

# Medicinal Plants Used for the Treatment of Hyperlipidemia by Traditional Practitioners in Kabul City, Afghanistan

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## ABSTRACT

Hyperlipidemia, which is characterized by an increase in the total amount of cholesterol, triglycerides and phospholipids of the plasma than its normal level is one of the main components of metabolic syndrome caused by various factors. As the capital of Afghanistan, Kabul city has an ancient history of employing traditional practices and usage of medicinal plants (MPs) for the management of various diseases. However, there is no sufficient documented data regarding the application of traditional medicine including phytotherapy for the treatment of hyperlipidemia. Therefore, the main purpose of this research was to identify and to introduce MPs used for the treatment of hyperlipidemia by traditional practitioners (TPs) in Kabul city. The study was a field research conducted on the months of July and August 2020. Kabul city was selected as the field of study. Cross-sectional convenience sampling was used for data collection. The required information was randomly collected from eight districts of Kabul city and accepted as sample. TPs were selected as participants and interviewed using pre-prepared questionnaires. The result of the study showed that 18 MPs were used by TPs for the treatment of hyperlipidemia in Kabul city. The effectiveness of MPs used to treat hyperlipidemia by TPs in Kabul city, in most of the cases, matches the rational phytotherapy. However, further studies are needed to ensure the identity, purity, quality and uniformity of MPs and their recommended dosage forms throughout the city. The unavailability of herbal-treated lipid profile data of patients suffering from hyperlipidemia who visited TPs for treatment purpose was the main limitation of this study.

**Keywords:** Hyperlipidemia, Medicinal Plants, Traditional Medicine, Safety, Standardization.

## INTRODUCTION

Hyperlipidemia, which is characterized by an increase in the total amount of cholesterol, triglycerides (TGs) and phospholipids (PLs) of the plasma than its normal level is one of the main components of metabolic syndrome caused by various factors. According to the guidelines of the National Cholesterol Education Program (NCEP), the cholesterol level higher than 240 mg/dL in adults is called hyperlipidemia. For children, this limit is less than 180 mg/dL [1].

Major blood lipids include chylomicrons, very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL). Hyperlipidemia is one of the main causes of atherosclerosis and related disorders such as; ischemic cerebrovascular diseases, coronary heart diseases and peripheral vascular diseases. The relationship between high plasma lipid levels and the development of atherosclerotic plaques is well established [2]. Atherosclerotic plaques may lead to occurrence of ischemic heart disease and acute coronary syndromes [3]. Epidemiological evidence shows that by reducing the level of TGs to approximately 150 mg/dL, the risk of cardiac diseases decreases [4].

Hyperlipidemia is divided into primary and secondary types. Primary hyperlipidemia is usually caused by genetic impairments and mutations, and secondary hyperlipidemia is acquired. The most common causes of acquired hyperlipidemia include nephrotic syndrome, chronic alcoholism, and medicines used in the treatment of myxoedema, diabetes, corticosteroids, oral contraceptives, and beta blockers [5].

Hyperlipidemia is an important risk factor in the initiation and progression of atherosclerosis. Therefore, the most important point for its treatment is to lower the plasma lipids' level [6]. The statins, cholesterol absorption inhibitors, fibrates, niacin, bile acids-binding resins, and omega-3 fatty acids are generally used for the treatment of hyperlipidemia [7].

The use of synthetic therapeutic agents for the treatment of various diseases, including hyperlipidemia, may cause various side effects. Myopathy, Rhabdomyolysis, increased levels of aminotransferase and creatine kinase (adverse effects of statins); impaired absorption of fat-soluble vitamins, hypernatremia, hyperchloremia, obstruction of the digestive system, and reduction of the bioavailability of acidic drugs and iron (adverse effects of bile acids-binding resins); digestive problems, dizziness, redness and skin rashes, increased formation of gallstones, myositis

syndrome, myalgia, weakness, increased level of creatine kinase and aspartate aminotransferase and synergistic effects with the oral anticoagulants (adverse effects of fibrates); hyperuricemia, hyperglycemia (adverse effects of niacin); thrombocytopenia and bleeding disorders (adverse effects of Omega-3 supplements) are some obvious examples of side effects caused by the consumption of different groups of synthetic anti-hyperlipidemic drugs [1,8].

Hyperlipidemia and atherosclerosis are the main causes of heart disease and mortality in most of the countries, both developed and developing. Afghanistan is one of the developing countries in Asia, where more than half of its population is poor. Poverty, illiteracy, unavailability and unaffordability of a healthy diet for the majority of people, inaccessibility of primary health care centers, and stressful living environment have caused various health problems including cardiovascular diseases (CVDs), high blood pressure, hyperlipidemia, diabetes among the residents of the country [9].

Dissatisfaction of hyperlipidemic patients with the use of common lipid-lowering drugs, the occurrence of side effects due to the excessive and long-term use of anti-hyperlipidemic medications, diseases caused by abnormal increase in the level of plasma lipids and the costs imposed on patients, the effectiveness of natural products in reducing blood lipids' level, safety, reasonable price and accessibility of these alternatives have caused most people to use MPs and other traditional preparations to control and treat hyperlipidemia. Recent studies on MPs used in traditional medicine indicates that presence of certain phytoconstituents such as flavonoids, sterols and other antioxidant compounds not only reduce the level of serum lipids but also inhibit the oxidation of LDL and consequently remove reactive oxygen species (ROS). In addition, these phytoconstituents may affect immune system and improve the body's overall strength that is more likely effective for the management of hyperlipidemia [10,11].

Considering the high prevalence of CVDs in the country, the importance of hyperlipidemia as the main risk factor for the occurrence and progression of CVDs, and the preference of patients to use natural remedies for the treatment of various health problems including hyperlipidemia a decision was made to investigate the use of MPs for the treatment of hyperlipidemia in different districts of Kabul city, one of the most populated provinces of the country. The main purpose of this research was to introduce MPs used in the treatment of hyperlipidemia by TPs in different districts of Kabul city, Afghanistan.

## Aims and Objectives

This research aimed to investigate the traditional phytotherapy for the control and treatment of hyperlipidemia employed by TPs across the different districts of Kabul city. In most specific words, the main objective of the study was: to introduce MPs and their recommended preparations used for the treatment of hyperlipidemia by TPs in different districts of Kabul city, Afghanistan.

## METHOD

The study was a field research conducted on the months of July and August 2020. Kabul city was selected as the study area. Cross-sectional convenience sampling was used to collect data. The required information was randomly collected from eight districts; including the first (Mandawi, Bagh-e-Qazi, Sar-e-Chawk), the third (Pol-e-Surkh), the fifth (Mirwais maidan, Afshar), the sixth (Pol-e-Sokhta, Alauddin), the seventh (Chehlseton, Dehmazang), the tenth (Taimani), the thirteenth (Pol-e-Khoshk, Naqash, Tank-e-Tel), and the eighteenth (Sorkhabad) districts of Kabul city and was accepted as sample. TPs were selected as participants and interviewed using pre-prepared questionnaires. The prepared questionnaires included the information regarding the demographic

characteristics of TPs, the type of MPs used for the treatment of hyperlipidemia by TPs, the MPs parts used for the treatment of hyperlipidemia and their methods of preparations, the reasons for using herbal medicine for the treatment of hyperlipidemia and some other general questions. The main limitation of this study was unavailability of pre- and post-herbal treated lipid profile data of patients suffering from hyperlipidemia who visited TPs for the treatment purpose.

## RESULT

In order to investigate the MPs used for the treatment of hyperlipidemia, a total of 80 pre-prepared questionnaires were distributed among the participants (TPs) in Kabul city. Totally, 48 TPs were surveyed. The participated TPs were aged between 25-55 years old and most of them had primary education.

The result of this research showed that TPs of different districts (the first, third, fifth, sixth, seventh, tenth, thirteenth, eighteenth districts) of Kabul city have used a total of 18 MPs for the treatment of hyperlipidemia. The used MPs along with their scientific and local names, plant families, parts used and method of preparations are summarized in Table 1.

**Table 1.** List of MPs used for the treatment of hyperlipidemia by TPs in different districts of Kabul city (researcher)

No.	Scientific Name	Local Name	Plant Family	Part Used	Method of Preparation
1	<i>Anethum graveolens</i> L.	Shebet	Apiaceae	Fruits, Herb	Infusion, Decoction
2	<i>Berberis</i> sp.	Zereshk	Berberidaceae	Fruits	Dried fruits
3	<i>Carum carvi</i> L.	Zira-e-sia	Apiaceae	Fruits	Infusion
4	<i>Cassia angustifolia</i> M. Vahl	Sanna-i-makki	Fabaceae	Leaves	Decoction
5	<i>Cichorium intybus</i> L.	Kasni	Asteraceae	Root, Leaves	Dried form, Infusion
6	<i>Citrus aurantium</i> L. var. <i>amara</i> Engl.	Narenj	Rutaceae	Leaves	Decoction
7	<i>Descurainia Sophia</i> (L.) Webb ex Prantl	Khakshir	Brassicaceae	Seeds	Mixture
8	<i>Ephedra</i> sp.	Bandak	Ephedraceae	Herb	Infusion
9	<i>Hibiscus sabdariffa</i> L.	Chai Makka	Malvaceae	Flowers	Infusion
10	<i>Olea europaea</i> L.	Zaitoon	Oleaceae	Fruits, Leaves	Fresh form, Decoction
11	<i>Stachys lavandulifolia</i> Vahl	Chai-e-kohi	Lamiaceae	Flowers	Infusion
12	<i>Terminalia chebula</i> Retz.	Halila-e-zard	Combretaceae	Fruit	Mixture
13	<i>Thymus</i> sp.	Awishan	Lamiaceae	Leaves and ers	Fresh form
14	<i>Trigonella foenum-graecum</i> L.	Shanbalila	Fabaceae	Seeds	Fresh and Dried forms
15	<i>Urtica dioica</i> L.	Atashak, Gazana	Urticaceae	Whole plant	Fresh and Dried forms, Decoction
16	<i>Vitis vinifera</i> L.	Angoor-e-sia	Vitaceae	Fruits	Fresh and Dried fruits
17	<i>Zingiber officinale</i> Roscoe	Zanjabil	Zingiberaceae	Rhizome	Fresh form, Powdered
18	<i>Ziziphus jujuba</i> Mill.	Onab	Rhamnaceae	Fruits	Dried fruits, Decoction

## DISCUSSION

Hyperlipidemia is an abnormal increase in the level of serum lipids (total cholesterol, TGs, IDL, VLDL, and LDL), which is responsible for the development and progression of various diseases such as CVDs, stroke, arteriosclerosis, etc. This study has introduced 18 types of MPs used by TPs of Kabul city for the treatment of hyperlipidemia. Existing scientific researchers have proven the anti-hyperlipidemic properties of these plants.

The therapeutic effects of *A. graveolens* have been compared with cholestyramine, nicotinic acid and gemfibrozil in patients with high level of serum lipid. The result showed that the lipid lowering effect of *A. graveolens* is not much different from the selected synthetic alternatives. However, *A. graveolens* had greater effect to reduce cholesterol level with lower effect on TGs and HDL compared to gemfibrozil. No side effects have been reported after taking the preparations of *A. graveolens*, but several problems including digestive system discomfort, increased risk of gallstone production, etc. have been recorded after usage of gemfibrozil [12]. The results of clinical studies have shown that the consumption of products containing the fruit and herb of *A. graveolens* in patients suffering from hyperlipidemia and hyperlipoproteinemia (high blood cholesterol and TGs) after two weeks reduced the amount of VLDL and LDL [12]. D-limonene, one of the main phytoconstituents present in the EO of *A. graveolens* fruit is an excellent solvent for cholesterol. This compound has been used clinically to dissolve gallstones containing cholesterol [13]. The plant crude extract can reduce lipid peroxidation in the liver and improve the activity of antioxidant enzymes in rats fed high-fat diet [14]. Using the ethanolic extract of *A. graveolens* at a daily dose of 1 ml (equivalent to 500 mg of herbal powder) for 10 to 30 days has caused a decrease in the serum lipid level in rats. In addition, a significant increase in the secretion of HMG-COA mevalonate in mice has been observed after treatment with ethanolic extract of plant for 30 days [15].

TPs have recommended *Berberis sp.* for the treatment of hyperlipidemia. Berberine is one of the most important alkaloids of the plant, which may be effective to prevent coronary disease and to reduce cholesterol and TGs levels. Berberine lowers the cholesterol level in a different mechanism than statins, so if used simultaneously with statins, it seems to control cholesterol level more effectively [16]. Berberine up-regulates the expression of specific type of receptor in the liver, which can bind to cholesterol and facilitate its excretion [17]. Moreover, there are other possible mechanisms

by which berberine can reduce the level of serum lipids including increasing mRNA of LDLR, LDLR protein of liver, phosphorylation and activation of adenosine monophosphate and protein kinase [18].

*C. carvi* exerts its anti-hyperlipidemic effects by reducing the biosynthesis of cholesterol, especially through reducing the activity of the enzyme HMG-CoA reductase or the level of NADPH required for cholesterol synthesis [19]. In addition, the fruits of plant may alleviate hypercholesterolemia by modifying the metabolism of lipoproteins, LDL absorption through up-regulation of LDL receptors, or by increasing the activity of lecithin cholesterol acyltransferase [19]. *C. carvi* may facilitate rapid LDL catabolism. Repeated administration of *C. carvi* fruits for 15 days has significantly decreased plasma TGs in normal diabetic rats [19].

The hypolipidemic activity of ethanolic extract of *C. angustifolia* in Triton X 100 induced hyperlipidemia in rats has been evaluated. The result showed that usage of 400 mg/kg of plant extract significantly lowers serum lipids level [20]. In the other study it was reported that short term treatment with hydroalcoholic extract of *C. angustifolia* significantly reduced the level of cholesterol, TGs, LDL-C and increased HDL-C in hyperlipidemic rats [21].

The use of *C. intybus* in traditional medicine has a long history. Ancient Egyptians had used it to treat CVDs and strengthen liver function. Studies have shown that the inulin of the plant has TGs lowering effects [22]. Inulin extracted from *C. intybus* reduces blood uric acid and TGs by regulating the level of acetyl CoA [23].

Anti-hyperlipidemic activities of many *Citrus sp.* including *C. aurantium* have documented [24]. The result of in-vivo experiments has shown that neohesperidin (NHP) derived from *C. aurantium*. significantly decreased serum TGs, total cholesterol, leptin level, and liver index in the KK-A(y) diabetic mice. In addition, inhibition of lipid accumulation in the liver and decreased size of epididymal adipocyte have been seen in the KK-A(y) mice after administration of NHP, which are due to modification in gene expression of fatty acid synthase (FAS), stearoyl-CoA desaturase 1 (SCD-1) and acyl-CoA oxidase (ACOX) [25].

The findings of several studies have shown that administration of extract of *E. sinica* Stapf can reduce the level of cholesterol, TGs, LDL and increase HDL level [26,27].

The aqueous and ethanolic extracts of *H. sabdariffa* flowers

and leaves prevent the oxidation of LDL and macrophages [28,29]. *H. sabdariffa* reduces the formation of foam cells and inhibits smooth muscle cell contractions, which helps to slow down the progression of atherosclerosis [30].

In the study on mice fed with high-fat diet, it was found that treatment with *O. europaea* leaf extract reduced the level of serum lipids (total cholesterol, LDL, and TGs), which is attributed to the increase in the antioxidant enzymes, catalase and superoxide dismutase [31].

The hypocholesterolemic effect of *T. chebula* fruit in mice fed with atherogenic diet has been evaluated. The oral administration of powdered fruit decreased the body weight, serum total cholesterol, TGs, thickening of the walls of aorta and shrinkage in aorta lumen of treated rats [32]. In addition, rats receiving treatment with *T. chebula* have shown increased level of HDL. It has been observed that the plant has an excellent lipid-lowering activity at concentrations of 1.05- 2.10 mg/kg body weight [33].

It has been stated that the anti-hyperlipidemic and cholesterol lowering activities of *Thymus sp.* is due to the effect of carvacrol on HMG-COA reductase, which can reduce the lipid absorption from the gut or decrease the lipid catabolism for the gluconeogenesis [34].

The seeds of *T. foenum- graecum* have been used by TPs in different districts of Kabul city to treat hyperlipidemia. It has been reported that *T. foenum- graecum* with a dose of 2.5 grams per day for three months has reduced total cholesterol and TGs in patients suffering from coronary artery diseases with and without type II diabetes and had no effect on HDL [35]. The exact mechanism of anti-hyperlipidemic effect of *T. foenum- graecum* is not yet clear. However, it is thought that the herbal preparations of the plant inhibit the absorption of cholesterol from the gut due to the formation of saponin and cholesterol complex [36].

*U. dioica* is a potent anti-hyperlipidemic plant, which can reduce the level of lipids and lipoproteins in the blood. Administration of plant aqueous extract at a dose of 150 mg/kg for 30 days in rats fed with a normal or high-fat diet has improved blood lipid profile [37]. The herbal preparations containing *U. dioica* have decreased serum total cholesterol, TGs and LDL, while increasing HDL in an animal model of polycystic ovary syndrome (PCOs). It seems that the continuous consumption of aqueous and petroleum ether extracts of *U. dioica* significantly affect blood lipid profile and directly

influence the synthesis and metabolism of lipoproteins [38]. It has also been found that *U. dioica* lowers blood TGs level, and its root reduces the activity of HMG-COA reductase, thereby reducing LDL levels in rats [39].

Recent studies have shown that the seed extract of *V. vinifera* significantly reduces plasma cholesterol levels in rabbits fed a high-cholesterol diet. Long-term use of plant seed extract may decrease plasma lipids by inhibiting the activity of pancreatic lipase, cholesterol esterase, and binding of bile acids [40].

Researchers conducted on diabetic animals have shown that *Z. officinale* significantly lowers serum total cholesterol, LDL, VLDL, TGs and phospholipids and reduces the risk of atherosclerosis. *Z. officinale* acts on the liver to reduce cholesterol biosynthesis and may stimulate the conversion of cholesterol into bile acids and increase its excretion [41]. *Z. officinale* has shown anti-hypercholesterolemic properties in rats fed with high cholesterol diet, which is due to its ability to inhibit angiotensin-converting enzyme (ACE). In addition, the activity of the liver hydroxylase enzyme has increased after consumption of the plant-containing products, which plays an important role in converting cholesterol to bile acids [42].

Studies have shown that consumption of 64 mg/kg per day fruit of *Z. jujuba* for 20 days can reduce total cholesterol and LDL levels and increase HDL in rats fed with natural diet [43]. The hydroalcoholic extract of the plant leaves at doses of 200, 400 and 600 mg/kg for 125 days lowers body weight, LDL, VLDL, TGs and increases HDL levels [44]. *Z. jujuba* inhibits intrahepatic production of bile, and increases hepatic synthesis of bile acids [45].

TPs have used *D. sophia* and *S. lavandulifolia* for the treatment of hyperlipidemia. There are some evidences showing LDL-lowering effects of *D. sophia* in cardiovascular patients with high LDL cholesterol [46]. However, more researches are needed to prove anti-hyperlipidemic effects of the plant. Anti-oxidative stress activity of *S. lavandulifolia* aqueous extract in human has been reported [47]. In order to ensure the effectiveness of plant and its preparations to treat hyperlipidemia, more studies are required.

## CONCLUSION

Hyperlipidemia is a prevalent disease and one of the components of metabolic syndrome caused by various factors. The main goal of treatment in hyperlipidemic patients is to reduce the risk of ischemic heart disease or the occurrence of other cardiovascular or cerebrovascular disorders. The results of

this study revealed that 18 MPs are used by TPs of Kabul city for the treatment of hyperlipidemia. The effectiveness of reported MPs for the treatment of hyperlipidemic have documented by the scientific studies, in most of the cases. However, to ensure the safety, interactions, efficacy, and rational use of MPs used for the treatment of hyperlipidemic, especially in the cases of *Ephedra sp.*, *D. sophia* and *S. lavandulifolia* extensive studies should be done. As MPs have a plethora of phytochemicals with different bioactivities, so it is important to rely on evidence-based findings not just empirical therapies. Moreover, establishment of successful treatment report is highly relied on the presence of clinical data showing the total lipid profile, both pre- and post-treatment, of hyperlipidemic patients visited TPs for the treatment purpose. There are some drawbacks for the usage of MPs and many herbal products to manage several chronic diseases including hyperlipidemia. As so many factors may affect the achievements or failures of traditional practices.

#### RECOMMENDATIONS

- Further researches is required to ensure the identity, purity, quality and uniformity of MPs used for the treatment of hyperlipidemia by TPs and their recommended dosage forms throughout the city.
- In order to document and report the effectiveness of MPs and the herbal products for the management of hyperlipidemia, the follow up practices are highly recommended.
- Although, the lipid lowering activities of *Ephedra sp.* extracts has established by several studies; it is recommended to use these preparations under the supervision of specialist.
- More studies are needed to reveal the anti-hyperlipidemic effects of *D. sophia* and *S. lavandulifolia*.
- In order to establish the rational usage of MPs for the treatment of various health concerns including hyperlipidemia, the general understandings of the people should be addressed.

#### REFERENCES

1. Dhaliya SA, Surya AS, Tomy DV, Carla B, Kumar AR, Christudas S. (2013). a review of hyperlipidemia and medicinal plants. *Int J APS BMS*. 2(4):19-237.
2. Feingold KR. (2024). Introduction to Lipids and Lipoproteins. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, et al. (Eds.). South Dartmouth (MA): MDText.com, Inc. 2000.
3. Bergheanu SC, Bodde MC, Jukema JW. (2017). Pathophysiology and treatment of atherosclerosis. *Neth Heart J*. 25(4):231-242.
4. Koo BK, Park S, Han KD, Moon MK. (2021). Hypertriglyceridemia Is an Independent Risk Factor for Cardiovascular Diseases in Korean Adults Aged 30-49 Years: a Nationwide Population-Based Study. *J Lipid Atheroscler*. 10(1):88-98.
5. Hill MF, Bordoni B. (2023). Hyperlipidemia. *Treasure Island (FL): Stat Pearls*. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK559182/>.
6. Li B, Li W, Li X, Zhou H. (2017). Inflammation: A Novel Therapeutic Target/Direction in Atherosclerosis. *Curr Pharm Des*. 23(8):1216-1227.
7. Schaiff RA, Moe RM, Krichbaum DW. (2008). An Overview of Cholesterol Management. *Am Health Drug Benefits*. 1(9):39-48.
8. Link N, Tanner M. (2001). Hyperlipidemia: Part 2. Pharmacologic management. *West J Med*. 175(6):396-401.
9. Peltzer K, Pengpid S. (2021). Cardiovascular diseases among adults in Afghanistan: Prevalence and associated factors from a national household survey in 2018. *Popul Med*. 3:1-8.
10. Duan H, Song P, Li R, Su H, He L. (2023). Attenuating lipid metabolism in atherosclerosis: The potential role of Anti-oxidative effects on low-density lipoprotein of herbal medicines. *Front Pharmacol*. 14:1161657.
11. Niknafs A, Rezvanfar M, Kamalinejad M, Latifi SA, Almasi-Hashiani A, Salehi M. (2021). The Effect of a Persian Herbal Medicine Compound on the Lipid Profiles of Patients with Dyslipidemia: A Randomized Double-Blind Placebo-Controlled Clinical Trial. *Evid Based Complement Alternat Med*. 2021:6631963.
12. Mirhosseini M, Baradaran A, Rafeian-Kopaei M. (2014). Anethum graveolens and hyperlipidemia: A randomized clinical trial. *J Res Med Sci*. 19(8):758-761.

13. Sun J. (2007). D-Limonene: safety and clinical applications. *Altern Med Rev.* 12(3):259-264.
14. Jana S, Shekhawat GS. (2010). *Anethum graveolens*: An Indian traditional medicinal herb and spice. *Pharmacogn Rev.* 4(8):179-184.
15. Yazdanparast R, Bahramikia S. (2008). Evaluation of the effect of *Anethum graveolens* L. crude extracts on serum lipids and lipoproteins profiles in hypercholesterolaemic rats. *DARU Journal of Pharmaceutical Sciences.* 16(2):88-94.
16. Kong W, Wei J, Abidi P, Lin M, Inaba S, Li C, et al. (2004). Berberine is a novel cholesterol-lowering drug working through a unique mechanism distinct from statins. *Nat Med.* 10(12):1344-1351.
17. Li XY, Zhao ZX, Huang M, Feng R, He CY, Ma C, et al. (2015). Effect of Berberine on promoting the excretion of cholesterol in high-fat diet-induced hyperlipidemic hamsters. *J Transl Med.* 13:278.
18. Cai Y, Yang Q, Yu Y, Yang F, Bai R, Fan X. (2023). Efficacy and underlying mechanisms of berberine against lipid metabolic diseases: a review. *Front Pharmacol.* 14:1283784.
19. Lemhadri A, Hajji L, Michel JB, Eddouks M. (2006). Cholesterol and triglycerides lowering activities of caraway fruits in normal and streptozotocin diabetic rats. *J Ethnopharmacol.* 106(3):321-326.
20. Nanumala SK, Nischal Y, Sarika M, Shravva GS. (2014). Hypolipidemic activity of ethanolic extracts of *cassia angustifolia* in triton- X 100 induced hyperlipidemia in Rats. *Asian Journal of Pharmaceutical and Clinical Research.* 7:189-191.
21. Karajibani M, Montazerifar F, Eslahi H, Yarmand S, Miri M, Naghizadeh M. (2023). The Effect of Hydroalcoholic Extract of *Senna* (*Cassia Angustifolia* Vahl.) on Lipid Profiles in Hyperlipidemic Rats. *JNFS.* 8(1):1-8.
22. SOCACI, M. V., MUDURA, E., COLDEA, T. E., & SALANTA, L. (2019). Therapeutic Properties of *Cichorium Intybus* L. Roots in Liver Diseases, Diabetes and Hypercholesterolemia. *Hop and Medicinal Plants.* 27(1-2).
23. Lin Z, Zhang B, Liu X, Jin R, Zhu W. (2014). Effects of chicory inulin on serum metabolites of uric acid, lipids, glucose, and abdominal fat deposition in quails induced by purine-rich diets. *J Med Food.* 17(11):1214-1221.
24. Mallick N, Alam Khan R. (2016). Antihyperlipidemic effects of *Citrus sinensis*, *Citrus paradisi*, and their combinations. *J Pharm Bioallied Sci.* 8(2):112-118.
25. Jia S, Hu Y, Zhang W, Zhao X, Chen Y, Sun C, et al. (2015). Hypoglycemic and hypolipidemic effects of neohesperidin derived from *Citrus aurantium* L. in diabetic KK-A(y) mice. *Food Funct.* 6(3):878-886.
26. Fan Y, Li J, Yin Q, Zhang Y, Xu H, Shi X, et al. (2015). Effect of extractions from *Ephedra sinica* Stapf on hyperlipidemia in mice. *Exp Ther Med.* 9(2):619-625.
27. Mohammad S, Masoumeh H, Gholamali J, Hoda T. (2017). Ephedraceae as a Treatment for Hyperlipidemia and Hyperglycemia: An Experimental Study. *Journal of Autoimmune Disorders.* 3(3):36.
28. Sabzghabae AM, Ataei E, Kelishadi R, Ghannadi A, Soltani R, Badri S, et al. (2013). Effect of *Hibiscus sabdariffa* Calices on Dyslipidemia in Obese Adolescents: A Triple-masked Randomized Controlled Trial. *Mater Sociomed.* 25(2):76-79. (Sabzghabae, et al., 2013)
29. Gosain S, Ircchiaya R, Sharma PC, Thareja S, Kalra A, Deep A, et al. (2010). Hypolipidemic effect of ethanolic extract from the leaves of *Hibiscus sabdariffa* L. in hyperlipidemic rats. *Acta Pol Pharm.* 67(2):179-184
30. Ali BH, Al Wabel N, Blunden G. (2005). Phytochemical, pharmacological and toxicological aspects of *Hibiscus sabdariffa* L.: a review. *Phytother Res.* 19(5):369-375.
31. Sindi HA. (2020). Evidence that supports the antidiabetic, antihypertensive, and antihyperlipidemic effects of olive (*Olea europaea* L.) leaves extract and its active constituents (oleuropein) in human. *J Biochem Tech.* 11(2):41-45.
32. Rathore HS, Soni S, Bhatnagar D. (2004). Hypocholesterolemic effect of *Terminalia chebula* fruit (Myrobalan) in mice. *Anc Sci Life.* 23(4):11-15.
33. Maruthappan V, Shree KS. (2010). Hypolipidemic activity of haritaki (*terminalia chebula*) in atherogenic diet induced hyperlipidemic rats. *J Adv Pharm Technol Res.* 1(2):229-235.

34. Adam A, Elsayed AH, Shihata S, Abd El-hady AM. (2020). Effect of Thyme (*Thymus Vulgaris*) on Productive Performance, Carcass Characteristics, Blood Hematology and Lipid Profile of Broiler Chicks of Broiler Chicks. *Egypt Poult Sci.* 40(III):715-727.
35. Yadav UC, Baquer NZ. (2014). Pharmacological effects of *Trigonella foenum-graecum* L. in health and disease. *Pharm Biol.* 52(2):243-254.
36. Al-Asadi JN. (2014). Therapeutic Uses of Fenugreek (*Trigonella foenum-graecum* L.). *Am J Soc Issues Hum.* 2:21-36.
37. Joshi B, Mukhija M, Kalia A. (2014). Pharmacognostical review of *Urtica dioica* L. *International Journal of Green Pharmacy.* 8(4):201-209.
38. Namazi F, Shomali T, Taghikhani P, Nazifi S. (2018). Protective effect of *Urtica dioica* leaf hydro alcoholic extract against experimentally-induced atherosclerosis in rats. *Avicenna J Phytomed.* 8(3):254-262.
39. Amiri Behzadi A, Kalalian-Moghaddam H, Ahmadi AH. (2016). Effects of *Urtica dioica* supplementation on blood lipids, hepatic enzymes and nitric oxide levels in type 2 diabetic patients: A double blind, randomized clinical trial. *Avicenna J Phytomed.* 6(6):686-695.
40. Adisakwattana S, Moonrat J, Srichairat S, Chanasit C, Tirapongporn H, Chanathong B, et al. (2010). Lipid-Lowering mechanisms of grape seed extract (*Vitis vinifera* L) and its antihyperlipidemic activity. *Journal of Medicinal Plants Research.* 4(20):2113-2120.
41. Nicoll R, Henein MY. (2009). Ginger (*Zingiber officinale* Roscoe): a hot remedy for cardiovascular disease? *Int J Cardiol.* 131(3):408-409.
42. Mohd Sahardi NFN, Makpol S. (2019). Ginger (*Zingiber officinale* Roscoe) in the Prevention of Ageing and Degenerative Diseases: Review of Current Evidence. *Evid Based Complement Alternat Med.* 2019:5054395.
43. Jeong O, Kim HS. (2019). Dietary chokeberry and dried jujube fruit attenuates high-fat and high-fructose diet-induced dyslipidemia and insulin resistance via activation of the IRS-1/PI3K/Akt pathway in C57BL/6J mice. *Nutr Metab (Lond).* 16:38.
44. Ganachar MS, Kumar S. (2004). Effect of *Ziziphus jujuba* leaf extract on body weight, food intake and serum lipid levels in sucrose-induced obese rats. *Indian Journal of Pharmaceutical Sciences.* 66(3):363-365.
45. Niaz K, Fatima A, Memon M, Hakro S, Murad S. (2016). New Slant on Hyperlipidemia: Prevention by Vitamin B-3 and Common Fruit *Ziziphus Jujuba*. *Journal of Drug Delivery and Therapeutics.* 6(6):22-24.
46. Mardani M, Bahmani M, Jalali S, Rafeian-kopaei M. (2016). Comparison of the *Descurainia sophia* and Levostatin effect on the LDL cholesterol reduction, a clinical trial study. *Journal of Chemical and Pharmaceutical Sciences.* 9(3):1329-1333.
47. Rahzani K, Malekiran AA, Zeraatpishe A, Hosseini N, Seify SM, Abdollahi M. (2013). Anti-Oxidative Stress Activity of *Stachys lavandulifolia* Aqueous Extract in Human. *Cell J.* 14(4):314-317.