HERBAL CURE TO NON-ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT

The phrase "non-alcoholic fatty liver disease" refers to a wide range of illnesses that can manifest in people who never drink alcohol. The primary characteristic of non-alcoholic fatty liver disease, also known as Kaphaja Yakrit dalludara in Ayurveda, is the retention of a sizable amount of fat in the liver tissues. Obesity, high blood fat (triglyceride) levels, hyperglycemia, and insulin resistance are the main risk factors for non-alcoholic fatty liver disease. Numerous conditions in which the liver has developed steatosis, steatohepatitis, or cirrhosis make up non-alcoholic fatty liver disease. Traditional medicine does not offer pharmacological therapy for fatty liver. One of the non-communicable diseases that an Ayurvedic approach can successfully treat is non-alcoholic fatty liver disease. In order to manage non-alcoholic fatty liver disease, the pathogenic variables such as Agnivaigunya, strotorodha, and kapha medo dushti should be broken down. It is possible to effectively manage the illness with a routine that combines rest, cleansing, and dietary changes tailored to the individual's constitution. Langhana (de-nourishing) and Deepana-Pachana (appetizer-digestives) therapy, two traditional science treatment modalities, may be advantageous.

Keywords: Non-alcoholic fatty liver disease, Yakrit, Rakta Dhatu, non-alcoholic steatohepatitis.

INTRODUCTION:

The liver is the largest organ in the human body and is responsible for metabolising all of the meals we eat. This process is known as metabolic processes[chayapachaya[1]. In vedas, liver is called Takima or Yakna. The various organs express themselves in different combinations of Maubhata and especially in the context of the liver, Rakhdhatu [blood tissue]. Yakrit dalludara is a general term used in Ayurveda for an increase in liver size[Yakrit Vridhi]. In response to an increase in Kapha Dosa, leads to an increase in the size of the liver takes place, resulting in Kaphaja Yakrit Dalludara. As a result, it increases the Meda inside the Yakrit Dalludara.

Varna(color): Vidradhi's color is comparable to that of Yakrit, i.e. Krishnalohitam (reddish-brown).[2]

Svarupa (appearance): As per the Brihadaranyaka Upanishad, Yakrit and Pleeha have the appearance of solid mountains.

Sthaana(site): According to Acharya Arundatta, the liver is located below and to the right of the heart

Karya(physiology of liver): According to numerous Acharyas, the fundamental objective of Yakrit is to bring red color to Rasa Dhatu, i.e. Ranjana of Rasa Dhatu. This function, according to Acharya Vagbhata, is performed in Amashaya (stomach). According to Sushruta, Pitta's role imparts distinct color (Ragakrit) to the Rasa Dhatu (lymph chyle), for which it is called Ranjakagni. The liver and spleen are home to Pitta. In regards to the production of blood, Acharya Sharangadhara holds a similar viewpoint.

The liver's general functions: The liver is known as the body's engine because it plays a critical role in digesting, metabolizing, and producing vital substances that keep the body healthy.[3]This organ converts Rasa Dhatu (clear plasma) into Rakta Dhatu (blood), as well as detecting and recognizing toxins in Rasa Dhatu and storing them to prevent them from entering the bloodstream. This helps to keep the blood pure by preventing ama (impurities) from combining with it.The liver produces and secretes bile, which is utilised to break down and digest fatty acids. It also produces blood-clotting factors while also producing protective elements that prevent blood clots from clogging the circulatory system.

Non-alcoholic fatty liver disease: Consumption of excessive alcohol does not cause non-alcoholic fatty liver disease.[4] The presence of (antimitochondrial antibodies) accumulated by undigested food causes the disease. As a result, the treatment strategy focuses on reinvigorating Agni, which enhances digestion and reduces (antimitochondrial antibody levels in the body. This form of fatty liver is caused by Atibhojana (eating too much) and Divaswapan (sleeping throughout the day). As a result, to complement the effect of the medicines, a specialized diet and lifestyle plan are also offered. The liver is the most important glandular essential organ in the abdomen, and it is placed on the right side. In addition to producing bile, the liver regulates the amount of fat, sugar, and proteins in the bloodstream. As the primary organ responsible for body metabolism, the liver works 24 hours a day, seven days a week to remove poisons and wastes from our bodies. When the liver cells are overworked as a result of a high volume of toxins, they fail to handle and cause gradual damage. Any type of liver disease is a severe worry that must be addressed as soon as possible.

Emotions and the body are not separated in Ayurveda. Yakrut is also seen as a significant repository of rage, hatred, envy, and jealousy. If these feelings aren't handled and digested, they can build up in the body and cause illnesses.

Causes: Obesity occurs when fat accumulates beneath the skin. It causes Fatty Liver when it builds up inside the liver. Fat is natural in the liver, but when the amount of fat contributes to a 5 to 10% increase in liver weight, the illness is known as fatty liver disease. Excessive alcohol use is one of the primary causes of fatty liver. Steatohepatitis is the inflammation of hepatic (liver) cells that occurs in conjunction with the accumulation of fat. Fatty liver disease can develop in people who do not use alcohol, and this is known as non-alcoholic fatty liver disease.

Symptoms: Fat liver disease is characterized by fatigue, weight loss, weakness, loss of appetite, lethargy, and sometimes nausea. Other symptoms include abdominal pain, enlargement of the liver, which is commonly noticed when palpitation occurs, and even blackness around the neck, underarms, and the groin area.[5]

Diagnosis of non-alcoholic fatty liver disease:

Nonalcoholic fatty liver disease should be recognised as soon as possible.When other specific etiologies of liver disease and excessive alcohol consumption (>20g/day) have been ruled out and a metabolic syndrome is present.

The investigation is frequently undertaken in response to high liver transaminases, however many patients with Non-alcoholic fatty liver disease have normal liver function tests, thus this method is limited. As a result, regardless of transaminase levels, the diagnosis should be evaluated in high-risk patients with type 2 diabetes or metabolic syndrome. Fatty liver disease is often suspected if blood tests show a high liver enzyme level.[6] Fatty liver disease is diagnosed with a variety of testing, including blood tests, radiographic tests such as MRI and ultrasound, and, in certain cases, a liver biopsy.

1. Blood tests: These demonstrate liver enzyme levels.

2. Radiography test

a) Ultrasound: This may show liver steatosis as a hyperechogenic image, i.e. 'Bright liver'. It is the initial step taken when Non-alcoholic fatty liver disease is suspected.

b) Computed topography or magnetic radiography imaging: These techniques cannot distinguish NASH (Non-alcoholic steatohepatitis: fat accumulation in the liver, which causes inflammation and damage) from Non-alcoholic fatty liver disease, but still may be used.

c) Transient elastography: This is the advanced form of ultrasound that measures the rigidity of the liver that indicates fibrosis. 3. Liver biopsy: If other tests are unclear, your doctor may recommend taking a tissue sample from your liver (liver biopsy).

The tissue sample is examined in a lab for signs of inflammation and scarring.

PATHOPHYSIOLOGY OF NON-ALCOHOLIC FATTY LIVER DISEASE

Non-alcoholic fatty liver disease is a complex metabolic condition that originated from the interaction of hereditary and environmental variables.[7] One key clinical challenge for the discipline is the development of diagnostic and evaluation criteria for non-alcoholic steatohepatitis that are predictive of disease outcome. The presence of fibrosis appears to be the best such marker at the moment, which is troublesome because it appears late in the illness development. Furthermore, cross-sectional research and epidemiology provide the majority of our understanding of the course and effects of non-alcoholic fatty liver disease. The use of animal models has tremendously aided the search for treatment targets as well as our understanding of the dynamic nature of the non-alcoholic fatty liver disease. However, an animal model that perfectly mimics the whole range of human diseases remains elusive. Well-controlled prospective clinical trials are required to help validate molecular markers that may signal a disease risk or could be used to better identify slow and fast progress, as well as other kinds of Non-alcoholic fatty liver disease. It will also be crucial to uncover distinct disease profiles among rapid progress that can be utilized to predict susceptibility to common outcomes like as Hepatocellular carcinoma (HCC), Cardiovascular disease (CVD), and cirrhosis. Continuous clinical and fundamental research is required to establish new diagnostic criteria and produce effective medications to treat the global epidemic of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis.

Several processes have been connected to the pathophysiology of non-alcoholic fatty liver disease. Not everyone with fatty liver gets hepatic fibrosis, according to the current two-hit hypothesis. Steatosis (fatty liver) happens from the 'first hit,' which is only worsened by inflammation if a second hit occurs. The release of free fatty acids and adipokines from central adipose tissue, which drain into the portal vein and produce insulin resistance, is the initial hit. Reduced hepatic fatty acid oxidation and enhanced fatty acid synthesis are the results of these activities. Insulin resistance leads to hepatic steatosis, which perpetuates the problem. Subsequent activation of Tumor

necrosis factor(TNF)– alpha, leads to the production of reactive oxygen species and the production of endotoxin then leads to inflammation. Mechanism of action: Hepatic steatosis occurs when numerous metabolic pathways become dysfunctional.[8] The pathophysiology of the fatty liver appears to be influenced by an increase in the circulating fatty acid pool. However, the importance of enhanced transcription factor activation, adipokine activity, abnormalities in hepatic fat oxidation, and very-low-density lipoprotein (VLDL) secretion is becoming more widely acknowledged. Hepatic fat accumulation and peripheral insulin resistance have a link. High-calorie consumption causes lipolysis, tumor necrosis factor(TNF) expression, and hypoadiponectinemia in sedentary and genetically predisposed people, resulting in peripheral insulin resistance and an elevated circulating fatty acid pool. Insulin resistance is caused by an aberrant intracellular insulin signaling element-binding tumor, which is induced by hepatic fat deposition. Both of these mechanisms result in hepatic insulin resistance and fatty deposition, as well as increased expression of sterol regulatory element-binding protein-1c(SREBP-1c), CB1, and maybe ghrelin, all of which are capable of promoting de-novo hepatic lipogenesis.

TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

Non-alcoholic fatty liver disease has no known treatment in conventional medicine. Weight loss through a mix of a nutritious diet and working out is usually the first line of treatment.[9]Losing weight can assist in addressing the causes of nonalcoholic fatty liver disease. Despite losing 10% of your body weight being optimal, changes in risk variables can be evident if you drop just 3% to 5% of your starting weight. Treatment of risk factors such as diabetes mellitus and hyperlipidemia, as well as the use of insulin-sensitizing drugs such as biguanides (metformin)and thiazolidinedione's (rosiglitazone, pioglitazone), antioxidants, and different hepatoprotective medications, have all been used to treat non-alcoholic fatty liver disease. The other drugs that are being studied for the treatment of non-alcoholic fatty liver disease include pentoxifylline, telmisartan, L-carnitine, and vitamin E.Non alcoholic fatty liver disease is a growing clinical and pathological disorder that can develop end-stage liver disease. The clinical implications of Non-alcoholic fatty liver disease stem primarily from its widespread prevalence in the general population, as well as its proclivity to develop into cirrhosis and liver failure. In today's medicine, there is no known pharmaceutical treatment for non-alcoholic fatty liver disease.

Non-alcoholic fatty liver disease treatment is still in its early stages, with no medicine that has been proved to be successful. As there is no known pharmaceutical treatment for Non-alcoholic fatty liver disease alternative treatment modalities in other systems of medicine are under investigation, which must be safe and cost-effective. Ayurveda is another system of medicine that can treat Non-Contagious Diseases, including Non-alcoholic fatty liver disease.

MATERIALS AND METHODS

ALLOPATHIC REMEDIES FOR NONALCOHOLIC FATTY LIVER DISEASE

Allopathic remedies that help treat Non-alcoholic fatty liver disease are classified into following[10]

A)Pharmacological treatment

1. Insulin sensitizers: metformin, thiazolidinediones, incretin-based therapies
2. Lipid-lowering agents: statins, fibrates, PUFA
3. Cytoprotective and antioxidant agents: URSO, Vitamin E, silymarin, betaine
4. Anti-tumor necrosis factor-alpha: Pentoxifylline, monoclonal antibodies

B)Phlebotomy

C)Surgical intervention and antiobesity drugs

1. Bariatric surgery

2. Orlistat

PHARMACOLOGICAL TREATMENT

1.Insulin sensitizers

Non-alcoholic fatty liver disease is characterized by insulin resistance. This approach has received a lot of attention in the treatment of nonalcoholic fatty liver disease. Two newer drugs in this category are GLP-1 receptor (GLP-1) agonists and dipeptidyl peptidase 4 (DPP-4) inhibitors (ie, incretins). Metformin has been studied in non-diabetic Non-alcoholic fatty-liver disease patients in several minor trials. Transaminase levels and hepatic steatosis have both been observed to improve with it. There are two disadvantages to using this class of drugs for treatment. One is the nearly uniform reversion of improvement after drug withdrawal, implying that long-term treatment with these drugs is likely. Second, Thiazolidinediones (TZDs) use is usually associated with lower extremity edema and weight gain (average 2 to 5 kg), which may limit the drug's beneficial effects.. Both of these are undesirable reasons for therapy cessation.

2.Lipid-lowering agents

Statins, fibrates, and omega-3 polyunsaturated fatty acids are all used to treat dyslipidemia (PUFAs).This, together with their putative antioxidant capabilities and favorable effect on adiponectin levels, implies that they may be beneficial to patients with nonalcoholic fatty liver disease. Several major studies have now shown that statins are safe in people with underlying Non-alcoholic fatty liver disease and dyslipidemia. Statins are a crucial element in managing these patients' metabolic risk factors, and gastroenterologists who see them should recommend them.

3. Cytoprotective and antioxidant agents

Since oxidative stress is likely to have a role in the development of Non-alcoholic fatty liver disease, potent antioxidants such as ursodeoxycholic acid (URSO), vitamin E, silymarin (milk thistle), and betaine are promising treatment agents. Ursodeoxycholic acid (URSO) in a moderate dose has no role in the treatment of nonalcoholic fatty liver disease, and high-dose ursodeoxycholic acid (URSO) is unlikely to provide significant benefit to consistently advocating its use at this time. Vitamin E acts as a powerful antioxidant and fat-soluble vitamin. It had only been studied in small, disparate research before recently. PIVENS and TONIC, two large, newly published randomized controlled studies, examined their efficacy on adult and pediatric NAFLD populations, respectively.Despite the fact that neither study met its primary objectives, both trials found that vitamin E treatment reduced hepatocellular ballooning and Neonatal abstinence syndrome This is certainly a therapeutically significant finding because ballooning indicates cellular and cytoskeletal damage and increases the probability of disease development.

4. Anti-tumor necrosis factor-alpha

Pentoxifylline: Inflammatory activation contributes to the evolution of Non-alcoholic fatty liver disease, with tumor necrosis factor-alpha (TNF-) likely playing a direct role in obesity and insulin resistance. Pentoxifylline is a TNF-alpha antagonist with a well-established safety profile. It's been tested in a few small non-alcoholic fatty

liver disease trials, two of which looked at histology responses and showed improvements in steatosis, inflammation, and ballooning.

PHLEBOTOMY

In patients with Non-alcoholic fatty liver disease and MS, elevated serum ferritin levels and increased hepatic iron deposition are typical observations, regardless of Human homeostatic iron regulator protein,genotype. Because iron is a powerful oxidative stress catalyst, serum ferritin may be a good indicator of oxidative stress and hepatocyte injury. In Non-alcoholic fatty liver disease , iron depletion has been shown to enhance metabolic indices and transaminase levels; however, the effect on hepatic steatohepatitis and fibrosis is uncertain. To answer this critical topic, the University of Western Ontario is conducting a prospective study comparing pre-liver and post-liver histology.

SURGICAL INTERVENTION AND ANTIOBESITY DRUGS

1. Bariatric surgery

Among morbidly obese patients, bariatric surgery is becoming a more popular treatment choice. To date, numerous studies have assessed bariatric surgery for non-alcoholic fatty liver disease, the majority of which have been retrospective or observational. Overall, the surgery was successful, with better liver histology. Advanced fibrosis, on the other hand, has not been shown to regress consistently, and one five-year prospective research indicated that, while steatohepatitis diminished, fibrosis deteriorated slightly. Cirrhosis is also a relative contraindication to bariatric surgery because of an elevated risk of short- and intermediate-term death**.** The absence of randomized and quasirandomized trials prevents the evaluation of bariatric surgery as a therapeutic option for individuals with Non-alcoholic fatty liver disease, according to a recent Cochrane review.

2. Antiobesity drugs

The medical treatment of obesity has been seen as a potentially helpful technique for non-alcoholic fatty liver disease therapy, given the documented benefit of weight loss for this condition. However, regardless of the effect of weight loss, pharmacological therapy has not been proved to have a direct positive effect on the liver. Some of these medicines' safety has also been questioned, with sibutramine being pulled off the market in the United States and Canada in 2010, and rimonabant manufacture ending in 2008. Despite occasional instances of hepatotoxicity, orlistat, a pancreatic lipase inhibitor, is nevertheless accessible.

AYURVEDIC PLANTS THAT HELP TO TREAT NONALCOHOLIC FATTY LIVER DISEASE

Allium sativum

Extracts from allium Sativa commonly known as garlic belonging to the family Liliaceae when administered were found to stimulate activity in high-fat diet (HFD) induced obese rats. The herbal medicine from allium sativum that plays a key role in treating Non-alcoholic fatty liver disease is S-allyl mercapto cysteine. Treatment with 3 doses of drug per week through the intraperitoneal route was found to decrease lipogenesis. S-allyl mercapto cysteine shows its impact by decreasing the levels of inflammatory modulators like Nuclear factor-κB (NF-κB) and activator protein-1(AP-1) which helps in treating Non-alcoholic fatty liver disease. The other responses of S-ally mercapto cysteine are a decrease in collagen formation and a decrease in oxidative stress. Alliin, allicin, ajoenes, vinyldithiins, and flavonoids like quercetin are sulfur-containing phytoconstituents prevalent in Allium

sativum. Extracted compounds from Allium sativum have been studied for antibacterial, antiviral, antifungal, antiprotozoal, antioxidant, anti-inflammatory, and anticancer effects, among others.

Polygonati rhizoma

Polygonati rhizoma commonly known as huangjing belongs to the family Liliaceae.[12] Its processed products have anti-diabetic, antiviral, anti-tumor, anti-oxidant, anti-fatigue, anti-aging, and immune-boosting properties and also help in treating Non-alcoholic fatty liver disease. Dioscin, a herbal medication derived from polygonati rhizoma, is used to treat non-alcoholic fatty liver disease (NAFLD). The extracts of polygonati rhizoma were found to stimulate activity in high fat diet-induced obese rats, high functioning depression-induced obese Wistar rats, and mice, and also dimethylnitrosamine-induced acute liver injury mice when orally administered. The effective doses of the above mentioned pharmacological models are 60mg/kg, 15-80mg/kg and 80mg/kg respectively. Treating high functioning depression-induced obese Wistar rats and mice with dioscin with about 15-80mg/kg dose has shown a gradual increase in silent information regulator-T1(SIRT1)/AMP-activated protein kinase(AMPK) and also decreased apoptosis. Similarly treating dimethylnitrosamine-induced acute liver injury mice with about 80mg/kg dose has shown a decrease in liver X receptor-α(LXRα) with decreased oxidative stress. When 60mg/kg dioscin is administered in high fat diet-induced obese rats there is a gradual decrease in the inflammatory modulators like a nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha(IκBα), and also decreased collagen formation. The other chemical constituents of polygonati are steroidal saponins, flavones, polysaccharides, and lectins which were isolated from the roots and rhizomes of polygonati.

Citrus reticulata

Tangerine oil is extracted from the fruit peel of Citrus reticulata, commonly known as mandarin, and contains chemical constituents such as monoterpenes and oxygenated compounds such as alcohols and aldehyde.[13] Tangerine oil can be used as an antibacterial, antispasmodic, stomachic, sedative, diuretic, and circulatory stimulant.. Naringenin is a prominent citrus flavonoid that is found mostly in oranges. Many pharmacological properties have been documented, including anti-dyslipidemic, anti-obesity, anti-diabetic, and antifibrotic and also help in reducing the fat accumulation in the liver. It has been established that it regulates(PPAR), which controls hepatocyte triglyceride accumulation. The citrus-derived flavonoids were found to stimulate activity in high fat diet-induced mice with the minimum effective dose of 1% or 3% wt/wt. This effective dose of naringenin was administered orally for about 4 weeks. The pharmacological activities shown were a decrease in very-low-density lipoproteins(VLDL) and also increased insulin resistance.

Silybum martanum (L.) Gaertn

Silybum marianum is a kind of thistle. This plant is also known as milk thistle, blessed milk thistle, Marian thistle, Mary thistle, Saint Mary's thistle, Mediterranean milk thistle, variegated thistle, and Scotch thistle. This Asteraceae species is an annual or biennial flowering plant.

Silymarin is an antioxidant present in Silybum martanumi stabilizes cell membranes, promotes detoxification pathways, regenerates liver tissue, slows the growth of some cancer cell lines, has direct cytotoxic activity against certain cancer cell lines, and improves the efficacy of some chemotherapy treatments. Milk thistle, unlike other plants, has a lot of preclinical data for its hepatoprotective and anticarcinogenic properties.

Silibinin is the herbal medicine present in silybium martanumm that helps to treat Non-alcoholic fatty liver disease. This silibinin extract was found to show its activity in methionine -choline-deficient(MCD) diet-induced

Nonalcoholic steatohepatitis mice when given orally for about 6 weeks with a minimum effective dose of 10 and 20 mg/kg/day. Silibinin has shown its pharmacological action by increasing the β-oxidation and decreasing Nonalcoholic steatohepatitis(NASH)via Caspase 8 and Fas-associated protein with death domain-like apoptosis regulator(CFLAR-JNK) pathway

Glycyrrhizae Radix et Rhizoma

Glycyrrhizae Radix et Rhizoma is acclaimed as **"**Gan-Cao"(in China) or licorice (in Europe) belonging to the family Fabaceae.[14] Glycyrrhizae Radix et Rhizoma (GRER) has been utilized as a medicinal plant and dietary supplement due to its immunomodulatory properties. Because of its simplicity and low cost, sulfur fumigation (SF) processing was frequently utilized in the preservation and maintenance of Chinese medicine. Ethyl acetate extract from Glycyrrhizae Radix et Rhizoma exhibit anti-inflammatory property. Glycyrrhizin is the herbal medicine found in this plant that helps in treating Non-alcoholic fatty liver disease to some extent. When induced with 50 mg/kg per day effective dose of glycyrrhizin via intraperitoneal route for about 2 weeks, mice with methionine -choline-deficient(MCD) diet show biological activities like decrease in lipogenesis and also decreases in inflammatory modulators like NLR family pyrin domain containing 3 (NLRP3) and Farnesoid X receptor (FXR). (The NLRP3 gene codes for the production of a protein known as cryopyrin.Cryopyrin is a member of the intracellular "NOD-like" receptor (NLR) protein family. Cryopyrin is mostly found in white blood cells and cells that produce cartilage)

Piper methysticum

Piper methysticum is commonly known as kava belonging to the family Piperaceae.[15] Some of the mechanisms of action proposed for kavakava include lower glutamate levels, an excitatory neurotransmitter, activation of dopaminergic neurons, interaction with Gamma-aminobutyric acid (GABA) receptors, direct action on muscles leading to relaxation, and elevation of dopamine and serotonin levels via inhibition of monoamine uptake. The principal constituents, kavapyrones (kavalactones), are said to have effects comparable to those of alcohol, such as relaxation, talkativeness, and euphoria, but still preserving mental clarity. The herbal medicine present in kava that helps in treating Non-alcoholic fatty liver disease is yangonin which when administered orally for about 16 weeks by high-fat diet-induced mice with a minimum effective dosage of 10, 20, or 40 mg/kg shows decreased fibrosis and increased fatty acid β-oxidation as well as increased insulin sensitivity.

Coptidis Rhizoma

Coptidis Rhizoma is commonly known as Huang Lian in China. Herbalists from china have been using the dried rhizome of medicinal plants from the Ranunculaceae family for over 2000 years. Rhizoma coptidis extract is widely known for its anti-inflammatory, antioxidative, antiviral antihyperglycemic agent, and antibacterial properties. The precise mechanisms of action are unknown. It is a Traditional Chinese Medicine used to treat bacillary dysentery, typhoid, tuberculosis, epidemic cerebrospinal meningitis, pyrosis, pertussis, and other ailments such as Non-alcoholic fatty liver disease. Berberine is the herbal medicine discovered in coptidis rhizoma was found to stimulate activity in pharmacological models like Mice fed with a high-fat diet(HFD) and Nonalcoholic steatohepatitis (NASH)-hepatocellular carcinoma(HCC) mice model. The above-mentioned pharmacological models were administered with berberine and the minimum effective dose for respective models are 300 mg/kg/day and 250 mg/kg. The stimulating activities of the berberine are decreasing Stearoyl-CoA

Desaturase (SCD1)via the AMP-activated protein kinase-Sterol regulatory element-binding transcription factor-1c(AMPK-SREBP-1c)pathway (SCD1 is a lipid metabolizing enzyme) and decreasing fibrosis.

Gastrodia elata Bl

Gastrodia elata, often known as Tianma, is a saprophytic perennial herb in the genus Gastrodia in the family Orchidaceae. It is used in medicine to 'calm the liver' and cure migraine, dizziness, tetanus, and epilepsy.

Its traditional use includes calming the liver and clearing the meridians by strengthening the patient's circulation. Gastrodia is reported to have calming and analgesic qualities in Western medicine. Gastrodia was used to treat migraine headaches, dizziness, or vertigo caused by liver inflammations, convulsions induced by heat excess, paralysis, general weariness, numbness in the hands or feet, and joint discomfort. Recently, gastrodia has been used to treat nervous headaches, trigeminal nerve pain, nocturnal emissions, difficulty breathing, stress-induced sleeplessness, and hypertension.

Gastrodin is the herbal protein extracted from the plant which when administered by the Larval zebrafish fed with high-fat diet mice shows a decrease in lipogenesis and fibrosis. Gastrodin also shows a gradual decrease in the immuno-modulators like TNFα Tumour Necrosis Factor-alpha(TNFα), Interleukin6(IL-6), and Interleukin-1-beta-1(IL1β). The minimum effective doses of gastrodin were found to be 10, 25, and 50 mg/L

Sparganium stoloniferum

Sparganium stolonifera (Simplestem Bur-Reed) is a perennial herb in the Typhaceae family.For the first time, beta-sitosterol, succinic acid, and daucosterol were extracted from the rhizome of Sparganium stolonifera and identified as beta-sitosterol, succinic acid, and daucosterol using known specimens. Using gas chromatography-mass spectrometry, twenty-one fatty acids were isolated and identified. Traditional medicinal herbs and microorganisms contain -glucosidase inhibitors such as acarbose, 1-deoxynojirimycin, and genistein, which aid in the treatment of diabetes. Some synthetic -glucosidase inhibitors cause unpleasant side effects such as stomach cramping and diarrhea, while others may raise the risk of hepatic syndrome and kidney malignancies. Furthermore, glycosidase inhibition has emerged as a significant therapeutic target for cancer and viral infections such as HIV and influenza, with several such medicines currently in clinical trials. Hence Sparganium stoniferum extracts have antioxidant and glucosidase Inhibitory activities.

Furthermore, the herbal remedy spartploninB aids in the treatment of non-alcoholic fatty liver disease by lowering Toll-like receptor 4 (TLR4) lipid raft trafficking (It is a protein expressed by the TLR4 gene in humans. TLR4 is a transmembrane protein that belongs to the pattern recognition receptor (PRR) family and is a member of the toll-like receptor family), and it also reduces fibrosis and NADPH oxidase activation. The minimum effective dose which shows efficient activity in high-fat-fed mice is 3mg/kg twice a week.

Laggera alata

Laggera alata also known as blumea alata, conzya nutans, and vermonia alata belongs to the family Asteraceae. The oils of Laggera alata contain monoterpenes α-pinene, sabinene, and filifolone, which have been shown to have significant antimicrobial activity, as well as sesquiterpenes α-copaene, β-bourbonene, β -elemene, and p-2,5- dimethoxycymene from Lippia rugose, which has also been shown to have significant antimicrobial activity. The herbal medicine isochlorogenic acid B when administered by the mice fed with methionine -choline-deficient(MCD) diet orally for about 4 weeks has shown a significant impact on decreased fibrosis and decreased oxidative stress. The minimum effective doses of isochlorogrnic acid are 5, 10, and 20 mg/kg. Scutellaria

baicalensis Georgi Scutellaria baicalensis is a flowering plant in the Lamiaceae family that is also known as the Baikal skullcap or Chinese skullcap. Scutellaria baicalensis, a traditional Chinese herbal medicine, has been demonstrated to be effective in the treatment of a variety of disorders, including hepatitis, diarrhea, vomiting, and high blood pressure. Flavonoids and their glycosides are regarded to be typical components of Scutellaria baicalensis, and more than 40 constituents have been found to date. The chemical ingredients of Scutellaria baicalensis are Flavanoids volatile oils terpenoids polysaccharides, β-sitosterol, benzoic acid, and benzyl alcohol. Baicalin is the herbal medicine extracted from Scutellaria baicalensis which when administered by the methionine-choline deficient (MCD) diet-induced Nonalcoholic steatohepatitis(NASH) shows a significant impact on decreased inflammation and decreased fnd hepatic apoptosis. Aralia elata Aralia elata, often known as Japanese angelica, Chinese angelica, or Korean angelica, is a woody plant in the Araliaceae family. In Japanese, it's called tara-no-ki, and in Korean, it's called dureup-namu. Aralia plants are commonly used in traditional Chinese medicine to treat rheumatism, arthralgia, stiffness in the waist and knees, bruises, lumps, abscesses, and other ailments. The chemical components with the highest content and pharmacological action in Aralia are triterpenoid saponins and terpenoids. Aralia's pharmacological activities are primarily anti-inflammatory, analgesic, anti-tumor, liver protection, and cardiovascular and nervous system protection. All the extracted saponins from the aralia elata when administered by Apolipoprotein E(APOE) or High fat diet mouse for about 2 weeks with minimum effective doses of 75, 150 mg/kg/day showed decreased inflammation and oxidative stress which helps get rid of the fatty liver.

Salvia miltiorrhiza

Red sage (Salvia miltiorrhiza) is a species of Salvia miltiorrhiza. It's a perennial plant of the Salvia genus that's been utilised in Chinese medicine for millennia. [16] It is native to China and Japan and thrives in grassy areas in forests, slopes, and along stream banks. It favours grassy areas in forests, hillsides, and along stream banks, and grows at an elevation of 90 to 1,200 metres. Salvia miltiorrhiza and its components were found to decrease blood pressure, improve atherosclerosis, and enhance myocardial ischemia-reperfusionreperfusion in several in vitro and in vivo preclinical investigations. Some of the active compounds discovered include danshensu, salvianolic acid B, protocatechuic acid, catechin, protocatechualdehyde, tanshinone, tanshinone IIA, tanshinone VI, lithospermate B, cryptotanshinone, and polysaccharides, which are thought to be responsible for its cardioprotective effects via various cell signaling pathways. When Aqueous extracts from salvia miltiorrhiza are administered by Ovariectomized (OVX)+ hyperlipidemic SD rats show significantly decreased fibrosis. The minimum effective dose for the pharmacological model is 600 mg/kg/d.

Cyclocarya paliurus

Cyclocarya is a Juglandaceae flowering plant genus with only one species, Cyclocarya paliurus, which was originally classified as Pterocarya paliurus in the Pterocarya genus. It is indigenous to China's eastern and central regions. It is a deciduous tree that can reach a height of 30 meters.Quinic acid, neochlorogenic acid, chlorogenic acid, 4-hydroxybenzoic acid, gallic acid, quercetin-3-glucuronide, kaempferol, loganin 7-pentoside, astragalin, kaempferol-3-rhamnoside, quercetin, quadranoside IV, and asiatic acid are some of the active compounds found in Cyclocarya paliurus. Cyclocarya paliurus is a multi-component, multi-target herbal medicine with significant cholesterol regulation capabilities in patients with dyslipidemia. The chloroform extract from cyclocarya paliurus when administered by the Sprague–Dawley (SD) fed with a high-fat diet (HFD) for 6 weeks shows an impact on

decreasing fibrosis that hits in decreasing the amount of fat deposited on the liver. This pharmacological model was fed with the chloroformic extract orally for about 4 weeks. Aristolochia manshuriensis Kom Aristolochia manshuriensis, often known as Manchurian pipevine, is a deciduous, woody, twining climber with peculiar apetalous flowers with a calyx like a dutchman's pipe hung on a thin stalk. The traditional medicinal herb Aristolochia manshuriensis Kom (AMK) is used to cure arthritis, rheumatism, hepatitis, and obesity. Because of the nephrotoxicity and carcinogenicity of Aristolochia manshuriensis Kom, no pharmacological studies on its anti-obesity potential have been conducted.Aristolochia species have been studied for about 164 compounds, including aristolochic acids and esters, aristolactams, aporphines, protoberberines, isoquinolines, benzylisoquinolines, amides, diphenyl ethers, coumarins, tetralones, terpenoids, benzenoids, steroids, and others. The ethyl acetate extract from this plant when administered by the high-fat diet(HFD) induced Nonalcoholic steatohepatitis (NASH)model with the minimum effective dose of about 2.5 mg/kg shows decreased oxidative stress apoptosis as well as decreased inflammation that helps get rid of the fat deposited on the liver thus treating Non-alcoholic fatty liver disease to some extent.

Aristolochia manshuriensis Kom

Aristolochia manshuriensis, often known as Manchurian pipevine, is a deciduous, woody, twining climber with peculiar apetalous flowers with a calyx like a dutchman's pipe hung on a thin stalk. The traditional medicinal herb Aristolochia manshuriensis Kom (AMK) is used to cure arthritis, rheumatism, hepatitis, and obesity. Because of the nephrotoxicity and carcinogenicity of Aristolochia manshuriensis Kom, no pharmacological studies on its anti-obesity potential have been conducted.Aristolochia species have been studied for about 164 compounds, including aristolochic acids and esters, aristolactams, aporphines, protoberberines, isoquinolines, benzylisoquinolines, amides, diphenyl ethers, coumarins, tetralones, terpenoids, benzenoids, steroids, and others. The ethyl acetate extract from this plant when administered by the high-fat diet(HFD) induced Nonalcoholic steatohepatitis (NASH)model with the minimum effective dose of about 2.5 mg/kg shows decreased oxidative stress apoptosis as well as decreased inflammation that helps get rid of the fat deposited on the liver thus treating Non-alcoholic fatty liver disease to some extent.

RESULTS AND DISCUSSION

Non-alcoholic fatty liver disease is a clinicopathological condition that can proceed to end-stage liver disease if traditional medicine fails to establish an appropriate management strategy.[17] The use of Ayurvedic therapy modalities in the treatment of various types of lifestyle disorders has a lot of promise. With promising outcomes, a vast number of natural substances, entire extracts, and herb formulations have been extensively explored against various Non-alcoholic fatty liver diseases. Polyphenols like resveratrol, quercetin (green tea, soy isoflavones), silymarin (extracted from Sylbum marianum), silybin, and rutin are the most commonly studied natural compounds in non-alcoholic fatty liver. The early stage of the Non-alcoholic fatty liver is steatosis, which is defined by fat buildup, and inflammation that disrupts the insulin signaling pathway is the primary event that causes early steatosis to progress to steatohepatitis. As a result, reducing steatosis and inflammation is critical for Non-alcoholic fatty liver treatment. Herbal medicine therapy has demonstrated remarkable anti-inflammatory, antioxidant, and anti-apoptotic capabilities, which may help to slow the course of Non-alcoholic fatty liver inflammation.[18] Their actions were always multi-pathways to better Furthermore, it has been demonstrated that

herbal therapy combined with other interventions has a far greater therapeutic effect than a single intervention alone. For example, combining Lingguizhugan decoction with calorie restriction therapy may help to reduce fasting blood cholesterol levels. Korean red ginseng and the probiotic Lactobacillus worked well to reduce hepatic inflammation. Therefore, For patients with Non-alcoholic fatty liver, herbal medicine supplements mixed with other therapeutic techniques may give viable therapeutic solutions.

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