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INTEGRATIVE EVALUATION OF AYURVEDIC INTERVENTIONS FOR NON-ALCOHOLIC STEATOHEPATITIS (NASH): A COMPREHENSIVE REVIEW OF PATHOPHYSIOLOGY, DIAGNOSIS, AND THERAPEUTIC APPROACHES

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ABSTRACT

Introduction: Non-Alcoholic Steatohepatitis (NASH) is a severe form of Non-Alcoholic Fatty Liver Disease (NAFLD) characterized by liver inflammation, cell injury, and progressive fibrosis. The condition poses a significant risk for advanced liver diseases including cirrhosis and hepatocellular carcinoma. Despite advancements in understanding, treatment options remain limited. Ayurveda, with its holistic approach, offers potential adjunctive strategies.

Methods: This review integrates current knowledge on NASH, including its epidemiology, pathology, and conventional management approaches. It also explores Ayurvedic concepts relevant to liver health, including diet, detoxification, and therapeutic herbs. A comparative analysis of Ayurvedic practices and conventional treatments is presented.

Results: NASH is prevalent in adults aged 35-55, with significant variations in prevalence across populations. Key diagnostic methods include liver imaging, serology, and biopsy. Conventional treatments focus on lifestyle changes, weight management, and medications like vitamin E and ursodeoxycholic acid. Ayurveda offers complementary approaches such as Panchakarma, dietary

modifications, and specific herbal formulations. Evidence suggests that Ayurvedic treatments can enhance liver function, reduce inflammation, and improve metabolic health.

Discussion: While conventional treatments address symptoms and progression, Ayurvedic practices provide additional benefits through detoxification and metabolic regulation. Ayurvedic formulations like Arogya Vardhini Vati and Patolakaturohinyadi Kashaya show promise in managing NASH, particularly by modulating lipid metabolism and inflammation. However, more rigorous clinical trials are needed to validate these findings.

Conclusion: Integrating Ayurvedic therapies with conventional treatments may offer a holistic approach to managing NASH. Further research is essential to establish the efficacy and safety of Ayurvedic interventions, potentially enhancing treatment outcomes and patient quality of life.

Keywords: NASH, Liver disorders, Panchakarma, Pathya-Apathya, Yoga

INTRODUCTION

Liver is considered to be the biggest chemical factory of the body as it is concerned with filtration, metabolism, detoxification and other vital functions. Non- alcoholic steatohepatitis (NASH) represents a part of a wide spectrum of non-alcoholic fatty liver disease (NAFLD).

Steatohepatitis is the preliminary and most common histological response to hepatotoxic stimuli. It is more prone in age group 35-55 years and there was a predominance of female. NASH constitutes around 6% of all chronic hepatitis cases **[1]**. Liver has difficulty for breaking down fat, which causes a buildup in liver tissue. These ranges from simple steatosis to steatohepatitis to advanced fibrosis and cirrhosis **[2]**. 20–25% of cases with NASH have or will progress to cirrhosis **[3]**.

Prevalence of the disease in Indian population about steatosis is the most common cause of raised transaminases and affects nearly 10-24% of general population while only 2-3% in the general population has steatohepatitis. In patients undergoing liver biopsy, prevalence of NAFLD and steatohepatitis ranges from 15-39% and 1.2-4.8% respectively. However, on imaging steatosis and steatohepatitis ranges from 9.7-23% and 1.2-4.8% respectively **[4]**. Balloon degeneration is a recognized form of liver cell injury and is a significant feature of NASH **[5]**.

A portion of individuals with non-alcoholic fatty liver disease progress to a condition known as non-alcoholic steatohepatitis (NASH), which is marked by liver cell damage, inflammation driven by innate immune cells, and the advancement of liver fibrosis. Hepatic dysfunction is frequently caused by non-alcoholic fatty liver disease (NAFLD). It is a metabolic disease with hepatic presentation that is linked to obesity, insulin resistance, and dyslipidaemia **[6]**.

In India, avoidable diseases are becoming recognised as public health issues. The Alcohol-related disorders and NAFLD are more common than above the severity of hepatitis virus. NAFLD is part of the national initiative. in order to avoid and manage non-communicable illnesses (NCDs), such as diabetes, cancer, and stroke **[7]** Ayurveda can greatly aid in the management of Due to Ayurveda's unique metabolic theory (Ama) and high acceptance rate, NAFLD eccentric action (prevent hepatic regeneration and fibrogenesis) secure and useful in several contexts **[8]**.

The mechanisms driving hepatic inflammation in NASH are not fully understood but seem related to the inflammatory environment created by lipotoxicity from toxic lipid-induced liver cell damage **[9]**.

There are two key concepts regarding the role of cell death in NASH inflammation:

(A) Apoptotic liver cells can trigger inflammation directly when their remnants are ingested by macrophages.

(B) Apoptotic liver cells may indicate widespread stress in surrounding cells, which could exacerbate inflammation through the release of pro-inflammatory extracellular vesicles **[10]**.

If NASH halted in initial stage can avert further progression of disease. Many studies have shown that Katuki, Nimba, Amritha, Bhringraj and Bhumyamalaki have been evaluated individually for their clinical efficacy in Hepatological disorders and found to have Hepato protective, Anti-inflammatory, Hepatotonic, Anti-hepatotoxic and Anti-viral properties. Effective management of NASH is crucial to prevent the potential risks of cirrhosis, end-stage liver failure, and hepatocellular carcinoma. Currently, the treatment options for NASH primarily focus on dietary changes and lifestyle modifications.

Methods

This review article utilizes a comprehensive literature review approach to evaluate Ayurvedic interventions for Non-Alcoholic Steatohepatitis (NASH). The methodology includes examining traditional Ayurvedic texts and recent clinical studies from databases such as PubMed and Google Scholar. Key search terms include “NASH,” “Ayurveda,” and “liver disease management.” The review focuses on peer-reviewed articles, clinical trials, and systematic reviews, applying inclusion criteria for relevant studies and exclusion criteria for unrelated or low-quality research. Data extraction involves assessing study design, interventions, and outcomes, with quality evaluated using tools like the Cochrane Risk of Bias. The synthesis includes reviewing therapeutic approaches, mechanisms of action, and clinical efficacy of Ayurvedic treatments, with

recommendations for integrating these treatments with conventional therapies.

Diagnosis and Assessment

Liver imaging and clinical variables work together to diagnose fatty liver. Detailed alcohol intake is part of the clinical evaluation process.

medicines, review of personal and family metabolic risk factors, serologic tests and medical history, including supplements. Diagnostic procedures for serology and MRI, transient elastography (TE) ultrasonography, and biomarker panels.

It is possible to stage fatty liver using elastography (MRE) the most reliable. A biomarker panel that determines likelihood is the liver fibrosis score (NFS).

indicating advanced fibrosis according to easily accessible clinical data, such as age, BMI, AST, platelets, albumin, ALT, and whether or not there is impaired fasting glucose. The gold standard for fatty liver diagnosis and evaluation is a liver biopsy **[11]**. Liver function test (LFT) these tests used to detect the presence of liver disease, distinguish among different types of liver disorders, gauge the extent of known liver damage, and follow the response to treatment **[12]**.

Pathology of NASH

The American Association for the Study of Liver Diseases defines non-alcoholic fatty liver disease (NAFLD) as the development of fatty liver in patients without a history of persistent excessive alcohol intake (i.e., alcohol intake of <20 g ethanol/day) **[13]**. The non-alcoholic fatty liver (NAFL) and the more severe non-alcoholic steatohepatitis (NASH) are the two histologically differentiated conditions that make up NAFLD, according to the recommendations set out by the American Association of Hepatology (AASLD). These pathophysiological abnormalities may progress into potentially fatal hepatic cirrhosis and hepatocellular cancer within a few decades **[14]**. Day and James presented the first "two-hit" theory for the pathophysiology of NASH based on the existing preclinical evidence. The same was widely acknowledged and continued to be the sole thorough explanation for NASH **[15]**.

This theory has been revised in light of new knowledge about the clinical signs of NASH and how it interacts with other metabolic illnesses. Hepatic steatosis was thought to be the “first hit” that eventually results in a “second hit” according to the “two hit hypothesis.” Recent studies have unequivocally shown that hepatic steatosis is the underlying cause of several other clinical symptoms, not only a "first hit." **[16]** As a result, the "multiple parallel hits" theory—which holds that insulin resistance serves as a priming condition for the development of NASH—has been updated in light of current data **[17]**.

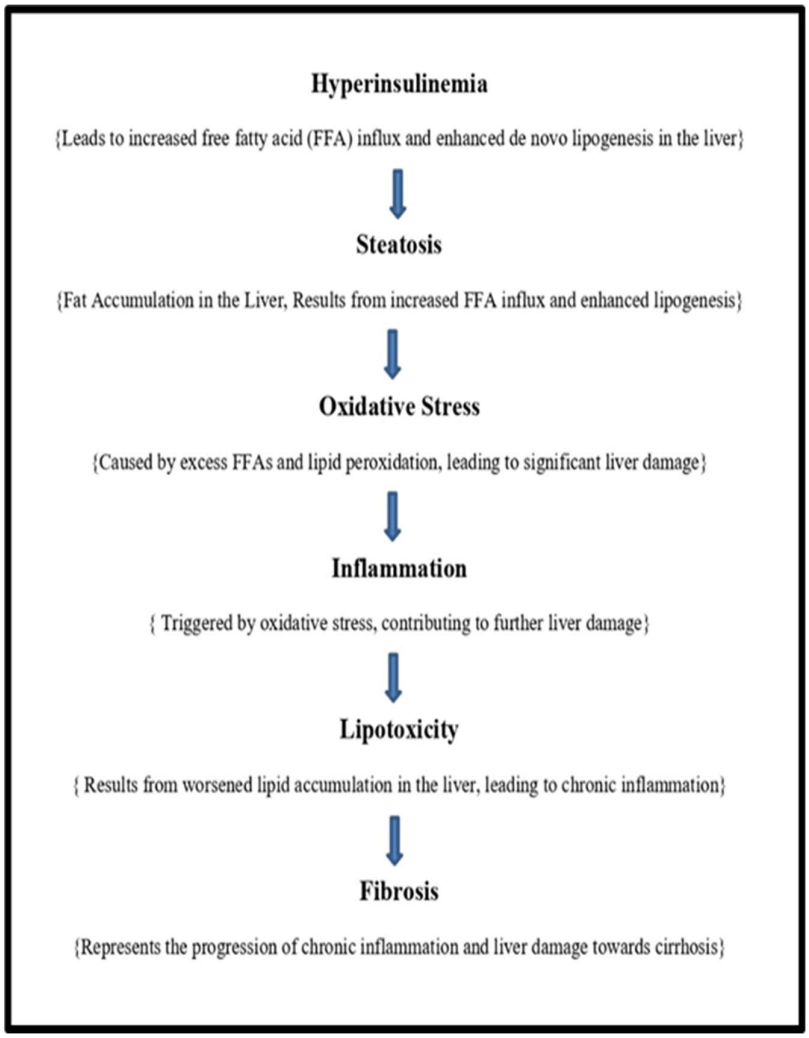

Figure 1: Pathogenesis of Non-Alcoholic Steatohepatitis (NASH)

Kaphaja Yakrutodara

This Non-alcoholic steatohepatitis can be compared with Kaphaja yakrut roga in Ayurveda as lakshanas are correlating to NASH.

Lakshana: Mandha vyatha, Kathinyata, Gouvravata, Arochaka, Agnimandhya according to Bhavpraksha.

Symptoms: Pain in right upper quadrant, Enlarged, Hard, Feeling of heaviness, Loss of appetite.

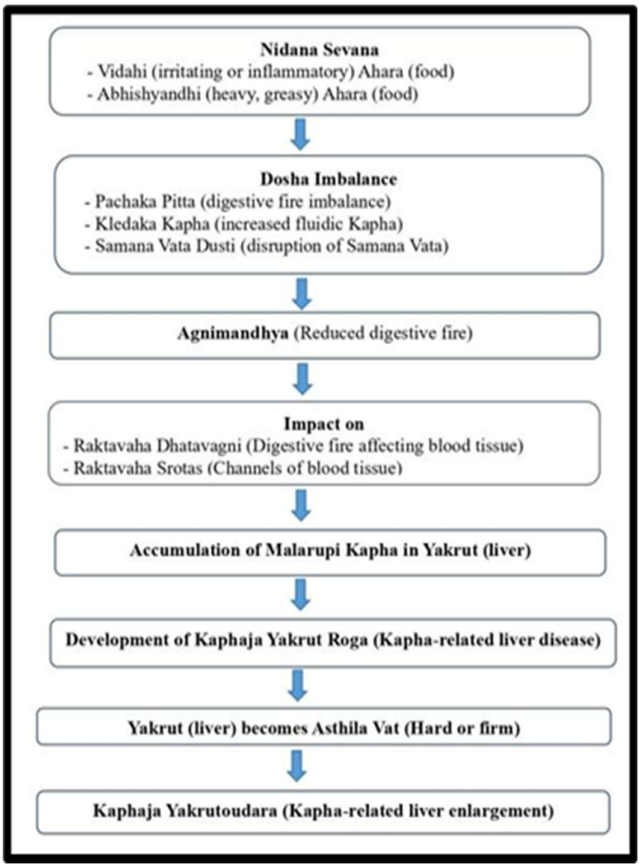

Figure 2: Pathogenesis of Kaphaja Yakrutodara

Histological Differential Diagnosis

Viral hepatitis, particularly hepatitis C, primary biliary cirrhosis, autoimmune hepatitis, 1-antitrypsin deficiency, and hemochromatosis are the disorders that can cause steatohepatitis. While it might be challenging to differentiate chronic hepatitis C with Mallory-type inclusions from steatohepatitis, portal or periportal hepatitis centrilobular hepatitis (inflammation in zone 3) is a common feature of chronic viral or autoimmune hepatitis. Focal fatty alterations can potentially be confused with a focal lesion of steatohepatitis.

Clinical features

Hepatomegaly (75%) and splenomegaly (25%) are the most common signs in NASH patients. The presence of ascites and spider angiomata indicates development of cirrhosis. Nonspecific constitutional symptoms of weakness, fatigue, and malaise precede in a third of NASH patients **[18]**. Despite similarities, patients of NASH are mostly asymptomatic whereas patients of alcoholic hepatitis are always symptomatic. NASH due to drugs or nucleoside analogues, antimitotic agents, or tetracyclines can present dramatically with rapid onset of fulminant hepatic failure.

Upadrava

Yakruttodara can be manifested if chikitsa is not adopted in proper avastha of the vyadhi. Further leading to jalodara.

Complications: Further stages of liver pathogenesis manifests like

- Fibrosis of liver
- Cirrhosis of liver
- CA of liver

Chikitsa

The primary goal of chikitsa is to restore the balance between the doshas and dhatus. This can be achieved either through shodhana or shamana in conjunction with nidana parivarjana. Treatment for Yakrut roga is similar to that of Pleeha roga, as stated inBhavpraksha **[19]**. Shodhana: virechana karma is advocated in pitta pradhana vyadhis. It is useful in pitta rogas and also suitable in vata and sanshrusta rakta and disorders of kapha. Since kapha plays a significant role in samprapti in this disease, ruksha virechana can be adopted for samprapti vighatana purposes, as well as pittahara, Yakrut uttejaka, and kaphahara.

Treatment

The various treatment options specific for NASH are limited and their role in the treatment of NASH.

Weight Reduction: It has been shown that weight loss is effective in getting serum amino transferases back to normal in obese individuals, both in adults and children. Not the quantity of weight lost, but the method of weight loss is crucial in weight reduction therapy for NASH patients; too fast weight loss may be detrimental and can worsen portal inflammation and fibrosis. Although a weight reduction goal of 230 grammes per day or 1.6 kg per week is not advised, it seems to be a rather safe target. After evaluating various calorie limitations, an adult should consume 45–100 grammes of high-quality animal protein, fewer than 100 grammes of carbs, and less than 10 grammes of fat per day to get a suitable diet that provides around 600–800 kcal of energy.

An essential lipid-soluble antioxidant, vitamin E (RRR--tocopherol) may scavenge free radicals and prevent lipid peroxidation. As a result of research conducted in recent years on the therapeutic effects of vitamin E supplementation on NAFLD and NASH, vitamin E is now recommended as a first-line medication for individuals without diabetes who have biopsy-proven NASH **[20-23]**.

However, vitamin E is not advised for the treatment of nonalcoholic steatohepatitis (NASH) in individuals with diabetes, cirrhosis-associated NASH (NASH with cirrhosis), or cryptogenic cirrhosis. Ursodeoxycholic acid has an influence on the immune system, cytoprotection, and membrane stabilisation. Transaminases and the degree of hepatic steatosis significantly improved in three open-label patient studies on the effect of UDCA in NASH (dosage of

10- 15 mg/kg/day for 6–12 months) as compared to baseline.

Liver Transplantation: Numerous NASH patients who experienced chronic liver disease underwent liver transplantation. Due to the possibility that orthoptic liver transplantation fails in NASH patients, NASH is regarded as a relative contraindication to liver transplantation since it recurs in about 2/3 of these patients in the new donor liver and in 1/3 of them in the replacement liver. Significant fibrosis developed in less than a year. Ayurveda approaches in health promotion of NAFLD. Although obesity is a major contributing factor to the death and morbidity of fatty liver disorders, insulin resistance and metabolic syndrome—which include intrahepatic triglyceride buildup and inflammation—also play a significant impact.

Genetic susceptibility combines with behavioural and environmental variables to cause fatty liver. Although the precise process leading to the buildup of hepatic fat and the development of non-alcoholic steatohepatitis (NASH) is not fully known, the development of fatty liver can be stopped by lowering the intrahepatic lipid (IHL) concentration. Within three months, lifestyle changes that incorporate both physical activity and food can lower the IHL by up to 40%.

According to Ayurveda, health is defined as the harmony of the body, mind, and soul. In Ayurveda, the process of renewal, regeneration, and reversal of aging and illness involves detoxification through Panchakarma, the use of herbs and minerals, specific diets, exercises, yoga, pranayama (breathing exercises), and meditation, all contributing to self-realization. Important elements of an Ayurvedic food plan for the prevention and treatment of liver illnesses include digestion capacity (Agni) and constitution (Prakriti).

Patients with impaired digestive function should have a liver function test first, and they should start with deepana (digestive) and pachan (carminative). The popular carminative and digestive herbs shown below can be utilised to maintain a healthy liver. persons who have Pitta prakruti are sensitive to alcoholic liver problems, whereas Kapha prakriti persons are prone to fatty liver. Stress is characterized by the subjective experience of negative emotions paired with physiological responses, often leading to uncomfortable physical symptoms such as muscle tension, elevated blood pressure and heart rate, digestive issues, and abnormal liver function tests.

1.1 Shodhan Chikitsa/Panchakarma therapy (detoxification)

By oxidation, reduction, and conjugation, the human body creates toxic chemicals such urea, carbon dioxide, ammonia, and

aldehydes. It also removes toxins from cells and tissues by breathing, urine, perspiration and stool via a natural detoxifying procedure. There are several examples of the accumulation of bioaccumulative persistent toxicants (PBT) in biological blood, urine, breast milk, and adipose tissues as a result of the release of contaminants in the environment, such as heavy metals, synthetic chemicals, and xenobiotics, pesticides on food, dust, water, air, and soil. Detoxification, or detox, is the phrase a huge hit among the younger generation. For detox, patients have shown self-motivation. treatment in recent years for liver disorders, weight reduction, and addiction recovery from excessive alcohol use and believed to be the cure-all for many non-infectious diseases with a psycho-somatic basis.

Detox treatment is also indicated for conditions such as gastrointestinal disorders, autoimmune diseases, chronic fatigue syndrome, and endocrine imbalances and disorders affecting the liver and kidneys. The act of converting poisonous parent substances into harmless metabolic forms or getting rid of toxins without endangering or injuring people is known as detoxification, or detox. Ayurvedic treatments known as panchakarma involve removing toxic chemicals via the use of snehana (Oil therapy), swedana (sudation), vamana (vomiting), virechana (purgation), and vasti (enema). Rakta mokshyana, or bleeding, is occasionally used in Panchakarma to expand the liver. Through the creation of bile acids, panchakarma can alter the makeup of gut bacteria and the metabolism of fats **[24]**.

1.2 Pathya-Apathya (Diet plan) for Liver disorders

A higher intake of fruits, legumes, vegetables, nuts, whole grains, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), along with a reduction in red meat and trans fats, has been associated with a lower incidence of steatosis. In cases of fatty liver disease, a diet high in minerals can lower intrahepatic lipid levels. In Ayurveda, there have been descriptions of the Pathya (wholesome diet) and the Apathya (unwholesome diet) for the liver **[25, 26]**. Diets low in carbohydrates, high in fibre, and mono-saturated fat are recommended, whereas diets heavy in fructose and sugar should also be avoided.

Table 1: Pathya-Apathya (Diet plan) for Liver disorders

Items	Pathya (Wholesome diet)	Apathya (Unwholesome diet)
Cereals	Shashtika, Yava, Godhuma, Laja, Manda	Rice flour, Tila, drugs having Ushna, Lavana , Amla, Vidahi Gunas
Pulses	Mudga	Masa
Fruits	Draksha, casted apple, pomegranate, apple, Ripened kiwi	Orange, lemon, mango, watermelon
Vegetable	Potala, Shigru, snake guard, Jeevanti, punnanova, Radish, beans, brinjal, potato	Chilly, bitter guard, pickle, all leafy vegetables (Saka)
Milk Product	Ghee, Milk, Takra	Curd
Non Veg	Mamsa Rasa with Dashamoola	All fish
Others	Gomootra, Asava, Arishta.	Sura, Madhya, salt

1.3 Yoga, Mindfulness, and Physical Conditioning (Yogic Poses, Meditation, and Exercise)

Over the past ten years, non-pharmacological techniques to treating several non-communicable illnesses have gained popularity in clinical practice. These approaches include pranayama (breathing exercises), asana (yogic postures), and dhyana (meditation). Yoga therapy has been shown to be effective in treating obesity, pre-diabetes, and healthy liver function.

Yoga practices like Kapalabhati Pranayama, Ardha Matsyendrasana, Gomukhasana, Dhanurasana, Balasana, and Dhyana (Meditation) have demonstrated benefits for both NAFLD and NASH **[27]**.

The skill of meditation is the effective and flexible control of neurobehavioral energy, involving complete involvement or non-participation in conscious thought and sensory awareness. Deep relaxation combined with a happy mood and increased energy may be achieved via practicing meditation for a minimum of 12 weeks, which can alter awareness, concentration and thoughts.

Long-term meditation practice (at least 12 weeks) has been shown to reduce alcohol and nicotine cravings, lower peer pressure, and lessen the physical withdrawal symptoms. Thus, practicing yoga and dhyana can either stop the onset of liver disease or stop it from getting worse.

1.4 Behavioural changes

More focus is being made on the application of short motivational strategies and/or evidence-based behaviour modification techniques to support effective lifestyle behaviour change. These strategies are designed to enhance volition by encouraging realistic approaches such as goal setting and identifying barriers to help patients plan and sustain behavioral changes over time. They also aim to boost motivation by addressing common misconceptions, identifying personal reasons for change, and finding effective ways for patients to successfully modify their lifestyle behaviors. To achieve the best outcomes, habits such as smoking, alcohol consumption, and the intake of

sugary drinks should be eliminated. For best results, the habits of smoking, drinking alcohol, and using drinks can be broken **[28]**.

Liver directed Ayurveda therapy

The only liver-directed Ayurvedic medications are Pitta saraka (bile excretion), Sothagna, and pittghna (which decrease bile production), as well as Yakrit uttejaka (liver stimulant). The botanicals used in Ayurveda medicine include Varuna, kakachchi Bringaraj, Daruharidra, Kumari, Katuki, Kalmegha, and Apamarga root. Takra vasti and Virechana have been practicing with positive results. Panchakarma and Ayurvedic medicines can alter the makeup of gut flora, enhance hepatic lipid metabolism, inhibit hepatic lipogenesis, control mitochondrial dysfunction, modify lipid metabolism through bile production, and reduce hepatic inflammation. The advancement of liver disorders brought on by alcohol can be slowed down by rohitaka.

DISCUSSION

Despite the registration of numerous clinical trials exploring the potential of various treatments, there remains a noticeable gap in published data, particularly in the form of case series, case studies, pilot clinical trials, and full-scale clinical trials. This is particularly evident in the context of Ayurveda, where traditional formulations have shown promise in improving liver health and metabolic functions.

Ayurvedic medications like Argya Vardhini Vati, Patolakaturohinyadi Kasaya, Rohitaka Churna, and Sarapankaha Churna have been observed to play a significant role in the management of liver-related disorders, particularly Non-Alcoholic Fatty Liver Disease (NAFLD). These formulations have been reported to enhance hepatic lipid metabolism, prevent hepatic lipogenesis, regulate mitochondrial dysfunction, and modulate lipid metabolism through bile synthesis. Additionally, they are believed to modulate hepatic inflammation by promoting apoptosis and autophagy and correcting gut bacterial composition, which is increasingly recognized as a critical factor in liver health.

The mechanism of action of these Ayurvedic formulations aligns with the underlying pathophysiology of NAFLD, which is characterized by an imbalance in lipid metabolism, oxidative stress, inflammation, and gut dysbiosis. By addressing these key factors, Ayurveda offers a holistic approach to managing NAFLD, which could complement existing medical treatments.

CONCLUSION

Currently, no pharmacological agent has been officially approved specifically for the treatment of NAFLD, leaving a significant gap in effective therapeutic options. The accumulated evidence from both traditional knowledge and emerging research suggests that Ayurvedic formulations like Argya

Vardhini Vati, Patolakaturohinyadi Kasaya, Rohitaka Churna, and Sarapankaha Churna hold potential for inclusion in the current practice guidelines for NAFLD management. However, to substantiate their efficacy and safety, there is a pressing need for more rigorous clinical trials and well-documented case studies.

The integration of liver-directed Ayurveda therapy into mainstream medical practice for NAFLD could offer a valuable adjunctive treatment option, particularly for patients who may not respond well to conventional therapies. Encouraging further research in this area could lead to the development of more comprehensive and effective treatment protocols for NAFLD, ultimately improving patient outcomes and quality of life.

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