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REVIEW ARTICLE

Review on Role of Herbs, Spices and Herbal Extracts in Non-alcoholic Steatohepatitis (NASH)

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Abstract

Non-alcoholic steatohepatitis or NASH is an advanced inflammatory variant of Non-Alcoholic Fatty Liver Disease (NAFLD), linked to disease progression, development of cirrhosis, and potential necessity for liver transplantation. Despite its epidemiological prevalence, NASH is underrecognised in clinical practice. It is a progressive liver disease which results from the impairment of hepatic steatosis and involves the incidence of inflammation and hepatocyte injury, and ultimately ends up in fibrosis, cirrhosis and hepatocellular carcinoma. Nevertheless, at the moment, the current pharmacological treatments for NASH are inadequate and exhibit only a varying amount of efficacy. Several spices and herbs, such as turmeric, coriander, cinnamon, cardamom, ginger, garlic, *kalmegh*, asafoetida, milk thistle, fenugreek, *ashwagandha*, *amaranth*, and many of them have been demonstrated to show hepatoprotective effects in different preclinical models of NASH. Phytochemicals of these plants can improve lipid metabolism, reduce oxidative stress and inflammation, and enhance insulin sensitivity. Not only do individual herbs, but their formulations, such as traditional Chinese medicines and Ayurvedic formulations, show promise in reducing liver steatosis and fibrosis in experimental and clinical studies. Despite promising preclinical data, clinical studies evaluating the efficacy of spices, herbs, and herbal extracts in NASH management and treatment are limited. Therefore, additional well-designed clinical trials are required to determine the therapeutic effect, offer some advantages, and determine their effective and safe doses in NASH management. Herbs, spices, and herbal extracts have potential advantages in reducing liver damage and slowing the advancement of NASH, are reviewed in this review. These can be beneficial to find promising supplementary therapies and might offer a comprehensive strategy for controlling NASH and enhancing patient outcomes.

Major Findings: This review highlights that NASH, a progressive and underrecognised form of NAFLD, lacks effective pharmacological therapies, but various herbs, spices, and their formulations demonstrate hepatoprotective effects through improving lipid metabolism, reducing oxidative stress and inflammation, and enhancing insulin sensitivity. While preclinical evidence is strong, clinical validation remains limited, underscoring the need for well-designed trials to establish their therapeutic potential, safety, and role as supplementary strategies in NASH management.

Keywords: Hepatoprotective Activity, Herbs, Non-Alcoholic Fatty Liver Disease (NAFLD), Non-Alcoholic Steatohepatitis (NASH), Spices

1. Introduction

Non-Alcoholic Steatohepatitis (NASH) is a progressive stage of non-alcoholic fatty liver disease (NAFLD) marked by inflammation of the liver, hepatocellular damage, and hepatic steatosis. NASH frequently progresses to cirrhosis, hepatocellular cancer, and fibrosis. As obesity, diabetes, and metabolic syndrome become more commonplace globally, NASH has emerged as a significant public health concern, contributing to substantial illness and mortality. Current pharmacological treatments for NASH are restricted and frequently yield only little benefits, emphasising the need for novel therapeutic methods. In recent years, interest has increased in the possible benefits of spices, herbs, and herbal extracts as supplemental or alternative treatments for NASH[1].

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NASH has become a significant global public health issue at the same time as obesity, metabolic syndrome, and type 2 diabetes are becoming more common. According to epidemiological research, NASH is a key factor in chronic liver disease, liver-associated morbidity, and liver-related death, affecting as much as 5–10% of the general population[2].

The pathogenesis of NASH is multifactorial and involves an intricate interaction of genetic, environmental, and metabolic factors. Hepatic steatosis and inflammation in NASH are primarily caused by insulin resistance, dyslipidemia, malfunction of adipose tissue, and oxidative stress. Hepatocytes that have accumulated triglycerides produce pro-inflammatory cytokines and activate hepatic stellate cells, which in turn cause hepatocellular damage, fibrogenesis, and finally liver cirrhosis and fibrosis.

Clinically, NASH patients may exhibit nonspecific symptoms, including fatigue, malaise, and stomach discomfort, or they may be asymptomatic. However, when the illness worsens, people may experience side effects such as ascites, portal hypertension, and hepatic encephalopathy. Furthermore, NASH poses a serious risk of developing hepatocellular cancer, especially when combined with severe cirrhosis and fibrosis[3].

The diagnosis of NASH involves a comprehensive approach, including clinical assessment, laboratory testing, imaging studies, and histological examination of liver biopsy specimens. Hepatocellular injury and inflammation may be reflected by increased serum biomarkers like Gamma-Glutamyl Transferase (GGT), Aspartate Transaminase (AST), and Alanine Transaminase (ALT). Hepatic steatosis can be identified and liver fibrosis can be assessed using imaging techniques such as Computed Tomography (CT), ultrasound and Magnetic Resonance Imaging (MRI). However, biopsy of the liver remains the definitive method for diagnosing NASH and evaluating disease severity[4].

Management of NASH involves a multidisciplinary approach aimed at addressing underlying metabolic risk factors, promoting lifestyle modifications, and targeting hepatic inflammation and fibrosis. The mainstay of NASH therapy is weight loss, which is attained by food modifications, consistent exercise, and behavioural therapies. While no single medication has yet obtained regulatory approval for the treatment of NASH, some patients may be eligible for consideration of pharmacological treatments that target inflammation, lipid metabolism, and insulin resistance[5].

The prevalence of NASH is rising, and it has a big impact on liver-related morbidity and mortality. In order to lessen the disease's impact and enhance patient outcomes, it is essential to comprehend the intricate pathophysiology of NASH and create efficient diagnostic and treatment plans. Further research is required for the complete understanding of the underlying mechanisms of NASH progression and to find new therapeutic options for this increasingly common liver disease. Several phytochemicals, herbs and spices used in different indigenous systems of medicine and therapy have shown potential benefit in different metabolic disorders and hepatic health. This review aims to analyse the evidence-based benefits of potential herbs, spices and herbal extracts on NASH.

2. Materials and Methods

In this review work, the effect of different herbs, spices and herbal extracts on NASH was reviewed using PubMed, Google Scholar and searching the keywords: "Non-alcoholic steatohepatitis (NASH), herbs"; "NASH, plant" and using the search filter of the last 30 years. References from previous reviews were also examined to prevent any potential biases. The search strategy was designed to encompass a wide range of research papers, reviews, and both preclinical and clinical studies, all in the English language, focusing on the medicinal properties of plants and their phytochemical components in the treatment of NASH and other hepatic disorders. Articles published in languages other than English were excluded from the study. Additionally, the articles were screened for relevance, and their references were carefully examined to identify other relevant publications. This thorough approach was adopted to compile a comprehensive and current review, synthesising the vast array of available scientific information on the role of medicinal plants in NASH.

3. Definition of NASH

Nonalcoholic steatohepatitis (NASH) is a prevalent chronic liver disease that affects both children and

adults. It can range from mild to advanced-stage liver disease. NASH is a type of NAFLD (nonalcoholic fatty liver disease). NAFLD is a condition associated with fat accumulation in the liver. "Nonalcoholic steatohepatitis, or NASH, is the most severe form of NAFLD, a condition in which the liver builds up excessive fat deposits[6]".

4. Epidemiology and Etiology of NASH

NASH is the inflammatory form of non-alcoholic fatty liver disease, linked to progression of disease, cirrhosis development, and potential need for a liver transplant. Despite its significance, NASH is often underdiagnosed in clinical settings.

NASH is estimated to impact 3% to 6% of the US population, and its prevalence is on the rise. NASH is closely linked to dyslipidaemia, obesity, type 2 diabetes, and metabolic syndrome. Although various non-invasive tests and scoring systems are available to characterise NAFLD and NASH, liver biopsy is the only definitive method for diagnosing NASH. Presently, no specific therapies are approved by the US Food and Drug Administration for the treatment of NASH. Lifestyle modification is the primary approach of the treatment, which includes dietary changes and exercise, with a focus on weight loss. Significant improvement in histological outcomes, including fibrosis of the liver, is directly associated with weight loss. In certain cases, bariatric surgery may be required to achieve and sustain the required weight loss for therapeutic effect. Approximately 20% of NASH patients will progress to cirrhosis, and NASH is projected to become the leading cause of liver transplants in the US. Mortality rates among individuals with NASH are significantly higher than those in the general population or patients without this inflammatory NAFLD subtype, with an annual all-cause mortality rate of 25.56 per 1,000 person-years and a liver-specific mortality rate of 11.77 per 1,000 person-years[7].

Non-Alcoholic Steatohepatitis (NASH) is an advanced form of NAFLD, defined by liver inflammation and damage to hepatocytes (ballooning) caused by fat accumulation.

NAFLD and NASH are associated with:

- Excess weight or obesity.
- Insulin resistance, where cells fail to respond properly to insulin.
- Hyperglycaemia, indicating prediabetes or type 2 diabetes.
- High blood lipid levels, particularly triglycerides.

5. Pathophysiology

The pathophysiology of NASH is intricate, involving multiple simultaneous factors. It is primarily characterised by steatosis, hepatocyte damage, and inflammation, with or without fibrosis. NASH is strongly linked to type 2 diabetes and is commonly associated with conditions of insulin resistance.

The pathophysiology of NAFLD is equally complex and influenced by various systemic changes. The earlier "two-hit" hypothesis proposed that the first "hit" was the intrahepatic accumulation of fatty acids, followed by a second "hit" involving oxidative stress or mitochondrial dysfunction. However, this model is now considered overly simplistic and has been replaced by the "multiple-parallel hits" hypothesis, which more accurately represents NAFLD development and progression. In this model, various factors act simultaneously and synergistically in individuals with a genetic predisposition[8].

The multiple-hits hypothesis proposes that environmental and genetic factors, particularly those associated with dietary habits, contribute to obesity, the development of insulin resistance, and alterations in the intestinal microbiome. Insulin resistance increases hepatic de novo lipogenesis and stimulates lipolysis of adipose tissue, leading to a higher influx of fatty acids into the liver. It also causes adipose tissue dysfunction, inducing the release of inflammatory cytokines. The accumulation of fatty acids in hepatocytes triggers several deleterious events, including endoplasmic reticulum stress, mitochondrial dysfunction, oxidative stress, and the production of reactive oxygen species.

Furthermore, intestinal microbiome imbalances promote increased production of intestinal fatty acids and enhanced intestinal permeability, collectively leading to the activation of inflammatory cytokines such as IL-6 and TNF-α. This sustained inflammatory response subsequently results in chronic hepatic inflammation, thereby promoting the development and progression of NAFLD and NASH[9]. Figure 1 explains the pathophysiology of NASH.

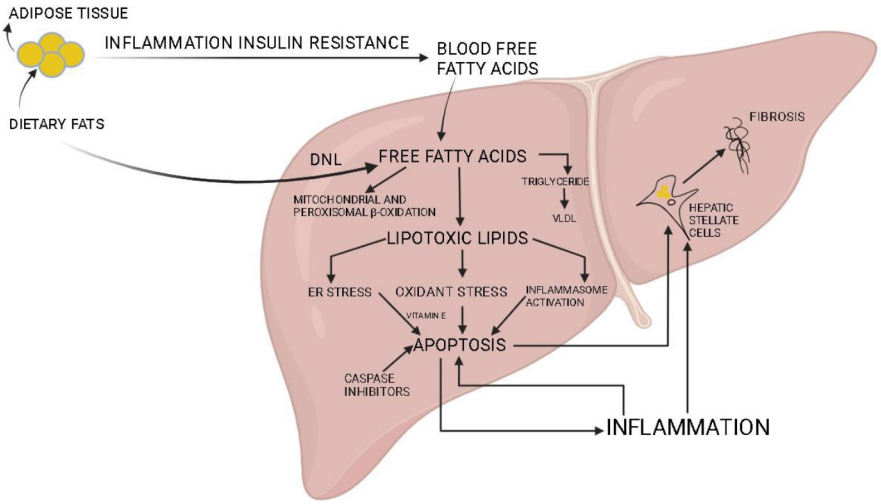


Figure 1. *Pathophysiology of NASH: Pathophysiological mechanisms linking dietary fats and adipose tissue dysfunction to the progression of NAFLD and NASH. Excess dietary fats and adipose tissue inflammation contribute to insulin resistance, leading to elevated circulating free fatty acids. These free fatty acids undergo de Novo Lipogenesis (DNL), mitochondrial and peroxisomal β-oxidation, and triglyceride/VLDL synthesis, resulting in accumulation of lipotoxic lipids. Lipotoxicity induces Endoplasmic Reticulum (ER) stress, oxidative stress, and inflammasome activation, which collectively trigger hepatocyte apoptosis. The apoptotic process, combined with persistent oxidative and inflammatory signaling, promotes hepatic stellate cell activation, inflammation, and fibrosis, ultimately driving NASH progression.*

6. Symptoms

NASH is often a silent condition, presenting with few or no noticeable symptoms. Individuals with NASH may experience fatigue or discomfort in the upper right abdominal area. Some possible symptoms of NASH include:

- Severe itching
- Abdominal swelling
- Increased tendency to bruise and bleed easily
- Jaundice
- Spider-like blood vessels under the skin
- Behavioural changes, confusion, or slurred speech
- Nausea
- Vomiting
- Loss of appetite
- Memory impairment

7. Diagnosis

Physicians diagnose NAFLD using a combination of medical tests, a review of medical history, and physical examinations. Blood tests, imaging studies, and liver biopsies are commonly used to identify NAFL and to distinguish it from NASH. A liver biopsy is performed if NASH is suspected[10]. Liver biopsy remains the gold standard for diagnosing NAFLD, NASH, and fibrosis, but it is invasive, costly, and carries risks such as pain, bleeding, and rarely death, in addition to sampling variability. Because of these limitations, it is not feasible or appropriate to biopsy all suspected cases in routine practice. Non-invasive biomarkers and imaging tests offer safer, repeatable, and more patient-friendly alternatives for diagnosis, risk stratification, and monitoring. Blood-based markers such as cytokeratin-18 (CK18), fibroblast growth factor 21 (FGF21), and inflammatory proteins, along with clinical scores such as the NAFLD fibrosis score (NFS) and fibrosis-4 index (FIB-4), can help detect fibrosis and NASH with reasonable accuracy. Imaging-based tools such as transient elastography (FibroScan), magnetic resonance elastography (MRE), and magnetic resonance imaging–proton density fat fraction (MRI-PDFF) provide reliable assessments of liver fat and stiffness. These non-invasive approaches reduce dependence on biopsy and hold promise for early detection, treatment monitoring, and predicting outcomes in patients with NAFLD[11].

8. Current Challenges in NASH Management and the Need for Novel Strategies

The treatment of NASH is currently challenged by the absence of FDA-approved drugs and the disappointing outcomes of clinical trials using single-drug therapies, particularly in addressing hepatic fibrosis, the most critical determinant of patient outcomes. The multifactorial nature of NASH pathogenesis, driven by obesity, insulin resistance, oxidative stress, inflammation, and fibrogenesis, demands therapeutic strategies that can simultaneously target multiple pathways. However, an incomplete understanding of the molecular and cellular mechanisms underlying disease progression, especially the activation and regulation of hepatic stellate cells in fibrosis, limits the development of effective mechanism-based interventions. Additionally, current diagnostic approaches rely heavily on invasive liver biopsies, which pose safety, feasibility, and interpretation challenges, while reliable non-invasive biomarkers are still under validation. These barriers underscore the pressing need for innovative and alternative treatment options. Combination therapies designed to act on complementary pathogenic mechanisms, along with novel RNA-based therapeutics capable of targeting previously undruggable molecular pathways, represent promising directions. Furthermore, integrating multi-omics platforms, precision medicine approaches, and advanced biomarker discovery will be essential to improve disease characterisation, optimise treatment selection, and ultimately enhance patient outcomes in NASH. Given the rapidly increasing prevalence, high economic burden, and potential progression to cirrhosis and hepatocellular carcinoma, the development of safe, effective, and accessible therapies for NASH is an urgent global health priority[12,13].

To treat NASH, doctors recommend weight loss. Shedding excess weight can reduce liver fat, inflammation, and fibrosis. Currently, there are no authorised medications to treat NAFLD or NASH. Some recommended treatments include:

- Weight loss
- Controlling diabetes
- Keeping cholesterol levels down
- Protecting the liver

9. Effect of Various Herbs, Spices and Herbal Extracts in NASH

Nonalcoholic Steatohepatitis (NASH) develops through multiple interlinked metabolic and inflammatory pathways, and therefore treatment strategies are focused on both the sources and fates of fatty acids in the liver. Since insulin resistance drives uncontrolled adipose lipolysis and increases fatty acid influx to the liver, interventions such as weight loss, lifestyle modification, and drugs like peroxisome Proliferator-Activated Receptor Gamma (PPARγ) ligands are used to improve adipocyte fat storage and reduce hepatic burden. Dietary restriction of fructose and sugar-sweetened beverages helps limit de Novo Lipogenesis (DNL), while pharmacological approaches, including Acetyl-CoA Carboxylase (ACC) inhibitors, Farnesoid X Receptor (FXR) agonists, and thyroid hormone receptor-beta (THR-β) agonists, suppress lipogenic pathways. Diversion of fatty acids toward safer storage or oxidation is also a therapeutic goal, with agents that activate brown adipose tissue, bile acid–related FXR/TGR5 agonists, and exercise-induced substrate utilisation providing metabolic benefit[14].

At the hepatic level, impaired β-oxidation and mitochondrial dysfunction promote toxic lipid accumulation; thus, PPARα/δ agonists, mitochondrial-targeted therapies, and controlled mitochondrial uncouplers are under investigation. Lipotoxic intermediates such as ceramides and diacylglycerols are targeted through specific inhibitors, while enhanced but safe disposal of triglycerides via Very-Low-Density Lipoprotein (VLDL) secretion is also being explored. To counteract hepatocellular injury, antioxidants like vitamin E and anti-apoptotic agents such as emricasan address oxidative and endoplasmic reticulum (ER) stress, while inflammasome activation is being targeted through caspase inhibitors, interleukin-1 (IL-1) blockers, and modulation of the gut microbiome[14].

Fibrosis remains a central therapeutic target given its role in disease progression, with therapies including chemokine receptor (CCR2/CCR5) inhibitors, lysyl oxidase-like 2 (LOXL2) inhibitors, small interfering RNA (siRNA) therapies against collagen regulators, and strategies to induce stellate cell apoptosis. The gut–liver axis also offers opportunities, as dysbiosis contributes to inflammation and fibrosis, and interventions such as

probiotics, prebiotics, faecal microbiota transplantation, and FXR–FXR-fibroblast growth factor 19 (FGF19) or FGF21 analogues aim to restore bile acid, lipid, and glucose homeostasis. Because no single therapy has proven sufficiently effective, combination approaches that pair metabolic modulators such as FXR agonists, glucagon-like peptide-1 (GLP-1) agonists, or PPAR agonists with antifibrotic or anti-inflammatory drugs are increasingly emphasised. Overall, while lifestyle interventions with sustained weight loss remain the cornerstone of therapy, emerging pharmacological strategies targeting fatty acid metabolism, lipotoxicity, inflammation, and fibrosis represent a promising path toward comprehensive NASH management[14].

Considering the challenges of limited treatment options for non-alcoholic steatohepatitis (NASH), natural products such as herbs, herbal extracts, and spices are gaining recognition as potential alternatives or adjuncts in its management. These natural agents are rich in bioactive compounds that exert multiple beneficial effects, including antioxidant, anti-inflammatory, lipid-lowering, and antifibrotic activities, which directly address the complex pathophysiological mechanisms of NASH. By reducing oxidative stress, improving insulin sensitivity, modulating inflammatory pathways, and preventing excessive fibrotic changes in the liver, they offer a holistic approach that targets several disease processes simultaneously. In addition, their relatively low toxicity, accessibility, and long history of use in traditional medicine systems make them appealing candidates for complementary therapies. However, despite their promising potential, further scientific validation through well-designed clinical trials, standardisation of extracts, and mechanistic studies is necessary before these natural interventions can be fully integrated into evidence-based treatment strategies for NASH.

In this review work, the effect of different herbs, spices and herbal extracts on NASH was reviewed using the PUBMED central database and searching the keywords: Non-alcoholic steatohepatitis (NASH), herbs and using the search filter of the last years, about 50 separate herbs and their effects on NASH were reviewed under Table 1.

A variety of herbs have demonstrated significant hepatoprotective effects, particularly against toxin-induced liver damage. Several phytochemicals (like curcumin) have shown an inhibitory effect on liver lipogenesis by decreasing the expression of genes associated with fatty acid synthesis, which are typically overexpressed in NAFLD.

Coriander reduces liver weight and enzyme levels (SGOT, SGPT, ALP), resulting in the elimination of fatty deposits and necrosis in liver tissues, while also enhancing liver function and aiding digestion. Cinnamon extract promotes protein synthesis, supports liver cell regeneration, and has antioxidant and lipid peroxidation-inhibiting properties. Cardamom and ginger exhibit strong hepatoprotective effects by reducing liver enzymes and oxidative stress, while cumin acts through various mechanisms such as minimising fat accumulation and inflammation. Black pepper and clove restore normal liver enzyme levels, with clove protecting against paracetamol-induced damage. Garlic and myristicin suppress oxidative stress and inflammation, and saffron offers antioxidant defence against liver toxicity. Fennel oil, *Laurus nobilis*, and amla provide hepatoprotection via antioxidant pathways, while silymarin, andrographolide, and capsaicin further shield the liver from toxic damage and inflammation. *Azadirachta indica* and *Ocimum sanctum* display liver-protective effects similar to silymarin. Other phytochemicals, such as bacoside A and andrographolide, support the antioxidant system and guard against toxin-induced liver injury. These findings highlight the significance of the diverse effects of these herbs, such as antioxidant, anti-inflammatory, and lipid-regulating properties, in protecting the liver from toxicity.

10. Clinical Trials on Herbal Interventions for NASH and NAFLD[70-77]

Herbal therapies have gained increasing attention as potential interventions for NAFLD and its progressive form, NASH. Among single-compound approaches, resveratrol, a polyphenol from grapes and berries, has shown mixed clinical outcomes. While some trials in NAFLD patients reported improvements in liver enzymes and inflammatory markers with 500 mg/day supplementation for 12 weeks, other studies, including those in obese and non-obese populations without metabolic disease, failed to demonstrate

Table 1. Effect of various herbs, spices and herbal extract in NASH

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
1	Turmeric (*Haldi*) Turmeric is obtained from the dried rhizome of *Curcuma longa* Linn. Family: *Zingiberaceae*	•Turmerone (44.1%) •β-turmerone (18.5%) •ar-turmerone (5.4%) •Curcumin (diferuloylmethane) •Dimethoxycurcumin •Bisdemethoxycurcumin	Bisdemethoxycurcumin exhibits a promising liver-protective effect. It also helps inhibit liver fat production by downregulating genes involved in fatty acid synthesis, which are typically overexpressed in NAFLD. Curcumin exerts its effects by reducing the inflammatory response in TNF-α-stimulated human endothelial cells through the inhibition of NF-κB signaling. Curcumin intake results in a reduction of total bilirubin and a decrease in activities of AST, ALT, ALP, LDH, GGT and increase in serum proteins.	*In vitro*	15-17
2	Coriander (*Dhania*) Dried ripe fruits of *Coriander sativum* Linn. Family: *Apiaceae*	•volatile oils (0.3-1%) •Volatile components are 90% of D-(+)-linalool (coriandrol),and coriandryl acetate along with other components like, geraniol, p-cymene camphor, borneol, limonene, and alpha-pinenes. The fruits also contain fatty oil and hydroxycoumarins. •Fixed oils include petroselic acid , oleic acid,linolenic acid •hydroxycoumarins •umbelliferone and scopoletine. •Fixed oil is 13% and proteins is 20%.	• Coriander sativum exhibits hepatoprotection by decreasing the liver weight as well as activities of SGOT, SGPT, and ALP, and direct bilirubin of CCl_4 induced hepatotoxicated animals. Administration of Coriander sativum extract at lead to the elimination of fatty deposit, ballooning degeneration and necrosis, indicating antihepatotoxic activity (at 300 mg/kg dose). • It is an antioxidant and activates liver activity and enhances the efficacy of GIT for food digestion.	*In vivo*	18,19
3	Cinnamon (*Dalchini*) Cinnamon comprises dried bark, from the shoots growing on the cut stumps of *Cinnamomum zeylanicum* Nees. Family: *Lauraceae*	Cinnamaldehyde: 65.00 to 80.00% Eugenol: 5.00 to 10.00% Volatile oil (0.5-1%) 1.2% tannins Mucilage Calcium oxalate, Starch and mannitol.	Extract of Cinnamon has raised serum total protein levels towards normal values, suggesting hepatoprotective effects. The enhancement of protein synthesis is considered a key mechanism of hepatoprotection, promoting liver cell regeneration and production. Cinnamon extract exhibits hepatoprotective effect may be due to both enhanced activity of the antioxidant- defense system and lipid peroxidation inhibition. The histopathological studies in the rat's liver also supported that cinnamon extract significantly mitigated the CCl4 toxicity and preserved the liver tissue architecture close to normal. These findings indicate that cinnamon extract is a potent hepatoprotective agent against CCl4 induced hepatotoxicity in animal model.	*In vivo*	20,21

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
4	Cardamom (*Elaichi*) Cardamom comprise dried ripe seeds and fruits of *Elettaria cardamomum* Linn. Maton. Family: *Zingiberaceae*	Volatile Oil- Cineole Terpinyl acetate Terpineol Borneol Terpinene	Hepatoprotection was evaluated by analyzing serum level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, albumin, and lipid profile. In the gentamicin induced acute liver damage, cardamom aqueous extracts significantly reduced the elevated serum levels of bilirubin, cholesterol, ALT, AST, triglycerides and low-density lipoprotein cholesterol. Aqueous extract of Cardamom significantly enhanced the reduced serum levels of albumin and high-density lipoprotein (HDL) cholesterol in gentamicin induced hepatotoxicity rats.	*In vivo*	[22]
5	Ginger (Adrak) Ginger consists of the dried or fresh rhizomes of *Zingiber officinale* Roscoe. Family: *Zingiberaceae*	•1-2% volatile oil •5-8% pungent principle, resinous matter, starch, mucilage. •Gingerol, Paradol, Terpenoids, Zingerone.	The methanol extract of ginger both alone and combination with chicory demonstrated hepatoprotective properties. However, the combination was more effective in lowering serum liver enzyme levels to or even below normal values compared to ginger alone. The reduced liver enzymes is likely attributed to a membrane stabilizing effect. The decreased lipid peroxidation in liver homogenates in CCl_4 induced hepatotoxicity may be attributed to the presence of triterpenoids and steroids.	*In vivo*	[23]
6	Black Cumin (*Kala Jeera*) Dried ripe fruits of *Nigella sativa* L. Family: *Ranunculaceae*	TQ, thymol, and α-hederin p-cymene and gamma-terpinene Terpenoid aldehydes, cuminic aldehyde Isomeric menthadiene carboxaldehydes.	Black Cumin and its components demonstrated hepatoprotective activity through several mechanisms including the inhibition of lipid peroxidation and oxidative stress, increased antioxidant enzymes and total thiol and GSH level, reduced fat accumulation, and preventing inflammation and other histopathological changes in the liver.	In vivo	[24]
7	Black Pepper (Kali Mirch) Dried unripe fruits of *Piper nigrum* L. Family: *Piperaceae*	Volatile oil (1-2.5%) Alkaloid [Piperine (5-9%)] Pungent resin (6.0%) Starch (about 30%) l-phellandrene Caryophyllene	The hepatoprotective property of methanolic extract of black peeper fruits were assessed in liver damage induced by ethanol-CCl_4. *Piper nigrum* exhibits significant hepatoprotective properties, attributed to the presence of piperine alkaloids, making it a promising therapeutic option for liver disorders.	*In vivo*	[25]
8	Clove (*Laung*) Dried flower buds of *Eugenia caryophyllus* L. Family: *Myrtaceae*	16-21% Volatile oil 1-13% tannins (gallotannic acid) Resin Eugenol Eugenin	Hepatoprotective potential of clove aqueous extract was assed using paracetamol induced hepatic damage assay. The degree of hepatic damage was determined by increased levels of cytoplasmic enzymes (aspartate aminotransferase and alanine aminotransferase). Clove extract restored the enzymes level in serum to their normal concentration.	*In vitro* and *In vivo*	[26]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
9	Garlic (*Lahsun*) It consists of bulb of *Allium sativum* Linn. Family: *Amaryllidaceae*	29% carbohydrates 56% proteins (Albumin) 0.1% fat, mucilage 0.06-0.1% volatile oil Allyl propyl disulfide Allin Allicin, Diallyl disulfide	*Allium sativum* safeguards the liver from oxidative stress by inhibiting cytochrome P450 2E1 and enhancing antioxidant enzymes catalase and glutathione peroxidase.	*In vivo*	[27]
10	Asafoetida (*Hing*) Oleo gum resin obtained by incising the living roots and rhizome of *Ferula asafoetida* L. Family: *Apiaceae*	Ferulic acid Luteolin Resin Gums Volatile oil	A combination of the methanol-insoluble fraction of the dried asafoetida resin, fresh garlic, ellagic acid, curcumin, butylated hydroxytoluene, and butylated hydroxyanisole, administered via gastric intubation to ducklings (at a dose of 10 mg/animal), demonstrated antihepatotoxic activity against aflatoxin B1-induced hepatotoxicity. Oleoresin when given to rats at a dose of 250 mg%, exhibited inhibition of hepatic oxidase.	*In vivo*	[28]
11	Fenugreek (*Methi*) Dried seeds of *Trigonella foenum-graecum* L. Family: *Fabaceae*	Fenugrin Carpaine Cystine Mucilage	The histological examination confirmed the hepatoprotective effect of methanol extract of fenugreek seed in animal model.	*In vivo*	[29]
12	Saffron (*Kesar*) It consists of dried stigmas and upper parts of styles of Crocus sativus L. Family: *Iridaceae*	Crocin Safranal Picrocrocin	The hepatoprotective effects of saffron extract and crocin have been demonstrated in models of liver injury induced by acetaminophen and acrylamide, respectively. The primary mechanisms of liver toxicity caused by acetaminophen and acrylamide are oxidative damage and depletion of GSH content. *Crocus sativus* L. shows antioxidant property and inhibit lipid peroxidation.	*In vitro* and *In vivo*	[30]
13	Fennel (*Saunf*) It consists of dried ripe fruits of *Foeniculum vulgare* Mill. Family: *Apiaceae*	3-7% volatile oil 20% fixed oil 20% proteins Anethole Fenchone	Essential oil of *F. vulgare* fruit demonstrated a potent hepatoprotective effect. Oral administration of *F. vulgare* essential oil reduced the levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin compared to the control group. *d*-limonene and β-myrcene of Fennel essential oil may have contributed significant role in the hepatoprotection from CCl4 toxicity.	*In vitro* and *In vivo*	[31]
14	Nutmeg (*Jaiphal*) It is the kernel of dried ripe seeds of *Myristica fragrans* Houtt. Family: *Myristicaceae*	Borneol Clemicine Myristicin Geraniol Camphene Dipentene Eugenol Safrol	Myristicin was found to possess hepatoprotective effects. It prevents the increase in serum AST and ALT levels in mice with intravenous LPS/D-GalN induced liver damage. Administration of LPS/D-GalN may have led to necrosis due to prolonged hepatic damage. Therefore, based solely on this study, it cannot be excluded that myristicin exerts its hepatoprotective effect by suppressing apoptosis.	*In vivo*	[32]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
15	Curry Leaves (*Kari patta*) It is the dried leaves of *Murraya koenigii* Linn. Family: *Rutaceae*	Tocophenol Girinimbine Lutein Carotene	Hepatoprotective activity of aqueous extract (WE) of curry leaves , carbazole alkaloids (CA), and tannin (T) fractions against ethanol-induced hepatotoxicity in Hep G2 liver carcinoma cell lines. Both tannins and carbazole alkaloids showed significant hepatoprotective effects, maintaining normal cell morphology even after ethanol exposure, similar to the standard drug L-ornithine L-aspartate (LOLA). The hepatoprotective activity was attributed to the modulation of liver enzymes, reduction in lipid peroxidation, and decreased cellular damage. Tannins obtained from crude aqueous extract of *M. koenigii* leaves exhibit potential hepatoprotective activity that may be therapeutically beneficial to treat alcoholic and other types of hepatic injury.	*In vitro*	[33]
16	Bay Leaf (*Tej patta*) It is the dried leaves of *Laurus nobilis* L. Family: *Lauraceae*	Essential oil Eucalyptol Terpinyl acetate Methyl eugenol Linalool Lauric acid	The methanolic extract of bay leaves demonstrates notable hepatoprotective effects, although the specific components responsible for its antioxidative activity remain unidentified	*In vitro* and *In vivo*	[34]
17	Indian Gooseberry (*Amla*) Biological Source: It is the dried as well as the fresh fruit of *Emblica officinalis* Gaertn. Family: *Phyllanthaceae*	Phyllemblin Tannins Emblicanin Pectin Gallic acid Phyllantine Quercetin ellagic acid	Amla exhibited significant hepatoprotective effects against different toxicants, mainly due to anti-inflammatory and free radical scavenging activity; Amla increases antioxidant enzymes and decreases lipid peroxidation; decrease in phase I enzymes; also enhances phase II enzymes; reduces ornithine decarboxylase, COX, and antimutagenic and immunomodulatory effects contribute toward the hepatoprotective effects. The bioactive compounds in amla, including quercetin, gallic acid, corilagin, and ellagic acid, have demonstrated hepatoprotective properties against toxicity induced by paracetamol, microcystins, galactosamine, and lipopolysaccharide. Amla's hepato protective effects are attributed to its antioxidant, anti-inflammatory, and lipid-lowering properties, as well as its ability to modulate detoxification enzymes.	*In vitro* and *In vivo*	[35]
18	Oregano Dried leaves of *Origanum vulgare* L. Family: *Lamiaceae*	Origanol A and B β-sitosterol Triacontanol Ursolic acid Oleanolic acid Carvacrol	The hepatoprotective effect was primarily attributed to its antioxidant properties, as treated mice exhibited reduced oxidative damage and enhanced antioxidant enzyme activity. This antioxidant mechanism likely contributed to liver protection by lowering plasma transaminase levels and minimizing microscopic liver damage.	*In vivo*	[36]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
19	Milk Thistle (Doodh patra) It is the dried seeds of *Silybum marianum* L. Family: *Asteraceae*	Silybin Isosilybin Apigenin Silybonol Betaine Silymarin	The hepatoprotective effect of silymarin is mainly due to its ability to neutralize the free radicals that are generated from the toxic substance's metabolism like ethanol, paracetamol, and carbon tetrachloride.	*In vivo*	[37]
20	Mace (Javitri) It is the dried seeds coat of *Myristica fragrans* Houtt. Family: *Myristicaceae*	Macelignan Myristicin Eugenol Safrol Elemicin Camphene	Myristicin significantly reduced LPS/D-GalN-induced increases in hepatic DNA fragmentation and serum TNF-alpha levels in mice. These results indicate that myristicin's hepatoprotective activity may be partially attributed to its ability to inhibit TNF-alpha secretion from macrophages.	*In vivo*	[38]
21	Green Chiretta (*Kalmegh*) It is the leaves or entire aerial part of *Andrographis paniculata* (Burm.f.) Nees Family: *Acanthaceae*	β-sitosterol glucoside Caffeic Andrographolide Carvacrol Eugenol Myristic acid	The hepatoprotective effect of andrographolide is associated with the regulation of specific metabolic enzymes. The suppression of hepatic cytochrome P450s (CYPs) activities by the plant extract and andrographolide contributes to its hepatoprotective properties.	*In vivo*	[39]
22	*Paprika* It is the dried red fruits of *Capsicum annuum* L. Family: *Solanaceae*	Capsaicin Capsanthin Capsorubin Oleo resin	Capsaicin has demonstrated liver-protective effects against carbon tetrachloride (CCl4)-induced hepatic damage. It enhances antioxidant enzyme defenses in the lungs and liver, contributing to its protective role.	*In vivo*	[40]
23	Phyllanthus (*Bhumi amla*) It is the aerial part of the plant *Phyllanthus niruri* L. Family: *Euphorbiaceae*	Phyllanthin Norsecurinine Hypophyllanthin Securinine	It promotes the improvement of fatty liver and reduces inflammatory damage. The decrease in pro-inflammatory cytokines (TNF-α) Phyllanthus may be attributed to its antioxidant properties, which inhibit the pro-inflammatory cytokines transcription produced by activated Kupffer cells.	*In vivo*	[41]
24	*Neem* It is the fresh dried leaves and seed oil of *Azadirachta indica* A. Juss. Family: *Meliaceae*	Nimbin Azadiradione Meliantriol Salannin Azadirachtin-A Silymarin	Various dilutions of chemically synthesized and Azadirachta indica Gold Nano Particles (GNPs) were tested for their impact on the cytokine profile. The co-culture treated with *Azadirachta indica* GNPs exhibited a significant increase in IL-10 compared to citrate GNPs, indicating a strong hepatoprotective effect of Azadirachta indica GNPs against LPS-induced inflammation. The protective effects of azadirachtin-A and silymarin were evaluated for their ability to mitigate biochemical, histopathological, and ultrastructural changes caused by CCl4 in normal liver tissues. Pre-treatment with herbal formulations from various plants helped restore total protein, albumin, and serum marker enzyme levels to near-normal values, demonstrating effects comparable to those of silymarin.	*In vitro* and *In vivo*	[42,43]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
25	*Tulsi* (Holy Basil) It is the fresh dried leaves of *Ocimum sanctum* L. Family: *Lamiaceae*	Eugenol Caryophyllene Estragole Methyl eugenol Cubebol Borneol	The alcoholic extract of Ocimum sanctum L. leaves exhibited notable hepatoprotective effects, as evidenced by improved liver function tests (LFTs) and histopathological analysis. A synergistic effect was observed when Ocimum sanctum L. extract was combined with silymarin, enhancing its protective benefits.	*In vivo* and *In vitro*	[44]
26	Pudina (*Mint*) It is the dried leaves of *Mentha spicata* L. Family: *Lamiaceae*	Menthone Methyl acetate Isomenthol Piperitone Neomenthol	Carbon tetrachloride (CCL_4) administration led to a significant rise in serum hepatic levels of sGOT, sGPT, sALP, and SB, indicating liver damage compared to normal controls. However, pre-treatment with chloroform, ethanol, and aqueous extracts before CCL4 administration significantly reduced the levels of sGOT, sGPT, sALP, and SB, with results almost comparable to those achieved with silymarin.	*In vivo*	[45]
27	Brahmi It is the fresh and dried leaves of *Bacopa monnieri* L. Family: *Scrophulariaceae*	Bacoside A loliolide Rosavin Bacopaside I Stigmastanol	It has a strong protective effect on liver and kidney functions damaged by morphine, as evidenced by improved serum levels of glutamate pyruvate transaminase, glutamate oxaloacetate transaminase, lactate dehydrogenase, alkaline phosphatase, gamma-glutamyl transferase, and reduced creatinine, urea, and uric acid levels. Pre-treatment with Bacoside A helps prevent the increase in lipid peroxidation (LPO) and serum marker enzyme activity, while preserving the antioxidant system, thereby protecting rats from Diethyl nitrosamine-induced liver toxicity.	*In vivo*	[46]
28	*Bhringraj* It is the fresh and dried leaves of *Eclipta alba* L. Family: *Asteraceae*	Amyrin Wedelolactone Demethylwedelolactone Saponins	The phytochemicals of bhringraj significantly decreases the accumulation of fat in liver, necrotic foci and mononuclear infiltration. The phytochemicals in Bhringraj stimulated the regeneration of hepatocytes in the liver.	*In vivo*	[47]
29	*Ashwagandha* It is derived from the roots of *Withania somnifera* (L.) Dunal Family: *Solanaceae*	Withanolide Withanoside Withaferin Withanone Anaferine Cortisol	It significantly decreases the LPO, boosts CAT, glutathione content, GPx and GR activity in liver. The withanolide-rich fraction of Ashwagandha have demonstrated significant reduction in serum bilirubin, AST, ALP, and ALT levels whereas, promising enhancement in hepatic SOD, GPx and total antioxidant capacity. The MDA and NO levels have been significantly reduced along with mRNA down regulation , expression of TNF-α, cyclooxygenase-II, IL-1b, and iNOS genes.	*In vivo*	[48]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
30	*Shatavari* It is derived from the dried tuberous roots of *Asparagus racemosus* Willd. Family: *Asparagaceae*	Sarsasapogenin Shatavarin I-IV Steroidal saponins Mucilage Alkaloids	The hepatoprotective effects of Shatavari were studied in male albino rats exposed to isoniazid, which caused necrotic changes and elevated levels of hepatic enzymes, including alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, and γ-glutamyl transpeptidase, indicating injury of liver. The increased levels of aspartate aminotransferase and alanine aminotransferase reflected higher liver cell permeability and damage. However, A. racemosus extract administration restored glutathione levels, mitigating the damage. The hepatoprotective activity was attributed to the inhibition of free radical production and scavenging of these radicals by reducing hepatic CYP2E1 activity. In a paracetamol-induced liver injury model, the ethanolic root extract of shatavari reversed elevated levels of SGOT, SGPT, serum bilirubin, and alkaline phosphatase, further supporting its hepatoprotective effects. Additionally, the extract improved the depleted antioxidant enzymes catalase and superoxide dismutase.	*In vivo*	[49]
31	*Reetha* It consists of the dried fruits of *Sapindus mukorossi* L. Family: *Sapindaceae*	Saponins Sugar Mucilage β-sitosterol Starch Linoleic acid Sapindic acid	In vitro, extract of Reetha protected primary hepatocyte monolayer cultures from CCl_4-induced damage. In vivo, the extracts effectively reduced liver damage in CCl_4-treated rats, as shown by improved serum marker enzyme activities.	*In vitro* and *In vivo*	[50]
32	Wild cassia /*Senna* Dried bark of *Senna singueana* (Delile) Lock Family: *Leguminosae*	(epi)gallocatechin (epi)catechin (epi)catechin-(epi) catechin (epi)catechin-(epi) afzelechin (epi)guibourtinidol-(epi) catechin (epi)guibourtinidol (ent)cassiaflavan (epi)afzelechin (epi)gallocatechin-(epi) catechin	The methanolic extract of *S. sengueana* demonstrated significant hepatoprotective effects in rats with d-galactosamine (d-GalN)-induced liver damage. It notably reduced elevated levels of aspartate aminotransferase and total bilirubin. Additionally, the extract of wild cassia enhanced cytoplasmic Bcl-2 expression, suggesting a suppression of apoptosis. Overall, the bark extract shows promising potential as a candidate for further research on antioxidants and liver protection.	*In vitro*	[51]
33	Licorice (Mulethi) It consists of the dried roots and rhizomes of *Glycyrrhiza glabra* L. Family: *Fabaceae*	Glycyrrhizin Isoliquiritin Glycyrrhetic acid Coumarins	Licorice decreases lipid peroxidation due to which there is increase in detoxification which helps in the hepatoprotective activity.	*In vivo*	[52]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
34	Spiny Amaranth (*Kateli*) It is obtained from the plant of *Amaranthus spinosus* L. Family: *Amaranthaceae*	Spinasterol Arginine	The 50% ethanolic extract of Amaranthus spinosus (ASE) demonstrated significant hepatoprotective and antioxidant effects against CCl4-induced liver damage in rats. ASE, administered at doses of 100, 200, and 400 mg/kg for 14 days, effectively normalized elevated liver enzymes at serum level (ALT, AST, alkaline phosphatase, and total bilirubin) in a dose-dependent manner. The highest dose showed the most significant protection. Histopathological examination of liver sections confirmed these improvements. Additionally, ASE improved in vivo antioxidant activities, including reduced levels of malondialdehyde (MDA), hydroperoxides, and increased levels of reduced glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT). These results suggest that ASE's hepatoprotective effects may be due to its flavonoid and phenolic compounds.	*In vivo*	[53]
35	Common Wormwood It is obtained from the aerial parts of *Artemisia absinthium* L. Family: *Asteraceae*	Sesquiterpene lactones Thujone Artemisinin Absinthin	The aqueous extract of *Artemisia absinthium* (AEAA) demonstrated significant hepatoprotective effects in mice, both against chemically induced (CCl4) and immunologically induced (LPS) liver injury. AEAA pretreatment effectively reduced elevated liver enzyme levels (AST, ALT), decreased lipid peroxidation in liver tissue, and restored antioxidant enzyme activities (SOD and GPx) to normal levels. AEAA also suppressed pro-inflammatory mediators (TNF-alpha and IL-1) and improved liver histopathology, reducing hepatocellular necrosis and inflammatory cell infiltration. Phytochemical analysis identified the presence of sesquiterpene lactones, flavonoids, phenolic acids, and tannins in AEAA. These findings support AEAA's traditional use as a liver protective agent, suggesting its antioxidative and immunomodulatory properties as the underlying mechanisms.	*In vivo*	[54]
36	Common Fig (*Ajneer*) It is obtained from the leaves of F*icus carica* L. Family: *Moraceae*	Rutin Catechin Bergapten Myricetin Kaempferol	The ethanolic extract of *Ficus carica* leaves demonstrated significant hepatoprotective effects in a CCl4-induced liver damage model. Mice pre-treated with the extract at doses of 200, 400, and 800 mg/kg showed a significant reduction in liver enzyme levels (ALT and AST), compared to the CCl4 control group. Histopathological examination revealed that the extract treatment resulted in less liver damage, with no fibrosis and moderate inflammation, in contrast to the severe liver damage observed in the control group. The results suggest that leaf extract (200 mg/kg) in animal model provides notable protection against CCl4-induced hepatic damage.	*In vivo*	[55]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
37	Indian Laurel It is obtained from the leaves of *Litsea coreana* H. Lév. Family: *Lauraceae*	Copaene Dodecanoic acid Decanal Ethenyl ester	The methanol extracts and total flavonoids of L. coreana (hawk tea) exhibited significant hepatoprotective effects in various rat models. The methanol extract at 400 mg/kg reduced serum levels of pro-inflammatory cytokines and suppressed inflammation-related gene expressions, such as TNF-α and COX-2, in CCl4-induced liver damage. Kaempferol-glucopyranoside inhibited hepatic stellate cell proliferation and fibrosis by modulating collagen and Smad gene expressions. The total flavonoids (TFLC) at 200 mg/kg significantly improved liver function by reducing triglycerides, MDA, ALT, and AST levels, while enhancing antioxidant activity (SOD). TFLC also alleviated liver fibrosis and hepatic steatosis by reducing liver markers like ALT, AST, and collagen proteins. In models of alcoholic fatty liver and insulin resistance, TFLC improved metabolic markers, reduced lipid accumulation, and promoted insulin sensitivity.	*In vivo*	[56]
38	Simple leaf Chastetree (*Legundi*) It is obtained from the leaves of *Vitex trifolia* Linn. Family: *Lamiaceae*	Casticin Vitexin Luteolin	Ethanolic extract of Vitex trifolia flowers (EVT) demonstrated significant hepatoprotective effects in rats with CCl4-induced liver injury. At a dose of 200 mg/kg, EVT reduced elevated serum levels of liver enzymes (SGPT, SGOT, ALP, GGTP, and total bilirubin) to near-normal values, showing activity comparable to the standard hepatoprotective drug, silymarin. Histopathological analysis further confirmed that EVT protected against liver damage caused by CCl4.	*In vivo*	[57]
39	Hogweed (*Punarnava*) It is obtained from the fresh and dried plant of *Boerhavia diffusa* L. nom. cons. Family: *Nyctaginaceae*	Boeravinones Xanthone Lignan Boerhavisterol	*Boerhavia diffusa* extract effectively protected against CCl4-induced liver damage in Swiss albino mice. Treatment with the extract at doses of 100, 200, and 300 mg/kg/day significantly reduced liver enzyme levels, bilirubin, and lipid peroxidation in a dose-dependent manner. It also improved liver tissue structure and reversed histopathological damage. The hepatoprotective effect is attributed to the antioxidant properties of *B. diffusa* extract.	*In vivo*	[58]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
40	*Rhubarb (Revand chini)* It is obtained from the dried rhizome and roots of *Rheum emodi* Wall. ex Meisn. Family: *Polygonaceae*	Emodin Physcion Rhein Emodin glycoside	Hepatoprotective effects of flavonoid-containing fractions derived from *Rheum emodi* (Chinese rhubarb) roots was st in rats with paracetamol-induced liver toxicity. Through column chromatography and thin layer chromatography, five fractions (F1 to F5) were identified as containing various flavonoids. Among these, fraction F2 demonstrated the most significant hepatoprotective activity, notably reducing elevated liver enzymes (ALT, AST, ALP) and bilirubin levels in a dose-dependent manner. The highest therapeutic effect was observed with a 0.5 mL/kg dose of F2, surpassing the effect of the standard hepatoprotective drug, silymarin. These findings suggest that the flavonoid fractions from *Rheum emodi* roots may offer notable liver protection, though further research is necessary to pinpoint the specific flavonoids involved and fully understand their mechanisms.	*In vivo*	[59]
41	*Chirata* It is obtained from the dried plants of *Swertia chirata* L. Family: *Gentianaceae*	Mangiferin Amarogentin Gentianine Gentiopicrin	The extract of Swertia chirayita demonstrated significant hepatoprotective effects in Swiss albino mice with paracetamol-induced liver toxicity. Treatment with S. chirayita extract (100–200 mg/kg) effectively mitigated liver damage by reducing elevated serum markers (GPT, GOT, ALP, bilirubin) and restoring antioxidant enzyme levels (SOD, catalase, GSH, GPx) in liver tissue. Additionally, lipid peroxidation was reduced, and hepatic tissue architecture was preserved.	*In vivo*	[60]
42	*Amaltas* It is obtained from the plant of *Cassia fistula* L. Family: *Fabaceae*	Anthraquinone Saponins Terpenoids Rhein	The hepatoprotective potential of the Cassia fistula leaf n-heptane extract was assessed in rats with liver toxicity induced by a carbon tetrachloride and liquid paraffin mixture (1:1). The extract exhibited a notable protective effect by reducing serum levels of transaminases , bilirubin, and alkaline phosphatase (ALP). At a dose of 400 mg/kg, the extract demonstrated significant hepatoprotective activity, comparable to that of a standard liver-protective drug.	*In vivo*	[61]
43	Chicory (*Kasni*) It is obtained from the roots of the plant of *Cichorium intybus* L. Family: *Asteraceae*	Resveratrol Salvianolic acid Hesperetin Luteolin Quercetin	In animal models of liver damage induced by acetaminophen and carbon tetrachloride, both aqueous and methanolic extracts from chicory seeds significantly reduced mortality and improved liver function by lowering serum levels of liver enzymes like AST, ALT, and alkaline phosphatase (AP). The extracts also alleviated elevated bilirubin levels and improved histological markers of liver damage. Additionally, the extracts improved oxidative stress markers, such as increasing antioxidant enzymes (superoxide dismutase, glutathione peroxidase, catalase) and reducing malondialdehyde levels.	*In vivo*	[62]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
44	Fumitory (*Pitpapra*) It is obtained from the plant of *Fumaria indica* L. Family: *Papaveraceae*	Protopine Fumariline Sitosterol Narlumidine Bicuculine	The hepatoprotective effects of the Fumaria genus have been supported by several studies. F. indica exhibited a chemo-preventive effect in liver cancer models, with its butanol fraction (containing protopine) showing the most effectiveness, comparable to silymarin. F. officinalis also contained protopine, which raised bile flow in dogs, and demonstrated hepatoprotective properties against CCl4-induced toxicity. Additionally, *F. parviflora* showed antioxidant-induced hepatoprotection, mainly due to alkaloids and fumaric acid. In another study, extracts of F. densiflora and F. officinalis displayed hepatoprotection against CCl4 toxicity, with alkaloids showing significant cytoprotective effects. Clinical research on F. officinalis in Tunisia revealed its protective effects against liver and kidney damage induced by the insecticide permethrin (PER). This was attributed to its phenolic compounds, such as polyphenols, flavonoids, and alkaloids. The extract restored liver function, reduced enzyme activity (AST, ALT), and reduced oxidative stress markers (TBARS, PCO, AOPP, NO) in both the liver and mitochondria. Histopathological analysis showed significant recovery from liver damage, including reduced DNA damage, likely due to quercetin and naringenin's antioxidant properties. Furthermore, an ethanolic extract of F. officinalis (at doses of 200 and 500 mg/kg) significantly reduced liver damage induced by CCl4, as evidenced by lowered serum enzyme levels, bilirubin, cholesterol, and triglycerides, with histopathological confirmation of its hepatoprotective activity.	*In vivo*	[63]
45	*Kabab chini* Fruits of *Piper cubeba* L.f. Family: *Piperaceae*	cubebin, hinokinin, yatein, dihydrocubebin	Piper cubeba fruit's ethanolic extract exhibited significant hepatoprotective and antioxidant effects in CCl_4-induced liver injury in rats by normalizing hepatic enzyme levels, enhancing antioxidant defenses, and modulating the expression of inflammatory and stress-related genes.	*In vivo*	[64]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
46	Wild guava Biological Source: It is obtained from the stem bark of *Careya arborea* Roxb. Family: *Lecythidaceaea*	Terpenoids Valepotriates Tannins Cardiac glycosides	The methanolic extract of Careya arborea (MECA) stem bark exhibited significant hepatoprotective and antioxidant effects in Wistar albino rats. CCl4-induced hepatotoxicity was treated with MECA at doses of 50, 100, and 200 mg/kg, as well as silymarin (25 mg/kg). Extract significantly reduced serum levels of transaminases (GOT, GPT), alkaline phosphatase (ALP), bilirubin, uric acid, and lipid peroxidation, while increasing antioxidant enzyme levels (SOD, CAT) and nonenzymatic antioxidants (GSH, Vitamin C, Vitamin E) in a dose-dependent manner. These results suggest that MECA has potent hepatoprotective and antioxidant activities.	*In vivo*	[65]
47	Indian Mulberry (*Noni*) It is obtained from the different plant parts of *Morinda citrifolia* L. Family: *Rubiaceae*	Proline Valine Digoxin Iridoids Scopoletin	Tahitian Noni Juice (TNJ) provided hepatoprotective effects against chronic liver damage induced by carbon tetrachloride (CCl4) in rats. TNJ treatment prevented hepatic steatosis and normalized serum levels of liver enzymes (ALP, AST, ALT) and lipids (cholesterol, triglycerides, LDL, VLDL), while increasing HDL levels compared to the placebo group. Histopathological examination indicated that liver damage was minimized in the TNJ-treated group, similar to the control group.	*In vivo*	[66]
48	Yellow gentian (*Kutki*) It is obtained from the dried roots of *Picrorhiza kurroa* Royle ex Benth. Family: *Plantaginaceae*	Cucurbitacins Apocynin Kutkiol Drosin	Equal ratios of extracts from *Andrographis paniculata*, *Boerhavia diffusa*, *Eclipta alba*, and *Picrorhiza kurroa* were combined and assessed for their hepatoprotective effects against liver damage induced by paracetamol and carbon tetrachloride in rats. The hepatotoxic substances enhanced the serum levels of transaminases, total bilirubin, and triglycerides, while decreasing albumin levels. Liver homogenates showed increased lipid peroxidation and reduced glutathione content. Administration of the combined extract helped restore these biochemical parameters, indicating liver function improvement. The combined extract demonstrated significant, dose-dependent hepatoprotective effects ($p<0.05$), with the 400 mg/kg dose showing the most substantial recovery, comparable to the effects of silymarin-treated rats.	*In vivo*	[67]

Table 1. Continued...

Serial Number	Name of spices/herb , Biological Source	Chemical constituents	Effect on NASH	Study Model	References
49	*Chinese wedelia* (*Bhimra*) It is obtained from the plant of *Wedelia calendulacea* L. Family: *Asteraceae*	Wedelolactone Demethylwedelolactone Coumestans	hepatoprotective effect of the ethanolic extract of *Wedelia calendulacea* (EEWC) was evaluated against CCl4-induced acute hepatotoxicity in rats. The extract demonstrated a dose-dependent reduction in elevated serum levels of liver enzymes (AST, ALT, ALP), while also increasing total protein and bilirubin levels, indicating that it helped maintain normal liver function. Additionally, the weight of organs such as the liver, heart, lungs, spleen, and kidneys were higher in EEWC-treated rats compared to the CCl4 control group, suggesting a protective effect on these organs as well.	*In vivo*	[68]
50	Indian Nightshade (*Makoi*) It is obtained from the aerial part of *Solanum nigrum* L. Family: *Solanaceae*	Coumarin Luteolin Quercetin Kaempferol	The water extract of Solanum nigrum (SNE) exhibited significant hepatoprotective effects against liver damage caused by carbon tetrachloride (CCl4) in rats. After 6 weeks of oral administration of SNE, there was a notable decrease in serum liver enzyme markers (GOT, GPT, ALP, and total bilirubin), along with a reduction in superoxide and hydroxyl radicals. Additionally, the extract helped restore hepatic glutathione (GSH) levels and the activities and expressions of antioxidant enzymes, such as SOD, GST Al, and GST Mu, which had been diminished by CCl4. Histological examination showed less liver damage, including reduced signs of swelling, lymphocyte infiltration, necrosis, and fibrosis. These findings indicate that SNE protects the liver by enhancing detoxification enzymes and exhibiting antioxidant and free radical scavenging properties.	*In vivo*	[69]

consistent metabolic benefits. Meta-analyses confirm its clinical efficacy remains inconclusive despite robust preclinical data, with proposed mechanisms involving Sirtuin 1 (SIRT1) and AMP-activated protein kinase (AMPK) activation, suppression of lipogenesis, and gut microbiota modulation.

Curcumin, the active polyphenol from turmeric, exhibits promising phase II/III clinical results. In a randomised trial of 80 Iranian NAFLD patients, curcumin supplementation significantly improved hepatic steatosis and aminotransferases. Mechanistically, it reduces oxidative stress, inflammation, and apoptosis while activating AMPK, NRF2, FXR, LXR, and PPARA, inhibiting NLRP3 inflammasome, and modulating gut microbiota, although larger multicenter trials are needed to confirm its therapeutic potential.

Berberine, an isoquinoline alkaloid, has shown consistent clinical efficacy. Trials in NAFLD patients (n = 184 and 80) demonstrated improvements in liver function, fat metabolism, serum lipid profiles, and ceramides, with ongoing phase 4 studies for NASH (NCT03198572). Its mechanisms involve AMPK activation, NRF2/PPARγ signalling, suppression of NLRP3 inflammasome, enhancement of adipose thermogenesis, and gut microbiota modulation through intestinal FXR signalling, making it one of the most clinically promising herbal agents.

Table 2: Clinical Evidence of Herbal Interventions in NASH [70-77]

Herbal Intervention	Dose / Regimen	Trial Size & Population	Duration	Key Clinical Outcomes	Proposed Mechanisms
Resveratrol	500 mg/day	50 NAFLD patients	12 weeks	Improved liver enzymes and inflammation in some studies; other trials no significant metabolic benefit	Activates SIRT1 & AMPK, induces adipose browning, suppresses lipogenesis, modulates gut–brain axis & gut microbiota
Curcumin	Not specified (varied)	80 NAFLD patients	12 weeks	Improved hepatic steatosis, reduced ALT/AST	Reduces oxidative stress, apoptosis & inflammation; activates AMPK, NRF2, FXR, LXR, PPARA; inhibits NLRP3 inflammasome; modulates gut microbiota
Berberine	Not specified	184 NAFLD patients + 80 patients (other trial)	12–16 weeks	Improved liver function, lipid metabolism, serum ceramides; ongoing phase 4 for NASH	Activates AMPK, NRF2/PPARγ; suppresses NLRP3 inflammasome; enhances adipose thermogenesis; modulates gut microbiota & bile acid metabolism via intestinal FXR
Silymarin	700 mg/day + Vitamin E & phospha tidylcholine	NAFLD/ NASH adults (phase I–IV trials)	12 weeks (varies)	Improved liver enzymes, oxidative stress, fibrosis markers; variable efficacy	Activates SIRT1/AMPK, FXR, NRF2; inhibits NLRP3 inflammasome; antioxidant, anti-inflammatory, antifibrotic
Ginger (Zingiber officinale)	1–2 g/day	44–76 NAFLD/ T2DM patients	12 weeks	Improved liver enzymes, insulin resistance, HDL-C, BP; reduced BMI & waist/ hip circumference	Antioxidant, anti-inflammatory, lipid metabolism regulation, reduced hepatic fat accumulation, enhanced antioxidant defenses
Anthocyanins	Not specified	74 NAFLD patients	Not specified	Reduced liver fat, ALT/AST, triglycerides; improved antioxidant status	Activates AMPK & PPAR signaling, NRF2-mediated antioxidant defense, inhibits lipid peroxidation & inflammation, improves gut microbiota & intestinal barrier
Zataria multiflora	700 mg/day	84 NAFLD patients	12 weeks	Reduced liver fat grade, BMI, fasting glucose, ALT/ AST	Antioxidant, anti-inflammatory, lipid-lowering, modulates hepatic oxidative stress & inflammatory cytokines
Compound Herbal Capsules (ZZTZ)	Multi-herb formulation	120 NAFLD patients	Not specified	Improved hepatic steatosis, liver enzymes, lipid profile, insulin resistance	Multi-target: reduces oxidative stress, modulates lipid & bile acid metabolism, improves insulin signaling, anti-inflammatory
Qushi Huayu (QSHY)	Multi-herb formulation	246 NAFLD patients	24 weeks	Reduced ALT, AST, FIB-4; improved liver fat	Modulates gut microbiota (Escherichia-Shigella, Bacteroides), microbial metabolites (p-Hydroxyphenylacetic acid), reduces liver fat & inflammation
Spleen-strengthening & liver-draining formula (SLF)	Multi-herb TCM	Not specified	12 weeks	Improved liver function, CAP, LSM, lipid profile, HOMA-IR	Restores gut microbiota: increased Coprococcus, Lachnospiraceae_ NK4A136, Ruminococcus; modulation of glucolipid metabolism
SPS (Silybum marianum + Pueraria lobata + Salvia miltiorrhiza)	3 tablets twice daily (23 mg silybin/tablet)	121 NAFLD patients	24 weeks	Trend toward reduced liver fat & steatosis; decreased hs-CRP, increased aldehyde dehydrogenase	Anti-inflammatory, antioxidant, hepatoprotective
Heptex® (Phyllanthus niruri + Silybum marianum)	1–2 capsules/ day	146 patients at risk of NASH	36 weeks	Reduced ALT (low/high dose), AST (high dose); reduced total cholesterol (low dose); safe & well tolerated	Hepatoprotective, antioxidant, anti-inflammatory

Silymarin, extracted from *Silybum marianum*, has been extensively investigated across phase I–IV trials in NAFLD/NASH patients. Evidence supports improvements in liver enzymes, oxidative stress, and fibrosis markers, though results are variable due to differences in formulation and bioavailability. Mechanistic studies indicate activation of SIRT1/AMPK, FXR, NRF2, and inhibition of NLRP3 inflammasome, underpinning its hepatoprotective, anti-inflammatory, and antifibrotic effects.

Ginger (*Zingiber officinale* Roscoe) supplementation has been evaluated in NAFLD and type 2 diabetes patients. Clinical trials (2 g/day for 12 weeks or 1000 mg twice daily) showed improvements in liver enzymes, insulin sensitivity, HDL-cholesterol, and blood pressure, attributed to gingerols and shogaols mediating antioxidant, anti-inflammatory, and lipid-modulating effects. However, studies remain limited in size and duration.

Anthocyanins, flavonoid pigments from berries and coloured grains, have demonstrated reductions in liver fat, ALT/AST, triglycerides, and improved antioxidant status in randomised trials. Their mechanism involves AMPK and PPAR activation, NRF2-mediated antioxidant defence, and gut microbiota modulation, supporting their potential as nutraceuticals in NASH prevention.

Zataria multiflora, rich in thymol and carvacrol, reduced liver fat, BMI, fasting glucose, and liver enzymes in a clinical trial of 84 NAFLD patients, exerting antioxidant, anti-inflammatory, and lipid-lowering effects, suggesting utility as adjunct therapy.

Compound herbal formulas, such as Zhenzhu Tiaozhi (ZZTZ) and Qushi Huayu (QSHY), provide multi-target interventions. ZZTZ improved hepatic steatosis, insulin resistance, liver enzymes, and lipid profiles in 120 NAFLD patients, while QSHY, in a 246-patient multicenter trial, improved ALT, AST, liver fat content, and fibrosis markers over 24 weeks. Both formulas exert effects via modulation of oxidative stress, lipid metabolism, bile acid homeostasis, insulin signalling, inflammation, and gut microbiota composition.

Spleen-Strengthening and Liver-Draining formula (SLF), a traditional Chinese medicine formulation, demonstrated efficacy in a 12-week RCT. SLF improved liver function, CAP, liver stiffness, lipid profile, and HOMA-IR in NAFLD patients. Gut microbiota analysis revealed restoration of beneficial genera such as Coprococcus, Lachnospiraceae_NK4A136, and Ruminococcus, highlighting microbiome-mediated mechanisms.

Other polyherbal combinations, such as SPS (*Silybum marianum, Pueraria lobata, Salvia miltiorrhiza*) and Heptex® (*Phyllanthus niruri* + *Silybum marianum*), have also shown hepatoprotective and anti-inflammatory effects, reducing liver enzymes and oxidative stress markers in clinical trials, though larger studies are warranted to establish definitive efficacy.

Among single-compound herbs, berberine and silymarin show the most robust clinical evidence for NASH management, while resveratrol and curcumin have promising but variable results. Nutraceuticals such as ginger, anthocyanins, and *Zataria multiflora* show early positive outcomes. Compound herbal formulas, including SLF, QSHY, and ZZTZ, offer multi-target benefits, often incorporating gut microbiota modulation as a key mechanism, representing a promising avenue for integrated herbal therapy in NAFLD/NASH management. Different clinical evidence of herbal intervention in NASH is described in Table 2.

11. Conclusion and Future Perspective

Non-alcoholic Steatohepatitis (NASH) is a complex and increasingly common liver disease marked by fat accumulation, inflammation, and liver cell destruction. It can develop into more serious diseases like cirrhosis, fibrosis, and even liver failure over time. The lack of effective treatment options and the increasing frequency of NASH have led to a major expansion of research into the disease in recent years. The inflammatory subtype of NAFLD, known as NASH, is linked to the development of cirrhosis, the need for a liver transplant, and the progression of the illness. In clinical practice, NASH is not given enough credit despite its significance[78].

A liver biopsy is necessary for the diagnosis of NASH and is still the gold standard for diagnosis. For a diagnosis to be made, the liver must have five per cent fat cells. A biopsy is necessary to differentiate NASH from simple steatosis. A liver biopsy can also be performed to determine the disease's stage (fibrosis) and

severity (grade). In NASH patients, the use of insulin-sensitising medications, such as biguanide metformin and thiazolidinediones (TZDs), has demonstrated promise in improving insulin sensitivity and lowering liver enzymes, steatosis, necroinflammation, and fibrosis.

Even though the pathophysiology of NASH has been greatly improved, much more remains to be discovered about the disease's underlying causes and risk factors. While food, exercise, and metabolic syndrome are important lifestyle factors, genetic susceptibility and other environmental factors also play a role in its development[79].

The critical need for efficient therapy is highlighted by the lack of licensed pharmaceutical medicines for NASH. Prospective treatment possibilities for NASH pathogenesis, including inflammation, fibrosis, and metabolic dysfunction, seem promising due to ongoing clinical trials addressing these factors. Finding therapies that are effective and safe for a wide range of patients is still difficult, though.

While there is ongoing research into potential treatments, including herbal remedies as well as home remedies, the conclusive evidence on the effectiveness of herbs, spices and herbal extracts in reducing NASH is still evolving. The different effects of NASH on herbs, spices, and the herbal extract show that it can provide a therapeutic effect to the liver and help contribute to the study of NASH. Some herbs, spices and herbal extracts have shown promising results in preclinical studies and small-scale human trials. The compounds found in herbs like milk thistle, turmeric, ginger, coriander, coumarin, cinnamon, fenugreek, asafoetida and many more of them have exhibited hepatoprotective activity, anti-inflammatory and antioxidant properties, which could potentially mitigate liver damage associated with NASH. The different spices show their hepatoprotective effect by decreasing the levels of bilirubin and also the activities of AST, ALT and ALP. It also shows a decrease in the levels of serum bilirubin, the activities of GOP, GPT and ALP, with a significant increase in protein[80].

Moreover, certain herbal formulations and traditional medicines from various cultural practices include ingredients believed to support liver health and may have potential in managing NASH symptoms. However, rigorous clinical trials involving larger sample sizes are necessary to validate their efficacy and safety for NASH patients[81].

It's important to approach the use of herbs, spices and herbal extracts in NASH management with caution and under the guidance of healthcare professionals. While some natural remedies may offer benefits, they should not replace conventional medical treatment or lifestyle modifications, and variability in product quality and dosage underscores the importance of informed decision-making and monitoring when incorporating herbal supplements into NASH management plans[82].

In conclusion, NASH is a serious public health issue that could have fatal outcomes for those who are impacted. In order to reduce the burden of NASH on global health and to improve our understanding of the disease, it is imperative that research efforts be sustained.

The future of NASH management requires multi-targeted therapies that go beyond current pharmacological options. Herbs, spices, and phytochemicals hold promise due to their hepatoprotective, antioxidant, and anti-inflammatory properties, but clinical validation remains limited. Well-designed trials with standardised formulations and larger cohorts are essential to confirm efficacy, safety, and dosing. Integrating herbal approaches with modern therapeutics and personalised strategies may provide a holistic and effective framework for slowing disease progression and improving patient outcomes.

12. Author Contribution

Hritwij Bharati (HB)- Data collection, Writing original draft, Investigation, Design creation, Formal Analysis. Soumya Bhattacharya (SB)- Writing -original draft, Writing -review and editing, Data Validation, Supervision, Methodology, Conceptualization. All authors have read and agreed to the published version of the manuscript.

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