



(REVIEW ARTICLE)

Review of medicinal plant associated with antihyper-lipidermia

Eric Omo Irinmwiniwa ^{1, *}, Prince Chiazor Unekwe ¹, Joseph Oyindamola Olanrewaju ¹ and Charles Cherechi Njoku ²

¹ Department of Pharmacology and Therapeutics, Faculty of Medicine, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Nigeria.

² School of Nursing Umuahia, Abia State, Nigeria.

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Abstract

Hyperlipidemia is a common disease around the world which has affected both developed and developing countries, in this disease blood level of lipids is elevated more than normal range. Elevated lipids levels (cholesterol, fats, and triglyceride) predispose the patient to various serious and sometimes lethal complications such as cardiovascular disease, cerebral strokes, hepatic and renal dysfunction. This review emphasizes on some plants (extracts) having anti-cholesterol actions, including; *Glycyrrhiza glabra*, *Legenaria siceraria*, *Medicago sativa*, *Curcuma longa*, *Syzygium cerasoideum*, *Leptopus Cordifolius Decne*, *Piper longum*, *Moringa oleifera*, *Zingiber officinale*, *Trigonella foenum-graecum*, *Carum carvi*, *Carica papaya*, *Gloriosa superba*, *Ficus religiosa*, *Eleusine coracana*, *Lycium europaeum* and *Hibiscus sabdariffa* for anti-hyperlipidemic potential. Increase in the levels of these lipoproteins like, triglycerides (TG), Total cholesterol (TC), Very low density lipoprotein (VLDL) and low-density lipoprotein (LDL) includes some mechanisms of actions of these medicinal plants observed in triton-x, cholesterol, high fat diet, Poloxamer-407, Dexamethasone and alloxan-induced in-vivo and in-vitro models. Additionally, this review gives proof to the fact that these medicinal plants can be used for the management and prophylaxis of hyperlipidemia, thus reducing complications associated with hyperlipidemia.

Keywords: Cholesterol; Hyperlipidemia; Medicinal plants; Lipids; Triglyceride

1. Introduction

Hyperlipidemia is a disease of lipid metabolism produced by the rise of plasma concentration of the different lipid and lipoprotein portions, which are the source of heart disease. It is characterized as the elevation of serum TC, TG, VLDL, LDL and low level of HDL, which are responsible for various complications like heart attack, coronary artery syndrome, stroke, atherosclerosis, myocardial infarction and pancreatitis. Hyperlipidemia can be either primary or secondary type; the primary syndrome might be treated by hypolipidemic drugs, however, secondary induced by diabetes, hypothyroidism or renal lipid nephrosis which is treated by treating the natural disease respectively than hyperlipidemia [1]. Genetic disorder, way of life, diet wealthy in calories, fat, and cholesterol assume a vital role to cause dyslipidemia around the world [2]. The primary factor responsible for hyperlipidemia includes sedentary lifestyle and changing habits in which the most vulnerable factor includes poor diet, for example, lipoprotein intake of more than 40 percent of total calories, intake of saturated fat more than 10 per cent of total calories; and ingestion of cholesterol more than 300 milligrams per day [3]. For the enormous hyperlipidemia, a number of manufactured medications available, not a bit is useful for all lipoprotein disorder, and every drug connected with various side effects. So, presently different materials are searched from natural sources with the severity of less toxic, less expensive, and provide better safety and

*Corresponding author: Irinmwiniwa Omo Eric; Email: ericirins@gmail.com

Department of Pharmacology and Therapeutics, Faculty of Medicine, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Nigeria.

efficacy on a long age practice. Characteristic items from plants are a rich wellspring of medication utilized for quite a long time to treat different disease [4]. Hyperlipidemia, a clinical state can be defined as increase in either all lipoproteins or any one of them in the blood [5]. The lipid metabolism is synchronized in many various ways. Enzymes are the most significant regulators of lipid metabolism, for example, 3-Hydroxy-3-methylglutaryl coenzyme which is a reductase enzyme responsible for the biosynthesis of cholesterol [6].

However, increase in the low-density lipoprotein cholesterol (LDL-C) is the major lipid responsible for causing atherosclerosis. Dyslipidemia occurs due to significant abnormal amount of total cholesterol (TC), triglycerides (TG), or low levels of high-density lipoprotein (HDL). Hyperlipidemia is a medical just as social issue, particularly connected with diabetes mellitus results in increased mortality rate and morbidity. The major factors leading to hyperlipidemia includes atherosclerosis, which however results in Cerebrovascular and ischemic coronary heart disease [7]. Various allopathic hypolipidemic drugs like statins are obtaining in the market, but they cause various adverse effects like hyperuricemia, looseness of the bowels, myositis, hepatotoxicity, and so on. As they are for the most enzyme inhibitors, so they may inhibit other grave enzymes in the body. Additionally, statins are taken on a long-term basis, thus causing chronic toxic effects over a lifetime use [8].

2. Pathophysiology of hyperlipidermia

According to the present studies and reviews, hyperlipidemia is started from endothelial damage of the blood vessels, leading to the loss of nitric oxide in the damaged site, this will result in increase in the inflammatory response around the affected area and accumulation of the lipids in the deepest layer of the endothelial wall, macrophage cell will engulf the lipids forming what is called (the foam cell) with cholesterol. The formation of foam cell will cause necrosis, apoptosis, and mitochondrial dysfunction. At the same time, the cells of the smooth muscle encapsulate the foam cell producing fibrotic plaque and destroying the foamy cells. On other hand, stimulation of the platelets activity with the tissue factors resulting in plaque rupturing and thrombosis. Development of plaque occur either rapidly resulting in obstruction of the blood vessels or slowly that cause stenosis of the blood vessels. In both mechanisms, lipid plaque remains the mainstay of the development of CVD and deterioration of patient health status.

In addition to the CVD, patients with hyperlipidemia can also suffer from tendon dysfunction especially patellar tendon. This is because with time hyperlipidemia will produce higher number of macrophages in the tendon tissues, collagen fiber damage and replaced by lipid instead of collagen resulting in less effective tendons that are exposed to harm easily [9].

3. Medicinal plant associated with anti-hyperlipidermia

3.1. *Glycyrrhiza Glabra*

Glycyrrhiza glabra belongs to family *Fabaceae*. The main chemical constituents includes saponins, glycyrrhizin, triterpene and glycyrrhetic acid. Srivastava and Srivastava [10] reported that *Glycyrrhiza glabra* is used as an anti-inflammatory, mild laxative, antiarthritic, antiviral, antiulcer, antibiotic, memory stimulant, antitussive, aphrodisiac, antineoplastic, anticholinergic, antidiuretic, antimycotic, estrogenic, antioxidant, anticaries agent and hypolipidemic agent.

The results concluded that the level of TG, TC, and LDL-C in serum ($P < 0.05$) was prominently elevated in HFD animals when compared with the control group. However, the ethanolic root extract of *Glycyrrhiza glabra* at a dose of 400mg/kg when administered to animals showed a prominent increase in the plasma HDL-C in animals treated with *Glycyrrhiza glabra* extract when compared to HFD rats.

In the study, the high-fat diet used contains saturated fatty acids which elevates the effect of HMG-CoA reductase enzyme due to increased availability of acetyl CoA thereby resulting in increased cholesterologenesis rate as reported by Tyagi [10].

3.2. *Lagenaria siceraria*

Lagenaria siceraria belongs to family *Cucurbitaceae*. It is used for treating different conditions, like jaundice, congestive heart failure (CHF), ulcer, piles, diabetes, insanity, colitis, skin disease, and hypertension. The pulp of the fruits is used both as laxative and emetic. It is also used for its cooling effect, antibilious and as diuretic. The dried pulp can also be used for treating insomnia and rheumatism [11].

The results demonstrate that *Lagenaria siceraria* obtains the prominent antihyperlipidemic potential. A total of 200 mL of freshly prepared *Lagenaria siceraria* fruit extract was administered daily on empty stomach for 90 days. Significant reductions ($P < .01$) were found in triglycerides and total cholesterol levels in blood. Cardiac risk ratio, atherogenic coefficient, and atherogenicity index of plasma were also improved. Appreciable reductions in body mass index ($P < .01$) and blood pressure (systolic $P < .01$, diastolic $P < .05$) along with a significant reduction ($P < .05$) in fasting blood glucose levels were also observed in these subjects. *Lagenaria siceraria* fruit extract exhibited significant antioxidant activity in dyslipidemic subjects as evident from elevations in SOD ($P < .05$) and GSH levels ($P < .01$) with marked improvement in catalase ($P < .01$) and TBARS levels ($P < .05$). The presence of phytochemical in the plant may increase Lecithin Acyl Transferase (LCAT) effects. LCAT is responsible for the regulation of blood lipids. LCAT is the principal enzyme responsible for the incorporation of cholesterol into HDLc. Saponins reduce the intestinal absorption of cholesterol by binding with it and thus elevating its fecal elimination [11].

3.3. *Medicago Sativa*

Medicago sativa, also known as alfalfa, which belongs to family *Fabaceae*. the plant *Medicago sativa* have nematocidal, cytotoxic and antimicrobial activity[12].The methanolic extract, chloroform, ethyl acetate, petroleum ether, and butanol fractions of sprouts of *M. sativa*, demonstrate a prominent treatment-duration related reduce in the TG, TC, LDL and VLDL levels compared to the untreated diabetic rats in a level alike to those of reference hypolipidemic drug rosuvastatin. The findings revealed that the methanolic extract of *M. sativa* showed antihyperlipidemic and improved antihyperglycemic activity in STZ diabetic hyperlipidemic rats [13].

The plant act by inhibiting HMG-CoA reductase enzyme which is the rate limiting enzyme in the synthesis of cholesterol thereby resulting in decreased cholesterologenesis.

3.4. *Curcuma Longa*

Curcuma longa belongs to family *Zingiberaceae*. It commonly named as turmeric. It is the most common condiment used all over the world. *C. longa* is herbaceous perennial plant. There are many medicinal properties of turmeric which include anti-inflammatory, antifungal, antifertility, antiprotozoal, antimutagenic, anti-carcinogenic, anticoagulant, antihepatotoxic, antiviral, anti-fibrotic, anti-venom, antiulcer, antidiabetic, and hypolipidemic properties.

The study on diabetic hyperlipidemic rats was conducted and a notable increase in serum HDL levels in diabetic hyperlipidemic rats was observed, which received turmeric at a dose of 300 mg/kg and 500 mg/kg respectively, for four weeks. Activity of ethanolic extract of turmeric at dose of 300 mg/kg/day and 500 mg/kg/day decreased serum TC and serum TG. There was no prominent rise in serum HDL-C levels in some of the study groups (III, IV, V, and VI) [14].

3.5. *Syzygium cerasoideum*

Syzygium cerasoideum plant belongs to the family *Myrtaceae* which is found in India. Several active principles from this plant have been identified which include phenolic compounds cyanidin, 3-glucoside, delphinidin 3-glucoside, ellagic acid, kaempferol, myricetin, quercetin, quercetin and rutin as reported by Sharma [15].

Antioxidant and antihyperlipidemic activities of the extracts of *Syzygium cerasoideum* were investigated by studying their in-vivo effects on triton and cholesterol induced hyperlipidemia. Highest antioxidant activity was exhibited by methanolic extract followed by chloroform extract of *S. cerasoideum*. In triton induced hyperlipidemic model, the groups treated with the extracts of *S. cerasoideum* and pitavastatin demonstrated a significant decrease in the levels of TC, TG, LDL-C, VLDL-C particularly treatment with CESC at the dose of 200 mg/kg b.w resulted in significant decrease in levels of TC (67.60%), TG (47.89%), LDL-C (85.80%) and VLDL-C (47.89%). In cholesterol induced hyperlipidemic model, the groups treated with the extracts of *S. cerasoideum* and pitavastatin demonstrated a significant decrease with the CESC and MESD at low doses in the serum levels TC (68.68%), TG (60.22%), LDL-C (85.44%), VLDL-C (70.71%) besides an increase in serum HDL-C (62.26%) levels when compared to cholesterol- induced hyperlipidemic control group as reported by Sadik et al., [16].

3.6. *Leptopopus Cordifolius Decn*

Leptopopus cordifolius Decne (syn. *Andrachne cordifolia*) is a medicinal plant belonging to the family *Phyllanthaceae*, commonly found in the low hills of Northern hilly areas of Pakistan and the Himalayan region, including Azad Jammu and Kashmir. It is a small shrub, about 1m tall, with ovate to elliptic leaves. The powder of the leaves of *L. cordifolius* is used for wound healing, hypolipidemic effect and as a hypoglycemic agent as reported by Munir and Qureshi, [17].

The antihyperlipidemic evaluation was conducted in Swiss albino mice at doses of 150–250 mg/kg for 15 days. Total cholesterol, triglyceride, LDL, HDL were estimated according to standard procedures. Hyperlipidemic activity was significant at 250 mg/kg. The biochemical parameters, such as total cholesterol, triglyceride, LDL, HDL, were significantly improved ($p < 0.01$). Hyperglycemia is accompanied by a rise in TC, TG, and LDL, and a fall in HDL levels [18]. The methanolic extract *L. cordifolius* and gibenclamide might act on reserved fats and inhibit the release of free fatty acids, decreasing the total cholesterol and triglyceride levels, and increasing the HDL level as reported by Rahman et al., [19].

3.7. *Piper longum*

Piper longum belongs to family *Piperaceae*. In Indian kitchen, the *Piper longum* is black, hot, and used as spices beside its medicinal purpose, where it's soothing and relieves muscular pains and inflammation.

Hyperlipidemia was induced in the animals by administering triton WR-1339 through intraperitoneal route. Extract of *Piper longum* along with aqueous gum *acacia* (1% w/v) suspension were macerated and were administered orally at 500 and 200 mg/kg, b.w. doses respectively. It was investigated that HFD rich in cholesterol when administered to rats induced hyperlipidemia, the result demonstrated that extract of *Piper longum* could excite hepatic LPL and PHLA action, both the components play a vital role in the catabolism of lipid and their functions in the body [20].

3.8. *Moringa oleifera*

Moringa oleifera Lam is specie of family *Moringaceae*. Commonly it is known as Drumstick. It is used as antimicrobial activity, anti-diabetic, hepatoprotective, cardiac stimulation and hypocholesterolemic activity.

The result showed that administration of high-fat diet for 21 days caused a significant increase in lipid levels characterised by increased triglycerides, VLDL, LDL ($p < 0.001$), and decreased HDL levels ($p < 0.001$) when compared with the normal and control group. However, an increased LDL level indicates hypercholesterolemia and treatment with MEMOL for 3 weeks resulted in decreased hyperlipidemia activity induced by high-fat diet ($p < 0.001$). MEMOL treated animals with extract dose of 200mg/kg and 400mg/kg resulted in prominent decrease in the atherogenic index. It concluded that *M. oleifera* methanolic extract can be used in weight management, which supports its traditional claim [21].

3.9. *Zingiber officinal*

Zingiber officinal belongs to family *Zingiberaceae*. Commonly it is known as ginger. It is a perennial herb. It used for gastrointestinal disorders and has anti-inflammatory effect.

The result revealed that decreased levels of low-density lipoprotein (LDL), and total cholesterol (TC) in rat serum were administered with ginger extracts when compared with the control groups. The extracts were also effective as it decreased LDL levels to same levels as that of standard group which was also comparable to the effect of atorvastatin 10 mg/day. It was concluded that reduced triglyceride, and increased high-density lipoprotein level was observed in ginger-treated groups [22].

3.10. *Trigonella foenum-graecum*

Trigonella foenum-graecum is a useful medicinal plant belonging to family *Fabaceae*. It is an annually grown herb which is cultivated throughout the world including Ethiopia. It is known commonly as Fenugreek. It is cultivated as a leafy vegetable, condiment and as medicinal plant. It used as anti-diabetic, anti-microbial, anti-fertility, antioxidant, anticancer, anti-parasitic and hair growth promotion activity. It used for reducing the body weight in folklore and hypocholesterolaemic lactation stimulant

A study carried out by Genet *et al.*, [23] revealed that by the end of the intervention period, the treatment group showed significantly lower total cholesterol ($P < 0.001$) than the control group ($P < 0.001$); triglyceride and low-density lipoprotein cholesterol, but the treatment group showed significantly increased high-density lipoprotein cholesterol. However, lipid profile levels in the control group were not significantly changed.

3.11. *Carum carvi*

Carum carvi L. belongs to family *Apiaceae*. It is commonly known as caraway. It is used as a food flavour, fragrance additive. It is used as an antibacterial agent with antispasmodic, carminative, and appetite stimulant properties. *Carum carvi* is also used in eye ailments, gastrointestinal disorders, genitourinary diseases like metritis, dysuria and

orchitis[24]. AZ is a distillate product and is prepared from four various herbs, namely ajwain (*Trachyspermum ammi* L., *Apiaceae*), ginger (*Zingiber officinale* Roxb., *Zingiberaceae*), black caraway (*Carum carvi* L., *Apiaceae*) and cumin (*Cuminum cyminum* L., *Apiaceae*).

Rafiul and Shahid [25], reported that Arq Zeera (AZ), a poly herbal unani formulation has been used traditionally as a remedy for reducing body fat and gastric disorder. The current study was designed to investigate the antihyperlipidemic activity of AZ against rat model of high fat diet (HFD)-induced obesity. AZ was prepared and administered orally 7.75 mL/kg/twice a day for 4 weeks to HFD induced obese rat. Body weight and serum biomarkers were evaluated. At the end of study, HFD significantly ($p < 0.001$) increased body weight, cholesterol, triglycerides, pancreatic lipase activity, malondialdehyde(MDA) levels as compared to normal diets control group. AZ treated rats significantly ($p < 0.001$) reduced body weight, cholesterol, triglycerides, pancreatic lipase activity and MDA levels as compared to HFD control, this result suggest that AZ has an antihyperlipidemic action against HFD induced obesity in rats, possibly through lipid lowering action of intestinal absorption of dietary fat, and increased antioxidant defense.

3.12. *Gloriosa superba*

Gloriosa superba belongs to *Liliaceae* family. This drug is a valuable plant found in Africa and tropical Asia. It used an anthelmintic, anti-inflammatory, Analgesic, Oxytocic, Abortifacient, Mutagenic and Antimicrobial activities.

Vikas *et al.*, [26], reported that a significant ($P < 0.01$) reduction in blood glucose level was observed at 150 and 300 mg/kg doses of extract in glucose loaded as well as STZ induced diabetic rats. The extract also showed significant increase in the body weight and HDL levels and decrease in serum cholesterol, triglycerides, LDL, urea, SGPT and SGOT levels. Conclusion: The results showed that GSLE possess potential anti-hyperlipidemic activity. The effect produced might be due to inhibition of cholesterol 7 α -hydroxylase, which facilitates cholesterol clearance and up-regulation of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase. Inhibitory effect of this enzyme reduces the rate at which triglycerides breaks down into free fatty acids to produce increase in triglycerides level.

3.13. *Carica papaya*

Carica papaya belongs to family *Caricaceae*. It is one of the most nutritional fruits consumed and grown in Africa. It utilized as a tonic for the heart, analgesic. It has antioxidant properties and treatment for stomach ache.

The result showed that *Carica papaya* aqueous leaf extract of low dose (200mg/kg/ml/day) significantly and progressively lowered the glucose level, TG, TC and LDL dose dependently while significantly causing a dose-related elevation in HDL concentration when compared to the untreated control and positive control groups (I&II) treated rats [27]. *C. papaya* leaf contains sterols among their main components. It is known that phytosterols with analogue structure to cholesterol may decrease cholesterol absorption displacing it from bile salt micelles and competing for intestinal absorption [28, 29]. Intestinal absorption plays a main role in the regulation of cholesterol homeostasis.

3.14. *Ficus religiosa*

Ficus religiosa is a large tree belonging to the family *Moraceae*. This tree is given the name of Budhidhidru or tree of wisdom by Buddhists. It is commonly known as *Pipal* and its leaves roots have been used for the treatment of diabetes mellitus and to treat infertility in women, it has antidiabetic action and antihyperlipidemic action.

The result indicated that the aqueous leaves extracts of *Ficus religiosa* (250 mg/kg) were administered orally for 21 days, in alloxan induced diabetic rats on Glucose, Lipid profile, Lipoproteins and Lipid metabolizing enzymes. The aqueous leaves extract of *F. religiosa* induced significant improvement in glucose, serum lipids, lipoproteins concentration and lipid metabolizing enzymes activity (Lipase, HMG CoA reductase and LCAT) [30].

3.15. *Eleusine coracana*

Is extensively cultivated and consumed in the tropics and sub-tropics. It is very common in Africa (especially Senegal, Niger and Nigeria), and Asia, where it is called different names including finger millet, African millet, Ragi (India), Tamba (Hausa-Nigeria), Dendi (Leeni-Niger), Kpana (Birom-Nigeria), Changari (Fulani-Nigeria), Sarga (Kaniri-Nigeria), Oka tamba (Ibo-Nigeria), and Oka. The leaf juice has been given to women in childbirth, and the plant is reported to be diaphoretic, diuretic, and vermifuge. Ragi is a folk remedy for leprosy, liver disease, measles, pleurisy, pneumonia, and small pox and hyperlipidemia.

There were significant differences ($P < 0.05$) in the serum levels of total cholesterol (TC) and low density lipoprotein (LDL) in the treated group as compared to normal control and metformin diabetic control groups. There were marked

reductions in serum total cholesterol at a dose of 400mg/kg, and serum low density lipoprotein (LDL) at a dose of 100mg/kg. There were steady reductions in the levels of serum triglycerides (TG's) and high density lipoprotein (HDL) in a dose dependent pattern in the treated group as compared to the metformin diabetic control group. *E coracana* extract also reduced the serum triglycerides (TG's) and high density lipoprotein (HDL) levels in all the doses tested [31].

3.16. *Lycium europaeum* (Boxthorn)

Lycium europaeum Belongs to the Solanaceae family and occurs spontaneously around the Mediterranean basin with three other species, namely *L. barbarum*, *L. shawii*, and *L. chinense*. These species have widely been used in traditional medicine. In fact, the *L. shawii* root decoction is widely renowned to treat mouth sores, cough, high blood pressure and diabetes. Fruit of this plant is also consumed for its antioxidant and other beneficial properties. Concerning *L. barbarum*, several studies have indicated its benefits on aging, neuroprotection, general well-being, fatigue/ endurance, metabolism/energy expenditure, glaucoma, immunomodulation, antitumor activity and cytoprotection as well as hypoglycemic and antioxidant effects in cell or animal experiments

Result: *Lycium europaeum* aqueous extract was orally administered at a dose of 20 mg/kg for 28 consecutive days. Serum concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were assayed at the end of the experimental period in all investigated groups. *Lycium europaeum* extract significantly increased ($p < 0.05$) HDL-C and reduced blood glucose, TC, LDL-C and TG as compared to the alloxan-control group [32].

3.17. *Hibiscus sabdariffa*

Hibiscus sabdariffa is belongs to family *Malvaceae*. It common name is Roselle. It is one of the most common medicinal plant known all over the world. It has a mild laxative activity, capability to elevate urination and cracks treatment in the feet, anti-helminthic, sedative properties, bilious, sores and wounds. It is used for wound healing, relief of sour throat, as a soothing cough remedy, antipyretic, antimicrobial, diuretic and emollient[33].

It assessed that the calyces and leaves of *Hibiscus sabdariffa* decrease total cholesterol and raise HDL level. It examined the anti-hyperlipidemia effect of *Hibiscus Sabdariffa* in decreasing the serum concentration of TC, TGs and LDL-Cholesterol. The study demonstrates a prominent raised in HDL-C($p < 0.05$) since HDL-C is a protective factor in coronary heart disease, the present finding showed that serum TGs and level of LDL reduced prominently after rats were administered with 1000 mg/kg and 500 mg/kg dose of *Roselle* extract (dried calyces). It also revealed that 5% and 10% ethanolic extract of *Hibiscus Sabdariffa* L. flowers, when administered to cholesterol-rich basal diet, resulted ineffective decrease of serum lipid level [34].

4. Conclusion

Traditionally, folkloric medicines have been utilized for centuries as a remedy for a few diseases. Seventeen herbaceous plants possessing anti-hyperlipidemic activity were reviewed. The anti-hyperlipidemia activity of plants plays a vital role in the decrease of CVD; where this is a leading cause of mortality around the world. Thus, there is need to focus on the lipid-lowering activity of herbs and should adopt a new approach to the protective role of these medicinal plants which depends on the reduction of LDL, with a view to reducing the progression of the disease. This review is an overview and up to date action of the anti-hyperlipidemic activity in folkloric medicine as a potential use for the development of new medicines used in the protection against dyslipidemia or atherosclerosis. However, we can safely state that folkloric medicines have enormous potential to provide some remarkable orthodox drugs as most drugs are sourced from plant.

Compliance with ethical standards

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