoptotic and necrotic liver cell death, and to counteract the effect of acetaminophen-induced bcl-XL expression changes in mice²³.

In one study, grape seed extract of approximately 50 mg/kg each day, which is administered orally for 28 days, protects the liver against oxidative damage in rats following ligation of the bile duct. Administration of grape seed extract at a dosage of 50 mg/kg orally for 15 days before chemicals /

reperfusion injury and repeated before reperfusion also decreased liver ischemia/reperfusion injury in rats in another study²⁴. As evidenced by near normal serum levels of ALT, AST, ALP, ACP, GGT, and complete bilirubin, administration of the seed extract to diabetic rats prevented hepatocyte destruction. Extracts of *Vitis vinifera* are abundant in phyto-compounds. It also serves as a free radical hunter and avoids biological molecules from free radical-mediated oxidation. Fruit extract showed strong antioxidant capacity *in-vitro*, and the extract is considered as a good source of phytochemicals and antioxidant. Laxative plants are used to clear the ingested toxins away from the digestive system²⁵. Grapes are more used as a laxative, because of their stool softener property²⁶.

6. Pharmacological Properties of Cumin: In the Middle East, Far East, and Asian countries, cumin seeds have historically been used as a food additive and also as herbal health help for thousands of years²⁷. Phytochemical analysis of *Cuminum cyminum* results with the presence of alkaloid, tannin, anthraquinone, coumarin, resin, flavonoid, protein, glycoside, saponin, and steroid²⁸.

The Carbohydrates, proteins, calcium, and phosphorus are found in *C. cyminum* seeds, along with vitamin A, vitamin C, and various fractions of different volatile oils²⁹. Owing to the availability of plenty of essential oil, *C. cyminum* has both antioxidant and free radical scavenging activities³⁰.

The two alkyl glycosides, Cuminoside A and B (sesquiterpenoid glucosides), and the five other known constituents are found to be in *C. cyminum*³¹. By increasing the liver function test parameters and also significantly reducing the level of MDA and increasing the level of antioxidant enzymes such as catalase, superoxide dismutase, and glutathione, *C. cyminum* extract prevents hepatic cell damage. The healing of hepatic cells is because of the property of tissue regeneration present in *C. cyminum*³². By the level of aspartate transaminase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT), cholesterol, triglycerides, and phospholipids in the plasma of rats, cumin may decrease lipid levels in alcohol and thermally oxidized oil-induced hepatotoxicity. This suggests that a lot of antioxidant properties are found in cumin³³.

7. Pharmacological Properties of Cardamom:

This research shows that supplementation with cardamom has the option of reducing the cholesterol increased by the HCHF diet. A previous report suggests that cardamom can prevent the increase in plasma cholesterol levels due to a high-fat diet in rats³⁴. The increase in cholesterol can potentially increase the risk of diseases of the fatty liver³⁵. HCHF diet feeding in rats increases the accumulation of fat in this study and increases lipid peroxidation in the liver of rats, and increases the wet weight of the liver. However, the increased activity of the plasma enzymes ALT, AST, and ALP was also observed in diet-fed HCHF rats. Oxidative stress-mediated liver tissue damage may increase the enzyme activities of the liver markers in plasma. It often occurs in the liver during injury or degradation. Liver damage increases ALT and AST leakage into the bloodstream. Cardamom increased liver function as it stabilized the wet weight of the liver and also normalized ALT, AST, and ALP plasma activities³⁶. Similarly, improved liver function was assessed for alcohol-induced liver damage with cardamom extract³⁷. Cardamom administration or dietary use of cardamom can be helpful in dyslipidemia, hepatic steatosis and fasting hyperglycemia due to excess glucocorticoids³⁸.

8. Pharmacological Properties of Cubeb: *P. cubeba*:

P. cubeba is used to treat acute jaundice by the traditional medicine practitioner. Cubeba fruits are known to possess pain and inflammation-reducing capacity in experimental animals³⁹. There are several lines of evidence that implicated oxidative stress and inflammation in the etiology of liver diseases, cardiovascular diseases, and cancer⁴⁰. The potential hepatoprotective effects of Piper cubeba ethanolic extract (PCEE) against the CCl₄-stimulates the hepatic wounds in the male Wistar rats⁴¹. The antioxidant activity of 16 isolated compounds from Piper cubeba was identified⁴². Also, it has been reported that fruits possess anti-inflammatory activities⁴³. The ethanolic extract of *Piper cubeba* fruits possesses significant antioxidant and hepato-protective activity in CCl₄ induced rats⁴⁴. The preliminary qualitative analysis indicates the presence of essential oil, terpenoids, and flavonoids which are known as antioxidants and anti-inflammatory agents⁴⁵.

The study is observed for phytochemical evaluation and antioxidant activity of *Piper cubeba*⁴⁶.

9. Pharmacological Properties of Rose:

Administration of the acetone fraction (AF) of *Rosa domescena* reduced the ALP, GPT, and GOT activity in serum and tissues ($P < 0.001$) of the treated group animals. Reduced levels of lipid peroxide in this treated group suggest that the drug might have protected the liver from the toxic effect of CCl_4 ⁴⁷.

The alcoholic extract of *R. damascena* flowering top, when taken for long periods of time, may prevent paracetamol-induced liver damage and may also prevent liver diseases⁴⁸. The flower of this plant is reported to have blood purifying properties⁴⁹. Jigrine, a herbal preparation in which *R. damascena* is a prime ingredient, has shown anti-inflammatory activity⁵⁰.

AF of *Rosa damascena* has the potential compounds for antioxidant activity. It inhibits superoxide radical formation, hydroxyl radical generation, and lipid peroxide formation *in-vitro*⁵¹. Thus, it can be assumed that the observed antioxidant activity of *R. damascena* may be responsible for its hepatoprotective activity *in-vivo*.

R. damascena significantly reduced the elevations of serum TG, cholesterol, LDL, and hepatic enzymes. Improvement of antioxidant status and hepatoprotective activity which was mediated by phenolic ingredients are the main potential mechanism of this natural remedy. Positive effects of *R. damascena* as a dietary supplement and alternative medicine in the management of NAFLD (Non-Alcoholic Fatty Liver Disease) has been demonstrated⁵².

10. Pharmacological Properties of Gale of Wind:

Phyllanthus amarus – whole plant with buttermilk enhances the liver function⁵³. *Phyllanthus urinaria*, with potential antioxidative effects, is used in herbal medicine. Steatohepatitis has been shown to improve in both cell cultures and in mice by reducing oxidative stress, relieving inflammation and reducing lipid accumulation⁵⁴. In traditional medicine, *Phyllanthus* sp is primarily used in India and China to treat many diseases⁵⁵. A morphological analysis of the sample *Phyllanthus* used in the raw drug trade in southern India states

that 76% of the market samples contain *P. amarus* as the predominant species of around (>95%). The other five different species such as *P. debilis*, *P. fraternus*, *P. urinaria*, *P. maderaspatensis*, and *P. kozhikodianus*, were found in the remaining 24% of the shops⁵⁶.

P. amarus has been broadly studied because it is mostly used in Indian Ayurvedic medicine for the treatment of gastrointestinal and genitourinary diseases. Its main active components are ligands, as phyllanthin and hypophyllanthin, and flavonoids, alkaloids, hydrolysable tannins, polyphenols, triterpenes, sterols, and volatile oil⁵⁷.

The *P. amarus* was studied for the anti-oxidant and hepato-protective properties⁵⁷. The leaf extracts of *P. amaruscan* protect the liver against ethanol-induced oxidative damage by reducing the lipid peroxidation rate and can increase the antioxidant defense mechanism in rats.

CONCLUSION: The phytochemical composition and pharmacological activity of the ingredients present in the Thiratchai Kudineer having antioxidant, hepatoprotective, anti-inflammatory, antipyretic, analgesic, anti-viral, anti-bacterial, anti-fungal, anti-diabetic, anti-asthmatic, and immunomodulatory activities.

Moreover, in the developing nations, increased the price of medicine, as well as their side effects, has become a great task when public health is concerned. Hence this simple homemade preparation of "ThiratchaiKudineer" can be suggested to public who are in need of adopting an alternative medicine. Based on this research literature survey strongly support this polyherbal formulations in the Siddha System of Medicine (SSM) can be used to prevent as well as treat various hepatic diseases. This Thiratchai Kudineer (polyherbal) formulation has not been studied for its synergistic pharmacological activities. So we are in need to support the literature evidence mentioned in the classical siddha text, by expanding further research to analyze its toxicological, pharmacological and clinical studies.

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