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MEDICINAL PLANT WITH HEPATOPROTECTIVE PROPERTIES- A REVIEW

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ABSTRACT

The abstract investigates the fascinating relationship between plants and non-alcoholic fatty liver disease (NAFLD). The relationship between the two points to the potential advantages of plant-based substances in slowing the progression of NAFLD. The abstract summarises recent studies on how phytochemicals, antioxidants, and dietary fibre from different plants can reduce lipid buildup and liver inflammation. The study highlights the therapeutic potential of plant-based treatments for NAFLD and promotes more research into the processes behind their efficiency.

Keywords: NAFLD, Pharmacological Intervention, Phytochemical, Plants

INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) represents a significant and increasingly prevalent global health concern, intricately intertwined with the modern epidemics of obesity, type 2 diabetes, and metabolic syndrome **[1]**. Unlike the classic alcoholic liver disease, NAFLD encompasses a spectrum of liver disorders characterized by excessive accumulation of fat within hepatocytes in the absence of significant alcohol consumption. As one of the most common chronic liver conditions, NAFLD presents a multifaceted challenge that spans both clinical medicine and public health **[2]**. Its prevalence has surged in parallel with the rise in obesity rates, placing an immense burden on healthcare systems worldwide

[3]. NAFLD encapsulates a range of conditions, from benign hepatic steatosis, characterized by fat accumulation alone, to the more concerning non-alcoholic steatohepatitis (NASH), characterized by inflammation and varying degrees of fibrosis. NASH, in turn, can progress to cirrhosis and hepatocellular carcinoma, imposing grave consequences on affected individuals **[4, 5]**.

The intricate interplay of genetic predisposition, metabolic factors, insulin resistance, and lifestyle choices drives the development and progression of NAFLD **[6]**. Researchers are unraveling the complex mechanisms underlying the disease, with emerging evidence highlighting the potential role of gut microbiota, adipose tissue dysfunction, and chronic low-grade inflammation **[7]**. Given its silent nature and the absence of specific symptoms in its early stages, NAFLD often goes undiagnosed until it reaches advanced states. As a result, an urgent need exists for accurate diagnostic tools and effective interventions **[8]**. Lifestyle modifications, including dietary changes and increased physical activity, remain the cornerstone of NAFLD management. Additionally, pharmaceutical interventions and experimental therapies are being explored to target the underlying mechanisms of the disease and mitigate its progression **[9]**.

Understanding NAFLD requires a comprehensive grasp of its pathophysiology, risk factors, diagnostic techniques, management strategies, and potential long-term consequences. As researchers continue to unravel the complexities of this intricate liver disorder, healthcare providers and public health entities must collaborate to address the multifaceted challenges it poses, with the ultimate goal of improving patient outcomes and stemming the tide of this growing health crisis **[10, 11]**. Pharmacological interventions hold promise in targeting the underlying mechanisms of NAFLD, from reducing inflammation and oxidative stress to modulating lipid metabolism **[12]**. While certain drugs have shown potential in clinical trials, it's essential to carefully consider their efficacy, safety profile, and long-term effects before widespread implementation **[13]**. Natural plants and dietary compounds have also garnered attention for their potential benefits in NAFLD management. Components like omega-3 fatty acids, polyphenols, and antioxidants found in various plant sources exhibit anti-inflammatory and hepatoprotective properties. Integrating these natural remedies into dietary strategies could complement conventional treatments and enhance overall outcomes **[14, 15]**.

However, it's important to approach NAFLD treatment with a holistic

perspective. Lifestyle modifications, including adopting a balanced diet, engaging in regular physical activity, and maintaining a healthy weight, remain the cornerstone of managing NAFLD **[16]**. Combining these lifestyle changes with evidence-based pharmacological interventions or plant-derived compounds could potentially yield a comprehensive and effective approach to combating NAFLD **[17]**.

As research continues to evolve, it's imperative for healthcare professionals to stay informed about the latest developments in NAFLD treatment and to tailor their recommendations based on individual patient needs. Ultimately, a multidisciplinary approach that integrates pharmaceutical options and natural plant-based therapies within the framework of lifestyle modifications holds the potential to significantly impact the management and prevention of NAFLD **[18]**.

PHARMACOLOGICAL INTERVENTION

Several drugs are being explored for the treatment of Non-Alcoholic Fatty Liver Disease (NAFLD) and its more severe form, Non-Alcoholic Steatohepatitis (NASH).

1. Pioglitazone

A thiazolidinedione medication used to improve insulin sensitivity, pioglitazone has shown potential in improving liver enzyme levels and reducing inflammation in NASH patients. Pioglitazone is an oral medication that belongs to the thiazolidinedione class of drugs. It has been investigated as a potential treatment option for Non-Alcoholic Fatty Liver Disease (NAFLD), particularly for cases where there is evidence of non-alcoholic steatohepatitis (NASH), a more advanced form of the condition **[19]**. Pioglitazone primarily works by improving insulin sensitivity and reducing insulin resistance in cells. It activates peroxisome proliferator-activated receptors (PPARs), specifically PPAR-gamma, which helps regulate glucose and lipid metabolism. Studies suggest that pioglitazone may help improve liver fat content, reduce inflammation, and potentially slow down the progression of fibrosis in individuals with NASH **[20]**. It can also have positive effects on other metabolic markers, such as improved glycemic control and lipid profiles. Pioglitazone may have side effects, including weight gain, fluid retention, and a potential increased risk of heart failure. These side effects should be carefully monitored and discussed with a healthcare provider. Not all individuals with NAFLD are suitable candidates for pioglitazone treatment **[21]**. The decision to use pioglitazone should be based on individual patient characteristics, such as the severity of the disease and underlying health conditions **[22]**. The long-term safety and efficacy of pioglitazone for NAFLD

treatment are still being studied. Regular medical monitoring is essential to assess the patient's response to treatment and any potential adverse effects **[23]**. Pioglitazone is often used in conjunction with lifestyle modifications, including dietary changes and increased physical activity. A comprehensive approach that addresses multiple aspects of NAFLD management is recommended. Treatment with pioglitazone should be carried out under the guidance of a healthcare professional experienced in NAFLD management. Regular monitoring of liver function and other relevant parameters is crucial **[24]**.

2. Metformin

Metformin, a widely used oral antidiabetic medication, has been studied for its potential in the treatment of Non-Alcoholic Fatty Liver Disease (NAFLD). Metformin primarily works by improving insulin sensitivity and reducing glucose production in the liver. It also has effects on lipid metabolism and inflammation, which are relevant to NAFLD **[25]**. Metformin may improve insulin resistance, a key factor in NAFLD development. By enhancing insulin sensitivity, it could reduce the accumulation of fat in the liver. Metformin might have anti-inflammatory properties that could help reduce liver inflammation, which is a characteristic of non-alcoholic steatohepatitis (NASH) **[26]**. The typical dosage of metformin varies depending on the individual's medical condition and response. Studies exploring its efficacy for NAFLD have used dosages ranging from 500 mg to 2000 mg per day **[27]**. Treatment duration may also vary, and patients should be monitored for both efficacy and potential side effects. Not all patients with NAFLD might benefit equally from Metformin **[28]**. Responses can vary based on factors like the severity of the disease, insulin resistance, and other health conditions. Metformin might be more effective when used in combination with lifestyle modifications, including dietary changes and exercise **[29]**. Metformin is generally well-tolerated, but gastrointestinal side effects like nausea, diarrhea, and stomach discomfort can occur, especially when starting the medication. Long-term use might also lead to vitamin B12 deficiency. Regular monitoring of liver function, glucose levels, and potential side effects is essential during metformin treatment **[30]**.

3. Vitamin E

Vitamin E supplementation has been studied for its potential to reduce inflammation and oxidative stress in NASH patients. However, its use should be carefully monitored due to potential side effects. Vitamin E has been investigated as a potential treatment for Non-Alcoholic Fatty Liver Disease (NAFLD) due to its antioxidant properties and its potential to mitigate oxidative stress and inflammation

in the liver **[31]**. Some studies have suggested that vitamin E might have a positive effect on liver enzymes and histological markers of NAFLD. However, it's important to note that the use of vitamin E for NAFLD treatment is still a topic of debate and ongoing research **[32]**. Studies have explored various dosages of vitamin E, typically ranging from 400 to 800 IU per day. However, the optimal dosage and duration of treatment are still uncertain. Vitamin E has shown promise in improving liver enzymes and histological features in some individuals with Non-Alcoholic Steatohepatitis (NASH), a more severe form of NAFLD **[33]**. Improvement is often seen in terms of reduced inflammation and hepatocellular ballooning. Vitamin E treatment might be more suitable for specific patient populations, such as those with biopsy-proven NASH and certain risk factors. It's important to identify appropriate candidates for this therapy. Regular monitoring of liver function, lipid profiles, and potential adverse effects is necessary during vitamin E treatment. Long-term use of high-dose vitamin E could have risks, so careful monitoring is essential **[34, 35]**. Vitamin E might be used in combination with other interventions, such as lifestyle modifications (diet and exercise), to enhance its effects on NAFLD management. While some studies have reported positive outcomes with vitamin E supplementation, others have shown limited benefits or even potential harm in specific populations. The response to vitamin E treatment can vary among individuals **[36]**.

4. Obeticholic Acid (OCA)

OCA is an FXR agonist that has been granted accelerated approval by the FDA for NASH treatment. It targets liver fat accumulation, inflammation, and fibrosis. Obeticholic acid is a synthetic bile acid derivative that activates the farnesoid X receptor (FXR), a nuclear receptor involved in regulating various metabolic pathways. Activation of FXR by OCA can help improve liver metabolism, decrease inflammation, and reduce fibrosis in NAFLD/NASH patients **[37]**. Clinical trials have demonstrated that OCA can improve liver enzymes, reduce liver fat accumulation, and even lead to histological improvements in liver inflammation and fibrosis in some NASH patients. OCA is typically considered for NASH patients who have fibrosis or are at higher risk of disease progression. It is not recommended for patients with decompensated cirrhosis or those with severe liver impairment **[38]**. OCA is usually administered orally in the form of tablets. The dosage may vary depending on the patient's condition and response to treatment. It's important for healthcare providers to closely monitor patients during treatment **[39]**. OCA treatment can lead to certain side effects,

including itching (pruritus), which can sometimes be severe. Patients need to be monitored for this side effect and other potential adverse events. OCA is sometimes used in combination with other medications or interventions, especially lifestyle modifications like diet and exercise, to achieve better results in managing NASH **[40]**.

5. Liraglutide

Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist that works by increasing insulin secretion, reducing glucagon production, slowing gastric emptying, and promoting weight loss **[41]**. These mechanisms are believed to contribute to its potential efficacy in NAFLD treatment. Liraglutide is not specifically approved by regulatory agencies for the treatment of NAFLD, but healthcare providers may consider it in cases where lifestyle modifications alone are not effectively managing the condition **[42]**. Liraglutide is usually administered as a subcutaneous injection. The dosing regimen for NAFLD treatment may vary, and it's important for patients to follow their healthcare provider's instructions closely. Liraglutide's ability to improve insulin sensitivity, promote weight loss, and potentially reduce liver fat accumulation makes it a candidate for NAFLD treatment **[43]**. These effects may lead to improvements in liver enzymes, liver histology, and overall liver health. Liraglutide's impact on weight loss can be particularly beneficial for NAFLD patients, as excess weight is a major risk factor for the disease. Weight loss can help reduce liver fat content and improve insulin sensitivity. Regular monitoring of liver function, blood glucose levels, and any potential side effects is crucial during liraglutide treatment. Healthcare providers will assess the patient's response and adjust the treatment plan accordingly **[44]**. Like any medication, liraglutide may have side effects. Common side effects include gastrointestinal discomfort, nausea, vomiting, and potential pancreatitis or thyroid issues. Patients should be aware of these possible effects and report any concerns to their healthcare provider. Liraglutide treatment should be integrated into a comprehensive approach to NAFLD management. This includes lifestyle modifications such as dietary changes, exercise, and weight loss, as well as addressing other comorbid conditions like diabetes and metabolic syndrome **[45]**.

6. Selonsertib

An investigational ASK1 inhibitor, selonsertib targets inflammation and fibrosis in NASH patients. Clinical trials are ongoing to evaluate its effectiveness. Selonsertib, also known as GS-4997, is an experimental drug developed by Gilead Sciences for the treatment of non-alcoholic steatohepatitis (NASH), a severe form of

non-alcoholic fatty liver disease (NAFLD). Selonsertib was being investigated in clinical trials, but there might have been developments beyond that point. Selonsertib is a selective inhibitor of apoptosis signal-regulating kinase 1 (ASK1), an enzyme involved in cellular stress responses and inflammation. It was intended to target fibrosis and inflammation, which are key components of NASH progression. However, it's important to note that the results of clinical trials for selonsertib have been mixed, and its efficacy and safety profile have been subjects of ongoing research and debate **[46]**.

7. Cenicriviroc

This CCR2/CCR5 antagonist has shown potential in reducing liver inflammation and fibrosis in NASH patients. Clinical trials are underway to further assess its efficacy. Cenicriviroc (CVC) is an investigational drug that has shown promise in the treatment of Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH). It is a dual antagonist of C-C chemokine receptor type 2 (CCR2) and C-C chemokine receptor type 5 (CCR5), which are involved in inflammation and fibrosis processes in the liver. In clinical trials, cenicriviroc demonstrated potential benefits in addressing NASH-related inflammation and fibrosis. Patients interested in cenicriviroc or any other potential treatment options for NAFLD/NASH should consult with a qualified healthcare professional to obtain the most current and accurate information, as well as guidance on available treatments and their suitability for individual cases **[47]**.

8. Resveratrol

This natural compound found in grapes and red wine has antioxidant and anti-inflammatory properties that may benefit NASH patients. Resveratrol, a natural compound found in certain foods like grapes and red wine, has been investigated for its potential in the treatment of Non-Alcoholic Fatty Liver Disease (NAFLD). Resveratrol has demonstrated anti-inflammatory properties that could help mitigate inflammation associated with NAFLD and its progression to Non-Alcoholic Steatohepatitis (NASH). Resveratrol acts as an antioxidant, which may help reduce oxidative stress in the liver, a key contributor to NAFLD development and progression. Some studies suggest that resveratrol may improve insulin sensitivity and regulate lipid metabolism, which could benefit individuals with NAFLD by reducing fat accumulation in the liver **[48]**. Resveratrol's potential to protect liver cells from damage might contribute to slowing the progression of NAFLD and NASH. Many positive effects of resveratrol have been observed in animal studies, but it's essential to remember that translating these

findings to humans might be complex due to differences in metabolism and other factors. Limited clinical trials have been conducted on resveratrol's effects specifically for NAFLD. The appropriate dosage of resveratrol for NAFLD treatment is not well-established. Moreover, the safety profile of long-term resveratrol supplementation is not fully understood. Resveratrol should be considered as part of a holistic approach to NAFLD treatment, including lifestyle modifications like dietary changes, weight management, and exercise **[49]**.

9. Pentoxifylline

Used in some cases to improve liver enzyme levels and reduce inflammation in NASH patients, pentoxifylline has anti-inflammatory effects. Pentoxifylline is a medication that affects blood flow and has anti-inflammatory properties. It has been studied for its potential to improve liver function and reduce inflammation in NAFLD patients **[50]**.

NATURAL PLANTS

Several plants and natural compounds have been explored for their potential to assist in the treatment of fatty liver. It's important to note that while some of these substances show promise in preliminary studies, more research is needed to establish their safety and efficacy for treating fatty liver.

1. **Milk Thistle (Silymarin)**

Milk thistle is a well-known herb that contains a compound called silymarin. Silymarin has antioxidant and anti-inflammatory properties and is often used to support liver health. It has been studied for its potential to protect the liver from damage and improve liver function in cases of fatty liver **[51]**. Milk thistle contains a compound called silymarin, which is believed to have antioxidant and anti-inflammatory properties. These properties could help mitigate oxidative stress and inflammation, which are key factors in the progression of NAFLD **[52]**. Milk thistle may influence lipid metabolism by reducing the accumulation of fats in the liver. This could potentially benefit individuals with NAFLD who have excessive fat build-up in their liver cells. Milk thistle has been investigated for its potential to reduce liver fibrosis, a process that can lead to cirrhosis in advanced NAFLD cases **[53]**. The anti-fibrotic properties of milk thistle could slow down disease progression. While some studies have suggested potential benefits of milk thistle in improving liver enzymes and reducing liver fat content, the results have been mixed and not consistent across all trials. More robust clinical research is needed to establish its efficacy **[54]**. Milk thistle is available in various forms, including extracts, capsules, and teas. Dosage recommendations vary, but it's important to follow the guidelines provided

by a healthcare professional or the product's label.

2. Turmeric (Curcumin)

Turmeric contains curcumin, a compound with anti-inflammatory and antioxidant properties. Curcumin has shown promise in animal studies for reducing fat accumulation in the liver and improving liver function. Curcumin has strong anti-inflammatory and antioxidant properties **[55]**. NAFLD is associated with inflammation and oxidative stress, and curcumin's effects could potentially mitigate these factors. Some studies suggest that curcumin supplementation can lead to a reduction in liver enzyme levels, indicating improved liver function **[56]**. Curcumin has been found to impact lipid metabolism by decreasing lipid accumulation in the liver and promoting the breakdown of fats. Curcumin might enhance insulin sensitivity, which could be beneficial for individuals with NAFLD as insulin resistance is a contributing factor. Early research indicates that curcumin might have anti-fibrotic effects, potentially slowing down the progression of liver fibrosis in NAFLD **[57]**. Some studies suggest that curcumin could enhance the effects of other treatments, such as lifestyle interventions, due to its anti-inflammatory properties. Curcumin has poor bioavailability, meaning that the body absorbs and utilizes it poorly. The effective dosage of curcumin for NAFLD is not yet well-established. Studies have used varying doses, and optimal amounts still need to be determined. Responses to curcumin can vary between individuals. What works well for one person might not have the same effect on another. While some studies suggest potential benefits, the evidence is not yet conclusive. More rigorous clinical trials are needed to establish curcumin's effectiveness as a standalone treatment for NAFLD **[58]**.

3. Green Tea

Green tea contains catechins, which are antioxidants that may have a positive impact on liver health. Some studies suggest that green tea consumption might help reduce fat accumulation in the liver and improve markers of liver function. The antioxidants in green tea can help reduce oxidative stress in the liver, which is associated with NAFLD progression **[59]**. Green tea's anti-inflammatory properties may help mitigate liver inflammation, a key factor in the development of non-alcoholic steatohepatitis (NASH). Green tea catechins may aid in the regulation of lipid metabolism, potentially decreasing the accumulation of fat in the liver. Some studies suggest that green tea consumption could enhance insulin sensitivity, helping to manage underlying insulin resistance often associated with NAFLD **[60]**. Drinking green tea regularly, preferably multiple cups per day may provide consistent benefits due

to its bioactive compounds. Green tea extracts and supplements are available and could provide concentrated doses of catechins, but their effectiveness can vary. Green tea should be part of an overall healthy diet that includes whole foods, vegetables, lean proteins, and limited sugar and saturated fats **[61]**.

4. Dandelion

Dandelion root and leaves have been traditionally used to support liver health. Dandelion (Taraxacum officinale) has been studied for its potential health benefits, including its possible role in managing non-alcoholic fatty liver disease (NAFLD). Dandelion contains compounds with anti-inflammatory properties. These properties could potentially help reduce inflammation in the liver, which is a key feature of NAFLD. Dandelion is rich in antioxidants like flavonoids, which can help combat oxidative stress and reduce cellular damage **[62]**. This could be beneficial in protecting liver cells from damage caused by NAFLD. Some studies suggest that dandelion might support liver function by promoting the flow of bile, which aids in digestion and detoxification. Improved bile flow might contribute to overall liver health. Dandelion has been traditionally used as a diuretic and mild laxative, potentially aiding in weight loss. Since obesity is a major risk factor for NAFLD, weight management could indirectly benefit NAFLD patients. Early research indicates that dandelion might help regulate blood sugar levels. Given that insulin resistance is closely linked to NAFLD, better blood sugar control could be beneficial. Dandelion can be consumed as herbal tea or in supplement form. Some individuals choose to incorporate dandelion products into their diet as a potential complementary approach to NAFLD management **[63]**.

5. Ginger

Ginger, known for its anti-inflammatory and antioxidant properties, has shown promise in supporting liver health, including potential benefits for Non-Alcoholic Fatty Liver Disease (NAFLD). Ginger contains bioactive compounds that have anti-inflammatory effects. Chronic inflammation plays a role in the progression of NAFLD, and ginger's anti-inflammatory properties may help mitigate this. The antioxidants in ginger, such as gingerol, have the potential to counter oxidative stress, which is a key factor in NAFLD development **[64]**. Oxidative stress damages liver cells and promotes inflammation. Some studies suggest that ginger may improve insulin sensitivity, which is important for individuals with NAFLD as insulin resistance is a hallmark of the disease. Improved insulin sensitivity can help regulate blood sugar levels and reduce fat accumulation in the liver. Ginger may aid in weight management by promoting

thermogenesis and enhancing metabolism. Since obesity is a major risk factor for NAFLD, maintaining a healthy weight can positively impact liver health. Early research indicates that ginger might have anti-fibrotic effects, potentially helping to reduce the development of fibrosis in the liver, a process often seen in advanced stages of NAFLD **[65]**.

6. Garlic

Garlic contains compounds that have antioxidant and anti-inflammatory properties. Some research indicates that garlic might have a positive impact on liver health by reducing fat accumulation. Garlic is believed to have potential health benefits, including its role in managing certain aspects of Non-Alcoholic Fatty Liver Disease (NAFLD) **[66]**. Garlic contains compounds that have been shown to possess anti-inflammatory properties. Inflammation plays a significant role in the progression of NAFLD to more severe stages, so garlic's anti-inflammatory effects could potentially have a positive impact. The antioxidants present in garlic, such as allicin, may help counter oxidative stress, which is a contributing factor in NAFLD development **[67]**. Oxidative stress can lead to liver cell damage, and garlic's antioxidant properties could help mitigate this damage. Some studies suggest that garlic may influence lipid metabolism, leading to reduced fat accumulation in the liver. This effect could potentially help in managing the fat buildup characteristic of NAFLD **[68]**. Garlic has been proposed to improve insulin sensitivity, which is important for managing NAFLD as insulin resistance is a key factor in its development. By enhancing insulin sensitivity, garlic might indirectly contribute to better liver health. Garlic might help regulate blood lipid levels, including cholesterol and triglycerides. Abnormal lipid profiles are often seen in individuals with NAFLD, so garlic's potential lipid-modulating effects could be beneficial **[69]**.

CONCLUSION

In conclusion, the treatment landscape for Non-Alcoholic Fatty Liver Disease (NAFLD) has expanded to encompass both pharmaceutical interventions and natural plant-based approaches. As our understanding of NAFLD's complex pathogenesis deepens, researchers and clinicians are exploring a diverse array of options to address this significant public health concern.

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