ejpmr, 2025, 12(7), 19-27

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A COMPREHENSIVE REVIEW ON HERBAL DRUGS ACTING ON FATTY LIVER DISEASE

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Article Received on 01/05/2025 **Article Revised on 21/05/2025** **Article Accepted on 10/06/2025**

ABSTRACT

Fatty liver disease (hepatic steatosis) is a growing global health concern, characterized by excessive fat accumulation in liver cells. It exists in two primary forms: Non-Alcoholic Fatty Liver Disease (NAFLD), which is associated with metabolic disorders such as obesity and diabetes, and Alcoholic Fatty Liver Disease (AFLD), triggered by excessive alcohol consumption. The disease progresses through mechanisms including insulin resistance, oxidative stress, inflammation, and fibrosis, potentially leading to cirrhosis or hepatocellular carcinoma. Conventional management focuses on lifestyle modifications, but growing evidence supports the use of herbal medicine as a complementary approach. Medicinal plants such as milk thistle (*Silybum marianum*), turmeric (*Curcuma longa*), *Phyllanthus niruri*, Guduchi (T*inospora cordifolia*), and licorice (*Glycyrrhiza glabra*) have demonstrated hepatoprotective, anti-inflammatory, and antioxidant effects, improving liver function and lipid metabolism. This review explores the pathophysiology of fatty liver disease and the role of herbal interventions in its management, with an emphasis on their active constituents, mechanisms of action, and potential risks.

KEYWORDS: Hepatic Steatosis, Non-Alcoholic Fatty Liver Disease (NAFLD), Hepatoprotective Herbs, Oxidative Stress, Insulin Resistance, Silymarin (Milk Thistle).

INTRODUCTION

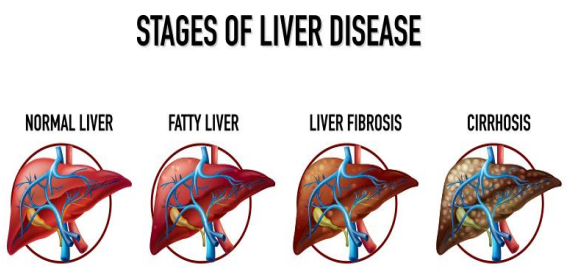
Fatty liver disease, also known as hepatic steatosis, develops when excessive fat builds up in liver cells. This condition is quite common and can vary from a mild, harmless fat accumulation to severe liver damage. It is primarily of two types.

- ➔ Non-alcoholic fatty Liver Disease (NAFLD) – This form is associated with obesity, insulin resistance, and metabolic syndrome but is not linked to alcohol consumption. If left untreated, it can advance to non-alcoholic steatohepatitis (NASH), which causes liver inflammation and scarring.
- ➔ Alcoholic Fatty Liver Disease (AFLD) – Triggered by excessive alcohol intake, AFLD can result in liver inflammation, fibrosis, and even cirrhosis.

Risk Factors: Obesity, diabetes, high cholesterol, excessive alcohol consumption, unhealthy diet, and a sedentary lifestyle.

Symptoms: Often asymptomatic in the early stages but may present as fatigue, abdominal pain, and, in severe cases, jaundice or liver failure.

Diagnosing fatty liver disease involves blood tests, imaging techniques like ultrasound and MRI, and, in some cases, a liver biopsy. Treatment primarily revolves around lifestyle modifications, including weight loss, a nutritious diet, regular physical activity, and alcohol avoidance. In advanced cases, medical intervention such as medication or liver transplantation may be required.



https://www.tenetdiagnostics.in/blog/post/fatty-liver-symptoms-causes-treatment-and-diet-chart

PATHOPHYSIOLOGY

Fatty liver disease arises from an imbalance between fat storage and fat breakdown in liver cells, leading to

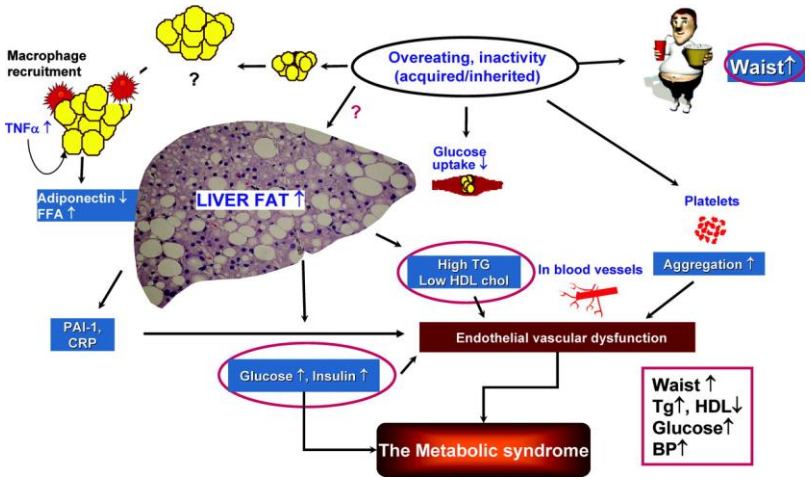
excessive fat buildup. Although the pathophysiology differs between Non-Alcoholic Fatty Liver Disease (NAFLD) and Alcoholic Fatty Liver Disease (AFLD), both conditions share key mechanisms such as insulin resistance, oxidative stress, inflammation, and fibrosis.

1. Fat Accumulation (Steatosis)
- In NAFLD, insulin resistance leads to an increased release of free fatty acids (FFAs) from adipose tissue and enhances triglyceride production in the liver.
- In AFLD, alcohol metabolism produces excess acetyl-CoA, which promotes fat synthesis while suppressing fat breakdown.

2. Oxidative Stress and Lipotoxicity
- The excess fat in liver cells undergoes peroxidation, leading to the production of reactive oxygen species (ROS).
- ROS cause mitochondrial dysfunction and endoplasmic reticulum (ER) stress, further disrupting fat metabolism.
- High levels of FFAs induce lipotoxicity, damaging hepatocytes and triggering an inflammatory response.

3. Inflammation and Liver Damage (Steatohepatitis)
- Injured liver cells activate Kupffer cells (liver macrophages), which release pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukins (IL-6, IL-1β).
- This inflammatory process can develop into Non-Alcoholic Steatohepatitis (NASH) or Alcoholic Hepatitis, depending on the underlying cause.

4. Progression to Fibrosis and Cirrhosis
- Persistent inflammation stimulates hepatic stellate cells (HSCs), leading to excessive production of the extracellular matrix (ECM) and fibrosis.
- Over time, fibrosis can develop into cirrhosis, significantly impairing liver function and increasing the risk of liver failure or hepatocellular carcinoma (HCC).[1][2]



https://www.ahajournals.org/doi/10.1161/atvbaha.107.147538

ALLOPATHIC MEDICINES USED TO TREAT FATTY LIVER DISEASE

Cytotoxic	Antibiotics	Other drugs	Nucleoside analogues
L-asparaginase	Azaserine	Amiodarone	Didanosine
Azauridine	Puromycin	Dichloroethylene	Stavudine
Methotrexate	Bleomycin	Ethyl bromide	Fialuridine
		Tetracycline	Hydrazine
		Isoniazid	Zidovudine
		Diltiazem	
		Coumadin	
		Estrogens	
		Glucocorticoids	
		Tamoxifen	
		Nifedipine	
		Chloroquine	

https://www.researchgate.net/publication/7090681/figure/tbl2/AS:601588167086080@1520441204079/Drugs-associated-with-nonalcoholic-fatty-liver-disease.png

COMPLICATIONS

Non-alcoholic fatty liver disease (NAFLD) has become the most prevalent chronic liver condition globally, closely linked to the rising incidence of metabolic syndrome and obesity. While NAFLD increases the risk of end-stage liver disease, hepatocellular carcinoma, and liver-related mortality, the primary cause of death in these patients is cardiovascular disease, followed by extrahepatic malignancies, with liver-related mortality being the third leading cause. NAFLD is associated with a wide range of extrahepatic complications, including chronic kidney disease, various cancers (such as colorectal cancer), psychological disorders, gastroesophageal reflux disease (GERD), obstructive sleep apnea syndrome (OSAS), periodontitis, hypothyroidism, growth hormone deficiency, and polycystic ovarian syndrome (PCOS). Despite the growing understanding of these complications, no standardized screening method has been established for their early detection. Given the diverse nature of these conditions, collaborative management with specialists

from various fields is essential. Further research is required to identify baseline risk factors and develop effective screening protocols for managing extrahepatic complications in NAFLD patients.[20]

HERBAL APPROACH

Herbs play a crucial role in supporting the management of fatty liver disease due to their natural antioxidant, anti-inflammatory, and liver-protective properties. Several medicinal plants, including milk thistle (*Silybum marianum*), turmeric (*Curcuma longa*), and licorice root (*Glycyrrhiza glabra*), have been researched for their ability to promote liver health. Milk thistle, which contains silymarin, helps lower liver inflammation and oxidative stress, while turmeric's active ingredient, curcumin, has been found to enhance liver function by reducing fat accumulation and fibrosis. Additionally, herbs such as green tea, dandelion root, and Andrographis aid in liver detoxification and improve fat metabolism, potentially slowing the progression of fatty liver disease. Combined with a healthy diet and lifestyle changes, these herbs may serve as a complementary approach to managing the condition.

GREATER CELANDINE (*Chelidonium majus*)

Chelidonium majus (CM), a plant from the Papaveraceae family, has been traditionally used for hepatobiliary disorders, digestive issues, and spasms. Its bioactive compounds, particularly benzophenanthridine alkaloids, contribute to its pharmacological effects. While CM has demonstrated hepatoprotective properties, concerns have been raised regarding its potential hepatotoxicity, particularly in individuals with pre-existing liver conditions such as fatty liver disease (FLD).

Studies suggest that CM and its nanoformulation can mitigate oxidative stress in liver tissues. In cadmium chloride ($CdCl_2$)-exposed mice, CM exhibited hepatoprotective effects, which could be beneficial in managing oxidative stress associated with FLD.

Interaction with Acetaminophen

Experimental models indicate that CM alone does not significantly impact liver function; however, its effects in the presence of hepatotoxic substances remain inconclusive. In FLD patients, where the liver is already vulnerable, potential interactions with medications such as acetaminophen require further investigation.

Enzyme Modulation and Metabolism

CM alkaloids have been found to inhibit monoamine oxidase (MAO) and mitochondrial respiration, suggesting a potential impact on liver metabolism. Given that mitochondrial dysfunction is a key factor in FLD progression, these effects warrant further exploration.

High-Dose Administration

Studies in rats receiving CM at doses 50–100 times higher than typical human consumption reported mild oxidative stress but no significant liver damage. However, the long-term impact of CM on fatty liver conditions remains unclear.

Idiosyncratic Reactions

CM-induced liver toxicity appears to be an unpredictable metabolic response rather than a direct toxic effect. Given the altered metabolic state in FLD patients, individual susceptibility to CM requires careful evaluation.[9]

BHUMI AMLA (*Phyllanthus niruri*)

Phyllanthus niruri, commonly known as Bhumi Amla, Stonebreaker, or Chanca Piedra, is a powerful medicinal herb widely used in Ayurveda, Traditional Chinese Medicine (TCM), and folk medicine for liver disorders. It is known for its hepatoprotective, antioxidant, anti-inflammatory, and lipid-lowering properties, making it highly effective in managing fatty liver disease (hepatic steatosis), including both Non-Alcoholic Fatty Liver Disease (NAFLD) and Alcoholic Fatty Liver Disease (AFLD).

Active Constituents of *Phyllanthus niruri*

Phyllanthus niruri contains various bioactive compounds that contribute to its liver-protective effects.

- ➔ Lignans – Phyllanthin, Hypophyllanthin
- ◆ Help protect liver cells from oxidative damage and inflammation.
- ➔ Flavonoids – Quercetin, Rutin, Kaempferol
- ◆ Act as strong antioxidants, preventing lipid peroxidation.
- ➔ Alkaloids – Phyllochrysine
- ◆ Support liver detoxification and prevent toxin-induced liver damage.
- ➔ Tannins – Corilagin, Geraniin
- ◆ It has anti-inflammatory and astringent properties that improve liver function.
- ➔ Saponins – Reducing fat accumulation and improving liver enzyme balance.[3]

CHICORY (*Cichorium intybus*)

The liver is highly susceptible to damage from toxins, metabolic imbalances, and chronic diseases. Fatty liver disease, including non-alcoholic fatty liver disease (NAFLD) and metabolic-associated fatty liver disease (MAFLD), is driven by oxidative stress, inflammation, and dysregulated lipid metabolism. The Farnesoid X Receptor (FXR), a nuclear receptor predominantly expressed in the liver, plays a crucial role in bile acid metabolism, lipid and glucose homeostasis, and liver regeneration. Impaired FXR function is strongly associated with chronic liver disease progression.

Traditional medicine has long recognized the hepatoprotective properties of medicinal herbs like milk thistle (*Silybum marianum*) and chicory *(Cichorium intybus*), both from the Asteraceae family. Given FXR's importance in liver health, recent studies have investigated the involvement of chicory in liver

protection and its potential benefits in managing fatty liver disease.

Key Mechanisms of Action

- ➔ Regulation of FXR Expression - Chicory extract (CE) has been shown to upregulate hepatic FXR expression, promoting improved bile acid metabolism and lipid regulation. This FXR activation may enhance liver regeneration and prevent fat accumulation in hepatocytes.
- ➔ Reduction of Oxidative Stress and Inflammation- Chicory contains bioactive compounds with strong antioxidant properties, reducing reactive oxygen species (ROS) and oxidative liver damage. It also exhibits anti-inflammatory effects by downregulating inflammatory cytokines involved in NAFLD progression.
- ➔ Lipid Metabolism Modulation- Experimental studies indicate that chicory may help regulate lipid homeostasis, reducing hepatic fat accumulation—a key pathological feature of fatty liver disease.
- ➔ Liver Function Improvement- In an acetaminophen-induced liver toxicity model, chicory extract significantly reduced liver enzyme levels (ALT and AST) and improved liver histology, suggesting its protective role in liver function.[11]

GUDUCHI (*Tinospora cordifolia*)

Guduchi, scientifically known as *Tinospora cordifolia,* is a widely recognized herb in Ayurveda, valued for its hepatoprotective, antioxidant, anti-inflammatory, and immunomodulatory properties. Traditionally used to promote liver health, it is now being explored for its potential in treating fatty liver disease (hepatic steatosis).

The following are the ways through which Guduchi helps in treating fatty liver disease.

- ➔ Liver Protection and Detoxification
- ◆ Guduchi enhances liver function by aiding detoxification and shielding liver cells from damage caused by toxins, alcohol, and fat accumulation.
- ◆ It promotes liver cell regeneration, preventing further damage.
- ➔ Antioxidant Properties
- ◆ This herb is packed with antioxidants that help combat free radicals, reducing oxidative stress in liver tissues.
- ◆ It also prevents lipid peroxidation, a process that contributes to the progression of fatty liver disease.
- ➔ Anti-Inflammatory Effects
- ◆ Guduchi helps lower inflammation by regulating pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β.
- ◆ This action helps prevent Non-Alcoholic Steatohepatitis (NASH), a severe form of fatty liver disease associated with inflammation and liver damage.
- ➔ Regulation of Fat Metabolism
- ◆ Research suggests that Guduchi reduces triglyceride and cholesterol levels, which are major contributors to fat buildup in the liver.
- ◆ It supports healthy fat metabolism, preventing excessive lipid accumulation.
- ➔ Improving Insulin Sensitivity and Glucose Metabolism
- ◆ Since insulin resistance plays a key role in Non-Alcoholic Fatty Liver Disease (NAFLD), Guduchi's ability to enhance insulin sensitivity may help in reducing fat deposits in the liver.
- ◆ It also aids in blood sugar regulation, lowering the risk of metabolic disorders linked to fatty liver disease.

Active Constituents

1. Alkaloids (Berberine, Palmatine, Magnoflorine).
2. Diterpenoid Lactones (Tinocordiside, Tinocordifolin, Cordifolide A)
3. Glycosides (Giloin, Tinocordifoloside)
4. Steroids (β-Sitosterol, Ecdysteroids)
5. Flavonoids (Quercetin, Rutin, Catechin)
6. Polysaccharides and Lignans.[4]

LICORICE ROOT (*Glycyrrhiza glabra*)

Licorice root (*Glycyrrhiza glabra*) is a widely used medicinal herb known for its hepatoprotective, anti-inflammatory, antioxidant, and antiviral properties. It has been traditionally used in Ayurveda, Traditional Chinese Medicine (TCM), and Unani medicine to support liver health. Studies suggest that licorice root can be beneficial for fatty liver disease (NAFLD and AFLD) by reducing liver inflammation, oxidative stress, and fat accumulation while promoting liver detoxification.

Active Constituents

- ➔ Glycyrrhizin (Glycyrrhizic Acid) - The primary active compound responsible for its anti-inflammatory and hepatoprotective properties. It also helps to reduce liver enzyme levels (ALT, AST), indicating improved liver function.
- ➔ Flavonoids (Liquiritin, Glabridin, Isoliquiritigenin) are powerful antioxidants that neutralize free radicals. They prevent lipid peroxidation and reduce fat accumulation in liver cells.
- ➔ Saponins - Support liver detoxification and bile production, helping in fat metabolism. Aid in lowering cholesterol and triglyceride levels, preventing fatty liver disease progression.
- ➔ Coumarins - Exhibit anti-inflammatory and immune-modulating effects. It helps to protect the liver from fibrosis and cirrhosis.[5][6]

GREEN TEA*(Camellia sinensis)*

Green tea has been studied for its potential role in the treatment of non-alcoholic fatty liver disease (NAFLD) due to its high content of polyphenols, particularly catechins (e.g., epigallocatechin gallate—EGCG), which have antioxidant, anti-inflammatory, and metabolic benefits.

Potential Benefits of Green Tea for Fatty Liver Disease.

- ➔ Antioxidant & Anti-Inflammatory Effects - Green tea polyphenols help reduce oxidative stress and inflammation, which play a major role in the progression of fatty liver disease. EGCG can lower liver enzyme levels (ALT, AST), indicating improved liver function.
- ➔ Reduction of Liver Fat Accumulation - Green tea may decrease lipid accumulation in the liver by regulating fat metabolism. Studies suggest it enhances fat oxidation and inhibits lipogenesis (fat production) in the liver.
- ➔ Improves Insulin Sensitivity & Blood Sugar Control - Green tea can improve glucose metabolism and reduce insulin resistance, a key driver of NAFLD. It helps lower blood sugar levels and decreases the risk of progression to NASH (non-alcoholic steatohepatitis).
- ➔ Weight Loss & Metabolism Boosting - Green tea extract has been linked to weight reduction and improved body fat composition, which are crucial for NAFLD management. It enhances thermogenesis (calorie burning) and improves gut microbiome health.
- ➔ Reduction in Liver Fibrosis Risk - Some studies indicate that green tea can help prevent fibrosis progression, reducing the risk of cirrhosis in NAFLD patients.

Active constituents

- ➢ Polyphenols (Catechins) – Green tea is rich in polyphenols, especially catechins, which have strong antioxidant, anti-inflammatory, and metabolic effects. The main catechins in green tea are:
- ➔ Epigallocatechin gallate (EGCG)
- ➔ Epicatechin gallate (ECG)
- ➔ Epigallocatechin (EGC)
- ➔ Epicatechin (EC)
- ➢ Alkaloids (Caffeine, Theobromine, Theophylline)
- ➔ Caffeine
- ➔ Theobromine
- ➔ Theophylline
- ➢ Saponins
- ➢ Vitamins & Minerals
- ➔ Vitamin C
- ➔ Vitamin E
- ➔ Manganese, Zinc, and Selenium
- ➢ Chlorophyll
- ➢ Tannins[7][8]

SILYMARIN

Silymarin, an extract from *Silybum marianum* (milk thistle), has been traditionally used for liver disorders due to its potent antioxidant and hepatoprotective properties. The primary active component, silibinin, undergoes hepatic metabolism and exerts beneficial effects on liver function. Legalon®, a standardized silymarin formulation, has demonstrated high bioavailability and pharmacological efficacy in clinical studies.

Clinical Evidence and Mechanisms

Silymarin has been extensively studied for its potential role in managing NAFLD. Its hepatoprotective effects are attributed to multiple mechanisms, including.

- ➔ Antioxidant Action: Silymarin reduces oxidative stress, a key factor in NAFLD progression.
- ➔ Anti-Inflammatory Properties: It modulates inflammatory pathways, potentially reducing hepatic inflammation in NAFLD.
- ➔ Lipid Metabolism Regulation: Studies suggest silymarin may help regulate lipid accumulation in hepatocytes, which is crucial in fatty liver disease management.
- ➔ Insulin Sensitivity Improvement: Some evidence indicates that silymarin may improve insulin resistance, a key driver of NAFLD progression.

Clinical Studies on Silymarin for NAFLD

Several studies have evaluated silymarin in NAFLD patients. A randomized controlled trial found that silymarin supplementation significantly improved liver enzyme levels (ALT and AST) and reduced hepatic steatosis in NAFLD patients. Additionally, Legalon® formulations have shown promise in reducing liver fat accumulation and fibrosis markers in metabolic-associated fatty liver disease (MAFLD).[10]

AMLA(*Emblica Officinalis*)

Fatty liver disease, particularly non-alcoholic fatty liver disease (NAFLD), is characterized by excessive lipid accumulation in the liver, leading to oxidative stress, inflammation, and hepatic damage. Conventional treatments for hyperlipidemia and liver disorders can have adverse effects, making herbal alternatives like *Emblica officinalis* (Amla) a promising option. Rich in polyphenols, flavonoids, and essential nutrients, *E. officinalis* is traditionally used in Ayurveda for liver protection and lipid regulation.

E. officinalis contains bioactive compounds that support liver health.

- ➔ Polyphenols & Tannins (Gallic acid, ellagic acid, emblicanin A & B) – Antioxidant and anti-inflammatory properties prevent lipid peroxidation and oxidative stress.
- ➔ Flavonoids (Quercetin, luteolin) – Regulate liver enzymes and enhance bile production.
- ➔ Fatty Acids (Linolenic acid, oleic acid) – Prevent excessive fat accumulation and support lipid metabolism.
- ➔ Vitamins & Organic Acids (Ascorbic acid, citric acid) – Reduce oxidative damage and improve detoxification.
- ➔ Sterols & Glycosides – Aid liver regeneration and repair.

Hepatoprotective Mechanisms

E. officinalis helps manage fatty liver disease through

- ➔ Antioxidant Action – Neutralizes free radicals, reducing oxidative stress.

- ➔ Lipid Metabolism Regulation – Lowers cholesterol and triglycerides, preventing fat buildup.
- ➔ Anti-inflammatory Effects – Suppresses inflammatory cytokines, reducing liver damage.
- ➔ Detoxification Enhancement – Improves bile secretion and liver enzyme function.[12]

BAEL (*Aegle marmelos*)

Aegle marmelos (Bael), a medicinal plant from the Rutaceae family, is rich in polyphenols, flavonoids, coumarins, tannins, and alkaloids, contributing to its strong antioxidant and hepatoprotective properties. Traditionally used in Ayurveda, Bael protects the liver by reducing oxidative stress, regulating liver enzymes, and enhancing detoxification. Bael has demonstrated significant protective effects against liver damage in various models.

CCl_4-Induced Liver Damage – Ethanolic extract (500 mg/kg) lowered SGPT, SGOT, and ALP levels, indicating liver function restoration.

Cisplatin-Induced Hepatotoxicity – Bael diet (2–4%) restored antioxidant status and reduced lipid peroxidation and liver enzyme levels.

Paracetamol-Induced Hepatotoxicity – Aqueous extract (100–400 mg/kg) reduced ALP, bilirubin, SGPT, and SGOT in a dose-dependent manner.

Mechanism of Liver Protection

- ➔ Antioxidant Action – Enhances SOD, catalase, and glutathione activity.
- ➔ Lipid Peroxidation Reduction – Prevents oxidative liver damage.
- ➔ Liver Enzyme Regulation – Lowers AST, ALT, ALP, and bilirubin levels.
- ➔ Anti-inflammatory Effects – Suppresses liver inflammation.[13]

NEEM (*Azadirachta indica*)

Azadirachta indica (Neem), a medicinal plant from the Meliaceae family, is known for its antioxidant, anti-inflammatory, and hepatoprotective properties. Rich in flavonoids, alkaloids, tannins, and terpenoids, Neem has been widely used in traditional medicine for liver protection and detoxification.

Hepatoprotective Activity

Neem leaf extracts have been shown to prevent liver damage and maintain normal liver function.

- ➔ Ethanol Extract in Rats – Doses of 100–300 mg/kg showed no liver abnormalities, with normal hepatocyte structure and stable AST/ALT levels, confirming its non-toxic nature.
- ➔ Liver Enzyme Regulation – Slight AST increase at higher doses was not linked to liver injury, while ALT levels remained stable, supporting Neem's hepatoprotective profile.

Mechanism of Liver Protection

- ➔ Antioxidant Action – Flavonoids and tannins neutralize free radicals, preventing oxidative stress.
- ➔ Liver Enzyme Stability – Maintains AST and ALT levels, ensuring liver function.
- ➔ Histopathological Integrity – No structural liver damage at tested doses.[14]

ARJUNA *(Terminalia arjuna)*

Non-alcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disorders, associated with obesity, insulin resistance, and metabolic syndrome. *Terminalia arjuna*, a medicinal tree from the Combretaceae family, has been traditionally used for its hepatoprotective and cardioprotective effects. Arjunolic acid (AA), a key triterpenoid found in its heartwood, exhibits potent antioxidant and lipid-regulating properties, making it a promising candidate for NAFLD treatment.

Hepatoprotective Activity of Arjunolic Acid

AA was isolated and tested in cellular and rodent NAFLD models:

- ➔ In HepG2 Cells – At 50 µM, AA reduced triglyceride accumulation by 66.36% and decreased ALT/AST leakage by 61.11% and 48.29%, respectively ($P < 0.005$).
- ➔ In HFD-Fed Rats – AA (25 & 50 mg/kg) significantly lowered transaminases, phosphatases, and GGT levels ($P < 0.005$), demonstrating liver function restoration.
- ➔ Histological Findings – AA reduced hepatic steatosis and mononuclear cell infiltration.
- ➔ Molecular Mechanisms – Upregulation of PPARα and FXRα (promoting lipid metabolism) and downregulation of PPARγ (reducing fat accumulation).[15]

GINGER (*Zingiber officinale)*

Ginger (*Zingiber officinale*) is a flowering plant whose rhizome has been widely used as a spice and herbal medicine for thousands of years. The ginger rhizome contains specific polyphenol compounds with antioxidative and anti-inflammatory properties, which help detoxify the liver. Evidence has shown that active ginger ingredients (e.g., gingerol and shogaol) suppress the production of prostaglandins, nitrite oxide (NO), and proinflammatory cytokines. Ginger and its derivatives display similar effects to nonsteroidal anti-inflammatory drugs (NSAIDs) by suppressing cyclooxygenase and lipoxygenase pathways. Ginger administration has been shown to increase superoxide dismutase (SOD) activity and total antioxidant capacity and decrease lipid peroxidation in mice. Sesquiterpenes in ginger inhibit the production of free radicals. Zingerone, which was also found in ginger, has antioxidant and antibacterial properties. The first meta-analysis investigation of the hepatoprotective effect of ginger supplementation suggests that ginger intake significantly improves lipid profile, liver enzymes, antioxidant/oxidative markers, and blood sugar.

Clinical evidence

The qualitative analysis included three clinical trials. Rahimlou et al.conducted a double-blind, randomized clinical trial in which 44 patients with NAFLD were randomly assigned to the ginger (2 g/day) or the placebo groups for 12 weeks. Both groups were recommended to follow an energy-balanced diet and perform physical activity. Ginger supplementation significantly reduced serum ALT and γ-GT levels and hepatic steatosis compared to placebo.[16]

BLUEBERRY (*Vaccinium ashei)*

Blueberry (*Vaccinium ashei*), a high-value crop rich in polyphenols, has been investigated for its potential benefits in managing non-alcoholic fatty liver disease (NAFLD). Extracts from blueberry pomace and juice have demonstrated antioxidant, hypoglycemic, hepatoprotective, and anti-obesity properties. Additionally, blueberry supplementation has been shown to enhance liver antioxidative capability by increasing metallothionein (MT) expression and superoxide dismutase (SOD) activity, leading to hepatic stellate cell (HSC) inactivation and reduced hepatic fibrosis.

Beyond the fruit, blueberry leaves also hold significant medicinal value, though their potential has been largely overlooked. Research indicates that blueberry leaves contain a more diverse range of polyphenols than the fruit, exhibiting stronger antioxidant activity. These polyphenols provide notable pharmacological benefits with minimal side effects, making blueberry leaves a promising alternative for phytotherapy in NAFLD treatment.

Furthermore, blueberry, in combination with Bifidobacteria, has been found to enhance liver protection by reducing hepatocyte injury, strengthening barrier functions, and improving antioxidant activity. Despite these promising effects, the precise mechanisms by which blueberry juice and extracts improve hepatic injury remain largely unknown, necessitating further research to optimize their therapeutic potential.[17] [18]

Rubus aleaefolius Poir

Rubus aleaefolius Poir (R. Aleaefolius), a species of the Rubus genus in the Rosaceae family, is a widely distributed medicinal herb known for its therapeutic properties. Traditionally used in Chinese medicine, it has been employed for heat-clearing, arresting bleeding, promoting blood circulation, and removing blood stasis. In Anxi County, Fujian Province, China, it has been specifically used for treating various types of hepatitis and has demonstrated significant efficacy in managing non-alcoholic fatty liver disease (NAFLD).

Studies show that total alkaloids extracted from *Rubus aleaefolius* (TARAP) provide hepatoprotective effects. In a carbon tetrachloride-induced acute liver injury model in rats, TARAP alleviated adipose degeneration, suggesting its potential as an effective therapy for NAFLD. Additionally, it has been a key component in various Traditional Chinese Medicine (TCM) formulations for centuries without apparent side effects.

Despite its promising therapeutic effects, the precise molecular mechanism underlying its anti-NAFLD activity remains unclear. Recent research indicates that TARAP positively influences lipid metabolism in NAFLD induced by a high-fat diet. Further studies are necessary to elucidate its exact mode of action, which could facilitate its development as a viable treatment for NAFLD.[19]

CONCLUSION

Fatty liver disease, whether non-alcoholic (NAFLD) or alcoholic (AFLD), is a growing global health concern with severe complications like cirrhosis and liver failure. Its pathophysiology involves fat accumulation, oxidative stress, inflammation, and fibrosis, leading to liver dysfunction. Standard treatments emphasize lifestyle changes, including weight management, a healthy diet, and physical activity, with medical treatments for advanced stages.

Herbal medicine presents a promising complementary approach, leveraging hepatoprotective, antioxidant, anti-inflammatory, and lipid-lowering properties. Medicinal plants such as milk thistle, turmeric, licorice root, green tea, Guduchi, Phyllanthus niruri, chicory, Amla, Bael, and Neem have shown potential in reducing liver fat, improving insulin sensitivity, normalizing liver enzymes, and combating oxidative stress.

However, caution is essential, as certain herbs, like Chelidonium majus, can be hepatotoxic, particularly for individuals with pre-existing liver issues. Standardized formulations like silymarin (from milk thistle) have demonstrated clinical efficacy in enhancing liver function in NAFLD patients.

Integrating herbal remedies with lifestyle modifications could improve liver health and slow disease progression. Yet, further clinical research is vital to validate the long-term safety, efficacy, and appropriate dosages of these interventions. Consulting healthcare professionals before using herbal supplements is crucial, especially for individuals with liver disorders or those on medication.

This balanced approach may offer hope in managing fatty liver disease effectively while minimizing risks.

Overview of the Herbal drugs used to treat fatty liver disease

Herb\Plant	Active Compounds	Mechanism Of Action	Potential Benefits	Concerns Or Risk
Milk Thistle (*Silybum marianum*)	Silymarin, Silibinin	Anti Oxidant, anti inflammatory, Lipid metabolism Regulator	Lowers liver inflammation, oxidative stress and Fat accumulation	Generally safe but can interact with certain medications
Turmeric (*Curcuma longa*)	Curcumin	Anti-inflammatory, Antioxidant, Lipid lowering	Reduces fat accumulation, fibrosis and improves liver function	High doses may cause GIT discomfort
Licorice Root 9	Glycyrrhizin, Flavonoids, Saponins, Coumarins	Anti-oxidant, Anti-inflammatory, liver detoxification	Lowers liver enzyme levels and reduces fat accumulation	High doses may cause hypertension
Green Tea	Catechins, Alkaloids and Polyphenols	Anti-oxidant, Anti-inflammatory, insulin sensitivity enhancer	Reduces oxidative stress and fat accumulation, improves glucose metabolism	Excessive green tea intake can cause liver toxicity; constipation is not typically a cause
Phyllanthus	Lignans, Flavonoids, Alkaloids, Tannins, Saponins	Hepatoprotective,Anti-oxidant,Anti-inflammatory	Protect liver cells, improves fat metabolism	Generally it is safe
Chelidonium majus	Benzophenanthridine Alkaloids	Anti-oxidant, Anti-inflammatory, Anti-tumor	Reduces oxidative stress	Potent hepatotoxic in patients with liver conditions
Chicory	Bioactive compounds, Polymorphs	FXR regulation,Anti-oxidant, Anti-inflammatory, Lipid metabolism modulation	Improves bile acid metabolism, reduces liver inflammation	Excessive intake may cause gastro-intestinal issues
Guduchi	Alkaloids, Diterpenoids, Lactones, Glycosides	Anti-oxidant, Anti-inflammatory, hepatoprotective	Reduces triglycerides and cholesterols, also reduces oxidative stress	Rare allergic conditions may occur
Emblica officinialis (Amla)	Polyphenols, Flavonoids, Fatty Acids, Vitamins, Sterols, Glycosides	Antioxidant, Anti-inflammatory, lipid regulation, Detoxification	Lowers cholesterol, triglycerides and Oxidative stress.	No major concerns, generally well tolerated
Aegle marmelos (Bael)	Polyphenols, Flavonoids, Coumarins, Tannins, Alkaloids	Antioxidant, Liver enzyme regulation, Lipid peroxidation reduction	Restores liver function, Prevents oxidative Stress and Reduce inflammation	Safe in moderate doses, but excessive intake may cause GIT discomfort
Azadirachta indica	Flavonoids, Alkaloids, Tannins	Antioxidant, Anti-inflammatory, hepatoprotective	Prevents liver damage, maintains liver enzyme stability	May cause hypoglycemic in diabetic patient
Terminalia arjuna	Arjunolic acid	Lipid regulation, Antioxidant, Anti-inflammatory	Reduces triglycerides accumulation, Improves liver function and prevents fat accumulation	Generally safe but prolonged high doses may cause GIT issues
Zingiber officinale (Ginger)	Gingerol, Shogaol, Sesquiterpenoids	Anti-oxidant, Anti-inflammatory	Lowers ALT levels and improves lipid profile	High doses may cause gastroi-ntestinal discomfort
Blueberry	Polyphenols, Flavonoids	Anti-oxidant, Anti-inflammatory, hepatoprotective, anti-obesity	Reduces hepatic fibrosis	Excessive intake may cause constipation
Rubus aleaefolius Poir	Total Alkaloids from *Rubus aleaefolius* (TARA)	Hepatoprotective, increases lipid metabolism	Alleviates adipose degeneration, Reduces hepatic steatosis, and improves liver function	Minimal reported side effects, but long term effects need further investigation

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