(REVIEW ARTICLE)

Blood lipids lowering effect of medicinal plants

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Abstract

Hyperlipidemia refers to elevated levels of lipids and cholesterol in the blood. It plays an important role in the development of atherosclerosis, the main cause of death in the world. Medicinal plants can lower blood lipids by many mechanisms included inhibition of the expression of fatty acid synthase, decreasing free fatty acid release, inhibition of HMG-CoA reductase, increasing the fecal excretion of fat and cholesterol, inhibition of the activity of pancreatic lipase and inhibition of cholesterol absorption. The current review will highlight the hypolipidemic effects of medicinal plants as promising effective and safe therapies.

Keywords: Hypolipidemia; Anti-hyperlipidemic; Medicinal Plants; Herbs

1. Introduction

Hyperlipidemia refers to elevated levels of lipids and cholesterol in the blood. It plays an important role in the development of atherosclerosis, the main cause of death in the world. The formation of atherosclerotic plaque involves accumulation of LDL in intima, LDL oxidation, and uptake of oxidized LDL by macrophage scavenger receptors, influence of macrophages on foam cells, and stabilization of plaque. Inflammatory cytokines are involved in all steps and make this process a chronic inflammatory disease [1-3]. Medicinal plants have always been considered as healthy source of treatment due to its therapeutic effect and safety. Different medicinal plants remedies were used to treat hyperlipidemia, it decreased blood lipids by many mechanisms included inhibition of the expression of fatty acid synthase, decreasing free fatty acid release, inhibition of HMG-CoA reductase, increasing the fecal excretion of fat and cholesterol, inhibition of the activity of pancreatic lipase and inhibition of cholesterol absorption [4-6].The current review was designed to introduce some promising medicinal plants effective in the prevention or treatment of hyperlipidemia.

2. *Allium* species

Garlic (1–4% in diet) and garlic protein administration in hypercholesterolemic rats induced by a high-cholesterol diet, significantly reduced serum cholesterol, triglyceride and LDL cholesterol. Long term feeding of garlic and garlic preparations on experimental atherosclerosis induced by a high-cholesterol diet in rabbits cause statistically significant reduction in serum lipids and atheromatous lesions. Water soluble extract of garlic inhibited the biosynthesis of cholesterol in hepatocytes. Garlic derived components are capable of miming with the sulphydryl (-SH) group. Reduced conversion of acetate into cholesterol has been observed both *in vivo* and *in vitro.* Eating of 10 g fresh garlic per day for 2 months significantly decreases (15%-28.5%) serum cholesterol levels among hypercholesterolemic patients. Garlic oil caused a steady decrease in LDL and VLDL levels with concomitant increase in HDL levels. Intake of enteric-coated garlic powder (equal to 400 mg garlic, 1mg allicin) twice daily in hyperlipidemic patients has significantly reduced total cholesterol, LDL-cholesterol and triglyceride and increased HDL-cholesterol. The level of cholesterol, triglyceride, phospholipids and ß- lipoproteins were significantly declined in the individuals consuming 10-50 g of garlic /week.

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These results indicate that routine consumption of garlic in the diet has a beneficial effect in maintaining the serum lipids at low or normal levels. In a placebo-controlled trial of patients with stage II peripheral arterial occlusive disease, garlic powder supplements, 800 mg daily were associated with a significant increase in walking distance by 46 meters; the improvement started after the fifth week of treatment. Patients treated with 900 mg daily of standardized garlic powder showed 9-18% reduction in plaque volume, a 4% decrease in LDL levels, an 8% increase in HDL concentrations, and a 7% decrease in blood pressure [7-27].

2.1. *Aloe vera*

Aloe vera gel lowered triacylglyceride levels in liver and plasma. Histological examinations of periepididymal fat pad showed that *Aloe vera* gel reduced the average size of adipocytes [28-29].

Five thousand patients of atheromatous heart disease, presented as angina pectoris, were studied over a period of five years. After adding the (Husk of Isabgol) and*(Aloe vera*) to the diet, a marked reduction in total serum cholesterol, serum triglycerides, increased HDL, decreased fasting and postprandial blood sugar level in diabetic patients were noted. Simultaneously the clinical profile of these patients showed reduction in the frequency of anginal attacks [30].

2.2. *Alpinia galangal*

2.3. **Ethanolic extract of Alpinia galangal** 20mg/day for 4 weeks in rats exerted hypolipidemic activity, with a significant increase in the serum levels of high density lipoproteins (HDL) in rats. *Alpinia galangal* constituents exerted platelet activating factor (PAF) antagonists. Methanolic extract showed significant inhibitory effects on PAF with IC_{50} value of 5.5ug/ml in rabbit platelets [31-33].

2.4. *Ammi visnaga*

A clinical study was carried out on 20 non-obese, normolipaemic male subjects to determine the effects of orally administered 50 mg khellin four times daily for 4 weeks on the plasma lipids. Plasma total cholesterol and triglyceride remained unchanged, but high-density-lipoprotein cholesterol concentration was significantly elevated during the treatment and till one week after cessation of treatment. In a comparison with glyceryl trinitrate, khellin (3 ml. Containing 150 mg. of khellin, alcoholic extract standardized to contain 50 mg/ml) was used in twelve patients for prevention of angina of effort and the electrocardiographic changes that may accompany it. Khellin was less potent but longer acting than glyceryl trinitrate, and it did not cause any unpleasant side effects [34-35].

2.5. *Anethum graveolens*

The crude extract of *Anethum graveolens* showed anti-hyper cholesterolaemic and anti-hyperlipidaemic activities. The crude extracts of *Anethum graveolens*. besides having strong anti-hyperlipidaemic effects, it improved the biological antioxidant status by reducing lipid peroxidation in liver and modulating the activities of antioxidant enzymes in rats fed with high fat [36-37].

Treatment of hyperlipidaemic rats with defatted ethanolic *Anethum graveolens* extract (single daily dose of 1 ml, equivalent to 500 mg of the plant powder) and high-fat diet for up to 10 and/or 30 days reversed the serum lipid levels compared to rats which were fed only high-fat diet. In addition, it induced significant increase in HMG-CoA/mevalonate ratio as compared to rats which were fed high-fat diet after treatment with defatted ethanolic *Anethum graveolens* extract for 30 days [38-39].

2.6. *Apium graveolens*

Many experimental studies showed that *Apium graveolens* significant lowered serum total cholesterol, triglycerides, LDL and VLDL and increased HDL level. *Apium graveolens* also reduced the formation of arterial plaques in experimental studies. However, the mechanisms suggested for lipid lowering action of *Apium graveolens* including inhibition of hepatic cholesterol biosynthesis, increasing fecal bile acid excretion and enhancing plasma lecithin: cholesterol acyltransferase activity and reduction of lipid absorption in the intestine. Some authors mentioned that blood lipids lowering effects was attributed to the compound 3n butylphthalideor (3nB) isolated from *Apium graveolens*, but, the active extract free from 3-n-butylphthalide has been reported to have lipid-lowering action. Instead, thin layer chromatography indicated that polar compounds with sugar or amino acid side chains (s) could be the hypocholesterolaemic constituents of celery extract [40-44].

In evaluation of the protective effects of ethanolic extract of *Apium graveolens* on ritonavir (a protease inhibitor) - induced dyslipidemia. It appeared that concurrent treatment with high dose of ethanolic extract of *Apium graveolens*

(150mg/kg) in mice with ritonavir, showed significant improvement in blood lipid profile. However, using of low dose of ethanolic extract of *Apium graveolens* (75mg/kg) showed no significant effects [45-46].

2.7. *Arachis hypogaea*

The effect of water soluble polyphenolic extract of peanut skin (PE) was investigated for its hypolipidemic properties and improvement of lipid homoeostasis in rats. 300mg/kg body weight of (PE) significantly reduced body weight and epididymal fat. Plasma and liver triglyceride (TG) and cholesterol (TC) levels were also significantly reduced, and the fecal secretion of TG and TC was greatly increased upon PE administration. Liver mRNA expression of enzymes involved in fatty acid synthesis, such as fatty acid synthase (FAS), sterol receptor element binding protein (SREBP)-1c, acetyl-CoA carboxylase (ACC1) and lipid uptake genes, such as PPARγ, were decreased, while PPARα was up-regulated by administration of PE [47-48].

Feeding a high-cholesterol diet with a water-soluble peanut skin polyphenol fraction to rats reduced their plasma cholesterol level, with an increase in fecal cholesterol excretion. The hypocholesterolemic effect was greater with the lower-molecular-weight rather than higher- molecular-weight polyphenol fraction. This effect attributed to some oligomeric polyphenols which reduced the solubility of dietary cholesterol in intestinal bile acid-emulsified micelles [49].

The effects of peanut (*Arachis hypogaea*) consumption on oxidant-antioxidant status and lipid profile in Streptozotocin (STZ) induced diabetic rats were investigated. Rats were given standard rat chow supplemented with 0.63 g % peanut for 12 weeks. The supplementation with peanut in the diabetic group led to significantly higher HDL-C levels and lower atherogenic index (AI) levels compared to diabetic group. Peanut consumption increased GSH levels significantly both in control and diabetic groups [50].

Most of peanet stilbenoids inhibited intracellular generation of reactive oxygen species (ROS) in PMA inducedHL-60 cells. Three stilbenids compounds produced a strongest antioxidant effect. Twelve compounds demonstrated significantly high antioxidant properties which were comparable to those of Trolox. Although, the majority of stilbenoids demonstrated moderate cytoxicity toward HL-60 cells, but the antioxidant effect was observed at much lower concentrations which confirmed that the antioxidant effect was not related to cytotoxic effect [51-52].

2.8. *Asparagus officinalis*

The hypolipidemic effect of *n*-butanol extract from asparagus by-products was evaluated in mice fed a high-fat diet. Asparagus butanol extract significantly decreased the levels of body weight gain, serum total cholesterol and low density lipoprotein cholesterol; it dramatically increased the high density lipoprotein level when administered at three different doses (40, 80 or 160 mg/kg body weight) for 8 weeks in hyperlipidemic mice. In addition, asparagus butanol extract decreased the levels of alanine transaminase, aspartate transaminase and alkaline phosphatase in serum. Superoxide dismutase activity and the total antioxidation capacity were evidently increased; in addition, the malondialdehyde level and the distribution of lipid droplets were reduced in liver cells of asparagus butanol extract -treated mice [53-55].

2.9. *Avena sativa*

Oat β-glucan exerted cholesterol-lowering properties. The consumption of oat meal and oat bran reduced total plasma cholesterol and LDL-cholesterol levels. This effect attributed to β-glucan, it interfered with the reabsorption of bile acid in the gut and reduces cholesterol levels The oat bran has been found to be the only fiber source that significantly lowered total and low density-lipoprotein cholesterol levels in mild hypercholesterolemics [56-57].

C57BL/6 NCrl mice responded to oat bran with 19 ± 1 % (P < 0.001) lower plasma cholesterol, 40 ± 5% (P < 0.01) higher excretion of bile acids and increased expression of the bile acid-producing hepatic enzymes CYP7A1 and CYP8B1, but none of these effects were found in control C57BL/6JBomTac mice [58].

To explored the dose-dependent effect of oat cereal β-glucan on improving metabolic indexes of obesity mice, C57-Bl mice were randomized to chow diet (N) group and high fat diet group and other three doses of oat β-glucan groups (low β-glucan, medium β-glucan, and high β-glucan). Energy intake, glucose, lipids, and appetite related hormones were tested. Dose-dependent relation was observed on oat β-glucan doses and body weight change, average energy intake, total cholesterol, HDL cholesterol, plasma neural peptide Y, arcuate neural peptide Y mRNA, and arcuate neural peptide Y receptor 2 mRNA level. Oat β-glucan helped to increase plasma peptide Y-Y and intestine peptide Y-Y expression in obesity mice [59].

The United States Food and Drug Administration (FDA) approved a health claim for β-glucan soluble fiber from oats for reducing plasma cholesterol levels and risk of heart disease in 1997. Similarly, in 2004 the United Kingdom Joint Health Claims Initiative (JHCI) allowed a cholesterol-lowering health claim for oat β-glucan. Studies conducted during the past 13 years support the suggestion that intake of oat β-glucan at daily doses, of at least 3 g, reduced plasma total and low-density lipoprotein (LDL) cholesterol levels by 5-10% in normocholesterolemic or hypercholesterolemic subjects. Studies also showed that oat consumption is associated with 5% reductions in total cholesterol levels [60].

A clinical trial was carried out to confirm the anti- obesity effect of oat. Subjects with BMI ≥27 and aged 18-65, were randomly divided into a control (n=18) and an oat-treated (n=16) group, taking a placebo or beta glucan-containing oat cereal, respectively, for 12 weeks. The result showed that consumption of oat reduced body weight, BMI, body fat and the waist-to-hip ratio. Profiles of hepatic function, including AST and ALT showed decrements in patients with oat consumption. Nevertheless, anatomic changes were not observed by ultrasonic image analysis. Ingestion of oat was well tolerated and there was no adverse effect during the trial [61].

The effect of oat consumption on serum lipid profiles in Thai hypercholesterolemic adults was studied. Following daily oat consumption, total cholesterol and LDL-cholesterol levels were significantly lower than baseline levels and lower than the levels observed with rice consumption. Oat consumption reduced total cholesterol by 5% and LDL-cholesterol by 10% from baseline levels. In addition, mean and percent changes were significantly different from the levels after consuming rice porridge ($p < 0.05$) [62].

2.10. *Bauhinia variegata*

The ethanolic and aqueous extracts of the root of *Bauhinia variegata* (200 and 400 mg/kg body weight) in rats, showed significant reduction ($P \geq 0.01$) in cholesterol and significant reduction ($P \geq 0.01$) in triglyceride level. The VLDL level was also significantly ($P \geq 0.05$) reduced, with a significant increase in HDL [63-64].

The anti-hyperlipidemic activity of fractions of total methanol extract of leaves of *Bauhinia variegata* was investigated against Triton WR-1339 induced hyperlipidemia in rats. Fractions were administered at a dose of 100mg/kg orally. Butanol fraction showed significant reduction ($p<0.05$) in serum cholesterol, triglyceride, LDL, VLDL and increase in HDL level in comparison with standard drug fenofibrate ($p<0.05$) [65].

The anti-obesity effect of methanolic extract of stem and root barks of *Bauhinia variegata* was examined in female rats fed with hypercaloric diet. The methanolic plant extract (200 and 400 mg/kg) exhibited a significant hypolipidemic effect with a reduction in the feed intake and body weight. Treatment of obese animals with the methanolic extract of *B. variegate* exhibited an increased brain serotonin level and high density lipoprotein with a concomitant decrease in total cholesterol, triglycerides and low density lipoprotein. Thus the anti-obesity activity of methanolic extract of *B. variegata* could be attributed to tendency of the extract to reduce lipid profile and elicit the brain serotonin level [66].

2.11. *Bellis perennis*

The methanolic extract and its saponin fraction (methanol-eluted fraction) of the flowers of *Bellis perennis* were found to suppress serum triglyceride elevation in olive oil-treated mice. Among these saponins, perennisosides I and II showed inhibitory effects on serum triglyceride elevation at doses of 25-50 mg/kg orally. As a result of hypolipidemic effect of saponin constituents isolated from the flowers of *Bellis perennis*, it also can be utilize as preventive drug in ischemic diseases and as an anti-obese remedy [67-69].

2.12. *Benincasa hispida*

Salad prepared by using 100gm of ash gourd (*Benincasa hispida*) and one gram of curry leaves (10 curry leaves) and five grams of skimmed milk powder (made into curd) and pepper and salt are added for taste. This salad was freshly prepared every day and given to hyperlipidemic diabetic patients in mid morning for a period of three months to find out the therapeutic effect of supplementation of ash gourd and curry leaves. Supplementation of ash gourd and curry leaves had significant hypoglycemic and hypolidemic effect and it reduced the blood glucose level (both fasting and post prandial), within the period of three months [70-71].

2.13. *Brassica rapa*

The effect of different doses ethanol extract of root on blood lipid changes was studied in hypercholesterolemic rabbits. Extract was given in as 100, 200, 400 mg / kg body weight of the rabbits. The results showed that the turnip root extract can prevent the occurrence of atherosclerotic in hypercholesterolemic rabbits which may be due to flavonoids and vitamins contents [72].

Caulilexin C, indole acetonitrile and arvelexin isolated from the root of *Brassica rapa* (at a concentration of 100 µg/ml) showed an inhibitory activity on human Acyl CoA: cholesterol transferase 1 (hACAT1) by 54.6±6.0%, 69.2±4.7% and 68.6±3.7%, and on human Acyl CoA: cholesterol transferase 2 (hACAT2) by 4.8±13.4%, 45.6±4.8% and 39.5±4.3%, respectively [73].

The influence of ethanolic extracts of *Brassica campestris* spp. rapa roots (EBR) on obesity was examined in imprinting control region (ICR) mice fed a high-fat diet (HFD) and in 3T3-L1 adipocytes. The molecular mechanism of the anti-obesity effect of EBR was investigated in 3T3-L1 adipocytes as well as in HFD-fed ICR mice. In the obese mouse model, both weight gain and epididymal fat accumulation were highly suppressed by the daily oral administration of 50 mg/kg EBR for 8 weeks, whereas the overall amount of food intake was not affected. EBR treatment induced the expression in white adipocytes of lipolysis-related genes, including beta3-adrenergic receptor (beta3-AR), hormone-sensitive lipase (HSL), adipose triglyceride lipase, and uncoupling protein 2. Furthermore, the activation of cyclic AMP-dependent protein kinase, HSL, and extracellular signal-regulated kinase was induced in EBR-treated 3T3-L1 cells. The lipolytic effect of EBR involved beta3-AR modulation, as inferred from the inhibition by the beta3-AR antagonist propranolol. Accordingly, EBR may have potential as a safe and effective anti-obesity agent via the inhibition of adipocyte lipid accumulation and the stimulation of beta3-AR-dependent lipolysis [74-75].

2.14. *Caesalpinia crista*

The methanol extract significantly (P<0.05) decreased the levels of lipid peroxidation and significantly (P<0.05) increased the levels of GSH, superoxide dismutase and catalase, when administered at the doses of 50, 100, and 200 mg/kg body weight per day for 14 days in mice [76].

Aqueous extract in isoproterenol treated rats significantly decreased plasma total cholesterol, TC (87.45 ±1.5), triglycerides TG (91.59±2.12), LDL (67.79±1.80), VLDL (12.46±0.68), along with a significant increased in HDL level (18.67±0.72) when compared to untreated isoproterenol group. Ethanolic extract of *Caesalpinia crista* + isoproterenol treated group showed decrease lipoproteins level except HDL of plasma. *Caesalpinia crista* aqueous extract treated group showed significantly decrement plasma TC (81.23±1.99), TG (73.82±1.34), LDL (60.34±1.56), VLDL (10.53±0.54), along with a significant (P<0.01) increased in HDL level (19.38±1.25) when compared to untreated isoproterenol group [77].

2.15. *Calotropis procera*

Serum lipid profile was measured in the diabetic rats. The extracts were significantly (p<0.001) decreased total cholesterol, triglycerides, phospholipids, LDL and VLDL cholesterol and significantly (p<0.001) increased HDL cholesterol [78-79].

2.16. *Capparis spinosa*

Leaves and flowers of *Capparis spinosa* were rich in either polyphenols or flavonoids, while roots are the poor ones. All extracts have anti lipid peroxidation and antioxidant effects with a dominance of flowers and leaves especially in the methanolic extracts (82.78 ± 2.64 and 80.94 ±1.57 respectively). Seeds exerted the acceptable effects followed by bud than roots [80-81].

2.17. *Capsicum annuum and Capsicum frutescens*

The anti-obesity effects of water extracts of seven *Capsicum annuum* L. varieties, Putgochu (Pca), Oyee gochu (Oca), Kwari putgochu (Kca), Green pepper (Gca), Yellow paprika (Yca), Red paprika (Rca) and Cheongyang gochu (Cca), were examined through the evaluation of lipoprotein lipase (LPL) mRNA expression level in 3T3-L1 cells (mouse pre-adipocytes). After capsaicin elimination by chloroform defatting, freeze-dried powder of Cca was treated to 3T3-L1 cells and anti-obesity effects were examined by determining the LPL mRNA level using the RT-PCR method. Of the primary fractions, only proven fractions underwent secondary and tertiary re-fractionating to determine anti-obesity effects. From seven different *Capsicum annuum*, there was a significant decrease of the LPL mRNA expression level of 50.9% in Cca treatment compared to the control group. A significant decrease of the LPL mRNA expression level was shown in primary fractions (Fr) 5 (36.2% decrease) and 6 (30.5% decrease) of the Cca water extracts. Due to the impurities checked by UPLC chromatography, Fr 5 and 6 were re-fractionated to determine the LPL mRNA expression level. Treatment of Fr 6-6 (35.8% decrease) and Fr 5-6 (35.3% decrease) showed a significant decrease in the LPL mRNA expression level. When analyzed using UPLC, major compounds of Fr 6-6 and Fr 5-6 were very similar. Subsequently, Fr 6-6 and Fr 5-6 were re-fractionated to isolate the major peak for structure elucidation. Treatment of Fr 5-6-1 (26.6% decrease) and Fr 6-6-1 (29.7% decrease) showed a significant decrease in the LPL mRNA expression level [82-83].

2.18. *Carum carvi*

The hypolipidemic effect of aqueous extract of *Carum carvi* seeds (60 mg/kg of body weight for eight weeks) was investigated in diet induced hyperlipidemia in rats. *Carum carvi* and simvastatin significantly decreased lipids levels in rats. *Carum carvi* extract reduced lipid levels more effectively than the simvastatin. *Carum carvi* constituents, especially flavonoids and carvone have strong anti-oxidant activity which might be involved in hypolipidemia [84-85].

Oral administration of caraway to rats, 1g/kg body weight, daily caused a significant decrease in blood glucose level (p=0.001) and alleviated their body weight loss (p = 0.037). Furthermore, it caused significant decrease in total cholesterol (p = 0.036), and low-density lipoprotein cholesterol levels (p = 0.001) compared with the diabetic control rats, and with no significant changes in triglyceride and high-density lipoprotein cholesterol levels were recorded [86].

The effect of single and repeated oral administration of the aqueous extract of *Carum carvi* fruits at a dose of (20mg/kg) on lipid metabolism was studied in normal and Streptozotocin-induced diabetic rats (STZ). After a single oral administration, *Carum carvi* extract produced a significant decrease on triglycerides levels in normal rats (p<0.05). In STZ diabetic rats, cholesterol levels were decreased significantly 6h after *Carum carvi* treatment (p<0.05). On the other hand, repeated oral administration of *Carum carvi* extract exhibited a significant hypo-triglyceridemic and hypo-cholesterolemic activities in both normal (p<0.01) and STZ diabetic rats (p<0.001), 15 days after *Carum carvi* treatment [87].

2.19. *Carthamus tinctorius*

The effect of the extracts from safflower was investigated on cholesterol metabolism in high cholesterol fed rats. After treatment for 14 and 30 days, a significant reduction in total cholesterol and total cholesterol/HDL-cholesterol and a significant induction in HDL-cholesterol were observed in the hypercholesterolemic rats treated with the dichloromethane extract. Higher expression of SRBI and ABCA1 in the liver of the control group was observed after 4 weeks whereas no significant difference in the expression level of SRBI and ABCA1 was found in groups treated with extract after 2 and 4 weeks. The authors suggested that the expression of SRBI and ABCA1 mRNA may not be regulated by the crude extract of safflower, which may not in part explain the decrease in HDL-cholesterol and gene encoding enzymes of the cholesterol biosynthetic pathway [88-89].

The inhibitory effects of defatted safflower seed extract (SSE) and serotonin derivatives (N-p-coumaroyl serotonin and N-feruloyl serotonin, CS+FS), were evaluated on hypercholesterolemia and atherosclerosis, using Pulse wave velocity (PWV) in Kurosawa and Kusanagi- hypercholesterolemic rabbits. The atherosclerotic lesioned area in the aorta was significantly reduced in the SSE and CS+FS groups, without significant changes in serum cholesterol and triglyceride levels among the three groups after supplementation. Local PWV (LPWV) in the middle thoracic and distal abdominal aortas was significantly smaller in the SSE and CS+FS groups than in the control group. PWV in the entire aorta was also significantly lower in the SSE and CS+FS groups, compared with that in the control group. Pressure-strain elastic modulus, an index of wall dispensability, was significantly lower in the middle thoracic and middle abdominal aortas in the SSE and CS+FS groups than in the control group. Wall thickness was also significantly smaller in the middle thoracic aorta in the SSE and CS+FS groups compared with that in the control group [90].

2.20. *Casuarina equisetifolia*

The effect of *Casuarina equisetifolia* bark incorporated into rat feed at 10-40% on the lipid profiles and blood sugar of albino rats was investigated. The parameters studied were triacylglycerol (TGL), total cholesterol (TC), total lipid (TL), phospholipids (PHOS), high-density lipoprotein (HDL) and random blood sugar (RBS). There was no significant change (P>0.05) in the TGL levels of all the rats, including the control, as they all range between 0.18-0.22 (mg/dl). The effects on TC and TL were irregular as they did not display any dose dependence. The mean plasma PHOS levels did not change significantly (P>0.05) between the control and the rats fed on 10% feed (0.19± 0.00 vs 0.18± 0.00 mg/dl), but was significantly lowered (P<0.05) at 20-40% feed content. The mean HDL level rose, although insignificantly (P>0.05) with the percentage contents of the bark in the feeds; by implication, the low-density lipoprotein (LDL) was decreasing with the increase in the bark contents of the feeds. The RBS also decreased as the percentage bark contents of the feeds increased, indication that it could have anti-diabetic properties [91-92].

The effect of extracts of *Casuarina equisetifolia* bark on serum lipid profile, total cholesterol, triglycerides, low density, very low density and high density lipoprotein was evaluated in the diabetic and non-diabetic rats. There was significant reduction in total cholesterol, LDL cholesterol, VLDL cholesterol and improvement in HDL cholesterol in diabetic rats [93].

2.21. *Cistanche tubulosa*

The hypocholesterolemic effect of the aqueous ethanol extract (CTE) of the roots of *Cistanche tubulosa* was evaluated in mice using gene chip and RT-PCR analysis of the livers of mice given CTE (400 mg/kg) for 14 days. The administration of CTE (400 mg/kg) for 14 days significantly suppressed serum cholesterol elevation in high cholesterol diet-fed mice. The mRNA expressions of VLDL receptor and cytochrome P450 SCC were significantly enhanced. In addition, acteoside, a major constituent of CTE, was found to enhance the mRNA expressions of apolipoprotein B, VLDL receptor, and cytochrome P450 SCC in HepG2 hepatocytes. According to these results, the authors concluded that CTE affected the mRNA expressions of molecules related to cholesterol transport and metabolism and exhibited hypocholesterolemic activity in diet-induced hypercholesterolemia mice. Acteoside was involved in the hypocholesterolemic activity of CTE [94-95].

2.22. *Citrullus colocynthis*

The hypolipidemic effect of *Citrullus colocynthis* was studied clinically. One hundred dislipidemic patients were randomly divided into two treated and placebo groups. They were treated daily with powdered seeds of *Citrullus colocynthis* (300 mg) and placebo for 6 weeks. A daily intake of 300 mg/ day of powdered seeds of *Citrullus colocynthis* can lower the triglyceride and cholesterol concentration significantly in nondiabetic hyperlipidemic patients [96-97].

The effect of *Citrus aurantifolia* peel essential oil was studied on serum triglyceride and cholesterols in Wistar rats. Thirty Wistar rats were divided into 5 groups: control, sham, and 3 experimental groups. The animals were treated in 2 phases: first, except for control group, which received normal saline, the rest of the groups were fed with a high cholesterol regimen to induce hyperlipidemia; then, the 3 experimental groups were treated with *Citrus aurantifolia* peel essential oil in 3 different doses: 25, 50, and 100 µl/kg. The sham group demonstrated a significant rise in mean serum triglyceride, cholesterol, and LDL level in comparison with the control group ($p<0.05$). The results of experimental groups treated with peel essential oil in 50 and 100 µl/kg doses demonstrated a significant reduction in triglyceride, cholesterol, and LDL ($p< 0.01$) [98].

The effect of *Citrus aurantifolia* on hepatic lipidomics was studied in female albino rats, it was found that the fresh juice of lime had different effects on cholesterol, riacylglycerol and phospholipid concentrations of the liver. The low concentration of lime juice (30µl) did not showed considerable effect on cholesterol concentration of the liver. Increase in cholesterol concentration was observed only after applying a concentration of 60 µl. Beyond this concentration, cholesterol concentration was decreased. Therefore, it was demonstrated that peak stimulation for lime juice is 60µl. Similar effect also occurred for triacylglycerol concentration. However, it caused dose-dependent increase in phospholipids concentration [99].

Eriocitrin (eriodictyol 7-rutinoside), a powerful antioxidative flavonoid in lemon with lipid-lowering effects was evaluated in a rat model of high-fat diet to investigate its mechanism of action. A feeding experiment was conducted in zebrafish with diet-induced obesity. Oral administration of eriocitrin (32 mg/kg/day for 28 days) improved dyslipidaemia and decreased lipid droplets in the liver. DNA microarray analysis revealed that eriocitrin increased mRNA of mitochondrial biogenesis genes, such as mitochondria transcription factor, nuclear respiratory factor 1, cytochrome c oxidase subunit 4, and ATP synthase. In HepG2 cells, eriocitrin also induced the corresponding orthologues, and reduced lipid accumulation under conditions of lipid loading. Eriocitrin increased mitochondrial size and mtDNA content, which resulted in ATP production in HepG2 cells and zebrafish [100]. *Citrus medica* cv Diamante peel extract lowered plasma cholesterol and triglycerides in mice [101].

2.23. *Clitoria ternatea*

The anti-hyperlipidemic effect of *Clitoria ternatea* was studied in experimentally induced hyperlipidemia in rats. The poloxamer 407-induced acute hyperlipidemia and diet-induced hyperlipidemia models were used in this investigation. Oral administration of the hydroalcoholic extract of the roots and seeds of *Clitoria ternatea* resulted in a significant ($p < 0.05$) reduction of serum total cholesterol, triglycerides, very low-density lipoprotein cholesterol, and low-density lipoprotein cholesterol levels. The atherogenic index and the HDL/LDL ratio were also normalized after treatment in diet-induced hyperlipidemic rats. The effects were compared with atorvastatin (50 mg/kg, po) and gemfibrozil (50 mg/kg, po) [102-103].

2.24. *Coriandrum sativum*

The antilipidemic activity of fresh leaves of *Coriandrum sativum* was studied against salbutamol induced cardiac injury in rabbits. Salbutamol administered rabbits (50mg/kg) showed elevated level of serum lipids (LDL-cholesterol, triglyceride) and decreased level of HDL-cholesterol and antioxidant enzymes (SOD, CAT). Both the pre- and post-

treatment of plant extract (100mg/kg) for three weeks exerted significant antilipidemic effect against salbutamol-induced myocardial infarction by lowering the level of serum LDL-cholesterol, triglycerides and peroxidase and increasing the level of HDL-cholesterol and antioxidant enzymes [104].

The hypolipidemic and antioxidant action of *Coriandrum sativum* were investigated in cholesterol-fed rabbits. Cholesterol feeding (500 mg/ kg bw/day) for 120 days caused a significant increase in serum total cholesterol, phospholipid, triglyceride, LDL-cholesterol and VLDL-cholesterol levels, whereas HDL ratio was decreased significantly when compared with control group. The changes in the antioxidant parameters were accompanied by an increase in hepatic lipid peroxidation and reduction in glutathione (GSH) and catalase activity. The level of lipid peroxidation was reduced whereas GSH content and catalase activity were elevated after the treatment with 70% methanolic extract of *Coriandrum sativum* at a dose of 500 mg/kg bw/day. Reduced serum lipid profile and elevated HDL ratio was observed after administration of *Coriandrum sativum*. *Coriandrum sativum* extract feeding increased the fecal excretion of cholesterol and phospholipids. Histological studies showed less cholesterol deposits in the aorta of high cholesterol diet animals given *Coriandrum sativum* compared to the high cholesterol diet untreated animals [105].

Coriandrum sativum seeds were incorporated into diet, and the effect of the of coriander seeds on the metabolism of lipids was studied in rats fed with high fat diet and added cholesterol. The seeds had a significant hypolipidemic action. In the experimental group of rats (tissue) the level of total cholesterol and triglycerides increased significantly. There was significant increase in beta-hydroxy, beta-methyl glutaryl CoA reductase and plasma lecithin cholesterol acyl transferase activities were noted in the experimental group. The level of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol were decreased, while that of high density lipoprotein (HDL) cholesterol was increased compared to the control group [106-108].

2.25. *Crocus sativus*

Serum triglycerides, total-, LDL-, cholesterol, fecal excretion of fat and cholesterol were significantly inhibited by crocin (100 mg/kg/day) compared to the control group [109].

Crocetin, was administered to rabbits to determine its effect on the development of atherosclerosis. New Zealand white rabbits were given three different diets for eight weeks: a standard diet, a high lipid diet (HLD), or a high lipid + crocetin diet. The HLD group developed hypercholesterolemia and atherosclerosis, while the crocetin-supplemented group decreased the negative health effects of a high lipid diet. However, the results did not show a significant difference in the plasma lipid levels (total, low density lipoprotein (LDL), and high density lipoprotein (HDL) cholesterol) between the HLD and crocetin groups but showed significant decrease in the aorta cholesterol deposits, atheroma, foam cells, and atherosclerotic lesions. The authors suggested that nuclear factor kappa B (NF-κB) activation in the aorta was suppressed by crocetin which in turn decreased the vascular cell adhesion molecule-1 (VCAM-1) expression [110].

Administration of a monthly intramuscular injection of crocetin reduced serum cholesterol concentrations by 50%, and the severity of atherosclerosis by 30% in rabbits fed an atherosclerosis-inducing diet. Crocin exerted antiatherosclerotic effects through decreasing the level of Ox-LDL that plays an important role in the initiation and progression of atherosclerosis [111-112].

Fifty milligrams of saffron dissolved in 100 ml of milk was administered twice a day to human subjects, the significant decrease in lipoprotein oxidation susceptibility in patients with coronary artery disease (CAD) indicated the potential of saffron as an antioxidant [113].

Healthy, mildly overweight women (N = 60) participated in a randomized, placebo-controlled, double-blind study to evaluated the efficacy of satiereal supplementation (Inoreal Ltd, Plerin, France), a novel extract of saffron stigma, on body weight changes over an 8-week period. They took twice capsule of satiereal (176.5 mg extract per day or a matching placebo. Caloric intake was left unrestricted during the study. At baseline, both groups were homogeneous for age, body weight, and snacking frequency. Satiereal caused a significantly greater body weight reduction than placebo after 8 weeks (p<0.01). The mean snacking frequency was significantly decreased in the satiereal group as compared with the placebo group (P < .05). Other anthropometric dimensions and vital signs remained almost unchanged in both groups. No subject withdrawal attributable to a product effect was reported throughout the trial, suggesting a good tolerability to satiereal [114-115].

2.26. *Crotalaria juncea*

The antihypercholesterolemic effects of 50 and 100 mg/kg bw per day of an ethanolic extract of *Crotalaria juncea* Linn (whole plant) were investigated in rats fed high-fat diet by evaluating food consumption, weight gain, fecal fat excretion,

serum and liver lipids, and biochemical profiles as well as by histopathological studies. The results were compared to animals fed with the standard diet and animals fed with a high-fat diet and atorvastatin (10 mg/kg bw). The animal group administered with the ethanolic extract for 35 days showed decreased levels of TC, LDL, VLDL, TG, HDL+VLDL, VLDL+LDL, LDL/TC, AI, SGOT, SGPT, and elevated levels of HDL, HDL/TC, significantly (p<0.01 and p<0.05) in a dose-dependent manner [116-117].

The antihyperlipidemic activity of alcoholic and methanol extract of leaves of *Crotolaria juncea* (CJ) was investigated against Triton induced hyperlipidemia in mice. CJ was administered at a dose of 100 and 200mg/kg (po) to Triton induced hyperlipidemic mice. Atorvastatin was used as reference standard. CJ showed a significant decrease in the levels of serum total cholesterol, triglyceride, LDL, VLDL and significant increase in the level of serum HDL at the dose of 100 and 200mg/kg (po) against Triton induced hyperlipidemia in mice [118].

The amino acid, 2-amino-5-hydroxyhexanoic acid isolated from the seeds of *Crotalaria juncea*, showed dose dependent lipid lowering activity in the *in vivo* experiments and also showed good *in vitro* antioxidant activity. The cyclized compound, 3-amino-6-methyltetrahydro-2H-pyran-2-one showed better lipid lowering and antioxidant profile than the parent compound [119]. The anti-obesity effect of *Crotalaria juncea* leaves extract was documented in high fat induced obesity in rats [120].

2.27. *Cuminum cyminum*

The hypocholesterolemic effect of methanolic extract of *Cuminum cyminum* (MCC) was evaluated in ovariectomized (OVX) rats. MCC 1000 mg/kg and estradiol benzoate equivalent to 0.15 mg/kg of estradiol were administered to OVX rats per orally for 10 weeks. The results indicated that estradiol as well as MCC protected OVX rats against increased cholesterol levels due to ovariectomy, MCC was better than estradiol [121-122].

The effect of cumin powder on body composition and lipid profile was studied in overweight and obese women in a randomized clinical trial. 88 overweight/ obese women were randomly assigned into two groups. The experimental group was given 3 g/day cumin powder with yogurt at two meals for 3 months. The same amount of yogurt without cumin powder was prescribed for the control group. All patients received nutrition counseling for weight loss in a similar manner. Anthropometric and biochemical parameters were determined before and after the intervention. Cumin powder reduced serum levels of fasting cholesterol, triglyceride, and LDL and increased HDL. Weight, BMI, waist circumference, and fat mass were also significantly reduced. However, it exerted no effect on FBS and fat-free mass [123].

The effects of cumin extract supplementation on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, High density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), apolipoprotein A1 (Apo A1), and apolipoprotein B (Apo B) were studied in the patients with hypercholesterolemia. The results demonstrated that there was a significant decrease in the level of oxLDL after receiving cumin. Paraoxonase and arylesterase activities increased in serum after taking cumin extract. Paraoxanase 1 (PON1) played a protective role against the oxidative modification of plasma lipoproteins and hydrolyzes lipid peroxides in human atherosclerotic lesions [124].

The effects of *Cuminum cyminum* intake on weight loss and metabolic profiles among overweight subjects was studied by a randomized double-blind placebo-controlled clinical trial which conducted among 78 overweight subjects (male, n = 18; female, n = 60) aged 18-60 years old. Participants were randomly assigned into three groups to receive: (1) *Cuminum cyminum* capsule (n = 26); (2) orlistat 120 capsule (n = 26) and (3) placebo (n = 26) three times a day for 8 weeks. Anthropometric measures and fasting blood samples were taken at baseline and after 8 weeks of intervention. Consumption of the *Cuminum cyminum* and orlistat120 resulted in a similar significant decrease in weight (-1.1 ± 1.2 and -0.9 ± 1.5 compared with placebo 0.2 ± 1.5 kg, respectively, p = 0.002) and BMI (-0.4 ± 0.5 and -0.4 ± 0.6 compared with placebo 0.1 ± 0.6 kg/m (2), respectively, p = 0.003). In addition, *Cuminum cyminum* L., compared with orlistat and placebo, led to a significant reduction in serum insulin levels (-1.4 ± 4.5 vs. 1.3 ± 3.3 and 0.3 ± 2.2 µIU/ml, respectively, p = 0.02), HOMA-B (-5.4 ± 18.9 vs. 5.8 ± 13.3 and 1.0 ± 11.0, respectively, p = 0.02) and a significant rise in QUICKI (0.01 ± 0.01 vs. -0.005 ± 0.01 and -0.004 ± 0.01, respectively, p = 0.02) [125].

2.28. *Cupressus sempervirens*

The effects of *Cupressus sempervirens* cone extract (CSE) on the lipid profile was studied in Wistar rats. The oral administration of the extract resulted in a substantial decrease of serum total cholesterol, which was significant even after 6 weeks of treatment. Moreover, these animals exhibited lower total cholesterol levels compared to the controls after the initiation of treatment (p<0.001). The administration of the extract also led to a substantial reduction in serum triglycerides (p<0.05), comparing 0 week to 6-24 weeks. However no significant differences in triglyceride levels were

observed between CSE animals and controls during the entire study period. No significant changes in HDL-cholesterol level [126-127].

2.29. *Cydonia oblonga*

The hypolipidemic effect of *Cydonia oblonga* was studied in a rat model. Low-, medium- and high-dose *Cydonia oblonga* leaf extracts (COM) were given orally for 56 days. The normal controls were fed a normal diet, all other groups a high fat diet. COM dose-dependently reduced TC, TG, LDL-C and MDA, inhibited the activity of ALT, AST and LPS, increased HDL-C content, increased the activity of SOD, GSH-PX, LPL and HL, and reduced liver steatosis in hyperlipidaemia rats, significant at medium and high doses. The effect of COM was similar to that of simvastatin except for increased lipoprotein lipase and hepatic lipase which were reduced by COM but not by simvastatin [128-129].

The effects of *Cydonia oblonga* Miller (COM) total flavonoids (TF) from leaves and fruit on the blood lipid and antioxidant potentials were studied using hyperlipidaemic rat models. Compared with the hyperlipidaemic model group, TF significantly reduced serum TC, TG, LDL-C (p<0.01), ALT and AST (p<0.01 or p<0.05) and increased HDL-C (p<0.05 or p<0.01). TF also reduced MDA (p<0.01 or p<0.01). The effects of hydromethanolic extract of quince leaf were investigated on the lipid profile of rabbits fed with cholestrol enriched diet (2% w/w for two months). Animals were treated as follow: no treatment (NT), atrovastatin (AT) (0.5 mg/kg/day) and quince extract (QE) (dried extract, 50 mg/kg/day) treatment, and then fed with normal diet for three months. Significant increases (p<0.05) in the mean values of cholestrol I, triglyceride, low density lipoprotein, aspartate aminotransferase, alanine transaminase, creatinine, and alkaline phosphatase with a significant decrease (p<0.05) in high density lipoprotein level, were recorded after receiving cholesterol enriched diet in comparison with the control group [130].

2.30. *Cyperus rotundus*

Hypolipidaemic activity of *Cyperus rotundus* rhizomes was evaluated in high fat diet induced hyperlipidaemic rats (70, 140 and 280 mg/kg bw). The results demonstrated statically significant reduction in serum lipid profile. Treatment with different doses of extract exerted statistically significant (p<0.05) reduction in serum total cholesterol, LDL, TG levels at the end of 15 days of intervention [131].

The biological efficacy of *Cyperus rotundus* tubers extract was studied on weight control in obese Zucker rats. Administration of 45 or 220 mg/kg/day of *Cyperus rotundus* tubers hexane extract for 60 days in Zucker rats induced a significant reduction in weight gain without affecting food consumption or inducing toxicity. *In vitro*, 250 microg/ml of this extract was able to stimulate lipolysis in 3T3-F442 adipocytes suggesting that this medicinal plant contained activators of beta-adrenoreceptors (AR). The binding assay performed on the rat beta3-AR isoform, known to induce thermogenesis, demonstrated that *Cyperus rotundus* tubers extract can consistently and effectively bind to this receptor. The data suggest that the effect on weight gain exerted by *Cyperus rotundus* tubers extract may be mediated, at least partially, through the activation of the beta3-AR [132-133].

2.31. *Daucus carota*

High-carbohydrate, high-fat diet-fed rats developed hypertension, cardiac fibrosis, increased cardiac stiffness, endothelial dysfunction, impaired glucose tolerance, increased abdominal fat deposition, altered plasma lipid profile, liver fibrosis and increased plasma liver enzymes together with increased plasma markers of oxidative stress and inflammation as well as increased inflammatory cell infiltration. Purple carrot juice reversed all these parameters [134].

The effect of a 3-week supplementation of the diet with carrot (15% dry matter) in lipid metabolism was studied in rats. A significant decrease of cholesterol level in liver (–44%; p= 0.0007) was observed together with a reduction of the level of liver triglycerides (–40%; P= 0.0005). Fecal total steroids excretion increased by 30% upon feeding the carrot diet as compared to the control. The secretion of bile acids was maintained, whereas the cholesterol apparent absorption was reduced in rats fed carrot diet [135-136].

2.32. *Dolichos lablab*

The hypocholesterolemic effect of germinated Indian bean (*Dolichos lablab* L. var lignosus) was studied in hypercholesterolemic rats. Supplementation of the diet with dried powder of soaked bean almost brought the plasma cholesterol to 72.5 ± 0.75 from 178 ± 1.85 compared with that of the control (61.5 ± 0.70), although the liver cholesterol was still three times higher compared with the control. The 24h germinated Indian bean cotyledons could effectively counteract the effects of added cholesterol on liver and plasma by their high fiber content coupled with enormous increase in ascorbic acid levels [137-138].

2.33. *Echinochloa crusgalli*

The anti-obesity effect of hydroalcoholic extracts of *Echinochloa crusgalli* grains was evaluated in high fat diet induced obesity in albino rats. Obesity was induced by administration of high fat diet for 4 weeks, the obtained obese rats were treated with hydroalcoholic extracts of *Echinochloa crusgalli* grains in a dose of 200, 400 and 600 mg/kg, bw orally for next 4 weeks. *Echinochloa crusgalli* caused significant decrease in body weights, adipose tissue weight, SGOT and SGPT levels, blood glucose levels, LDL-C, VLDL-C, total cholesterol, triglyceride levels, atherogenic index, with a significant increase in HDL-C levels compared with high fat diet control [139-140].

The curative effect of *Echinochloa crusgalli* extract as anti-hypercholesterolemic therapy was evaluated by performing in vivo studies and identifying its effects by on food consumption, weight gain, fecal fat excretion, serum lipid and biochemical profiles. The animal group administered methanolic extract of the plant has shown decreased levels of TC, LDL, VLDL, TG, HDL+VLDL, VLDL+LDL, LDL/TC, AI, SGOT, SGPT and elevated levels of HDL, HDL/TC in a dose dependent manner significantly (p<0.01 & p<0.05). Body weight and food intake in treated groups were significantly lower than that in model control [141].

2.34. *Foeniculum vulgare*

The effect of *Foeniculum vulgare* fruit extracts in high fat diet and their possible role in obesity and associated cardiovascular disorders were studied in rats. Three fractions prepared by successive solvent technique from methanol extract of *Foeniculum vulgare* Mill. Fruits were administered at a dose of 300 mg/body weight by oral gavage and volatile oil obtained by hydrodistillation at a dose of 0.2 ml/bw intraperitoneally once daily along with high fat diet to the female albino rats for six weeks. Results revealed that body weight and fat pad weights were reduced in extracts fed animals in a variable pattern. Cholesterol and triglycerides levels, which were elevated in high fat diet fed animals, improved in a significant manner. Maximum activity was observed with methanol fraction of the extracts which contained maximum amount of phenolic (48.37 mg/g) and flavonoidal contents (21.44 mg/g) [142-143].

2.35. *Glycyrrhiza glabra*

Ethanolic extract and its ethyl acetate soluble, water soluble and hexane soluble fractions decreased serum level of total cholesterol by 25.9, 38.0, 39.0 and 26.3%, respectively in high fructose diet induced dsyslipidaemic in Syrian golden hamsters. Furthermore, they also increased the serum HDL-cholesterol level by 14.8, 34.3, 27.3 and 17.2%, and decreased triglyceride level by 31.3, 37.2, 41.2 and 28.9%, respectively. The reduction in LDL-cholesterol level by ethanolic extract, ethyl acetate soluble fraction and water soluble fraction were 43.9, 31.0, 33.4 and 24.6%, respectively [144-145].

2.36. *Helianthus annuus*

The anti-obesity activity of the methanolic extract of *Helianthus annuus* seeds was studied in mice model. The mice received cafeteria diet, atorvastatin (10 mg/kg) and *Helianthus annuus* 200 mg/kg daily for 6 weeks. Parameters such as food consumption, locomotor activity, body weight, body mass index (BMI), lee index of obesity (LIO), total cholesterol, triglyceride, LDL, HDL and glucose were studied. The methanolic extract of *Helianthus annuus* seeds significantly increased locomotor activity (rearing, grooming, ambulation) with HDL and significantly decreased food consumption, body weight, BMI, LIO, total cholesterol, triglyceride, LDL and glucose [146-147].

2.37. *Hibiscus cannabinus*

The hypolipidemic effect of50% hydroalcoholic extract of *Hibiscus cannabinus* leaves was evaluated in high fat diet fed rat model. The extract exhibited a strong dose dependent antihyperlipidemic activity and at dose level 400mg/kg po, the extract showed a significant decrease in the levels of serum TC, TG, LDL-C, VLDL-C and TBARS. The extract also markedly prevented the liver microvesicular steatosis in hyperlipidemic rats [148-149].

2.38. *Hibiscus rosa sinensis*

The hypolipidimic activity of flowers extract of *Hibiscus rosa sinensis* was studied in Alloxan induced diabetic rats oral administration of flowers extract in doses 50,100,200 mg/kg po, showed significant improvement in dyslipidemia caused by diabetes mellitus as evidenced by reduced level of total cholesterol, triglycerides, VLDL, LDL and elevated in HDL levels significantly [150].

The antidiabetic, hypolipidimic, antioxidant and histopathological effects of *Hibiscus rosa sinensis* were investigated in Alloxan induced diabetes in rats. HEFHR (Hydroalcoholic extract of flower *Hibiscus rosa-sinensis*) (50-200 mg/kg bw) possessed significant and sustained oral antidiabetic activity, comparable with the hypoglycemic effect of glibenclamide

and sulphonylurea. Flower extract of HRS was more efficacious in lipid lowering effect and in antioxidative activity than glibenclamide. After 28 day treatment with flower extract, size of islets was significantly increased and necrosis and atrophy of islets were significantly improved; also increase in number and diameter of cell islets compared to the diabetic group [151].

Blood glucose and total lipid levels were determined in Streptozotocin induced diabetic rats after oral administration of an ethanol flower extract of *Hibiscus rosa sinensis*. Ethanol flower extract possessed hypoglycemic effect after 7 and 21 days of oral administration of the extract. Maximal diminution in blood glucose (41-46%) was noticed after 21 days. The extract lowered the total cholesterol and serum triglycerides by 22 and 30%, respectively. HDL-cholesterol was much higher increased (12%) by the extract compared to glibenclamide (1%). The hypoglycemic activity of this extract is comparable to that of glibenclamide but is not mediated through insulin release [152].

The hypolipidemic activity of *Hibiscus rosa sinensis* root extract was studied in triton and cholesterol-rich high fat diet (HFD) induced models of hyperlipidemia in rats. Root extract (500 mg/kg body wt/day orally), possessed lipid-lowering effect , as assessed by reversal of plasma levels of total cholesterol (TC), phospholipids (PL) and triglycerides (TG) and reactivation of post-heparin lipolytic activity (PHLA) of plasma in triton model. The root extract (500 mg/kg body wt/ day orally) for 30 days also caused lowering of lipid levels in plasma and liver homogenate and reactivation of plasma PHLA and hepatic total lipoprotein lipase activity in cholesterol-rich high fat diet model [153-154] .

2.39. *Hibiscus sabdariffa*

The hypolipidemic effect of ethanolic extract of the leaves of *Hibiscus sabdariffa* (HSEE) (100, 200, and 300 mg/kg) was investigated in hyperlipidemic rats. Administration of HSEE (200 mg/kg and 300 mg/kg) together with continuous cholesterol feeding for four weeks showed significant reduction in serum cholesterol level by 18.5% and 22%, respectively ($p < 0.05$); serum triglyceride level by 15.6% and 20.6%, respectively ($p < 0.05$); serum LDL level by 24% and 30%, respectively ($p < 0.05$), and serum VLDL level by 15.5% and 20.5%, respectively ($p < 0.05$), as compared to cholesterol group. However, no significant change in HDL level was observed [155].

The effect of *Hibiscus sabdariffa* dried calyx ethanolic extract on the serum lipid profile was studied in Sprague-Dawley rats. The rats were fed during 4 weeks with either a basal diet, containing high cholesterol (1%), cholic acid (0.25%), lard oil (10%), or a supplemental diet with *Hibiscus sabdariffa* extract at 5%, 10%, and 15% levels (SD5, SD10, SD15). Weight gain and feces dry weight were both very significantly less ($p <or= 0.01$) in SD10 and SD15 groups as compared to the control group. Triacylglycerols and LDL levels were both significantly less ($p <or= 0.05$) in all groups (SD5, SD10, and SD15) as compared to the control. For total lipids, SD10 and SD15 showed significantly lower levels ($p <or= 0.05$), whereas very significant differences ($p <or= 0.01$) were observed in SD5 group. All groups had lower cholesterol levels compared to controls; however, only the SD5 group was statistically significant ($p <or= 0.05$) [156].

The effects of *Hibiscus sabdariffa* calyx aqueous extract on the serum cholesterol, body weight and liver marker enzymes activities were studied in normal albino rats. The aqueous extract was orally administered (100 – 800 mg/kg bw for 28 days) to normal male albino rats. *Hibiscus sabdariffa* administration significantly reduced serum cholesterol and body weight in a dose and duration dependent pattern [157].

The hypolipidemic and antiatherosclerotic effects of *Hibiscus sabdariffa* extract (HSE) were investigated in rabbits with experimental atherosclerosis. Rabbits were fed with a normal diet, high cholesterol (1.3%), lard oil (3%) diet (HCD) with or without 0.5 or 1% HSE for 10 weeks. The levels of triglyceride, cholesterol, and low-density lipoprotein cholesterol (LDL-C) were decreased in the serum of rabbits fed HCD plus HSE than in the serum of rabbits fed HCD. Feeding HSE (0.5 and 1% in the diet) to rabbits significantly reduced severe atherosclerosis in the aorta. Histopathological examination showed that HSE reduced foam cell formation and inhibited smooth muscle cell migration and calcification in the blood vessel of rabbits. These results suggest that HSE inhibits serum lipids and shows an antiatherosclerotic activity [158].

The antioxidant and antihyperlipidemic activities of the extracts of leaves and calyces of *Hibiscus sabdariffa* were investigated by studying in vitro inhibitory activity on lipid peroxidation and in vivo effects on cholesterol induced hyperlipidemia. Highest antioxidant activity was exhibited by ethanolic extract of calyces followed by ethanolic extract of leaves followed by aqueous extract of leaves of *Hibiscus sabdariffa* . In cholesterol induced hyperlipidemic model, the groups of rats treated with extracts of calyces and leaves of *Hibiscus sabdariffa* showed a significant decrease in the serum TC, LDL-C, VLDL-C, TAG values along with an increase in serum HDL-C levels. The treated groups also showed significant decrease in the atherogenic index, LDL-C: HDL-C risk ratios, and in the levels of SGOT, SGPT and ALP activities compared to cholesterol induced hyperlipidemic control group [159].

The effects of aqueous extract of *Hibiscus sabdariffa* (Hs) on body weight gain and its protective effects on the liver by improving lipid metabolism were studied in high fat diet-induced obese C57BL/6NHsd mice. Oral administration of the Hs extract reduced fat tissue accumulation, diminished body weight gain and normalized the glycemic index as well as reduced dyslipidemia compared to the obese mice group that did not receive Hs treatment. Hs treatment also attenuated liver steatosis, down-regulatedSREBP-1c and PPAR-γ, blocked the increase of IL-1, TNF-α mRNA and lipoperoxidation and increased catalase mRNA [160].

The effect of a standardized *Hibiscus sabdariffa* calyces aqueous extract on body weight was evaluated in an obese mice model induced by the administration of monosodium glutamate. *Hibiscus sabdariffa* aqueous extract was orally administered (120 mg/kg/day) for 60 days to healthy and obese mice. *Hibiscus sabdariffa* administration significantly reduced body weight gain in obese mice and increased liquid intake in healthy and obese mice. ALT levels were significantly increased on the 15th and 45th days in obese mice, but AST levels did not show significant changes. Triglycerides and cholesterol levels showed non-significant reductions in animals treated with *Hibiscus sabdariffa* [161].

Hibiscus sabdariffa water extract (HSE) treatment reduced fat accumulation in the livers of hamsters fed with fat diet (HFD) in a concentration-dependent manner. Administration of HSE reduced the levels of liver cholesterol and triglycerides, which were elevated by HFD. Analysis of the effect of HSE on paraoxonase 1, an antioxidant liver enzyme, revealed that HSE potentially regulated lipid peroxides and protects organs from oxidation-associated damage. The markers of liver damage such as serum alanine aminotransferase and aspartate aminotransferase levels that were elevated by HFD were also reduced on HSE treatment. The effects of HSE were as effective as treatment with anthocyanin; which indicated that anthocyanins present in the HSE may play a crucial role in the protection established against HFD-induced obesity [162-163].

The effect of *Hibiscus sabdariffa* L. (Hs) calyx extract on fat absorption-excretion and body weight was studied in rats. Rats were fed with either a basal diet (SDC = Control diet) or the same diet supplemented with Hs extracts at 5%, 10% and 15% (SD5, SD10 and SD15). Only SD5 did not show significant increases in weight, food consumption and efficiency compared to SDC. The opposite occurred in SD15 group which showed a significant decrease for these parameters. The SD10 responses were similar to SD15, with the exception of food consumption. In both SDC and SD5 groups, no body weight loss was observed; however, only in the latter group was there a significantly greater amount of fatty acids found in feces [164].

Hibiscus sabdariffa polyphenols (HPE) exhibited more potency to decrease plasma cholesterol and LDL cholesterol than the crude extract HSE, and increased HDL cholesterol dose-dependently. It decreased the lipid content of hepatocyte through the activation of AMPK and reduction of SREBP-1, thus inhibiting the expression of fatty acid synthase and HMG-CoA reductase. LDLR and LDL binding of HepG2 cells were enhanced when treated with HPE [165].

The effects of *Hibiscus sabdariffa* on adipogenic differentiation of 3T3-L1 cells were studied at the cellular and molecular levels. Hibiscus extract inhibited the adipocyte differentiation of 3T3-L1 preadipocytes induced by insulin, dexamethasone, and isobutylmethylxanthine (IBMX) in a dose-dependent manner. Hibiscus blocked the cytoplasmic lipid accumulation when administered at the onset of differentiation and 4 days after induction of differentiation. The inhibitory effect of hibiscus on adipogenic lipid accumulation of preadipocytes was significant (p < 0.01) between control cells and cells treated with hibiscus [166].

Hibiscus sabdariffa extract inhibits the adipocyte differentiation through the modulation of PI3-K/Akt and ERK pathway that play pivotal roles during adipogenesis [167].

The cholesterol-lowering potential of *Hibiscus sabdariffa* extract (HSE) was investigated in human subjects, a clinical study was conducted using an oral preparation of HSE capsules. The study consisted of 42 volunteers with a cholesterol level of 175 to 327 mg/dl. They were randomly divided into 3 groups: group I (1 capsule of HSE during each meal), group II (2 capsules), and group III (3 capsules). HSE caused significant decrease in serum cholesterol level in subjects from groups I and II after 4 weeks. HSEafter2 weeks, decreased serum cholesterol levels in all groups (*P* < .05 for groups I-III) compared with baseline values by 7.8% to 8.2%, while, a reduction in serum cholesterol level by 8.3% to 14.4%, was recorded after 4 weeks. The serum cholesterol level for 71% of group II volunteers was significantly lowered with a mean reduction of 12% (*P* < .05) [168].

In a sequential randomized controlled clinical trial, 60 patients with diabetes were randomly assigned into two groups: sour tea (*Hibiscus sabdariffa*, ST) and black tea (BT). They were instructed to consume sour tea or black tea two times a day for 1 month to investigate the hypolipidemic effects of sour tea in patients with diabetes and compare them with black tea. In the *Hibiscus sabdariffa* group, the mean of high-density lipoprotein-cholesterol (HDLc) increased

significantly (p = 0.002) at the end of the study, whereas changes in apolipoprotein-A1, and lipoprotein (a) were not significant. Also, a significant decrease in the mean of total cholesterol, low density lipoprotein-cholesterol, triglycerides, and Apo-B100 were seen in this group. In the BT group, only HDLc showed significant change (p = 0.002) at the end of the study, while, the changes in the other measures were not statistically significant [169].

A triple blind randomized placebo-controlled clinical trial was carried out to determine effects of *Hibiscus sabdariffa* (HS) calices on controlling dyslipidemia in 72 obese adolescents. They received 2 grams of fine powdered calices of *Hibiscus sabdariffa* per day for one month, while controls received placebo powder with the same dietary and physical activity recommendations and duration of exposure. Full lipid profile and fasting blood sugar were measured before and after the trial. In the *Hibiscus sabdariffa* calyces treated group, serum total cholesterol, low density lipoprotein cholesterol and serum triglyceride showed a significant decrease but high density lipoprotein cholesterol level was not changed significantly [170].

A clinical trial was carried out to confirm the metabolic-regulating and liver-protecting effect of *Hibiscus sabdariffa* extracts (HSE). Subjects with a BMI ≧ 27 and aged 18–65, were randomly divided into control and HSE-treated groups, for 12 weeks. The results revealed that consumption of HSE reduced body weight, BMI, body fat and the waist-to-hip ratio. Serum free fatty acids were also lowered by HSE. Anatomic changes revealed that HSE improved the illness of liver steatosis. Ingestion of HSE was well tolerated and there was no adverse effect during the trial [171].

A total daily dose of 100 mg of *Hibiscus sabdariffa* extract powder (HSEP) was orally administered in capsules for one month to determine its effect on lipid profiles of individuals with dyslipidemia associated with metabolic syndrome (MeSy).The MeSy patients treated with HSEP had significantly reduced glucose and total cholesterol levels, increased HDL-c levels, and an improved TAG/HDL-c ratio, a marker of insulin resistance (p<0.05). Furthermore, a triglyceride-lowering effect was observed in MeSy patients treated with HSEP plus diet, and in individuals without MeSy treated with HSEP. Significant differences in total cholesterol, HDL-c, and the TAG/HDL-c ratio were found when the means of absolute differences among treatments were compared (p<0.02) [172].

In a double blind, placebo controlled, randomized trial, sixty subjects with serum LDL values in the range of 130-190 mg/dl and with no history of coronary heart disease were randomized into experimental and placebo groups. The experimental group received 1 gm of the extract for 90 days, while the placebo received a similar amount of maltodextrin in addition to dietary and physical activity advice for the control of their blood lipids. Body weight, serum LDL cholesterol and triglyceride levels decreased in both groups, there were no significant differences between the experimental and placebo group. At a dose of 1 gm/day, *Hibiscus sabdariffa* leaf extract did not appear to have a blood lipid lowering effect [173-174].

2.40. *Jasminum sambac*

The anti-lipid peroxidation effect of *Jasminum sambac* was evaluated using the standard antioxidants BHT, Vitamin C, Vitamin E and Rutin. The methanolic extract of the *Jasminum sambac* flowers shows anti-lipid peroxidative effect which was similar to that of all standards [175].

The ethanolic extract of*Jasminum sambac*flowers was evaluated as the anti-obesity in an *in vitro* assay using pancreatic lipase enzymeand *in vivo* on high-fat diet-induced mice. The ethanolic extract of *Jasminum sambac* flowers at a dose 100 mg/kg and 300 mg/kg bw caused significant decrease of mice body weight, fat index, and food intake. In *in vitro* assay, the ethanolic extract of *Jasminum sambac* flowers inhibited pancreatic lipase enzyme activity [176-177].

2.41. *Juglans regia*

Diet supplemented with walnuts possessed beneficial effect on blood lipids, lowering blood cholesterol and lowering the ratio of serum concentrations of low density lipoprotein: high density lipoprotein by 12% [178].

In cross-sectional surveys, it appeared that high levels of HDL cholesterol and apo A1 were associated with a high amount of walnut consumption (oil and kernel) in the regular diet [179].

A randomized, double blind case-control study was conducted to evaluate the lipid-lowering effect of Persian walnut oil (encapsulated in 500 mg capsules, 3 g/day, for 45 days) in the population of southern Iran. Lipid profiles were checked before; on days 15, 30, and 45 after the beginning; and 15 days after termination of the study. Plasma TG concentrations decreased by 19% to 33% of baseline (p value < 0.05). No statistically significant change was observed in other measured parameters [180].

In a randomized, double-blind, placebo-controlled clinical trial, consumption of walnut oil by type 2 hyperlipidemic diabetic patients (15 ml Persian walnut oil)resulted in a significant decrease in total cholesterol levels (treatment difference (TD)=-30.04, P<0.001), triglyceride level (TD=-15.04, P=0.021), low-density lipoprotein level (TD=-30.44, P<0.001) and total cholesterol to high-density lipoprotein ratio (TD=-0.72, P<0.001) compared to the control group. There was an increase in the HDL level with consumption of walnut oil (TD=2.28, P=0.06). Frequency of patients reaching a LDL level below 100 was higher in the case group (20 vs 0%) [181].

The polyphenol of walnut (WP) was evaluated for its hypolipidemic effect in high fat diet fed mice. Oral administration of WP (100 and 200 mg/kg) significantly reduced liver weight and liver and serum triglycerides (TG). Hepatic beta-oxidation in cytosol, including peroxisome, was enhanced by WP (50-200 mg/kg). mRNA expressions of hepatic peroxisome proliferator-activated receptor (PPAR) alpha and acyl coenzyme A oxidase (ACOX) 1 were enhanced by WP (50-200 mg/kg). The mRNA expressions of PPARalpha, ACOX1, and carnitine palmitoyltransferase (CPT) 1A in HepG2 cells were significantly enhanced by addition of WP (100 microg/mL). Tellimagrandin I, a polyphenolic constituent in WP, enhanced ACOX1 expression at 1-100 microg/ml [182].

The walnut diet improved endothelium-dependent vasodilation and reduced levels of vascular cell adhesion molecule-1 (P<0.05). The walnut diet significantly reduced total cholesterol (-4.4±7.4%) and LDL cholesterol (-6.4±10.0%) (P<0.05) [183-184].

2.42. *Juniperus communis*

Juniperus communis was evaluated for the antidiabetic and antihyperlipidemic activity on Streptozotocin (STZ)-nicotinamide induced diabetic rats. The methanolic extract of *Juniperus communis* (100 and 200mg/kg bw) was administered orally in diabetic rats.The extract showed significant (P<0.01) reduction in blood glucose levels total cholesterol, triglyceride, LDL, VLDL, with elevation of HDL levels in diabetic rats. The effects were dose dependent [185].

Juniperus Communis Lynn (JCL) (50, 100, 200 mg/kg JCL oil for 30 days were given to hypercholesterolemic rats to determine their hypolipidemic effects. The administration of cholesterol increased the TC level significantly with a significant increase in Ox-LDL levels, but the administration of JCL together with cholesterol prevented these changes [186-187].

2.43. *Kochia scoparia (Bassia scoparia)*

The effect of ethanol extract of *Kochia scoparia* fruit was evaluated for prevention of obesity induced in mice by a high-fat diet for 9 weeks. The ethanol extract of *Kochia scoparia* fruit prevented the increases in body weight and adipose tissue weight induced by the high-fat diet. Consumption of a high-fat diet containing 1% or 3% *Kochia scoparia* extract significantly increased the fecal content and the fecal triacylglycerol level at day 3 compared with those in the high-fat diet group. The ethanol extract (250 mg/kg) and total saponins (100 mg/kg) of *Kochia scoparia* inhibited the elevation of the plasma triacylglyccerol level 2 or 3 h after the oral administration of the lipid emulsion. Total saponins, momordin Ic, 2'-O-beta-d-glucopyranosyl momordin Ic and 2'-O-beta-d-glucopyranosyl momordin IIc isolated from *Kochia scoparia* fruit inhibited the pancreatic lipase activity (in vitro) [188-189].

2.44. *Lallemantia royleana*

The hypolipidemic activities of *Lallemantia royleana* was studied in rabbits fed diets supplemented with cholesterol (0.5%) for 12 weeks to evoke hypercholesterolemia. Hypercholesterolemic rabbits were treated with different doses of whole *Lallemantia royleana* seeds (0, 5, 10, and 20%) for 12 weeks. The serum total cholesterol and triglyceride decreased in all groups treated with *Lallemantia royleana* seeds (p<0.05), however, *Lallemantia royleana* seeds increased of atherogenic index in all treated groups [190-191].

2.45. *Lawsonia inermis*

The hypoglycemic and hypolipidemic effects of *Lawsonia inermis* hydroalcoholic extract (100, 200 and 400 mg/kg) were studied in Alloxan induced diabetic dyslipidemia in rats. The percentage reduction in blood glucose level of *Lawsonia inermis* hydroalcoholic extract at dose of 400 mg/kg was 39.08% on day 21 compared to baseline, which was comparable to glibenclamide (44.77%) and metformin (46.30%). The hypoglycemic effect of the extract exhibited significant improvement in lipid profile, plasma albumin, total plasma protein and serum creatinine [192-194].

2.46. *Lepidium sativum*

The total cholesterol, triacylglycerol and alanine transaminase (ALT) activity were increased significantly in the rats fed with high cholesterol diet as compared to control group. *Lepidium sativum* reduced total cholesterol and ALT; however, higher dose (6 g/kg diet) was found better than lower dose (3 g/kg diet) in reducing serum triacylglycerol. Histopathological findings revealed that liver of cholesterol-treated rats showed varying degrees of vacuolar degeneration, fatty changes, fatty cysts, and lobular disarray. Livers of the *Lepidium sativum*- treated rats showed mild to moderate degree of recovery [195].

The effects of *Lepidium sativum* extract (20 mg/kg, orally for4 weeks) on the blood glucose and lipid profile were studied in hypercholesterolemic rats. *Lepidium sativum* treated group showed a significant lower value of plasma glucose 30%, cholesterol 22%, triglycerides 25%, LDL 23% and increase in HDL 32% [196-197].

2.47. *Linum usitatissimum*

The antihyperlipidemic effect of flax lignan concentrate was investigated in triton induced hyperlipidaemic rats. Triton (200 mg/kg, ip) significantly ($p < 0.001$) increased total cholesterol, triglyceride, very low density lipoprotein at 24 h and 48 h. Flax lignan concentrate showed dose dependant decrease in the total cholesterol, triglyceride and very low density lipoprotein, whereas, it increased high density lipoprotein cholesterol. Administration of triton alone increased both coronary risk index and low density lipoprotein and flax lignan concentrate and atorvastatin treatment decreased both the indices [198].

The effects of flaxseed oil consumption on serum lipids and lipoproteins were investigated in 34 hemodialysis patients using a randomized double-blinded controlled trial. The patients in the flaxseed oil group received 6 g/day of flaxseed oil for 8 weeks, whereas the control group received 6 g/day of medium chain triglycerides oil. Serum triglyceride concentration decreased significantly up to 23% in the flaxseed oil group at the end of week 8 compared to baseline, and the reduction was significant in comparison with the medium chain triglycerides oil group ($p < 0.01$). There were no significant differences between the two groups in the mean changes of serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and lipoprotein (a) [199].

The potential hypolipaemic and anti-atherogenic effects of linseed were studied in rabbits fed a hyper-cholesterolaemic diet (1 % cholesterol extracted from lyophilised egg). Group I, control group, andgroup II, fed a hypercholesterolaemic diet for 56 day and ground linseed was added from day 29 to day 56. Animals underwent aortic arch and descending aorta dissection on day 56 for histological, morphometric and immunohistochemical analysis. At the end of the experiment, group II showed lower levels of total cholesterol (TC, 10 068·3 vs. 16 767·0 mg/l; p< 0·05) and lower levels of LDL-cholesterol (LDL-C; 10 743·2 vs. 15 961·2 mg/l; p< 0·05) compared with the GI control group. There was no significant difference in serum HDL-cholesterol and TAG between the two groups. Almost all animals exhibited type III atherosclerotic lesions in the descending aorta. There was no statistically significant difference between the intima area and the intima: media layer area ratio in both groups. There was no difference between the positive areas for vascular cell adhesion molecule-1 and intercellular adhesion molecule-1 molecules between the groups [200].

The effects of dietary flaxseed on plasma cholesterol were studied in patients with clinically significant mild biomarkers of cardiovascular disease (CVD) and in those administered cholesterol-lowering medications, statins. Dietary flaxseed (foods that contained30 g of milled flaxseed) resulted in a 15% reduction in circulating LDL cholesterol as early as 1 month into the trial (P= 0.05). The concentration in the flaxseed group (2.1 ± 0.10 mmol/l) tended to be less than in the placebo group (2.5 ± 0.2 mmol/l) at 6 months (P= 0.12), but not at 12 months (P = 0.33). Total cholesterol also tended to be lower in the flaxseed group than in the placebo group at 1 month (11%, P= 0.05) and 6 months (11%, P = 0.07), but not at 12 months (P= 0.24). In a subgroup of patients taking flaxseed and statins, LDL-cholesterol concentrations were lowered by 8.5% ± 3.0% compared with baseline after 12 months, which differed from LDL-cholesterol concentrations in the placebo + statins subgroup, which increased by 3.0% ± 4.4% (P= 0.030) [201].

2.48. *Lippia nodiflora*

γ-sitosterol showed antihyperlipidemic activity as evidenced by significant decrease in serum total cholesterol, triglycerides and very low density lipoprotein-cholesterol levels coupled with elevation of high density lipoprotein-cholesterol levels in Streptozotocin (STZ) induced diabetic rats. A significant decrease in the activities of alanine aminotransaminase, aspartate aminotransaminase, alkaline phosphatase and acid phosphatase in γ-sitosterol treated rats were recorded compared to diabetic control rats which indicated its protective role against liver damage [202-203].

2.49. *Luffa acutangula*

The antidiabetic and antihyperlipidemic potentials of methanolic and aqueous extracts (100, 200 and 400 mg/kg, po) of *Luffa acutangula*(LA) fruits were studied in Streptozotocin (65 mg/kg, ip) and nicotinamide (120 mg/kg, ip) induce non-insulin dependent diabetes mellitus in rats. The methanolic extract at a dose of 100 mg/kg was found to be active (p< 0.05) but the antidiabetic activity was increased significantly (p< 0.01) at a dose of 200 and 400 mg/kg as compared to the aqueous extract, the methanolic extract also showed dose dependent pronounced (p<0.01) antihyperlipidemic activity in comparison with the aqueous extract [204-205].

2.50. *Lycium barbarum*

The hypolipidemic effects of powdered *Lycium barbarum* fruits (250 and 500 mg/kg) were studied in high fat diet-induced hyperlipidemia in rats. *Lycium barbarum* powdered extract showed a significant reduction in the total cholesterol, triglycerides and very low density lipoprotein-cholesterol levels at both doses employed (p< 0.05). However, reduction in low density lipoprotein-cholesterol levels was significant (p<0.05) only at the dose of 500 mg/kg when compared to the standard drug group. The increase in high-density lipoprotein levels was significant only at 250 mg/kg [206].

Polysaccharide fraction from *Lycium barbarum* (LBP) in addition to its hypoglycemic effect in diabetic mice, it also significant decrease total cholesterol and triglyceride[174].Basal diet supplemented with 10 and 20 g/kg bw dry wolfberry fruit powder for 4 weeks also decreased TG, TC, VLDL and VLDL and increased the mean values of HDL in diabetic rats [207].

The anthropometric and biochemical parameters in patients with metabolic syndrome were investigated after the consumption of goji berry. After 45 days of supplementation with goji berry a significant reduction in transaminases as well as an improvement in lipid profile was observed. A significant reduction in the waist circumference was also recorded with an increased glutathione and catalase levels associated with a reduction of lipid peroxidation [208].

2.51. *Mangifera indica*

The hypolipidemic effects of Vimang treatment were studied on risk factors of the atherosclerosis prone model of familial hypercholesterolemia. Mice were treated with Vimang during 2 weeks and were fed a cholesterol-enriched diet during the second week. The Vimang treated mice showed significantly reduced levels of plasma (15%) and liver (20%) cholesterol, increased plasma total antioxidant capacity (10%) and decreased reactive oxygen species (ROS) production by spleen mononuclear cells (50%) (P< 0.05). However, Vimang has protective effects on systemic and tissue-specific risk factors, but it was not sufficient to promote a reduction in the initial steps of atherosclerosis development [209].

Mangiferin (10 and 20 mg/kg, ip) showed significant antihyperlipidemic and antiatherogenic activities as evidenced by significant decrease in plasma total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C) levels, together with elevation of high-density lipoprotein cholesterol (HDL-C) level and diminution of atherogenic index in diabetic rats [210].

The anti-obesity effects of tea from *Mangifera indica* were studied in obese rats fed a high-fat diet (HFD). The consumption of *Mangifera indica* tea (24.7±2.1ml/day) exerted antioxidant and anti-inflammatory effects, increasing total antioxidant capacity and interleukin-1 serum concentrations, reduced abdominal fat accumulation, upregulated PPAR-γ and LPL and downregulated FAS expression. According to the results, *Mangifera indica* tea has therapeutic potential in treating obesity and related diseases through regulating the expression of transcriptional factors and enzymes associated with adipogenesis [211-212].

2.52. *Marrubium vulgare*

The hypocholesterolemic and hypotriglyceridemic activities of four *Marrubium vulgar* herb extracts were evaluated using Triton WR-1339-induced hyperlipidemia in mice. After, 7and 24 h intragastric administration of extracts, caused a significant decrease of plasma total cholesterol. Triglyceride levels were also significantly lowered by all extracts while petroleum ether extract produced the lowest decreasing level. Similar results were observed for LDL-cholesterol concentrations. Furthermore, the more polar extracts (methanol and ethyl acetate) showed a significant ameliorative action on elevated atherogenic index and LDL/HDL-C ratios, while these atherogenic markers were not statistically suppressed by the chloroform and petroleum ether extracts [213].

The aqueous extracts of *Marrubium vulgare* inhibited LDL oxidation and enhanced reverse cholesterol transport and can prevent cardiovascular diseases development. Incubation of LDL with the aqueous extracts of *Marrubium vulgare*

significantly prolonged the lag phase (P=0.014), lowered the progression rate of lipid peroxidation (P=0.004), reduced the disappearance of electrophoretic mobility in a dose-dependent manner. Furthermore, incubation of HDL with the aqueous extracts significantly increased HDL-mediated cholesterol efflux from THP-1 macrophages implicating an independent ATP binding cassette A1 (ABCA1) pathways [214-215].

2.53. *Melissa officinalis*

The hypolipidemic effect of ethanolic extract of *Melissa officinalis* (25, 50, and 75 mg/kg) was evaluated in rats with high-fat diet for 21 days. The amount of cholesterol, triglyceride and LDL were decreased significantly in the group receiving the extract compared to the model group (P<0.05) [216].

The hyperlipidemic effects of *Melissa officinalis* extract (orally, 2 g/kg/day, for 28 days) was studied in lipogenic diet (consisting of 2% cholesterol, 20% sunflower oil and 0.5% cholic acid) induced hyperlipidemic rats. Hyperlipidemic rats showed histological degenerative changes by light and electron microscopically, increase in the levels of serum cholesterol, total lipid, alanine transaminase, aspartate transaminase and alkaline phosphatase, decrease in the levels of liver tissue glutathione (GSH), increase in the levels of tissue lipid peroxidation. The extract reduced the total cholesterol, total lipid, liver enzymes levels, and lipid peroxidation levels in liver tissue and increased glutathione levels [217].

The hypolipidemic effects of *Melissa officinalis* essential oil were investigated in mice and lipid-loaded HepG2 cells. Plasma triglycerides were decreased significantly in mice orally administered essential oil (12.5 mg/d for 2 wk) than in the vehicle-treated group. Cellular triglycerides and cholesterol concentrations were also significantly decreased in a dose- (400 and 800 mg/l) and time- (12 and 24 h) dependent manner in HepG2 cells stimulated with essential oil compared with controls. Essential oil feeding altered several lipid metabolic pathways, including bile acid and cholesterol synthesis and fatty acid metabolism in mice. In HepG2 cells, the rate of fatty acid oxidation was unaltered; however, the rate of fatty acid synthesis was significantly reduced by treatment with 400 and 800 mg/l essential oil, due to the decreased expression of sterol regulatory element-binding protein-1c (SREBP-1c) and its responsive genes in fatty acid synthesis, including FAS, SCD1, and ACC1 [218].

The effects of *Melissa officinalis* alcohol extract (25 mg/kg, 50, and 75 mg/kg, ip) on the activity of liver enzymes were studied in fatty diet induced hyperlipidemic rats. At the end of 21-daytreatment period, the activity of liver enzymes and cholesterol in the group received the extract were decreased significantly [219].

3. Conclusion

Hyperlipidemia refers to elevated levels of lipids and cholesterol in the blood. It plays an important role in the development of atherosclerosis, the main cause of death in the world. Many recent studied confirmed the experimental and clinical efficacy and safety of medicinal plants in the treatment of hyperlipidemia. The current review was designed to introduce some promising medicinal plants effective in the prevention or treatment of hyperlipidemia.

Compliance with ethical standards

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