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**Review Article** 

# AROGYAVARDHINI VATI - A BOON FOR LIVER DISORDERS FROM AYURVEDA (FATTY LIVER) Dasi Padmaja<sup>1\*</sup>, T Maheshwar<sup>2</sup>, D Anuradha<sup>3</sup>, Ch VS Koteswara Rao<sup>4</sup>

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#### **ABSTRACT**

(NAFLD) or the Non-alcoholic Fatty Liver Disease is a global problem affecting a wide range of population associated with co-morbidities. Management of NAFLD is aimed both at managing the liver disease and also its co-morbidities. This is followed with an umbrella of therapeutic modules including lifestyle modifications, diet and the medications. Though both the modern medicine and Ayurvedic medicine follow the comprehensive approach in managing the disease, physicians will be very cautious with medications prescribed as those are associated with adverse effects. In this particular situation, Ayurvedic medicine such as *Arogyavardhini vati* plays a vital role in relieving the liver disorder, maintaining its health and also the health of digestive system thereby improving the overall health and the quality of life of the patient that is greatly disturbed with the liver disorders. *Arogyavardhini vati* that is considered one of the best for the liver disorders is critically reviewed in this study.

# **INTRODUCTION**

(NAFLD) or the Non-alcoholic Fatty Liver Disease is one of the distinct hepatic conditions that have become the global problem and one of the most common causes of chronic liver disease. [1] Chronic liver disease has a worldwide prevalence irrespective of age, sex, region or race. [2] In Western countries, the prevalence of NAFLD in the general population is about 20-30% and this may progress to hepatocarcinoma and liver cirrhosis. [3] As per UK National statistics, liver diseases are steadily increasing over the years and have been ranked as the fifth most common cause of death. [4] They have also been identified as the second leading cause of mortality amongst all digestive diseases in the US. [5]



Asian countries like Japan and China have well documented the increased incidence of NAFLD and Diabetes mellitus (DM), obesity, hyperinsulinemia are said to be its predisposing factors. [6] In India in last two decades, a rise has been observed in incidence of DM, obesity, insulin resistance and NAFLD in India. [7,8] This can be directly correlated to the rise of NAFLD in India due to its limited data on the prevalence. [9,10]

Fatty liver disease is also termed as nonalcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH). Than affecting only the liver, NAFLD is now recognized as a multisystem disease and has been associated with mortality-related cardiovascular disease, chronic kidney disease, extra-hepatic malignancy osteoporosis, with increased liver-related morbidity and mortality. [11] Obese people are also said to have increased prevalence of NAFLD ranging from overweight to obese and severely obese, is associated with NAFLD. [12] Based on the current guidelines, the diagnosis of NAFLD is done the following criteria; 1) the presence of hepatic steatosis (>5% of hepatocytes determined by histology or >5.6% determined by nuclear magnetic resonance techniques); 2) no significant alcohol consumption (defined as ongoing or recent alcohol consumption of >21 drinks/week for men and >14 drinks/week for women) and 3) no competing etiologies for hepatic steatosis. Treatment of NAFLD should be aimed at decreasing disease activity, delaying the progression of fibrosis, and reducing the risk factors associated with their high cardiovascular risk: [13,14]

The management of NAFLD comprises of treating liver disease as well as the associated metabolic comorbidities such hyperlipidemia, insulin resistance, and T2DM. Many studies indicate that lifestyle modification may reduce aminotransferases and improve hepatic steatosis when measured by either US or MR imaging and spectroscopy. [13] Potential therapeutic modules for NAFLD are managed with weight loss lifestyle modification medications, orlistat, sibutramine and bariatric surgery for obesity, insulin sensitizers, metformin and thiazolidinediones (tzds) for insulin resistance lipid lowering agents, statins, fibrates and polyunsaturated fatty acids for dyslipidaemia and antioxidants such as Vitamins E and C, Betaine, Nacetylcysteine and Probiotics like VSL#3 and Oligofructose for Oxidative stress.[15]

The pandemic Covid-19 has made people perceive the significance of immunity, wellness and the importance of Ancient and Alternative Medical sciences such as Ayurveda. Ancient Medical practitioners like Acharya Sushrutha, Charaka and others had discovered the properties of medicinal herbs and minerals centuries ago after years of research and trials and enlisted them in Granthas or the Samhithas which are used as the source of knowledge in the present era. About 70-80% of the world populations rely mainly on the herbal sources also called as nonconventional medicines in the healthcare according to the World Health Organization.[16]

There is a huge diversity in the approach of Modern medicine and Ayurvedic medicine. Ayurveda, an ancient science has evolved as a holistic system with the aim of maintaining the positive health and the prevention of diseases since ages. Modern medicine contributes greatly in the fields of emergency medicine, diagnostic techniques, and surgery where the practice of Ayurveda has proven its effectiveness in the management of chronic diseases. Both the systems of medicine if integrated would be a great benefit to the society in the healing of ailing and the same would be implied for the liver diseases too. [17]

Ayurvedic science is treating liver diseases since centuries and thereby proved its safety and efficacy. As Ayurveda drugs used for liver disorders have less toxicity compared to modern medicine which has more of systemic toxicity and therefore physicians are reluctant to prescribe them for an extended use. [18] Many studies on Ayurveda have shown that Ayurvedic herbs and products comprises bioactive molecules that protect liver from oxidative stress, anti-inflammatory, immune-modulating, liver regenerating, promote virus elimination, block fibrogenesis and inhibit tumor growth *in vitro* and *in vivo* studies. [19]

However, In India more than 50% of the patients with liver disorders depend on Ayurvedic medicine to overcome the problem. Hence, in this study, an attempt has been made to evaluate the efficacy of a formulation named *Arogyavardhini vati* that is described in the *Samhithas* of Ayurvedic science.

#### Yakrut rogas/Liver disorders in Ayurveda

The description of liver can be traced out to Vedas and Ayurveda Samhithas' such as Susruta Samhita, Charaka Samhita and Astang Hrudaya. In Vedas, liver is termed as "Takima" or "Yakna". Yakritkhanda, Yakritpinda, Kalakhanda, Jyotisthana, Raktadhara and Raktashaya are its other synonyms available in the ancient texts. According to Sushruta liver is perceived as Jyotisthana and Acharya Vagbhata quotes it as Yakritkhanda in Ashtanga Hridaya. Yakrit is developed from the Matrijabhava or the structural parts of the Mother and its main function is Ranjana of Rasa dhatu which means transformation of Rasa Dhatu to Rakta dhatu as Yakrit is the seat of Ranjaka pitta. [20]

Yakrit is an important Koshthanga and is the Mulasthana of Raktavahasrotas, Raktavahi and Mamsavahi dhamani. In Ayurveda, the manifestations of diseases are either through Vrudhi (Increase of specific quantity) or Kshaya (decrease of specific quantity) such as Rasa Vrudhi, Rasa Ksyaya, Rakta Vrudhi, Rakta Ksyaya, Mamsa Vrudhi, Mamsa Ksyaya etc. Likewise the disorders of Yakrit are manifested through Yakrit Vrudhi and Yakrit Kshava that can be correlated to hepatomegaly and the cirrhosis of liver as per the conventional medicine. Sushruta explains about Yakridalyudara which can be perceived as Yakrit vridhi but the term Yakrit Kshaya is available in *Bhaisajya Ratnavali*.[21] Charaka samhitha speaks of Yakrit under the management of Plihodara or the management of splenomegaly. The detailed description of Yakrit roga is found in Bhavaprakash as Yakrit vridhi along with its classification and symptomology. The Yakrit vridhi again classified in to Chyuta (displacement from own place due to accident) and *Achyuta* (due to *Rasadi dahtu* and *Rasa*, *Rakta* and *Mamsa vaha srotos*).

In Ayurveda, liver disorders and its management are described in vast and scattered through the entire ancient texts and these are dealt under *Udara roga* or the abdominal disorders. *Yakrit Vridhi* (Hepatomegaly), *Yakrit dalludara*, *Yakritdora*, *Yakrit gata dosa*, *Yakrit Kshaya* (Cirrhosis of Liver), *Yakrit Vidradhi* (Liver abscess), *Yakrit granthi* (hepatic cyst) are some of the disorders based on its structure and *Kamala*, *Kumbhakamala*, *Panaki*, *Halimala*, *Alasa* etc based on its functions that are found in Ayurvedic literature. [22]

Regarding the management, Ayurveda is also known to be far more cost effective and affordable treatment compared to modern medicine or synthetic drugs that have long been associated with side effects. For the liver disorders, Ayurveda advocates the integrated management with lifestyle modification, diet and the Ayurvedic formulations including herbal and herbo-mineral products and these plays a vital role in the management of the disorders. The herbo-mineral products or the *Rasaushadhas* refers to the metal or mineral formulations used for therapeutic purpose.

Ancient classics have very selected and sparing references regarding the usage Rasaushadhas in the management of a disease. Their administration is pressed into usage from the medieval period with Rasaushadhas getting more popular in very short time due to their quicker absorption, faster assimilation and almost instant action even in minute doses without significant sideeffects. As these drugs penetrate into deeper and minute channels of the body to exert instant results, their usage has gained more popularity and acceptance in the management of debilitating and life threatening diseases, where quick and instant result plays a vital role in the recovery as well as cure of the disease.

There are many number of Ayurvedic formulations described for liver disorders such as Phalatrikadi Kasaya, Potala katurohinyadi Kasaya, Varunadi Kasaya, Indukanta Kasaya, Suta sekhara Rasa, Agni kumar rasa, Sanjeevani vati, Arogya Rasa.[23-26] Vardhini Lokanath Rasa. Siddha Makardwaia. Punnavadi kasava. Potala Katu Rohinyadi Kasaya, Vardhamana Pippali Yoga, Panchagobya grita, Paurasaki avaleha, Gomutra Haritaki.[27-29] Arogyavardhini vati is considered as the prime and highest prescribing medicine in liver disorders. The current study focused on the Arogva vardhini vati, herbo-mineral compound preparation that is prescribed by most Ayurvedic practitioners

for liver disorders which is described in detail in the 'Rasa Ratna samucchaya and also Rasa Chandansu and Rasendra kalpa Druma.

# Arogvavardhini vati

*Arogyavardhini Vati* is one among Avurvedic polyherbo-minerals mentioned in formulary.[30] Since centuries it has been used in the management of jaundice, liver disorders, and various skin disorders due to its efficacy and safety. The term 'Aroqva' means good health and 'Vardhini' means the one that enriches and therefore Arogyavardhini means the one which enriches or improves good health. This is indicated to treat the imbalances of all the three *Doshas* (humour). The formulation or the yoga has been mentioned in Rasaratnasamucchaya in the context of Kustha vikaras [31] and in the context of *Yakrit vikaras* of Bhaishyajyaratnavali.<sup>[32]</sup> Though Rasaratnasamucchaya advised Arogyavardhini vati as Sarvarogaprashamani as its main indication, it is also used to treat lack of appetite, indigestion and irregular bowls, hepatic disorders or liver disorders and skin diseases, leprosy, fever, oedema, obesity, jaundice, and also as an alternative, carminative stomachic. [33]

# Ingredients of Arogyavardhini vati

It consists of Terminalia chebula (Haritaki), Terminalia bellerica (Bibhitaka), Emblica officinalis (Amalaki), Asphaltum (Silajatu-Suddha), Commiphora wightii (Guggulu Shuddha), Ricinus communis (Eranda), Picrorrhiza kurroa (Katuka), leaf juice of Azadirachta indica (Nimba) and metals including Shuddha Rasa (purified mercury), Shuddha Gandhaka (purified sulfur), Lauha Bhasma (iron compound in ash form), Abhraka Bhasma (mica in ash form), and Tamra Bhasma (copper compounds in ash form).

# Preparation of Arogyavardhini Vati

All the above ingredients are taken and made into a fine powder and is grounded with the juice of *Nimba* leaves for two days. After making into a fine paste, pills are prepared equal to the size of *Rajakola* or the Indian jujube fruit. Acharya Hariprasanna Sharma quotes that the size of the pills should be like that of *Kshudrakola*. These pills finally presents in black colour and with bitter taste. Scholars advise 500mg-1gm as per day dose. [31-33, 34]

#### Indications of *Arogyavardhini Vati*

With respect to Eminent Acharyas like Rasaratna samucchaya, Bhaisajyaratnavali and Bharatbhaisajya ratnakara, *Arogyavardhini vati* is indicated in *Kushta* due to its *Kushtanashaka* properties and said to alleviate all types of skin disorders if administered for 1 *Mandala* or 14 days. As it is *Tridosha jvara nashaka*, it is also indicated for the same and administered for 5 days. Apart from its

above properties it is also a *Hridya* (cardio protective), *Medonashaka* (can hyperlipidemia), *Malashuddhikari* (cleansing of waste materials), increases hunger or *Kshudha* (appetizer), *Sarvaroga prashamani*, one which alleviates all the *Rogas*, *Pachani* (digestive), *Dipani* (appetizer) and *Pathya*. [30] Last, but not the least it is indicated in the liver disorders in Rasarathna samucchaya as the most effective medicine.[31]

# Anupana (Adjuvant)

Arogyavardhani vati is prescribed with various types of Anupanas or the adjuvant based on the Vyadhi, its stage and the strength of the patients. These are Moong dal (Vigna radiate (L.) R. Wilczek,) Masur dal (Lens culinaris Medik.; Arhar- Cajanus cajan (L.) Millsp), Ghee (ghee made from cow milk), Barley (Hordeum vulgare L.; Parwal Trichosanthes dioica Roxb), curds from cow milk, milk (cow milk), Urad dal (Vigna mungo (L.) Hepper, sugarcane juice, jaggery, butter milk, Dashamula kwatha and Punarnavadi kwatha. [35]

#### DISCUSSION

Ayurvedic science aims at maintaining positive health by balancing the three *Doshas* such as *Vata*, *Pitta* and *Kapha*. Any imbalance in these leads to the disorders and in turn these are the causes for liver disorders too. Ayurvedic management of liver disorders comprises the integrated approach with proper diagnosis after the evaluation of *Dosha*, *Srotas*, *Bala kala* etc. Since NAFLD is a multi-factorial disease, single target based therapy has limited implications. Hence Ayurvedic approach with the lifestyle modification, *Pathya* and herbo-mineral formulations like *Arogyavardhini vati* would be very effective in alleviating the liver disorders.

Aroavavardhini vati consists of many ingredients among which Haritaki (Terminalia chebula), the chief is an astringent and laxative is effective in relieving liver disorders and very effective in fatty liver and cirrhosis of liver. Bibhitaki (Terminalia belerica) is a laxative, anthelmintic and effective in digestive disorders. Amalaki- (Emblica officinalis) being an astringent, antibacterial, carminative, hypoglycaemic, stomachic, hypotensive is effective because of its anti-hepatotoxic, antioxidative, and immuno-modulatory properties. Along with the herbal ingredients *Arogyavardhini vati* also consists of the minerals such as *Shuddh shilajit*, which like a nectar and an effective for vitality. With its powerful antioxidant properties it can delays the process of aging, effective in kidney diseases, liver diseases, digestive disorders and mental illness. Guggulu (Commiphora mukul) is an oleo-gum-resin helps in reducing cholesterol by converting it into

bile. This is also effective in removing the unwanted fats and balancing the cholesterol levels. The formulation also consists of *Chitraka* (*Plumbago zeylancia*) that is effective in relieving loss of appetite, indigestion, piles, liver diseases, worms, colitis and various. Including *Picrorrhiza kurroa* to the formulation makes it effective in liver disorders. It is said to be more effective in liver damage caused by chemicals such as carbon tetrachloride, alcohol, paracetamol etc. [30]

Ayurvedic herbs have demonstrated the wide range of biological activities including liver fibrosis attenuation, NAFLD prevention, hepatic protection, cholestasis elevation, Hepatic carcinoma inhibition by their anti-inflammatory, anti-oxidant and immune regulation mechanism etc. [36]

# Clinical Applications of *Arogyavardhini Vati* Chronic Liver Diseases (CLD)

With Ayurvedic formulations, the reduction in hepatic cancer invasion, metastatic adhesion and induction of apoptosis are observed in hepatocellular carcinoma. Few studies have reported that Ayurvedic medications have significantly increased the thrombocytes in thrombocytopenia of alcoholic liver diseases [37,38] with a positive outcome in chronic liver diseases (CLD).

#### **Auto Immuno Liver disease**

A case study report showed Ayurveda complex regimen is excellent in the management of Asatymyaja or Swabhava satmya viparyaya Yakrit vikara (Auto Immuno Liver diseases). [39] Snehana, Swedana, Nitya Virechana and Vamana are also found useful in chronic liver diseases. [40]

#### **Hepatitis**

In a double-blind trial of Antarkar et al, acute viral hepatitis was treated with *Arogyavardhini* and it showed significant hepato-protective effects with the improvement in hepatitis. [41]

A case study of 53 years old male patient with the complaints of yellowish coloured urine, reduced appetite along with generalized weakness, nausea and mild pain in right hypochondriac region was treated with herbomineral preparations such as *Phalatrikadi Kwath, Arogyavardhini Vati,* Liv52 HB and *Rohitakarishta* etc. described in classical texts of Ayurveda for 6 months. Both the subjective and objective assessments were done (pathological) before during and after the treatment. Significant changes were observed in both subjective and objective parameters after the completion of treatment.<sup>[42]</sup>

## Non Alcoholic Fatty Liver Disease

In the study of Panda et al, two Avurveda formulations such as Argyavardhini vati and Phalatrikadi kwatha having high concentration of Katuki (Picrorhiza kurroa) were selected for the study on NAFLD. This involved two cases one male and one female and the treatment was administered for a period of 12 weeks. Liver function test, Haemogram, Renal function test and cholesterol profile along with ultrasound of liver were performed D<sub>0</sub>, after 4 weeks, 8weeks and 12 weeks for both the cases. 12 weeks of treatment showed that the elevated liver enzymes and elevated echogenicity were normalized with no adverse effects. [25]

# **Alcoholic Fatty Liver**

An Open Randomized Clinical Trial (RCT) was at Bharati Vidvapeeth Foundation's Avurveda Hospital and Research Centre, Katraj, Dhankawadi, Pune. 40 Patients with the features of AFL were screened and included for the study and were allotted into two groups by random lottery method. The trial group was administered 500mg of Arogyavardhini vati and the control group Tab LIV 52 DS twice daily with Koshana jala Anupana after meals for 90 days. Subjective parameters such as anorexia, vomiting, abdominal distention, abdominal pain, nausea, fatigue and the objective parameters such as USG abdomen and LFT blood reports were assessed before and after the treatment. Trial group with Arogyavardhini vati showed significant changes compared to the control group. [43]

#### **Alcoholic Liver Disease**

In Sahoo et al, a case report of Alcoholic liver disease was studied who presented with symptoms such as nausea, vomiting, swelling in bilateral foot, weakness in the body, reduced appetite, gradually weight reduction and semisolid stool with frequency of 6-7 times/ day associated with reduced appetite and frequent vomiting. In this patient, Ayurvedic treatment was administered for 2 months among which one medication was *Arogyavardhini vati* that showed significant changes both in subjective and objective parameters. After 7 months of treatment, the patient was free from complications. [44]

A case report of 44 year old male patient with jaundice, abnormal liver functions (high transaminases and hyper bilirubinemia) and positive hepatitis B marker and fatty liver diagnosed as viral hepatitis and reports suggesting of acute viral hepatitis B and Alcoholic Liver Disease (ALD) was administered Ayurvedic medications along with dietary advices. After 72 days of treatment,

significant improvement was observed in clinical findings, reduction in liver transaminases, and fatty infiltration after the treatment. The patient became hepatitis B surface antigen negative, though no studies on reduction in viral load of Hepatitis B Virus (HBV) and anti-HBc (Hepatitis B core antibody) was done, but the clinical improvements and reduction in transaminase and fatty liver indicate a possible role of Ayurvedic therapy in hepatic injury due to HBV and ALD. [45]

# Animal experimentations on Liver disorders and *Arogyavardhini vati*

A study that evaluated the hepato-protective effects of *Arogyavardhini rasa* or *Vati* on paracetamol (PCM)-induced liver damage in rats showed that *Arogyavardhini rasa* prevented the hepatotoxicity and the protection of liver tissue from PCM-induced hepatotoxicity by supporting the histo-pathological examinations. [46]

One of the studies evaluated the protective effects of Arogyavardhani on D-galactosamine (d-GalN)- induced fulminant hepatic failure, where rats were administered an intraperitoneal injection of d-GalN (270mg/kg). *Arogyavardhani* (10mg/kg and 50mg/kg) was administered orally for 14 days continuously, and on the last day at 1hour before the d-GalN injection. Rats were sacrificed 24 hours after the d-GalN. Silymarin (100mg/kg body weight) was given orally as a standard hepatoprotective drug.

The liver injury was assessed biochemically. investigating biochemical parameters like ALT, AST, ALP, Bilirubin, Total Protein, and Albumin. The survival rates after the application of Arogyavardhani at 24 h were also observed. D-galactosamine administration induced a significant increase (P≤0.01) in total bilirubin associated with a marked the activities elevation of aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) as compared to control rats. The pretreatment of *Aroavavardhani* attenuated these changes in a dose dependent manner. The survival rate of the OC groups was significantly higher than that of the d-GalN group. Our results suggest that Arogyavardhani has hepatoprotective effects against D-galactosamine induced hepatic damage. Therefore, Arogyavardhani may be used as a hepatoprotective agent against various liver diseases including toxic liver injury. [47]

# Katuki (Picrorrhiza kurroa)

Katuki, being one of the main ingredient of the Arogyavardhini vati has also been studied to assess its effect in liver disorders. Katuki (Picrorrhiza kurroa)- Kutaki is bitter in taste, cooling and removal of excessive fire energy from the body, best of removal of excessive *Pitta* from the body via colon. *Katuki* helps in restoration of Liver functions by overcoming fatty liver changes. Research on animal studies suggested *Picrorrhiza kurroa* effective in hepatitis B infection and promising effect on bilirubin, SGOT, SGPT, preventing liver toxicity and improves hepatic glycogen preservation. It also promotes liver regenerating activities by restoring cytochrome. [48, 49]

Apart from liver disorders or the *Yakrit rogas*, *Arogyavardhini vati* has also proved its effects on other health disorders such as

#### Cardiovascular Disorders

Safety of *Arogyavardhini Vati* on liver, kidney, and brain has been evaluated in earlier studies.<sup>[50]</sup>

# Dyslipidemia

In a prospective clinical study conducted at All India Institute of Medical Sciences, New Delhi, 108 patients were screened and ninety-six patients with dyslipidemia and a poor history of lipid control were enrolled for the study. They were treated with Arjuna powder (5 g, twice a day) for 3 weeks followed by *Arogyavardhini Vati* (500mg, twice a day) for next 4 weeks brought about significant reduction in the level of risk factors of CVD arising from dyslipidemia and inflammation. Use of *Arjuna* powder and *Arogyavardhini Vati* to the currently available hypolipidemic therapy would offer significant protection against atherosclerosis and CAD with a reduction in the dose and adverse effects of hypolipidemic agents. [51]

# Metabolic Syndrome (MS)

In a double blind placebo controlled randomized clinical trial, seventy five patients were registered for the trial and randomly divided into two groups and were treated with lifestyle modification with and without *Arogyavardhini* compound for 8 weeks.<sup>[52]</sup>

# **PCOS- Polycystic Ovary Syndrome**

In a study conducted in the department of Prasuti tantra and Stree roga of National Institute of Ayurveda, Jaipur that included 110 women of 18-40 years diagnosed to have PCOS were divided in two groups with 50 patients in each. Group A received Pathadi Kwatha and Arogyavardhini vati and Group B received Kanchnaradi kwatha and Arogyavardhini vati. The study showed significant in the group A compared to Group B and was effective in reducing Dermatologic manifestations of PCOS (Dhatvagnimandya Janya Beejagranthi Vikara). [53]

From the above critical extraction and evaluation of *Arogyavardhini vati* from the Ayurvedic literature and the studies conducted, it definitely shows promising results in providing the effective

results in the liver disorders and particularly the fatty liver also called as NAFLD, one of the commonest among the current digestive disorders. More clinical studies are needed to authenticate its efficacy so that it can be administered as the main medication foe the fatty liver disorders.

#### CONCLUSION

Arogyavardhini vati as the name itself indicates that it improves the *Aroyaa* of the person who consumes it apart from all its other benefits. Though it is a herbo-mineral formulation, it is free from adverse and toxicological effects as it will be prepared according to the classical method and principles without compromising the qualities. It is considered as the best medicine for liver disorders as it maintains the health of the liver and thereby a healthy digestive system apart from relieving the liver disorders. Though it has proved its efficacy through few animal experimentations, case studies and case series, larger clinical studies are needed to be conducted with a larger sample size to validate its efficacy and to make it applicable to the larger population.

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