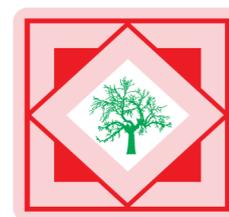




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Der Pharmacia Sinica, 2011, 2 (3):51-59



Der Pharmacia Sinica

ISSN: 0976-8688
CODEN (USA): PSHIBD

Herbs: Now in arena of hyperlipidaemia

¹Hitesh K. Dhamija and ²Ankit S. Chauhan

¹Department of Pharmaceutical Sciences, Manav Bharti University, Solan, H.P. (India)

²Department of Physiotherapy, Manav Bharti University, Solan, H.P. (India)

ABSTRACT

Herbal medicines are the oldest remedies known to mankind. Man's dependence on plants for health care is as old as the civilization. Herbs had been used by all cultures throughout history but India has one of the oldest, richest and most diverse cultural living traditions associated with the use of medicinal plants. It is being globally recognized that medicinal plants play a significant role in providing health benefits to human beings. The World Health Organization (WHO) has estimated that 80% of the earth's (6 billion) inhabitants rely upon traditional medicine for their primary health care needs and major part of this therapy involves the use of plant extracts or their active principles. Major Pharmaceutical companies are currently conducting extensive research on plant materials for their potential medicinal value. Hyperlipidaemia is widespread and common health problem now a day. Hyperlipidaemia is a major cause of atherosclerosis and atherosclerosis associated conditions, such as coronary heart disease (CHD), ischemic cerebrovascular disease, and peripheral vascular disease. Objective of the present review is to explore some of the medicinal plant and their phytoconstituents for their anti-hyperlipidaemic activity.

Keywords: Atherosclerosis, Cholesterol, Hyperlipidaemia, Lipids, Plants.

INTRODUCTION

Plasma lipids are transported in complexes called lipoproteins. Metabolic disorders that involve elevations in any lipoprotein species are termed as Hyperlipoproteinaemia or Hyperlipidaemia. Hyperlipidaemia denotes increased level of triglyceride. The two major clinical sequelae of Hyperlipidaemias are acute pancreatitis and atherosclerosis. The former occurs in patients with marked Hyperlipidaemia. Control of triglycerides can prevent recurrent attack of this life threatening disease.^[1]

Despite a continuous decline in incident of atherosclerosis-related deaths in the past 35 years, death from coronary heart disease (CHD), cerebrovascular disease, and peripheral vascular disease accounted to be 30% of the 2.3 million deaths in the US during 1997. Two-thirds of atherosclerosis deaths were due to CHD. About 85% of CHD deaths occurred in individuals over 65 years of age. Among the 15% die prematurely (below age 65), 80% died during their first CHD event. Among those died due to sudden cardiac death in 1997, 50% of the men and 63% of the woman had been previously asymptomatic. [2] These statistics illustrate the importance of identifying and managing risk factor for CHD. The major known risk factors are low density lipoproteins-cholesterol (LDL-C), reduced high density lipoproteins- cholesterol (HDL-C) level etc. [3]

Cut-off levels of lipids in humans
“Table 1: Cut-off levels of lipids in humans”

Groups	Total cholesterol (mg/dl)	Triglycerides (TG) (mg/dl)	LDL cholesterol (mg/dl)	HDL cholesterol (mg/dl)
Desirable levels	<200	<150	<130	>35
Borderline risk	200-239	150-200	130-159	30-35
High risk	>240	>200	>160	<30

Types of Lipoproteins
“Table 1: Cut-off levels of lipids in humans”

Lipoprotein class	Density of floatation (g/ml)	Major lipid constituent	Site of synthesis	Mechanism of catabolism
Chylomicrons and Remnants	<<1.066	Dietary triglycerides and cholesterol	Intestine	Triglycerides hydrolysis by lipoprotein lipase.
Very low density lipoproteins (VLDL)	<1.006	Endogenous or hepatic triglycerides	Liver	Triglyceride hydrolysis by lipoprotein lipase.
Intermediate density lipoproteins (IDL)	1.006-1.019	Cholesteryl esters and endogenous triglycerides	Catabolic product of VLDL	50% converted to LDL mediated by hepatic lipase.
Low density lipoproteins (LDL)	1.019-1.063	Cholesteryl esters	Catabolic product of VLDL	ApoB-100 mediated uptake by LDL receptor (75% in liver)
High density lipoproteins (HDL)	1.063-1.21	Phospholipids, cholesteryl esters	Intestine, liver plasma	Transfer of cholesteryl ester to VLDL and LDL.

The treatment of Hyperlipidaemia includes the use of many allopathic drugs like Niacin (Nicotinic Acid), Fibrates (Clofibrate and Gemfibrozil), HMG-Co-A reductase inhibitors (Lovastatin, Pravastatin Sodium), Bile acid binding resins (Cholestyramine and Cholestipol), and Probucof etc.

But these modern drugs are associated with certain side effects, also the cost of these drugs is very high, and also it will take almost a decade to develop a new drug. On the other hand plant based drugs have long history of use and better patient tolerance as well as public acceptance. They are easily available at low cost as compare with modern drugs. Also phytoconstituents isolated from them may act as a lead compound for new pharmaceuticals.

In the recent years, there is growing interest in herbal medicines all over the world. Traditional medicinal plants having antilipidaemic property can prove to be the useful source for the development of new oral hypolipidaemic agents or simple dietary adjuvant to existing therapies. Ethno-pharmacological surveys indicate that more than 1200 plants are used in traditional medicine for their hypolipidaemic activity.^{[4],[5]} The hypolipidaemic activity of a number of plants/plant products has been evaluated and confirmed in animal models,^{[6],[7]} as well as in human beings.^[8]

Plants with anti-hyperlipidaemic activity: There are lots of plants which have reported to possess hypolipidaemic activity. Brief description of some of the important plant used in the treatment of Hyperlipidaemia is:-

***Acorus calamus* Linn. (Vacha):-** Doses of 10, 20 and 40 mg/kg of the F-3 fraction of *Acorus calamus* Linn. demonstrated 11.42, 23.76 and 31.18% decreases in total cholesterol level. The decrease was found to be significant ($P < 0.05$) at the doses of 20 and 40 mg/kg but it is less effective when compared to fenofibrate and simvastatin which resulted in significant decreases by 47.14 and 33.59% ($P < 0.05$) respectively in total cholesterol levels.^[9]

***Allium cepa* Linn. (Onion):-** S-methyl cysteine sulphoxide (SMCS), a sulphur containing amino acid isolated from onion showed anti-diabetic and anti-hyperlipidaemic effects. Oral administration of SMCS daily at a dose of 200 mg/kg body weight for a period of 45 days to alloxan diabetic rats controlled significantly their blood glucose and lipids in serum and tissues and altered the activities of liver hexokinase, glucose 6-phosphatase and HMG Co-A reductase towards normal. The above effects of SMCS were comparable to those of glibenclamide and insulin.^[10]

***Allium sativum* Linn. (Garlic):-** Several animal and human studies have proven the efficacy of garlic as a herbal remedy to reduce a multitude of risk factors, which play a decisive role in the genesis and progression of arteriosclerosis including decreases in total cholesterol, LDL-C, HDL-C, serum triglyceride and fibrinogen concentrations.^[11]

***Apium graveolens* Linn. (Celery):-** The aqueous extract significantly lower TC and LDL-C level in rats which is fed with a high-fat diet for 8 weeks to induce Hyperlipidaemia. An aqueous celery extract significantly lowers the systolic blood pressure.^[12]

***Apocynum venetum* Linn. (Dogbane):-** Ethanolic extract decreased the serum TC and LDL-C levels and the atherogenic index, as well as the hepatic TC level in hypercholesterolemic rats, but they increased the HDL-C level. Clinical report on the Luobuma extract indicates that it decreases TC and triglyceride levels of patients with Hyperlipidaemia.^[13]

***Asparagus racemosus* (Shatavari):-** *A. racemosus* as 5 g% feed supplementation to hypercholesterolemic animals resulted in a decrease of total lipids (29%), total cholesterol (29%), triglycerides (39%), LDL-C (33%), VLDL-C (39%), atherogenic index (37%) and an increase in HDL-C content (11%). With 10g% *A. racemosus* treatment, a further reduction occurred in total lipids (64%), total cholesterol (38%), triglycerides (52%), LDL-C (44%), VLDL-C (52%) and atherogenic index (49%). This reduction in total lipids, total cholesterol, triglycerides, LDL-C, VLDL-C and atherogenic index was dose-dependent and significant. A

further increase in HDL-C (21%) level was also noted at dose 10g% as compared to animal treated with 5g% dose. *A. racemosus* also reduced total lipids (26% and 36%, respectively), total cholesterol (46% and 57%, respectively) and triglycerides (38% and 57%, respectively) in the liver of treated groups as compared to control. [14]

***Bauhinia variegata* Linn (Kachnar):-** A significant decrease in serum levels of cholesterol, triglycerides, VLDL, and LDL was noticed in the animals treated with *B. variegata* Linn. root and stem extracts (ethanol and aqueous) when compared with the control group and Simvastatin (standard). [15]

***Boswellia serrata* Roxb. (Gond):-** Alcohol extracts of *Boswellia serrata* Roxb. have been shown to significantly lower serum cholesterol and serum triglyceride levels, and reduce body-fat accumulation in hyperlipidaemic animals. In fact the extracts prevented, or reversed, atherosclerosis in animals who received high-fat diets. [16]

***Cassia glauca* Lam. (Amaltas):-** The acetone extract produced significant reduction in the blood glucose level which is comparable to that produced by glibenclamide treatment. Further acetone extract was purified by column chromatography that led to isolation of a several specific compounds; of the isolated compounds, Cg-1 possesses significant blood glucose-lowering and cholesterol-lowering activities. [17]

***Cicer arietinum* Linn. (Chick Pea):-** The hypocholesterolemic property was detected in lipid extracts of the plant as well as in the defatted portion, the former being more potent in this respect. Its lipid-lowering action could possibly be attributed to inhibition of the synthesis of cholesterol in the liver and increased catabolism and excretion of cholesterol end products in the feces. [18]

***Commiphora mukul* (Guggul):-** Guggulipid, an oleoresin and mixture of several steroid lipids, in the dose of 1.2 g/day for 6 weeks reduced cholesterol by 15% and triglycerides by 20%. When guggulipid was administered in a dose of 1.5 g/day for 12 weeks, it brought down the levels of cholesterol by 16.9% and triglycerides by 27%. The effect of guggul powder (8 g/day) in 135 patients with ischemic heart disease for a duration of 12 weeks showed reductions in serum cholesterol (27%), serum triglycerides (36%), phospholipids (20%), and free fatty acids (37%). [19]

***Curcuma longa* Linn. (Turmeric) and *Nardostachyas jatamansi*:-** It has also been reported that sodium curcumin isolated from *C. longa* is an active constituent which causes an increase in total excretion of bile salts, bilirubin and cholesterol. Ethanol extracts of *C. longa* (tuber) and *Nardostachyas jatamansi* (whole plant) feeding elevate the HDL cholesterol/TC ratio. The extract also caused a significant reduction in the ratio of TC/phospholipids. *C. longa* exhibited better cholesterol and triglyceride lowering activity (Ch ¼ 285%; TG ¼ 288%) as compared to *N. jatamansi* in Triton-induced Hyperlipidaemia. The cholesterol- lowering effects of curcumin span all levels of lipid-lowering mechanism, including lowering total and LDL cholesterol (by 11% normally), increasing HDL cholesterol (by 29% normally), and reducing lipid peroxidation, thereby limiting the oxidation of LDL cholesterol rats. [20]

***Emblica officinalis* Gaertn. (Amla):-** *E. officinalis* has been found to reduce serum TC, aortic cholesterol and hepatic cholesterol significantly, without any effect on the serum triglyceride levels in both normal and cholesterol induced hypercholesterolemic rabbits. The effect of *E. officinalis* on total serum cholesterol and its lipoprotein fractions was also studied in normal and hypercholesterolemic individuals aged 35–55 years. When the supplement was given for a period of 28 days in the raw form, both normal and hypercholesterolemic subjects showed a decrease in cholesterol levels. Two weeks after withdrawing the supplement, the total serum cholesterol levels of the hypercholesterolemic subjects rose significantly almost to the initial levels.^[21]

***Embelia ribes* Burm (False black pepper):-** Administration of the aqueous extract of *Embelia ribes* (100 and 200 mg/kg, *p.o.*) for 30 days, to hyperhomocysteinemic rats, significantly ($P < 0.01$) decreased the levels of homocysteine, LDH, total cholesterol, triglycerides, LDL-C and VLDL-C and increased the HDL-C levels in serum.^[22]

***Inula racemosa* Hook. f. Puskarmool:-** It has been found to possess a propranolol like beneficial effect in prevention of coronary ischemia and has been reported for its potent hypolipidaemic and cardioprotective activity.^[23]

***Moringa oliefera* Lam. ():-** A crude extract of the leaf of *M. oliefera* Lam. has been shown to possess hypocholesterolemic activity. A dose of 1 mg/g extract when co-administered with a high-fat diet, daily for a period of 30 days, had a cholesterol-reducing effect in the serum, liver, and kidneys, compared to the high-fat-fed group. The presence of the phytosterol, β -sitosterol, has been established in the leaf of this plant which is presumably the bioactive component that lowers the plasma concentration of LDL and exerts the cholesterol-lowering property.^[24]

***Oenothera biennis* Linn. (Evening primrose oil):-** Seeds of *O. biennis* contain 14% of a fixed oil known as OEP. This oil contains 50–70% *cis*-linoleic acid and 7–10% *cis*-gamma-linoleic acid (GLA). Essential fatty acids are important as cellular and structural elements, and as precursors of prostaglandins, which help to regulate metabolic function. GLA may inhibit a number of cardiovascular pathologies, including cardiac arrhythmia, hypertensive responses, platelet aggregation and Hyperlipidaemia. Linoleic acid can reduce elevated serum cholesterol levels, but GLA has cholesterol-lowering activity about 170 times greater than the parent compound. GLA, the major active ingredient in the evening primrose oil, inhibits platelet aggregation, reduces blood pressure and restores the motility of red blood cells.^[25]

***Phyllanthus niruri* (Stonebreaker):-** The lipid-lowering activity of *P. niruri* has been studied in Triton-induced and cholesterol-fed Hyperlipidaemic rats. Serum lipids were lowered by *P. niruri* extract orally fed (250 mg/kg *b.w.*) to the Triton WR-1339 induced Hyperlipidaemic rats. Chronic feeding of this plant (100 mg/kg) in animals simultaneously fed with cholesterol (25 mg/kg) for 30 days caused lowering of the lipids and apoprotein levels of VLDL and LDL in experimental animals. The anti-hypercholesterolemic effect of this plant may be mediated through the inhibition of hepatic cholesterol biosynthesis, increased excretion of fecal bile acids, and enhanced plasma lecithin: cholesterol acyl transferase activity.^[26]

***Phyllanthus reticulatus* Hook f non Linn. (Amalaki):-** Administration of aqueous extract of *P. reticulatus* (250 and 500 mg/kg per day) showed statistically significant decrease in total

cholesterol ($P < 0.05$), triglyceride ($P < 0.001$), LDL-C ($P < 0.05$), VLDL-C ($P < 0.001$) and protein carbonyl level ($P < 0.05$) while increase in HDL-C level ($P < 0.05$) as compared to hypercholesterolemic animals. The animals treated with above extract showed decrease in the atherogenic index and increased percentage of protection at both the doses, i.e. 250 and 500 mg/kg.^[27]

***Plantago psyllium* (Psyllium):-** In a study of 28 patients who took 3 doses (3.4 g/dose) per day compared with placebo for 8 weeks, the psyllium-treated patients showed decreases in total serum cholesterol levels compared with the placebo group after 4 weeks. Decreases were also seen in LDL- C and LDL/HDL ratio. At the end of 8 weeks, values for TC, LDL- C and the LDL/HDL ratio were 14, 20, and 15%, respectively, below baseline. This study suggested that a high cholesterol level could be managed safely and easily by including psyllium preparations in the diet.^[28]

Salvadora oleoides* Linn. (Pilu):-S. oleoides* produced significant beneficial effects in the lipid profile in euglycemic rats, reducing triglycerides, total cholesterol, LDL, and VLDL, and increasing HDL, significantly. The ethanolic extract increased secretion of insulin from b-cells of pancreas; this increased secretion of insulin stimulates fatty acid biosynthesis and also the incorporation of fatty acids into triglycerides in the liver and adipose tissue.^{[29], [30]}

***Satureja hortensis* Linn. (Summer savory):-**Administration of flavonoids isolated from *S. hortensis* Linn. along with cholesterol in rabbits has resulted in a significant attenuation of rise in serum cholesterol value after 8 weeks, when compared to the cholesterol alone group. This suggests the cholesterol-lowering effect of fraction F in a situation of rising serum cholesterol.^[31]

***Sphaeranthus indicus* Linn. (Mundi):-** Ethanolic extract of *Sphaeranthus indicus* root (EESIR) at the dose 100 and 200 mg/kg to the Streptozosin-induced diabetic rats showed significant ($P < 0.01$) reduction in elevated TC, TG, and LDL levels and increased HDL level. The dose of 200 mg/kg showed significant ($P < 0.05$ and $P < 0.01$) higher reduction in elevated TC, TG and LDL levels when compared to glibenclamide and 100 mg/kg dose of EESIR. The HDL level at the dose of EESIR 200 mg/kg was significantly increased compared to glibenclamide and EESIR 100 mg/kg ($P < 0.01$). Administration of EESIR and glibenclamide to diabetic rats showed significant ($P < 0.01$) reduction in VLDL level than diabetic control.^[32]

***Solanum nigrum* Linn. (Mayoya):-** An increased level of total cholesterol, LDL-C, VLDL-C, triglycerides, phospholipids, free fatty acids and decreased level of HDL-C were observed in ethanol-intoxicated rats. Oral administration of aqueous extract of fruit of *Solanum nigrum* significantly improved the lipid profile levels, which were brought to near normal. Above effect was comparable with that of the standard drug silymarin.^[33]

***Terminalia arjuna* Rob. (Arjuna bark):-** The alcoholic decoction of this bark powder significantly increases euglobin lysis time, prolongs prothrombin time and lowers the serum cholesterol levels in ischemic heart disease patients. The bark powder lowered the systolic blood pressure and body mass index, decrease in circulating catecholamine levels, while in adrenal glands its concentration and increased the HDL- C. The administration of the bark powder of *T. arjuna* causes a significant goes up. It might be acting by inhibiting the catecholamine release

from adrenal glands into the circulation, thus protecting the heart from catecholamine toxicity.^[34]

***Trigonella foenumgraecum* Linn. (Methi):-** The oral administration of *T. foenumgraecum* showed significant hypocholesterolemic and hypotriacylglycerolemic effects in cholesterol-induced Hyperlipidaemic rabbits, restoring the normal serum lipid levels and substantially lowering the tissue lipids.^[35]

***Triticum aestivum* Linn. (Wheat):-** Fresh grass juice of *Triticum aestivum* administered to rat produced dose related significant ($P < 0.05$) reduction in total cholesterol, triglycerides, LDL-C and VLDL-C levels in normal rats as compared to control.^[36]

***Vitis vinifera* Linn. (Grapes):-** Grapes are a rich source of polyphenolic compounds and flavonoids including quercetin, catechins, myricetin, kaempferol, and the isomers of resveratrol are the main constituents. Flavonoids, especially quercetin, are said to be far more effective than vitamin E in preventing the oxidation of LDL cholesterol, which is a contributor to the development of atherosclerosis. Proanthocyanins in grapes are both radical scavengers and xanthine oxidase inhibitors. *In vivo* lipid peroxidation has been implicated in many coronary malfunctions, including atherosclerosis and other ailments like aging and cancer. Phenolic constituents also inhibit cyclooxygenase and LOX in platelets and macrophages, thereby reducing thrombotic tendencies.^[37]

CONCLUSION

Among many disease or disorders, Hyperlipidaemia is one of the serious disorders effecting large population of the world. Hyperlipidaemia is associated with serious health risks and increased mortality. Hypertension, insulin resistance and glucose intolerance are known as cardiac risk factors that cluster in obese individuals. The persistence of hypercholesterolemic state causes enhanced oxidative stress, leading to the development of atherosclerosis, coronary artery disease (CAD) and other complications of obesity. Although the contribution of modern synthetic medicine for treatment of Hyperlipidaemia cannot be under-estimated, equally true is the fact that most of them have unwanted side effects. Hence in last few years the world has started exploring the herbs as agents for therapy which is safe, economical, and easily available as well as the minimum or no development of resistance towards causative organisms. Scientific validation of several plant species has proved the efficacy of the botanicals in reducing the cholesterol levels. From the reports on their potential effectiveness against hypercholesterolemia, it is assumed that the botanicals have a major role to play in the management of Hyperlipidaemia, which needs further exploration for necessary development of drugs and nutraceuticals from natural resources. However, many herbal remedies used today have not undergone careful scientific assessment, and some have the potential to cause serious toxic effects and major drug-to-drug interactions. Continuing research is necessary to elucidate the pharmacological activities of the many herbal remedies now being used to treat Hyperlipidaemia, atherosclerosis and other cardiovascular diseases.

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