

A Systematic Review on Important Risk Factors and Possible Involved Mechanisms of Medicinal Plants on Nonalcoholic Fatty Liver Disease

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Abstract

Nonalcoholic fatty liver disease (NAFLD) is one of the most common diseases in the industrialized world. Hyperlipidemia, obesity, hypertension, and diabetes are known to be major risk factors for NAFLD, and chemical drugs are rarely effective in treating this disease and may cause significant complications. It is believed that medicinal plants with antioxidant properties and several other mechanisms have high preventive and therapeutic effects. This study was conducted with the aim of determining the effective mechanisms of plants on NAFLD and its risk factors. First, efficient plants and disease risk factors were identified; then, by reviewing scientific information sources and 6523 articles, the positive effects of plants on each risk factors were investigated. This information was recorded in checklist 1. Another 1100 articles (a total of 7623 articles) were systematically reviewed, and the mechanisms of the selected factories regarding the above risk factors were recorded in Checklist No. 2. Plants, their scientific names, family names, the used parts, and their possible mechanisms were identified in the case of 43 effective plants, and their molecular and genetic mechanisms were recorded. According to the results, 33 plants affect all four risk factors, eight of which affect three factors and two affect only two factors. In general, most of the mechanisms were in the prevention and treatment of NAFLD. Identification of plants and their effective mechanisms in NAFLD will reduce the incidence of this disease and produce new potent and selective herbal medicines that inhibit each of the risk factors.

Keywords: Herbal plants, hypolipidemic, nonalcoholic fatty liver disease, obesity

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INTRODUCTION

Liver is one of the most important organs of the body with many functions including producing bile, eliminating materials cytotoxicity, and converting drugs to active metabolites and facilitating their excretion by increasing drugs solvency in water.^[1] Unfortunately, the common lifestyle (eating unhealthy foods, regular smoking, increased stress, self-treatment, and overeating) has caused great development in liver disease incidence.^[2] In 1980, nonalcoholic fatty liver disease (NAFLD)

was detected for the first time by Huang *et al.* in people without the history of alcohol consumption.^[3]

Nonalcoholic fatty liver disease

Indeed, NAFLD includes a wide variety of disorders ranging from a simple fat accumulation manifesting as large vesicles of fat to fat accumulation accompanied with inflammation, liver cell damage, and cirrhosis.^[4] Currently, NAFLD is

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considered the hepatic expression of metabolic syndrome and usually associated with clinical manifestations of this syndrome such as type 2 diabetes, obesity, dyslipidemia, and hypertension.^[5] The prevalence of NAFLD was estimated to be 20%–30% in general populations. Since there is a rapid increase in prevalence of metabolic syndrome's risk factors, NAFLD is known as the most common cause of liver disease in western countries.^[6]

NAFLD was classified into two types: nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver (NAFL). In NAFL, hepatic steatosis occurs with no inflammation, while in NASH, hepatic steatosis progresses to the inflammation-associated condition. In histopathological examinations, NASH could be distinguished from alcoholic steatohepatitis.^[6]

NAFLD is diagnosed mainly by an unreasonable increase of liver aminotransferase in patients with radiological findings of hepatic liver infiltration or less frequently cryptogenic cirrhosis. First, the most important diagnostic clue is to differentiate NASH from steatosis. Clinical examinations require serious consideration of metabolic risk factors such as glucose intolerance, central obesity, hypertension, hypertriglyceridemia, and low HDL cholesterol. These factors can contribute to the diagnosis of NAFLD, but they may not be considered specific.^[7] Secondary causes of NAFLD, such as medications and intestinal bypass surgery, should be excluded because these conditions may manage differently.^[8] Hepatic steatosis can be confirmed by imaging, although liver biopsy is required in some cases. Among suspected NAFLD, patients with chronic elevated aminotransaminases, clinical evaluation, and serological testing should be excluded as other causes of chronic liver disease.^[9] Liver biopsy is needed to stage fibrosis and differentiate NASH from steatosis. This would be helpful to provide prognosis, exclude other hepatic diseases, and monitor the response of treatment or the progression of disease. Clinical characteristics, especially diabetes, obesity, and age, can lead to stratify patients at risk for advanced fibrosis, but they are not adequately accurate to be used instead of triglyceride liver biopsy.^[10] Briefly, these factors can be considered as the causes of NAFLD: obesity, glucose intolerance, hypertriglyceridemia, low HDL cholesterol, hypertension, protein-calorie malnutrition, rapid weight loss, gastrointestinal bypass surgery, total parental nutrition, glucocorticoids, estrogens, tamoxifen, amiodarone, methotrexate, diltiazem, zidovudine, valproate, aspirin, tetracycline, cocaine, lipodystrophy, hypopituitarism, dysbetalipoproteinemia, Weber-Christian disease, Amanita phalloides mushroom, phosphorus poisoning, petrochemicals, bacillus cereus toxin, human immunodeficiency virus, hepatitis C, and small bowel diverticulosis with bacterial overgrowth.^[10]

Treatment strategies of NAFLD have revolved around identification and treatment of associated metabolic conditions such as diabetes, hypertension, obesity, and hyperlipidemia;

improving insulin resistance by weight loss, exercise, or pharmacotherapy; and using hepatoprotective agents such as antioxidants to protect the liver from secondary insults. Unfortunately, no essential and specialized drugs have been developed yet to treat NAFLD; also, available drugs fail to remove all the symptoms. Unfortunately, during treatment, the side effects due to fatty liver drugs may prevent keeping to the optimal efficacy of these drugs.^[10,11]

Historically, orlistat, sibutramine, metformin, pioglitazone, vitamin E, ursodeoxycholic acid (UDCA), betaine, probucol, pentoxifylline, losartan, vitamin E + C, pravastatin, Omega-3 fatty acids, clofibrate, and gemfibrozil have been used in the treatment of NAFLD.^[10]

Hyperlipidemia, obesity, diabetes, and hypertension can aggravate the disease. Obesity (waist circumference >94 cm for men, >80 cm for women), glucose intolerance (fasting glucose >6.10 mmol/l), hypertriglyceridemia (1.70 mmol/l), low HDL cholesterol (<1.30 mmol/l in women, 1.03 mmol/l in men), and hypertension (>135/80 mm Hg) are associated with cardiovascular morbidity and mortality. These features are commonly present in subjects with NAFLD, with 67%–71% obesity, 12%–37% having impaired fasting glycemia, 57%–68% having disturbed lipid profiles, and 36%–70% being hypertensive. Therefore, patients with newly diagnosed NAFLD should be screened for mentioned conditions and appropriate treatment instituted in an effort to ameliorate the vascular risk and to recover NAFLD.

However, NAFLD at early stages has no severe manifestations and mostly is diagnosed incidentally by radiological findings. This disease may become associated with severe hepatic damage finally. Therefore, prevention contributes greatly, reducing the incidence of NAFLD and considered even more important than treatment.

In recent years, research on natural products and their derivatives has had a certain ferment. The use of plants as therapeutic agents has very ancient origins and still holds considerable interest today. Some valid alternatives to the treatment of NAFLD and its progression into NASH can be exemplified by using specific chemical compounds naturally produced by some plants.^[10]

Medicinal plants have been prescribed since long ago to prevent and treat various diseases including liver complications.^[12] In traditional medicine, a great emphasis was placed on prevention of NAFLD. Hence, many herbal drugs have been recommended for it. Public acceptance of medical plants and their efficacy on the one hand and use of plants and fruits in diets on the other hand have caused people to welcome the use of plants to treat NAFLD and other diseases.^[13,14]

The aim of this study was to introduce the medicinal plants effective on NAFLD and the potential risk factors of this disease (hypolipidemia, obesity, diabetes type 2, and hypertension) also to present the mechanisms of herbal medicines on these conditions.

METHODS

In this study, 7623 articles [723 Review (R), 3754 full texts (FT), and 3146 article abstracts (A)] were studied. The international research databases including MEDLINE, Google scholar, Web of Science, SCOPUS, EBSCO, Academic Search, Cochrane, Central Register of Controlled Trials (CENTRAL), Pubmed, and a Chinese database [China Network Knowledge Infrastructure (CNKI)] up to August 2016 were searched. To identify herbs used to treat fatty liver and especially NAFLD, the keywords match the MESH: “phytomedicines in fatty liver”, “herbals in steatosis”, “medicinal plants in NAFLD”, “Medicinal plants in steatosis”, “herbal therapy in fatty liver”, and “herbal therapy in NAFLD” were used. Then, according to the most important risk factors for fatty liver (hypertension, hyperlipidemia, obesity, diabetes, and inflammation), we used the key words such as “Botany in hyperlipidemia”, “Herbal in hyper-cholestrolemia”, “Herbal therapy in hypertriglyceridemia”, “Systematic review of herbal in hyperlipidemia”, and “Natural remedies for hyperlipidemia”.

“Herbal medicine for cholestrolemia”, “Herbal with antilipid effect”, and “Hypolipidemic diet” were used. In addition, for more information on hypotensive plants, main keywords such as “Herbal as diuretics”, “Herbal therapy for edema”, “Herbal medicine as diuretics”, “Herbal diuretic list”, “Herbal diuretic review”, “Herbal tea as diuretic”, “Herbal in hypertension”, “Phytomedicine in hypertension”,

“Herbal therapy in hypertension”, “Botany in hypertension”, “Medicinal plants in hypertension”, “Chinese herbals in hypertension”, “Review of herbals in hypertension”, and “Ayurvedic herbal in hypertension” were studied. To identify medicinal plants affecting obesity, the key words “Botany in obesity”, “Herbal in obesity”, “Herbal therapy in obesity”, “systematic review of herbal in obesity”, “Natural remedies for obesity”, “Herbal medicine for obesity”, “Herbal with anti-obesity effect”, and “herbal in weight gain” were used, and to identify the medicinal plants influencing diabetes, the key words “Phytomedicine in diabetes”, “Herbal therapy in diabetes”, “Botany in diabetes”, “Medicinal plants in hyperglycemia”, “Chinese herbals in diabetes”, “Review of herbals in diabetes”, and “Ayurvedic herbals in diabetes” were used. To understand the effects of herbals on hepatic inflammation, key words such as “Herbal therapy in liver inflammation” were used. Then, the plants that were mentioned more than twice in the articles were selected and the check list (1) that included scientific name, common name, family, and part of plants used was chosen. Then, 1100 review articles, containing possible mechanisms of herbals with the titles “name of herb + lipid mechanisms”, “name of herb + diabetes mechanisms”, “name of herb + hypotension mechanisms”, “name of herb + obesity mechanisms”, “name of herb + NAFLD mechanisms”, and “name of herb + fatty liver mechanisms”, were investigated [Chart 1] and recorded in check list 2. Then, check lists 1 and 2 were merged and Table 1 was prepared.

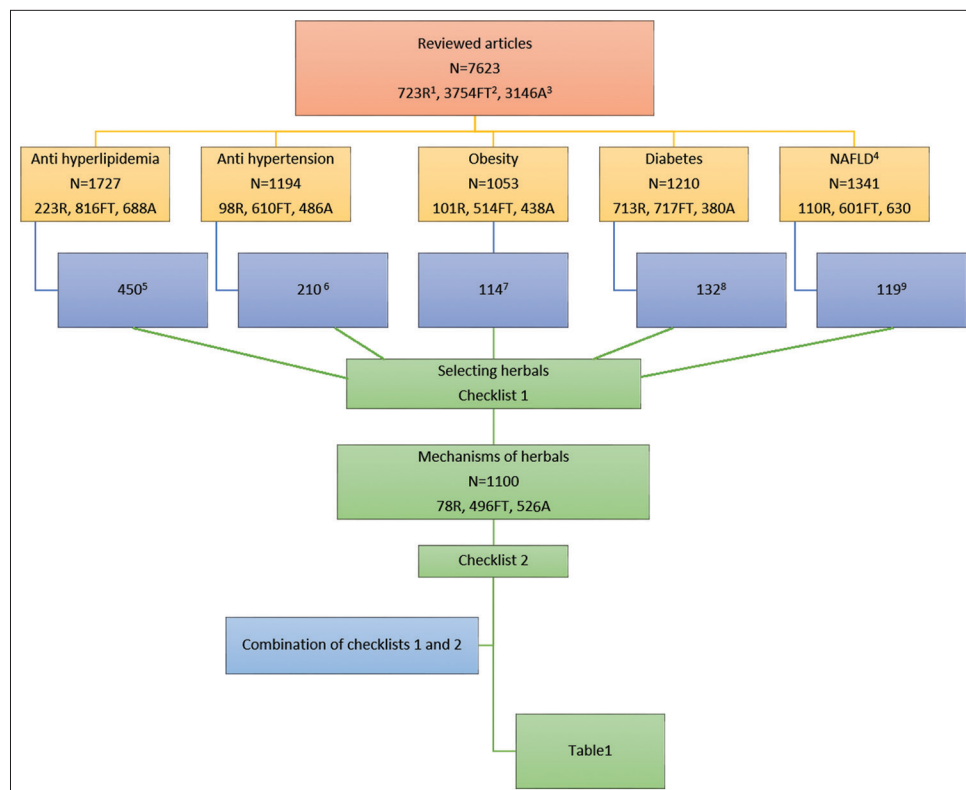


Chart 1: Design study based on the number of articles, plant disease risk factors, and potential mechanisms

Table 1: Possible mechanisms of plant effects on NAFLD and its risk factors

Scientific name	Common name	Family	Part used	Mechanisms of hypolipidemic effects
<i>Achillea millefolium</i> ^[15-17]	Yarrow	Asteraceae	Leaf	↓ HDL, ↓TG, ↓LDL – C
<i>Aesculus turbinata</i> ^[18-20]	Japanese horse-chestnut	Sapindales	Fruit, Seed	↑HDL, ↓TG,
<i>Allium cepa</i> ^[21-23]	Onion	Liliaceae	Leaf, Bulb	↑HDL, ↓TG, ↓LDL – C
<i>Allium sativum</i> ^[24-27]	Garlic	Liliaceae	Leaf, Bulb	↑HDL, ↓TG, ↓LDL activity of LCAT
<i>Aloe vera</i> ^[28-30]	Cap aloe	Liliaceae	Leaf	↓ TG, LDL, VLDL and HDL
<i>Anethum graveolens</i> ^[31-34]	Dill	Apiaceae	Leaf, Seed	↓ TG, LDL, ↓HDL, Inhibition of the activity of HMG-CoA reductase.
<i>Apium graveolens</i> ^[35-38]	Celery	Umbellifera	Leaf	↓ TC, TG, LDL-C, VLDL-C. HMG CoA reductase (HMGCR) was significantly repressed by flavone luteolin-7-glucoside.
<i>Arctium loppa</i> ^[39-41]	Burdock	Compositae	Root	↓ TC, TG, LDL-C, VLDL-C and ↑HDL
<i>Asparagus officinalis</i> ^[42-44]	Gorden Asparagus	Asparagaceae	Root	
<i>Avena sativa</i> ^[45-47]	Oats	Germinaceae	Fruit	Impaired dietary triglyceride absorption from the small intestine, ↑ clearance of chylomicron particles and chylomicron remnant uptake, ↓ liver very-low-density lipoprotein (VLDL-C) secretion, or ↑d VLDL-C catabolic rate
<i>Berberis vulgaris</i> ^[48-50]	Barbery	Berberidaceae	Root and fruit.	Regulators of hepatic cholesterol levels and activate genes involved in the synthesis of cholesterol and free fatty acids.
<i>Boswellia carteri</i> ^[51-53]	Indian tree	Burceraceae	Resin	↑ Blood HDL levels as well as a remarkable ↓ in cholesterol, LDL, fructosamine. ↓TG
<i>Cassia absus L.</i> ^[54]	Chaksu	Caesalpinaceae	Seed	↓ TG, LDL-C. ↑HDL. ↑3-hydroxy-3-methyl glutaryl coenzyme A reductase Inhibitors (HMGCR).
<i>Chicorium intybus</i> ^[55-57]	Chicory	Compositae	Root	↓ TG, LDL and ↑ HDL
<i>Cinnamomum verum</i> ^[58-60]	Cinnamon	Lauraceae	Bark	↓ LDL and ↑ HDL Cholesterol.
<i>Citrus aurantium</i> ^[61]	Bitter orange	Rutaceae	Fruit	↓ Total lipid, total cholesterol, triglycerides, low density lipoprotein cholesterol.
<i>Citrus limon</i> ^[62]	Lemon	Rutaceae	Fruit	↑ Insulin resistant sensitivity. Inhibition of hepatic gluconeogenic phosphoenol pyruvate carboxykinase mRNA expression.
<i>Cornus mas</i> ^[63,64]	Cran berry	Cornaceae	Fruit	Ameliorating-induced hypertriglyceridemia, ↓ TG, LDL – C and ↑ HDL
<i>Crataegus microphylla C. Koch</i> ^[65,66]	Howthorn	Rosaceae	Leaf-Fruit	Depress hepatic cholesterol synthesis by upregulating hepatic LDL-receptors resulting in greater influx of plasma cholesterol into the liver. ↓ triacylglycerol synthesis
<i>Curcubita pepo</i> ^[67-69]	Pumpkinseed	Curcubitaceae	Fruit	Prevented elevated activity of serum alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT) and creatine phosphokinase (CPK). ↓ LDL, VLDL, TG and ↓HDL.
<i>Curcuma longa</i> ^[70-73]	Turmeric	Zingiberaceae	Rizome	↓ Total lipid, total cholesterol, triglycerides, low density lipoprotein cholesterol.
<i>Ferula assa-foetida</i> ^[74,75]	Asafetida	Umbelliferae	Gum	↓ Serum cholesterol levels.
<i>Ficus carica</i> ^[76,77]	Fig	Moraceae	Leaf and fruit	(Leaf) ↓TG and IL-6 levels and ↑HDL
<i>Ginco biloba</i> ^[78-80]	Ginkgo	Ginkgoaceae	Leaf	↓ LDL, VLDL, TG AND ↑ HDL. ↑Activities of lipoprotein lipase and hepatic lipase and excretion of fecal bile acid in rats.
<i>Glycine soja</i> ^[81-83]	Soy	Legomuminosae	Seed	↓ Absorption of TC intestines, ↑ in bile acid production and excretion via the feces as investigated in rabbits and rats. ↑ Activity of (HMG CoA) reductase inhibitors. Inhibit the relocation and proliferation of smooth muscle cells, thus contributing a lot towards the control of atherosclerosis.
<i>Glycyrrhiza glabra</i> ^[84,85]	Licorice	Leguminosae	Root	↓ LDL, VLDL and TG

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Table 1: Contd...

Scientific name	Common name	Family	Part used	Mechanisms of hypolipidemic effects
<i>Gymnema sylvestre</i> ^[86-88]	Gymnema	Asclepiadaceae	Leaf	↓ TC and LDL – C ↓ Blood lecithin-cholesterol acyltransferase (LCAT) activity.
<i>Hibiscus sabdariffa</i> ^[89-91]	Hibiscus	Malvaceae	Flower	Inhibit LDL oxidation, foam cell formation, as well as smooth muscle cell migration and proliferation. ↓ LDL, VLDL
<i>Nigella sativa</i> ^[92,93]	Black cumin	Ranunculaceae	Seed	Depressant action on heart. Vasorelaxation. Calcium channel blockers.
<i>Ocimum basilicom</i> ^[94-96]	Basil	Labiatae	Leaf	↓ Serum total cholesterol, triglyceride, phospholipid and LDL-cholesterol levels ↑ HDL and total fecal sterol contents.
<i>Petroselinum crispum</i> ^[97-99]	Parsely	Umbelliferae	Leaf	↓ Plasma lipid concentrations ↓ TC, ↓ LDL ↓ HDL.
<i>Pronus avium</i> ^[100-102]	Cherry	Rosaceae	Fruit, Cherry tails	Inhibit copper triggered low density lipoproteins (LDL) oxidation, increased plasma lipophilic antioxidant capacity.
<i>Punica granatum</i> ^[103-105]	Pomegranate	Punicaceae	Fruit, Leaf	Total serum cholesterol (TC), triglycerides (TG), serum low density lipoprotein cholesterol (LDL-c), VLDL-C (very low-density lipoprotein cholesterol) and tissue LPO (lipid peroxidation) level.
<i>Solanum lycopersicum</i> ^[68,106-108]	Tomato	Solanaceae	Fruit	Inhibition of lipid digestion and absorption. Inhibitory effect during adipogenesis. ↓ LDL, VLDL, TG and ↑ HDL. ↓ DNA damage in lymphocytes subjected to oxidative stress.
<i>Tea sinensis</i> ^[109-111]	Tea, Green tea	Theaceae	Leaf	Total cholesterol, LDL, and triglycerides serum concentrations
<i>Taraxacum officinale</i> ^[112-114]	Dandelion	Compositae	Root, Leaf	Inhibitory effect during adipogenesis. decreased lipid droplet accumulation
<i>Terminalia chebula</i> ^[115-117]	Haritali	Combretaceae	Fruit	Reduction in total cholesterol, triglycerides, total protein and elevation of high density lipoprotein cholesterol
<i>Theobroma cacao</i> ^[118-121]	Cacao	Sterculiaceae	Fruit	↓ Plasma levels of LDL and oxidized LDL. ↑ HDL serum concentrations.
<i>Thymus vulgaris</i> ^[122-124]	Thyme	Labiatae	Leaf	↓ TG, TC, LDLc and VLDL-c, ↓ Proportional and absolute liver weight and proportional abdominal fat weight.
<i>Trigonella foenum</i> ^[125-127]	Fenugreek	Leguminosae	Seed	↓ Serum total cholesterol, LDL, VLDL TG and ↑ HDL levels. ↓ Triacylglycerols, phospholipids, and free fatty acids. Activating lecithin-cholesterol acyltransferase, postheparin lipolytic , triglyceride lipase, lipoprotein lipase and ↑ excretion of fecal bile acids
<i>Urtica dioica</i> ^[125,128-130]	Nettle	Urticaceae	Root, Leaf	↓ Total and LDL cholesterol, plasma Apo B, and the LDL/HDL.
<i>Vaccinium myrtillus</i> ^[131-133]	Bilberry	Ericaceae	Fruit, Leaf	↓ TG. Prolongation of the lag-phase of conjugated diene Production. Reduction in the formation of lipoperoxides. Inhibition of modification in the net negative charge of LDL.
<i>Vitis vinifera</i> ^[134,135]	Grape	Vitaceae	Fruit, Leaf, Seed	Inhibition of lipid digestion and absorption. Inhibit xanthine oxidase activity, glycosidases hyaluronidase and beta-glucuronidase.
<i>Zingiber officinalis</i> ^[136-138]	Ginger	Zingiberaceae	Root	↓ Cholesterol biosynthesis and in enhanced hepatic uptake of circulating LDL cholesterol. Development of infarct size and it's microscopically grade and also can ↓ serum level of cholesterol in animal models.
Scientific name	Mechanisms of hypotensive effects	Mechanisms of antiobesity effects	Mechanisms of antidiabetic effects	Mechanisms of antidiagonalcoholic fatty liver
<i>Achillea millefolium</i> ^[15-17]	↓ Systolic and diastolic BP, Diuretic effects	↓ Fatty absorption in GI, ↓ TG in liver	↓ FBS, ↑ Insulin-resistant	↓ SOD, ↓ ALT, ↓ AST
<i>Aesculus turbinata</i> ^[18-20]		↓ BMI and Abdominal fatty due polymeric proanthocyanidins from seed	↓ FBS, ↑ Insulin-resistant	↓ ALT, AST

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Table 1: Contd...

Scientific name	Mechanisms of hypotensive effects	Mechanisms of antiobesity effects	Mechanisms of antidiabetic effects	Mechanisms of antidiabetic fatty liver
<i>Allium cepa</i> ^[21-23]	↓ Systolic and diastolic BP, diuretic effects ↑ nitrate/nitrite (products of nitric oxide (NO)) excreted in urine and the NO synthase (NOS) activity in the kidneys in SHRSP.	↓ Body weight and level of epididymal fat tissue. ↓ Total cholesterol, glucose and leptin.	↓ blood glucose levels due to producing active nitrogen compounds	Preventive effect on liver cells damages by reducing number of apoptotic cells in Liver, ↑ SOD, ↓ ALT, ↓ AST. ↓ Cytokines TNF- α and IL-6 via regulating the expressions of Sirt1, NF- κ B p65 and iNOS.
<i>Allium sativum</i> ^[24-27]	Stimulated the production of the vascular gasotransmitter (H ₂ S), ↑ the regulation of endothelial (NO), vasodilation, and BP reduction.	↑ SOD and Catalase ↓ Lipid peroxidation	Allicin decreases glucose reuptake, ↑ Insulin resistance sensitivity	↓ Body weight, white adipose tissue deposits. ↓ Hepatic lipid accumulation through AMPK pathway.
<i>Aloe vera</i> ^[28-30]		↓ Glucose absorption, mild laxative, ↑ anti-inflammatory cytokines in the white adipose tissue and liver	Modulate glucose transporter-4 mRNA expression.	↓ Obesity-induced inflammatory responses by ↓ levels of the proinflammatory cytokines, PPAR γ /liver X receptor α , and 11 β -hydroxysteroid dehydrogenase 1, and ↑ anti-inflammatory cytokines in white adipose tissue and liver.
<i>Anethum graveolens</i> ^[31-34]	ACE Inhibitor, mild diuretic	↓ Glucose uptake, ↓ Fatty accumulation in abdomen.	↓ FBS, ↑ Insulin Sensitivity	↑ Hepatic SOD, CAT and GSH, ↓ ALT and AST
<i>Apium graveolens</i> ^[35-38]	ACE Inhibitor, moderate diuretic. ↓ BP and ↑ the HR in hypertensive rats,	↓ Body weight gain and feed intake, prevent the accumulation of white adipose tissue.	↓ FBS	↓ Levels of serum AST and ALT and serum total protein and albumin. Upregulation of AMPK signaling in adipocytes (3T3-L1 cells). Downregulation of HSL and lipolysis in adipocytes (3T3-L1 cells). Upregulation of CPT-1 (HepG2 cells) AMPK-dependent ACC phosphorylation (HepG2 cells).
<i>Arctium loppa</i> ^[39-41]	Suppressed upregulation of intercellular adhesion molecule (ICAM)-1, vascular cell adhesion molecule (VCAM)-1, and E-selectin in the aorta. Chronic treatment with EAL also suppressed increases in matrix metalloproteinase (MMP) - 2 expression.	Activation of AMP-activated protein kinase in human HepG2 cells. Pancreatic Lipase Inhibitors. Inhibition of Fat Absorption	↓ FBS	↓ NO, SOD, GSH, NADPH and GSH- x, ALT and AST. reduced lipid accumulation on hepatocytes in the presence of pathophysiologically relevant concentrations of palmitic acid and oleic acid in a dose-dependent manner. repressed the FFA-induced mRNA expression of SREBF1c, leading to reduced expression of FAS and lipid synthesis
<i>Asparagus officinalis</i> ^[42-44]		↓ Alanine transaminase, aspartate transaminase and alkaline phosphatase in serum. ↓ MDA, ↑ SOD.		Potent cytoprotective properties, including a strong, wide range of antioxidant activities in HepG2 cells. Promoted activities of ADH and ALDH in the enzymatic assay using liver cell homogenate as an enzymatic source.

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Table 1: Contd...

Scientific name	Mechanisms of hypotensive effects	Mechanisms of antiobesity effects	Mechanisms of antidiabetic effects	Mechanisms of antidiabetic fatty liver
<i>Avena sativa</i> ^[45-47]	Improve endothelial function, Vasodilation	Rapidly convert to gel forming, delays stomach emptying making you feel full longer which helps with weight loss.	↑ FBS	↑ ALT, AST. ↑ SOD and CAT
<i>Berberis vulgaris</i> ^[48-50]	↓ Systolic arterial blood pressure and heart rate. Sympatolytic effects.	Mediating Insulin Resistance.	Stimulate insulin secretion in HIT-T15 cells and pancreatic islets.	Inhibit cholesterol and triglyceride synthesis in human hepatoma cell line (HepG2) cells and primary hepatocytes, ↓ ALT, AST.
<i>Boswellia carteri</i> ^[51-53]			↓ the level of blood glucose and HbA1c after 17 th days.	↑ Insulin sensitivity and ↓ in liver index, activities of liver enzymes, serum TNF- α and IL-6 as well as hepatic iNOS expression. ↓ AST and ALT.
<i>Cassia absus L.</i> ^[54]	Anthraquinone glycoside inhibited activity against ACE	↓ Glucose reuptake, MDA and ↓ weight. ↑ SOD, ↓ abdominal fatty.	Emodin and obtusifolin in <i>Cassia tora L</i> ↓ FBS.	Up-regulating CYP7A1, LDL-R, FXR mRNA and PPAR- α protein produced in the process of fat metabolism
<i>Chicorium intybus</i> ^[55-57]	Diuretic effect, ↓ systolic blood pressure (SBP)	Inhibition of protein tyrosine phosphatase 1B and regulation of insulin signaling markers. ↓ BMI	↓ Blood glucose levels without inducing adipogenesis in 3T3-L1 adipocytes.	↓ AST, ALT and modulation of PPAR α and SREBP-1. Protected hepatocytes from injury and inflammation to aid its lipid-lowering properties.
<i>Cinnamomum verum</i> ^[58-60]	A vasorelaxant effect on the rat thoracic aortic ring segments, and Inhibiting extracellular Ca ²⁺ through L-type voltage-sensitive channels. Potent inhibitor of VEGFR2 kinase.	post-prandial intestinal glucose absorption by inhibiting the activity of enzymes involved in carbohydrate metabolism (pancreatic α -amylase and α -glucosidase)	↓ Fasting blood glucose, stimulated cellular glucose uptake by membrane translocation of GLUT-4, stimulating glucose metabolism and glycogen synthesis. ↓ HbA1c and ↑ circulating insulin levels	Inhibiting gluconeogenesis by effects on key regulatory enzymes and stimulating insulin release and potentiating insulin receptor activity. ↓ ALT, AST and ↑ SOD, CAT, High-sensitivity C-reactive protein.
<i>Citrus aurantium</i> ^[61]	↑ HR, ↑ BP	Increase in basal metabolic rate, lost a significant amount of weight. ↑ RMR, ↑ Kcal use	↓ FBS	↓ Liver enzymes (ALT, AST and alkaline phosphatase),
<i>Citrus limon</i> ^[62]	↑ NO ↑ Vasodilation and Diuretic effects	↑ superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), and glutathione <i>S</i> -transferase (GST)] in the liver Up-Regulation of mRNA Levels of the Enzymes Involved in β -Oxidation in Mouse White Adipose Tissue	↓ glucose uptake Food, ↓ FBS	Inhibited apoB100 secretion by activating Signaling cascades in HepG2 cells. ↓ AST, ALT ↓ The hepatic TG accumulation induced by OA, ↓ activity of TG synthetic enzyme, PAP.
<i>Cornus mas</i> ^[63,64]	Diuretic effects, reduced carotid femoral pulse wave velocity	↓ Weight gain and reduced visceral adiposity. protects from diet-induced obesity	Improved insulin sensitivity. ↓ HbA1c and ↑ circulating insulin levels	Lowering hepatic TG accumulation. ↑ T-Protein, ↓ ALT, AST and ALP
<i>Crataegus microphylla C. Koch</i> ^[65,66]	ACE Inhibitor, ↑ NO levels in epithelial cell, functional NO-synthase. Decrease in heart rate (HR) and mean arterial pressure (MAP)	↓ Body weight, epididymal adipose tissue. Stimulated glycerol release and liver weights.	↑ Hepatic protein contents of AMP-activated protein kinase (AMPK) phosphorylation. ↓ Expression of phosphoenol pyruvate carboxykinase (PEPCK) and glucose production.	↓ ALT, AST and ALP

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Table 1: Contd...

Scientific name	Mechanisms of hypotensive effects	Mechanisms of antiobesity effects	Mechanisms of antidiabetic effects	Mechanisms of antidiabetic fatty liver
<i>Curcubita pepo</i> ^[67-69]	↓ NO, vasodilator effects.	↓ Weight gain, Pancreatic Lipase Inhibitors.	Amelioration of glycemia, insulinemia, and lipid dysmetabolism.	↓ LD, ALT, AST and ALP.
<i>Curcuma longa</i> ^[70-73]			↓ The levels of glucose, hemoglobin (Hb), and glycosylated hemoglobin (HbA1C) in blood and improve insulin sensitivity od.	Inhibition of HSC activation, reduced lipogenesis, and improved insulin sensitivity. suppressed macrophage infiltration in liver tissue with lowered NF-B, SOCS3, MCP- 1, and TNF- in HFD-fed mice and leptin-deficient (ob/ob) mice
<i>Ferula assa-foetida</i> ^[74,75]	↓ Arterial blood pressure, ACE Inhibitor, Vasodilation effects.		↓ FBS, Improved insulin sensitivity.	
<i>Ficus carica</i> ^[76,77]	Vasodilation effect, peripheral, autonomic α -adrenoceptor blockade. Activation and/or stimulation of nitric oxide synthase.	(Leaf) Pancreatic Lipase Inhibitors. Inhibition of Fat Absorption	↓ HbA1c (Leaf) ↓ FBS, Improved insulin sensitivity. ↓HbA1c	↓Alanine (ALT), (AST), (ALP), (LDH) activities, inhibiting lipid peroxidation and increasing antioxidant enzyme activities.
<i>Ginco biloba</i> ^[78-80]	↑ ACE I, Mild diuretic effects.	↑ Adipo R1 and IL-10 gene expressions and IR and Akt phosphorylation. ↓NF- κ B p65 phosphorylation and TNF- α levels	Regulation effect on blood sugar and insulin resistance. ↓FBS.	Flavonoid ingredients (quercetin, kaempferol, and isorhamnetin) could lessen the lipid accumulation associated with upregulation of the rate-limiting enzyme, carnitine palmitoyl transferase 1A (CPT1A), in the β -oxidation of long-chain fatty acids.
<i>Glycine soja</i> ^[81-83]	ACE inhibitory activity.	Genistein present in the soybean has the ability to reduce the size of the fat pads which cause obesity.	↓The ratio of insulin and glucagons. Stimulate the lipogenesis. Inhibitor α -glucosidases activity. Suppressions of hepatic endoplasmic reticulum stress	Modulating lipid metabolism and regulating the expression of related transcription factors. Soy intake decreases the expression of sterol regulatory-element binding protein-1c (SREBP-1) and increases the expression of SREBP-2,
<i>Glycyrrhiza glabra</i> ^[84,85]		↓ Weight		Improve lipoprotein lipase expression, insulin sensitivity, and serum lipid levels. ↓ ALT, AST Improvement of fatty degeneration of hepatocytes and changes in genes implicating regulation of lipid metabolism with 2% concentration
<i>Gymnema sylvestre</i> ^[86-88]		hydroxycitric acid (HCA-SX) decreased the amount of food intake efficiently. ↑ Excreted neutral and acid sterols in feces, ↓ Body weight	↓ blood glucose levels, ↓ glucose uptake, ↑ Serum Insulin, C-peptide, ↓ Perirenal, mesenteric and epididymal fat mass, ↓ Serum leptin, insulin, glucose, LDH, apo-B, ↑ reproinsulin expression and insulin secretion	↑ Gpx, GR, GST, SOD, catalase, ↓ ALT and AST. ↑Protein kinase activity

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Table 1: Contd...

Scientific name	Mechanisms of hypotensive effects	Mechanisms of antiobesity effects	Mechanisms of antidiabetic effects	Mechanisms of antidiabetic fatty liver
<i>Hibiscus sabdariffa</i> ^[89-91]	Vasodilator mediated through the endothelium-derived nitric oxide-cGMP-relaxant pathway and inhibition of calcium (Ca ²⁺)-influx into vascular smooth muscle cells	↓Body weight↓BMI, ↓serum NEFA, ↓Appetite	↓ FBS, ↑ SOD, GSH, CAT and ↓ MDA	↓TAG, ↓Steatosis↓Adipocyte size in adipose tissue↓Insulin resistance↓Liver steatosis ↓ALT and AST↓Albumin.
<i>Nigella sativa</i> ^[92,93]	Reduction in cardiac lipid peroxidation product, NADPH oxidase, angiotensin-converting enzyme activity and plasma nitric oxide. ↑ In heme oxygenase-1 activity in the heart improve HbA1c	↓Appetit	↓ FBS. Protection of β -cells against oxidative stress. Decreasing morphological changes and preserving pancreatic β -cell integrity. ↓ Glucose and HbA (1C) levels. ↑ Insulin sensitivity.	Inhibit inflammatory cytokines such as interleukin-1 and 6 and the transcription factor, nuclear factor κ B. Protects hepatic tissue from deleterious effects of toxic metals. Protects the rat liver against hepatic ischemia reperfusion injury. ↑ ALT, AST. ↑ SOD.
<i>Ocimum basilicom</i> ^[94-96]	Inhibited renovascular hypertension-induced hypertrophy of heart and increase in ET-1 and Ang II levels. vasorelaxant effect in rat aortic rings,		↓ Blood glucose level.	↓ Serum total cholesterol, triglyceride, phospholipid and LDL-cholesterol levels ↑HDL and total faecal sterol contents.
<i>Petroselinum crispum</i> ^[97-99]	Mild diuretic and ↓ ACE activity.	Decrease in body weight gain.	Decrease blood glucose.	↓ ALT, AST and ↑ SOD, GSH. provide blood glucose homeostasis
<i>Pronus avium</i> ^[100-102]	Stalk: mild diuretics. Urinary sodium and chloride rising less than loop diuretics but higher than the others. ↑ Mild urine volume.	Inhibit nitric oxide (NO) production and other pro-inflammatory factors such tumor necrosis factor-alpha (TNF- α) in activated macrophages. ↓ The levels of proinflammatory molecules in plasma (interleukin-6, TNF- α) and the activity nuclear factor kappa and ↑ peroxisome proliferator-activated receptors (PPARs) in abdominal fat and in hepatic tissues. ↓ Of levels of serum glucose, triglycerides and cholesterol.	↓ Blood glucose and urinary microalbumin.	↓ enzymes SOD (liver, blood) and Gpx (liver) and a decrease of lipid peroxidation, ↓ALT and AST
<i>Punica granatum</i> ^[103-105]	↓Angiotensin-II activity.	↓ Body weight. ↓ Energy intake.↓ Various adipose pad weight. Activating hepatic expression of genes responsible for fatty acid oxidation. Inhibition of the pancreatic lipase activity, suppressing energy intake by appetite suppressant.	↓Blood sugar level and ↑number of β cells. ↑ Stimulation and activation of insulin receptor ↓fasting blood glucose. ↑Peripheral glucose utilization or retardation of intestinal glucose absorption. ↓ Aldose reductase, α -amylase, and protein tyrosine phosphatase PTP1B.	ameliorates diabetes and obesity-associated fatty liver, reducing Ratio of liver weight to tibia length, hepatic triglyceride contents and lipid droplets.

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Table 1: Contd...

Scientific name	Mechanisms of hypotensive effects	Mechanisms of antiobesity effects	Mechanisms of antidiabetic effects	Mechanisms of antidiabetic fatty liver
<i>Solanum lycopersicum</i> ^[68,106-108]	Carotenoid ↓ systolic and diastolic BP. γ -aminobutyric acid (GABA) rich tomato ↓ SBP.	Serum concentrations of C-reactive protein (CRP), tumor necrosis factor (TNF-), and interleukin (IL)-6 are significantly correlated with weight, body mass index (BMI), and waist circumference C3G (cyanidin 3-glucoside) was reported to upregulate the expression of adiponectin that can increase insulin sensitivity at the level of human adipocytes controlling obesity.	↓ FBS. ↑ Insulin sensitivity.	Inhibitory activity on the expression of TNF- α and IL-1 β cytokine. Prevention of liver steatosis. reduce the expression of TNF- α and IL-1 β in LPS-activated macrophages
<i>Tea sinensis</i> ^[109-111]	↓ systolic and diastolic BP.	Inhibition of pancreatic lipase. ↓Hormone-sensitive lipase and perilipin in mesenteric adipose tissue. Reduced body weight. ↓ Peptide repression activity. ↓adipogenesis downregulation thermogenesis.	Reductions in fasting serum glucose and insulin levels and insulin resistance	Attenuates fat liver through decreased lipogenesis and improved Hepatic oxidative stress conditions. Lowers liver enzymes. Decreased SREBP1c.
<i>Taraxacum officinale</i> ^[112-114]	Diuretic effects	Inhibitory actions on porcine pancreatic lipase. reduce fat absorption,	an insulin secretagogue effect (i.e., stimulating pancreatic beta-cell release of insulin)	Increase AMP protein kinase (AMPK) signaling. ↓cytokines IL-6 and TNF- α
<i>Terminalia chebula</i> ^[115-117]	✓	↓ Cholesterol absorption and cholesterol excretion. Enhanced lecithin: Cholesterol acyl transferase activity, lower TG and TC.	Insulin like action of its constituents and promotion of insulin release.	↓ALT, AST, ALP, bilirubin, and β^2 microglobulin.
<i>Theobroma cacao</i> ^[118-121]	Inhibit angiotensin-converting enzyme (ACE). ↑ eNOS activity. ↓ Vascular arginase activity in human endothelial cells. Peripheral vasodilatation. Increase in levels of nitrosated and nitrosylated species	↓The expression of Sterol Regulatory Element-Binding Proteins (SREBP)-1 and Fatty Acid Synthase (FAS), and by increasing Acetyl-CoA Carboxylase (ACC) phosphorylation. ↓ BMI.	↑Insulin sensitivity.	Improved hepatic β -Ox, activated PPAR α -signaling and up-regulated both gene and protein expression of SOD. Improved the lipid-metabolizing activity and oxidative stress.
<i>Thymus vulgaris</i> ^[122-124]	↓Systolic and diastolic blood pressure and total peripheral resistance in Spontaneously hypertensive rat.	Reduced production and gene expression of the pro-inflammatory mediators TNF- α , IL-1 β , and IL-6 and highly increased these parameters on the anti-inflammatory IL-10 cytokine.	Inhibit the formation of advanced glycation end products. ↓ FBS.	Reduced production and gene expression of the proinflammatory mediators TNF- α , IL-1 β , and IL-6 and highly increased these parameters on the anti-inflammatory IL-10 cytokine.
<i>Trigonella foenum</i> ^[125-127]	✓	↓Hepatic triglyceride level. ↓ Liver-weight. ↓Both the soluble and bound forms of TNF- α protein. ↓ Postprandial plasma glucose (PPG). ↑ Satiety. ↑ Serum C-peptide levels.	Inhibit α -amylase activity. Galactomannan rich soluble fiber fraction, saponin, and an amino acid called 4-hydroxyleucine that ↑ insulin sensitivity. Inhibition of glucose uptake. Direct pancreatic β -cell stimulation, delayed gastric emptying, and inhibition of glucose transport.	↓ mRNA expression levels of inflammatory genes. Inhibited IL-1 and IL-6 along with TNF- α . ↓ In serum enzymes, liver TGs, LPO, expression of liver ER stress marker proteins, and ↑ liver glycogen content and antioxidants. ↓ ALT, AST, GGT and ↑ SOD, GSH and Catalase.

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Table 1: Contd...

Scientific name	Mechanisms of hypotensive effects	Mechanisms of antiobesity effects	Mechanisms of antidiabetic effects	Mechanisms of antidiabetic fatty liver
<i>Solanum lycopersicum</i> ^[68,106-108]	Diuretic effects. Natriuretic effects. Negative inotropic activity and vasodilatory effects.	Improve glucose homeostasis. ↓ Fasting plasma glucose. ↓ Ceramide accumulation and PP2A activity in skeletal muscle. ↑ skeletal muscle insulin sensitivity ↓ PP2A (protein phosphatase 2A activity) through posttranslational modification.	↓ Glucose absorption in the small intestine. ↓ Malonyl-CoA Decarboxylase.	↑ Insulin sensitivity. ↓ Hepatic necrosis. ↓ Inflammation and improve metabolic symptoms. ↓ ALT, AST, GGT and Hepatic peroxidation. ↑ SOD, Catalase and GSH.
<i>Vaccinium myrtillus</i> ^[131-133]	Inhibit smooth muscle contraction and platelet aggregation. ↓ (ACE) activity	Lowering fat absorption. Regulate human adipocyte function. Activated adenosine monophosphate (AMP)-activated protein kinase (AMPK) in adipocytes without increasing the AMP/adenosine triphosphate (ATP) ratio.	↓ In serum glucose and fructosamine. ↑ Glucosidase activity	↑ Mitochondrial complex II activity, elevated sodium/potassium ATPase activity, ↑ mitochondrial membrane potential.
<i>Vitis vinifera</i> ^[134,135]	(Seed, Fruit, Leaf). Vasodilator and antioxidant actions. ↓ Systolic blood pressure.	(Seed), (Fruit). ↓ Leptin. ↓ NEFA in plasma ↓ ACAT, ↑ PPAR α , ↑ CPT gene expression. ↑ adiponectin. ↓ Fat mass. ↓ Body weight. ↑ adiponectin, ↓ NEFA in plasma	(leaf) Inhibited pancreatic lipase and cholesterol esterase. ↓ FBS.	↑ GSH, SOD, and CAT. ↓ Adiposity and hepatic steatosis. ↓ Hepatic cholesterol and TAG. ↓ ChREBP, ↓ PARG, ↓ SCD1 ↓ FAS, ↑ β -oxidation, FAS, ME activity. ↓ ALT, AST, ALP, ACP, GGT, and total bilirubin.
<i>Zingiber officinalis</i> ^[136-138]	↓ Systolic BP, diastolic BP, and the heart rate.	Inhibition of intestinal absorption of dietary fat.	Inhibition α -amylase and α -glucosidase. ↑ Insulin sensitivity. ↓ Glucose uptake.	Suppressed the gene and protein expression of hepatic inflammation markers, TNF α , and IL-6 and decreased NF- κ B activity. ↓ ROS

Arrow indicates an increase (↑) or decrease (↓) in the levels of gene expression, protein concentrations or activity. p-AMPK α , phosphorylated AMP-activated protein kinase α ; ACC, acetyl-CoA carboxylase; CPT-1, carnitine palmitoyl transferase 1; FAS, fatty acid synthase; free fatty acids (FFA) ROS, reactive oxygen species; SREBP-1c, sterol regulatory element-binding protein 1c; p-ACC, phosphorylated ACC; SIRT-1, sirtuin-1; GSH, reduced glutathione; GSSG, oxidized glutathione; TNF α , tumor necrosis factor α ; CAT, catalase; phosphatidate phosphohydrolase (PAP), RMR=resting metabolic rate; SOD, superoxide dismutase; GPx, glutathione peroxidase; ALT, alanine aminotransferase; HGMCR, 3-hydroxy-3-methylglutaryl coenzyme A reductase; GPAT, glycerol-3-phosphate acyltransferase; mtGPAT, mitochondrial GPAT; PKC, protein kinase C; p-JNK, phosphorylated, c-Jun N-terminal kinase; MDA, malondialdehyde; HFD, high-fat diet., triacylglycerol (TAG), Non esterified fatty acids (NEFA)

RESULTS

Among 7623 articles reviewed in this study, almost 43 plants were identified to be remarkably effective on NAFLD. In particular, 33 plants were realized effective on all four risk factors (hypertension, hyperlipidemia, obesity, and diabetes), eight of them effective on controlling three risk factors, and two only effective on two risk factors.

Generally, the most mechanisms in recovering hyperlipidemia were a decrease in LDL, VLDL, TG, TC, MDA, TG absorption from GI, HMG CoA reductase and an increase in HDL, chylomicron particles clearance, lipoprotein lipase, and LCAT activity.

Mechanisms that keep on by reducing obesity were a decrease of body weight and appetite, an increase in β cell function and energy expenditure as well as regulation of lipid metabolism, carbohydrate metabolism, and POP activity.

Probable mechanisms influenced by treating diabetes were decreases in FBS, blood glucose level, and glucose reuptake and also increases of insulin receptors, modulation of glucose transfer, and stimulation of insulin secretion.

In addition, diuretic effects, a decrease of systolic and diastolic BP, ACE inhibition, impression of endothelial function, and vasodilation were the possible mechanisms for hypertension.

Also, increases of TNF receptors, IL6 receptors, and TNF and decreases of IL6 and IL7 possibly arise by inhibiting inflammation.

Then, the possible mechanisms of these plants on NAFLD and its risk factors are indicated in Table 1, which help promising molecular and genetically observations in future studies.

DISCUSSION

NAFLD is a consequence of industrial urbanism concomitant with hypertension, hyperlipidemia, obesity, and inflammation, the most important of the risk factors. Although many factors have been offered to cause NAFLD, hypertriglyceridemia obviously comes on with NAFLD in all patients. The studied plants lead to lower glyceride through several mechanisms (a decrease in absorption of foods fat, fat breakdown into basic units, and an increase in insulin sensitivity).

Furthermore, despite the associations of aforesaid factors to the incidence of NAFLD, some patients may not present any of these risk factors. In addition, some patients come by NAFLD even with extreme dieting and hence having suitable BMI, significantly decreased triglyceride, and normal glycemia.

According to recent assumptions, two major factors were determined for development of fatty liver, including triglyceride invade to hepatic adipose tissue and stress oxidative invade from various sources. Moreover, stress oxidative is considered to be more effective than the first factor. To be noticed, all patients have been shown obviously low levels of plasma antioxidants.^[139]

There is stress generated by mitochondrial reactive oxygen species (ROS), cytotoxins, aflatoxins, and peripheral toxins. At the acute phase, lipid peroxidation occurs first, which is the major biomarker of hyperlipidemia. At the chronic phase, decreased SOD, catalase, and GSH are the original reasons for exacerbation of the disease.^[140]

The studied plants are rich in certain antioxidants such as polyphenols, flavonoids, flavonols, and saponins, which react easily with oxidants and neutralize free radicals through increasing SOD and catalase levels, and glutathione peroxidase helps to convert the produced OH and H to H₂O.^[12]

In addition, the plant secondary metabolites trigger lowering hepatic inflammatory biomarkers. Oxidative stress causes an increase in the secretion of proinflammatory cytokines, activation of hepatic asterisk cells, and finally fibrosis, progressive inflammation, and apoptosis.^[13]

ROS play an important role in enhancing the inflammation by activating NF- κ B and AP-1 transcription factors and nuclear histone acetylation and deacetylation in liver inflammation. The phenolic compounds in these herbs are mainly derivatives and/or isomers of flavones, isoflavones, flavonols, tocopherol catechins, and phenolic acids that modulate important cellular signaling. Moreover, they modulate NF- κ B activation, glutathione biosynthesis, chromatin structure, and nuclear

redox factor (Nrf2) activation; scavenge the effect of ROS directly or via glutathione peroxidase activity; and as a result regulate inflammatory genes in liver epithelial cells and macrophages. On the other hand, polyphenols may avert cellular disturbance in hepatocytes associated with NAFLD, followed by the various mechanisms including (a) reducing de novo lipogenesis through sterol regulatory element-binding protein 1c (SREBP-1c) downregulation, (b) increasing β -fatty acid (FA) oxidation by PPAR α upregulation, (c) improving insulin sensitivity, (d) reducing oxidative stress through increasing the antioxidant defense levels via nuclear factor-erythroid 2-related factor 2 (Nrf2), and (e) attenuating the inflammatory pathways.^[139]

Therefore, polyphenols, anthocyanins, saponins, and phytosterols not only decrease lipids, obesity, blood pressure, and glycemia but also prevent oxidative stress through their antioxidant properties. This is a marked finding on these compounds in comparison to other drugs used to treat NAFLD patients with no other risk factors.^[140]

CONCLUSION

Results of this study revealed that herbal medicine supplement combined with other therapeutic approaches might provide feasible therapeutic strategies for patients with NAFLD. Identification of the plants and their impressive mechanisms on NAFLD would cause lower incidence of this disease and produce new potent and selective herbal drugs restraining each risk factor. So, this study provides useful information for further research and development of new drugs and nonchemical products to improve the cure rate of nonalcoholic fatty liver.

Strength and limitation

The current review provides a detailed and updated description of the most widely used herbal medicine and herbal formulas in alleviating chronic liver disease. But there are some limitations such as no access to full text of some articles and non-English language of some articles.

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Conflicts of interest

There are no conflicts of interest.

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