A REVIEW ON MEDICINAL PLANTS WITH POTENTIAL HYPOLIPIDEMIC ACTIVITY

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ABSTRACT

Hyperlipidemia is the greatest risk factor contributing to atherosclerosis & occurrence of coronary heart disease & cerebrovascular accidents. Hence hypolipidemic drugs are extensively used as prophylactic agents to prevent such atherosclerosis induced disorders. But these hypolipidemic drugs are not free from adverse effects. Pancreatitis due to atorvastatin is a well known adverse effect and HMGCoA reductase inhibitors have also been reported to cause hyperglycemia and FDA has given a warning to this effect. Many plant derivatives and domestic remedies have been screened for their hypolipidemic action. More than 70 medicinal plants have been documented to have significant hypolipidemic action. This paper reviews these reports published in literatures in the last 5 years. This review indicates that the research has stopped with just reporting the effect of plant derivates and the findings are not translated into clinical research. Hence further research into identifying the active principle, conducting preclinical studies & if possible clinical studies is needed.

KEYWORDS: Hyperlipemia, Hypolipidemia, Medicinal plants.

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INTRODUCTION

Heart diseases have been implicated as leading causes of death in all racial and ethnic groups. The elevation of serum total cholesterol and low density lipoprotein (LDL) cholesterol has been reported as a primary risk factor for cardiovascular disease. Hyperlipidemia and reduced high-density lipoproteins (HDL-C) several risk factors such as lifestyle, genetic factors & metabolic disorders. Oxidative modification of human low density lipoprotein may play an important role in atherosclerosis. Hence hypolipidemic drugs are extensively used as prophylactic agents to prevent such atherosclerosis induced disorders but these hypolipidemic drugs are not free from adverse effects. Pancreatitis due to atorvastatin is a well known adverse effect. HMGCoA reductase inhibitors have been reported to cause hyperglycemia and FDA has given a warning to this effect. A number of plants have been used traditionally in the treatment of various cardiovascular diseases. The use of medicinal plants in the management of various illnesses is due to their phytochemical constituents and dates back to antiquity. However, during the last decade, an increase in the use of medicinal plants has been observed in metropolitan areas of developed countries. The advantages of herbal medicines reported are effectiveness, safety, affordability and acceptability.

The herbal medicines are categorized into 4 types

Category 1: Indigenous herbal medicines traditionally used by a community or a region.
Category 2: Herbal medicines in systems-reported in traditional systems such as Ayurved & Siddha
Category 3: Modified herbal medicines
Category 4: Imported herbal products

This review includes the herbal products in categories 1 to 2

Many plant derivates and domestic remedies have been screened for their hypolipidemic action. More than 70 medicinal plants have been documented to have significant hypolipidemic action. Aashish S Padkhe has already reviewed the studies on hypolipidemic activity of the following medicinal plants and herbs including Apium graveolans, Terminalia arjuna, Allium sativum, Zingiber officinalis, Achyranthes asparagus, Phyllanthus niruri, Musa sapientum, Coconut oil, Linum usitatissimum, Ginkgo biloba, Commiphora mukul, "Guggulu medhoanilaharanam sreshtam"-(Ashtanga Sangraham), Curcuma longa, Momordica charantia, Cymbopogon, Pterocarpus marsupium, Nigella sativum, Plantago psyllium, Soya bean, Ocimum sanctum, Embelia rebes burm. He suggested that collaborative works involving traditional, modern medical science & modern basic science have to be carried out to bring out solution for dyslipidemias.

1. Animal models used in this studies were the following Cholesterol-diet induced atherosclerosis in rabbits
2. Diet induced hypercholesterolemia in rats
3. Triton-induced hyperlipidemia- Triton WR 1 339 (isooctyl-polyoxyethylene phenol)

The other models which can be used are
1. Hereditary hypercholesterolemia in rats
2. Hereditary hyperlipidemia in rabbits
3. Transgenic animals- apo E knock out model
4. Fructose induced hypertriglyceridemia in rats

The earlier author Aashish S Padkhe has reviewed all the studies conducted during a period of 10 years from 1988-2005 the current author is reviewed articles published 2004 to 2013.

1. Capparis decidua (Sanskrit Name :- Karira)

Capparis decidua belongs to the family Capparidaceae. It is commonly found in the dry regions in India, Pakistan, Egypt and Tropical Africa. It’s a struggling, glabrous shrub. The bark has analgesic, diaphoretic, alexeteric, laxative, anthelmintic actions. It is good in cough, asthma, ulcers, boils, vomiting, piles and all inflammations.
Neelkamal Chahlia et al studied the ethanolic extract of various parts like fruit, bark & flower of Capparis decidua on lipid profile in Streptozotocin induced diabetic rats. The extract of fruit, bark & flower was given at a dose of 500mg/kg for 30 days. The serum and tissue samples of liver, heart and adrenal gland were assayed for biochemical parameters. Results showed significant decrease in total cholesterol, TG, LDL levels & it was more with bark and flower extracts than other parts and there was significant increase in HDL cholesterol compare to diabetic control. The underlying mechanism explained for lipid lowering activity was due to inhibition of lipid absorption by saponins and tannins.

2. Aconitum heterophyllum (Sanskrit Name :- Ativisha)
Aconitum heterophyllum commonly known as ‘Ativisha’or ‘Patis’ in Ayurveda; Aconitum heterophyllum is used traditionally to control obesity and included in lekhaneyagana a pharmacological classification mentioned in charaksamhita. Methanolic extract of Aconitum heterophyllum root was investigated for its hypolipidemic activity in diet induced obese rats against standard drug lovastation (mevinolin). After 4 weeks of treatment with extract, blood samples, faeces & liver tissue were used for estimation of serum cholesterol, TG, HDL-c,LDL-c, HMGCoA reductase, lecithin cholesterol acyltransferase and apolipoproteins. Results showed significant reduction in total cholesterol, TG, apolipoprotein B and increase HDL cholesterol& apolipoprotein A in serum samples and HMG CO A activity in liver samples. Activity of LCAT had increased & also there was increase faecal fat excretion. The mechanism explained for hypolipidemic activity was due to inhibition of HMG COA reductase activity and decrease fat absorption from intestine.

3. Dalbergia latifolia (Sanskrit Name: Simsapa)
Dalbergia latifolia (synonym Amerimnon latifolium) is an economically important timber species native to low elevation tropical monsoon forests of eastern India. Common names are blackwood, Bombay blackwood, rosewood, Roseta osewood, East Indian rosewood, black rosewood, Indian palisandre, and Java palisandre. Traditionally used for aphrodisiac, abortifacient, expectorant, anthelmintic, antipyretic, appetizer, allays thirst, vomiting, cures skin diseases, ulcers, diseases of the blood, reduces obesity, used in leucoderma, dyspepsia, dysentery, ring worm, syphilis, scabies leprosy. Mohammad Khalid et al conducted an in vivo study to investigate the hypolipidemic and hypoglycaemic potential of dried Dalbergia latifolia Roxb. bark extract in Sprague-Dawley rats induced with high fat diets. The treatment of dried Dalbergia latifolia bark extracts (DL-extract) at doses of 100, 200 and 400 mg/kg daily, together with continuous high fat diet feeding to hypercholesterolemic rats for 8 weeks significantly decreased serum cholesterol, triglycerides, low density lipoprotein (LDL) level with 200 and 400 mg/kg. Effect with 100mg/kg was not significant. Presence of phyto constituent β-sitosterol compound has been speculated for hypolipidemic effects of DL-extract.

4. Aloe vera gel (Sanskrit Name :- Ghrita kumari)
The Aloe vera plant has been known and used for centuries for its health, beauty, medicinal and skin care proper. Each leaf is composed of three layers with an inner clear gel that contains 99% water and rest is made of glucomannans, amino acids, lipids, sterols and vitamins. It has healing property, protective effect on skin against UV & gamma radiation, antitumor, antiviral, antifungal, antiseptic immunomodualtor, antiinfalmmatory effect & antiageing properties. Effect of processed Aloe vera gel (PAG) on lipid & blood glucose level was studied in a C57BL/6J mouse model of non-insulin-dependent diabetes mellitus. Oral administration of PAG for 8 weeks reduced circulating blood glucose concentrations to a normal level probably by decreasing insulin resistance. PAG has also significantly lowered triacylglyceride levels in liver and plasma. On histological examinations of peripipidymal fat pad showed that reduced the average size of adipocytes. This effect may be due to presence of phystosterols present in aloevera gel. They also examined the
expressions of adipogenic genes in adipose tissue which showed PAG suppressed the expressions of the adipogenic genes SREBP-1a, FAS, and GPAT\textsuperscript{12}.

5. \textit{Hibiscus cannabinus} L. (Sanskrit Name :- \textit{Sana})

Hibiscus is ornamental plant throughout India & popularly known as Kenaf\textsuperscript{a} in the western world. The plant has been used as an antidote for chemicals (acid, alkali, pesticides) poisoning and venomous mushrooms, to treat bruises, bilious conditions, fever etc. The stem peelings are being used in treating dysentery and blood & throat disorders. It is also having aphrodisiac, as well as fattening, purgative and stomachic\textsuperscript{13}. The effect of oral administration of 50\% hydroalcoholic extract of \textit{Hibiscus cannabinus} L. leaves (HC) on experimentally induced hyperlipidemia in rats was investigated. The extract exhibited a strong dose dependent(100mg/kg, 200mg/kg, 400mg/kg) antihyperlipidemic activity and at dose level 400mg/kg showed a significant decrease in the levels of serum TC, TG, LDL-C, VLDL-C and TBARS. In addition, the extract markedly prevented the liver microvesicular steatosis in hyperlipidemic rats. The presence of lignans, alkaloids and flavonoids as pharmacologically active compounds in HC may likely to have contributed for the observed hypolipidemic activity\textsuperscript{14}.

6. \textit{Eclipta prostrata} (Sanskrit Name :- \textit{Bringaraj})

Is a perennial herb belong to Asteraceae, used as tonic, deobstruent in hepatic and spleen enlargement and in skin diseases, and plant juice is administered for catarrhal jaundice in ayurvedic system of medicine. Aqueous extract of leaves of eclipta prostrata was investigated for hypolipidemic activity in atherogenic diet induced hyperlipidemic rats with 100mg/kg & 200mg/kg against standard drug atorvastatin. Results showed significant decrease in serum total cholesterol, TG & LDL compared to hyperlipidemic animals & increase HDL cholesterol with decrease in atherogenic index was observed\textsuperscript{15}. This is due to the presence of high amount of saponins & phytosterols in eclipta\textsuperscript{16}.

7. \textit{Moringa oleifera} Lam (Sanskrit Name :- \textit{Sobhanjana})

Horseradish plant or drumstick tree have been studied for several pharmacological actions like wound healing, antirolithiasis activity, antibacterial activity, antifungal, antitubercular activity and hypotensive actions. Pankaj G. Jain al et al studied the hypolipidemic activity of \textit{Moringa oleifera} Lam., on high fat diet induced hyperlipidemia in albino rats with simvastatin as standard drug. Methanolic extract of this plant in the dose of 150, 300 and 600 mg/kg, was given p.o., for thirty days. The hypolipidemic activity was assessed by faecal cholesterol excretion, HMGOA reductase activity & lipid profile in serum. Treatment with methanolic extract, at three different doses significantly decreased the levels of total cholesterol and LDL-c as compare to the controls. The cholesterol lowering effect may be due to inhibition in reabsorption of cholesterol from endogenous sources in association with a simultaneous increase in its excretion into faeces in the form of neutral steroids.\textsuperscript{17,18}.

\textsuperscript{a} This article can be downloaded from www.ijpbs.net

P - 732
8. **Terminalia Chebula** (Sanskrit Name :- Haritaki, Pathya)

Haritaki (Terminalia chebula) belongs to family Combretaceae and is one of component of the classic Ayurvedic combination “Triphala”. Terminalia chebula was given at doses of 1.05 and 2.10 mg/kg body weight and Ayurslim (250 mg/kg body weight) for 14 days for atherogenic diet induced hyperlipidemic rats. At the end of treatment lipid profile was estimated. There was significant decrease in all lipoproteins except HDL. Hypolipidemic effect was due to high amount of saponins, phytosterols, chebulinic acid and corilagin present in Haritaki19&20.

9. **Pithecellobium Dulce** (It is a Chinchabedha i.e Vanachincha or Adavichinta)

Pithecellobium native to tropical America cultivated throughout the plains of india, belonging to leguminosae family. The leaves have been reported to possess astringent, emollient, and anti diabetic properties. Aqueous extract of Pithecellobium Dulce 200mg/kg per oral has been given for 7 days after inducing hyperlipidemia by single dose of triton and compared with standard drug fenofibrate. Triton Wr-1339 induces acute hyperlipidemia in animals by blocking clearance of triglyceride-rich lipoproteins. On 8th days blood samples & liver tissues were tested for lipid profile. The Pithecellobium dulce markedly lowers the levels of serum cholesterol and VLDL. The decrease in cholesterol may be due to increased oxidation of mobilized fat 21.
10. Ougeinia Oojeinensis (Sanskrit Name :- Jinghini, Atimukta)
The plant Ougeinia oojienensis (Roxb.) belonging to family Fabaceae and commonly known as Atimukta in Sanskrit. The ayurvedic formulation of this plant being used clinically for burning syndrome, skin disease, urinary disorder, obesity, anti inflammatory, anti spasmodic, and anti hypertensive activity. C Velmurugan et al. studied anti Diabetic and Hypolipidemic Activity of Bark of Ethanolic Extract of Ougeinia Oojeinensis (ROXB.) in alloxan induced diabetic rats. The effect of extract on various biochemical parameters & body weight was studied in diabetic rats. Ougenina Oojeinensis at 200 mg/kg showed significant reduction in lipid profile and increased level of HDL in diabetic model rats. The hypolipidemic properties of Ougenina Oojeinensis may be due to presence of different types of active metabolites like saponins, flavonoids phenolic compounds and triterpenoids.

11. Randia dumetorum & Paederia foetida (Sanskrit Name :- Madana & Prasarini)
Randia dumetorum commonly known as indigo berry belonging to family Rubiaceae & Paederia foetida commonly known as stinkvin family Rubiaceae. Triton WR-1339 was used for inducing hyperlipidemia in this study. The dried and ground parts of fruit of Randia dumetorum and aerial part of Paederia foetida were used for this study at a dose of at the dose of 400 mg/kg/day respectively as single dose for two days. The Blood samples of each animal were collected at 0, 18, 24, 40 and 48 hrs post treatment and the results were analyzed and compared with standard drug fenofibrate. Results showed Randia dumetorum when compared with Paederia foetida showed comparatively better hypolipidemic activity.

12. Sesbania grandiflora (Sanskrit Name :- Agastya)
Sesbania grandiflora (Fabaceae), native to many Asian countries like India, Malaysia, Indonesia and Philippines. Sesbania grandiflora L. is popularly known as “Basna” is an ornamental plant and is found in plains of western Himalayas to Sri Lanka. Sesbania grandiflora is a folk remedy for bruises, catarrh, dysentery, eyes, fevers, headaches, small pox, sores, sore throat and stomatitis. Anti-hyperlipidemic activity of aqueous extract of leaves of SG against triton induced hyperlipidemia in rats was evaluated against standard drug fenofibrate. SG administered at a dose of 200µg/kg (p.o) to the triton induced hyperlipidemic rats for 7 days. SG shows a significant decrease in the levels of cholesterol, phospholipid, triglyceride, LDL, VLDL and significant increase in the level of serum HDL at the dose of 200µg/kg (p.o) in serum as well as in liver tissue. Flavonoids and anthocyanins, a heterogenous group of polyphenols present ubiquitously in this plant could be attributed to hypolipidemic activity.

13. Luffa aegyptiaca (Sanskrit Name :- Raja-koshataki)
Luffa aegyptiaca Mill fruits commonly known as Luffa, belonging to family Cucurbitaceae is a climbing herb. The medicinal uses of Luffa are as Dyslipidemic, Anti-Diabetic, Hepatoprotective, Anti-Hypertensive and Diuretic. British people are extensively using Luffa aegyptiaca Mill fruits along with egg preparations as a food habit, which is possibly reduces the cholesterol from the egg. Luffa aegyptiaca tender fruit is taken as vegetable,
the course sponge of mature fruit is used as a bath scrub and juice of leaves cures conjunctivitis. Abdul hameed thayyil et al evaluated hypolipidemic activity of *Luffa aegyptiaca* fruits in cholesterol fed hypercholesterolemic rabbits. Methanolic extract of *Luffa aegyptiaca* fruits at 300mg/kg significantly reduced serum lipid profile This hypolipidemic activity is attributed to the presence of chemical ingredients in *Luffa aegyptiaca* fruit such as Ascorbic acid, Niacin, Fiber, MUFAs (Linoleic acid, Oleanolic acid, Oleic acid) and stearic acid.

14. *Lycium barbarum* (Sanskrit Name :- Chirachata)
Lycium barbarum L. Belongs to family Solanaceae is well-known in traditional Chinese herbal medicine and nowadays fruit has been widely used as a popular functional food, with a large number of therapeutic beneficial effects, such as reducing blood glucose and serum lipids, anti-aging, immunomodulating, anticancer, anti-fatigue, and male fertility-facilitating. Qiong Luo et al evaluated the hypoglycemic and hypolipidemic and antioxidant activity of *Lycium barbarum* fruit water decoction, crude polysaccharides, and its purified polysaccharide fractions in alloxan-induced diabetic rabbits. After the treatment with *lycium* fruit extract for 10 days there was significant reductions in serum lipids & increase in HDL-c. *Lycium barbarum* extracts were rich in antioxidant components, such as carotene, ascorbic acid, thiamine, riboflavin, nicotinic acid, zeaxanthin, cryptoxanthin, and coumarin (scopoletin) which were responsible for its this property.

15. *Tinospora cardifolia* (Sanskrit Name :- Guduchi , Amrita)
Stem of the plant have reported to possess memory enhancing, antistress, antidepressant, anti-inflammatory, antioxidant, antiischemic, antiallergic, antifertility & antineoplastic properties. Evaluation of antiobesity activity of petroleum ether extract of tinospora cardifolia stems in rats was done by Dhingra Dinesh. Obesity was induced by cafeteria diet.
& antipsychotic drug sulpiride at a dose of 200mg/kg for 28 days. They measured body weight, lipid profile after 41 days in cafeteria diet group & 29 days in sulpiride group. Cafeteria diet induces obesity by causing hyperphagia, increase fat stores & down regulation of striatal D2 receptors. Antiobesity activity of tinospora extract was due to the presence of tannins & flavonoids, which can cause weight reduction, increase dopaminergic transmission, increase in thermogenesis \(^{27,28}\).

16. **Bauhinia purpurea** (Sanskrit Name :- Kanchan)

*Bauhinia purpurea* is a species of flowering plant in the family Fabaceae, native to South China (which includes Hong Kong) and southeastern Asia. Common names include Hong Kong Orchid Tree, Purple camel's foot, and Hawaiian orchid tree. Several species of this plant are known to possess pharmacological activities. Leaves have antinociceptive, anti-inflammatory, antipyretic, hypoglycaemic, nephroprotective, antimalarial, antimycobacterial, antifungal and cytotoxic activities, antioxidant and hepatoprotective activities. Hypolipidemic activity of ethanol extract of leaves and unripe pods at a dose of 300mg/kg was evaluated in diet induced hyperlipidemic rats. After 30 days treatment with unripe pods extract and leaf extract showed a marked reduction lipid profile & significant rise in HDL-c levels in all the groups. The probable mechanism for the cholesterol lowering effect of the extracts might be due to inhibition of dietary cholesterol absorption and/or esterification. The active compounds responsible for this effect are polyphenolic compounds flavonoids, tannins and proanthocyanidines \(^{29}\).

17. **Piper longum** (Sanskrit Name :- Pippali)

*M. longum* L. Commonly called as “Long pepper”. The Roman emperors valued it even more highly than black pepper due to its high commercial and economical importance. Fruit had reported to possess insecticidal activity, anti fungal, analgesic activity, anti depressant activity, anti ulcer activity, anti microbial activity, anti depressant activity, anti asthmatic activity, anti cancer activity. Shaik Abdul nabi et al. investigated anti diabetic and anti hyperlipidemic activity of piper longum root aqueous extract in streptozotocin induced diabetic rats. In this study aqueous extract of *Piper longum* root significantly reduced the TC, TG, LDL-C and VLDL-C levels with an increase of HDL-C in treated diabetic rats \(^{30}\).

18. **Urtica dioica** [L] (Sanskrit Name :- Vrischikasaka)

*Urtica dioica* commonly known as stinging nettle belonging to family urticaceal. It is having anti viral, antifungal actions. It has favourable effects on cardiovascular system. Preliminary studies revealed that *U. dioica* is having diuretic and hypotensive effect. Other medicinal uses are allergic rhinitis, diabetes, prostatic hyperplasia, in inflammation. M.das et al., evaluated anti hyperglycemic and anti hyperlipidemic activity of Urtica dioica on type 2 diabetic model rats. treated with aqueous extract of urtica dioica at a dose of 125mg/kg for 28 days. They were observed that aqueous extract significantly lowered the cholesterol levels & other lipoproteins except HDL-c in type 2 model in rats \(^{31}\).
19. **Psidium guajava Linn** (Sanskrit Name :: Perala, Amrutafalam)

Plant Psidium guajava belonging to family Myrtaceae commonly known as guava, is a shrub often grows naturally in the house gardens in the tropical regions. Traditionally the leaves of the guava tree are used to treat diarrhea, gastric disorders, wound healing, cancer, epilepsy. Shinde et al. Investigated hypolipidemic activity of psidium guajava linn leaves extracts in hyperlipidemic rats. Treatment of hyperlipidemic rats with methanolic and aqueous extract of Psidium guajava L. at a different doses 200 mg/kg, and 400 mg/kg along with cholesterol diet shown significantly decrease in serum TG, TC and LDL-C levels as well as significant decrease in Atherogenic index value.

20. **Piliostigma thonningii** (Sans. Not available)

Piliostigma thonningii also known as schumcamel’s foot / monkey bread. Traditionally it is used in the management of malaria, fever, wound, ulcers, dysentery, diarrhoea, infections, snake bites and cough. Dasofunjo K., et al investigated the effect of ethanolic leaf extract of Piliostigma thonningii on serum lipid profile of male albino rats at a dose of 50,100 and 200mg/kgfor 21 days. Results showed significant decrease in serum LDL-c and TC and significant increase of HDL-cholesterol but no significance changes in TG levels in all treatment groups. Phytochemical screening revealed the presence of flavonoids, tannins, steroids, phlobatannin, terpenoid (highest conc), cardioglycosides and saponin at varying concentrations which may be responsible for this effect.

**Phytochemical constituents – its effect on hyperlipidemia**

The presence of bioactive phytoconstituents such as saponins, tannins, flavonoids, terpenoid, cardioglycocides and steroids are known to perform several general and specific function in plants and many exhibits different biochemical and pharmacological actions in different species of animals when injected. The action ranges from cell toxicity to cell protective effect. VLDL is the transporter for triglycerisdes and Saponins is known to lower triglyceride level due to their lytic role which may lead to reduced VLDL cholesterol in serum. Phytosterol are reported to displace intestinal cholesterol and reduce cholesterol absorption from intestine. Saponins are also found to inhibit enterohepatic circulation of bile acid, making it unavailable for intestinal absorption which leads to decrease cholesterol absorption from intestine. Several authors reported from different parts of India that many traditional plants have hypolipidemic activity & mechanism of action of these plants vary but ultimately all reduce cholesterol level. This review has identified a long list of lipid lowering plants, the use of many of which has not reached the common public as regulated formulations exceptionally the preparations like Triphala (contains emblica, terminalia chebula, terminalia bellerica) & Trimada (contains embelia, cyperus rotundus, plumbago), Arogyavardhini, Medhohara guggulu andMedhoharavidangadiguggulu are available in the market as ayurvedic preparations for hyperlipidemia.
CONCLUSION

The present review has provided an overview of plants having hypolipidemic activity. It shows that currently used hypolipidemic drugs are associated with so many adverse effects and withdrawal is associated with rebound phenomenon which is not seen with herbal preparations. Plant parts or plant extract are sometimes even more potent than known hypolipidemic drugs. This review indicates that the research has stopped with just reporting the effect of plant derivates and the findings are not translated into clinical research. Taking these finding forward is mandatory to develop new drugs in this area. Hence further research into identifying the active principle, conducting preclinical studies & if possible clinical studies is needed.

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