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Research article

Antihyperlipidemic activity of herbs commonly used in Siddha Medicines based on Taste – A Review

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ABSTRACT

Hyperlipidemia is one among the Non communicable disease with its incidence on the raise across the globe. High-energy, high-fat, and high-saturated fatty acid diet, which can promote the synthesis of cholesterol, is the most common risk factor of hyperlipidemia, especially hypercholesterolemia. Hypercholesterolemia, a significant cardiovascular risk factor, is one of the major oxidative stresses that generate excess of highly reactive free radicals. This exacerbates the development and progression of atherogenesis induced hypercholesterolemia with a risk of increased LDLc or more accurately LDLc/ HDLc ratio. The atherogenic index can be decreased by reduction in LDLc and increment in HDLc. Further health risks due to hypercholestremia could be kept in check with drugs having the property to reduce the cholesterol level and to scavenge the free radicals. Siddha system of medicine uses a wide range of herbs with the similar potency based on taste. This paper is a collection of some herbs like fenugreek, garlic, onion, turmeric, cumin seeds that are commonly used in day to day life, as medicines in treating ailments, as *kayakalpam* and to explore their lipid lowering activity that are commonly used in Siddha system of medicine on scientific background.

Keywords:

Hyperlipidemia, Siddha Medicine, taste, free radicals, fenugreek, garlic, turmeric, onion, *kayakalpam*.

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INTRODUCTION

Hyperlipidemia refers to disorder of lipid metabolism manifested by increase of plasma concentrations of the various lipid and lipoprotein such as increase of serum total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG) concentrations and a decrease in the high-density lipoprotein (HDL) concentration [1-2].

Life style modification, very less physical activity westernized food intake pattern is also known to increase risks of hyperlipidemia and comorbidites[3-8].The most common pattern of dyslipidemia is hypertriglyceridemia and reduced HDL cholesterol levels. Hyperlipidemia commonly presents itself as an associated complication of diabetes mellitus. The small dense LDL particles found in type 2 DM are more atherogenic because they are more easily glycated and susceptible to oxidation. There is increased risk of atherogenic dyslipidemia and hypertension in diabetes, hence increased prevalence of coronary artery diseases, heart failure, and stroke in diabetic population [9].

Traditional system of medicine has been increasingly used for the treatment of dyslipidemia and cardiovascular disease. Recently, much progress has been made in studies on the mechanisms of action of the lipid-regulating e□ect of these medicines in animal experiments. Herbs with antioxidant and antihyperlipidemic property could be the best solution in preventing atherogenicity and development of CVD as they possess scavenging activity against high reactive oxygen molecules & oxidative stress. Recent findings also suggest that plant sterols (e.g., stigmasterol and β-sitosterol actively influence cellular cholesterol metabolism within intestinal enterocytes and, in response to the reduced supply of exogenous cholesterol, receptor-mediated lipoprotein cholesterol uptake is probably enhanced, as shown by increased LDL receptor expression**.** In addition, cellulose, pectin, and agar, which are also rich in many herbal medicines, can reduce the absorption of cholesterol by forming a complex with cholate to impede the formation of cholesterol microparticles in the intestine [10,11]**.**

Medicinal plants also inhibit hepatic cholesterol biosynthesis and reduction of lipid absorption in the intestine. Siddha system of medicine can prevent and treat metabolic diseases & ageing process by kaya kalpa medicines coined by various Siddhars.

This paper provides an overview& scientific evidence of the herbs and raw drugs commonly used in day to day life and in Siddha system of medicine that are capable to regulate the increased lipid levels. These age-old medications need to be validated scientifically for implications in future development of lipid-lowering drugs.

HYPERLIPIDEMIA:

Hyperlipidemia refers to a disruption of lipid metabolism with exceeding serum levels of cholesterol (TC), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), and/or lower level of high-density lipoprotein-cholesterol (HDLC). Serum levels of lipids and lipoprotein lipids are among the most potent and best substantiated risk factors for atherosclerotic diseases, particularly coronary heart disease (CHD)[12]. Lipid homeostasis is regulated by well-balanced mechanisms of intestinal uptake, endogenous synthesis and metabolism, transport in lipoprotein particles, and biliary excretion. Failure in the maintenance of lipid homeostasis leads to Hyperlipidemia. Drugs that alter lipids concentration act mainly by altering the kinetics of one or more parts of the metabolic cycle. Traditional system of medicine has been increasingly used for the treatment of Hyperlipidemia and cardiovascular diseases as they interfere with the excess absorption, endogenous synthesis and promotes the metabolism and excretion.

METHODS

. This review article includes information on antihyperlipidemic activity of some herbs with details of animal studies and clinical studies to add a scientific validation to the herbs that are commonly used in Siddha system of Medicine based on taste. Specific literature evidences are also included in this paper.

Herbs (common name)	Taste	Uses
Garlic	Pungent	Cough, bronchial asthma, indigestion [13]
Fenugreek	Bitter	Fever, burning sensation, thirst, cough, hepato&spleenomegaly[13]
Cardamom	Pungent	Pitha diseases, indigestion, cough, hepatomegaly[13]
Malabar tamarind	Sour	Dyspepsia[13]
Arjun tree	Astringent	Cardiac tonic[13]
Myrrh tree	Bitter	Diuretic , fever, joint pain[13]
Turmeric	Bitter	Jaundice, cough, fever, indigestion, insect bites. [13]
Jeera	Pungent, Sweet	Indigestion, fever, cough, gastritis. [13]
Onion	Bitter	Irregular menstruation, gastritis, hepatomegaly[13]
Cinnamon Tree	Pungent,Sweet	Bronchial asthma, cough, indigestion, dysentery[13]

Taste	Basic elements		Property
Inippu(Sweet)	*Manbootham* (Earth)	*Neerbootham* (Water)	Delay digestion, increases body weight
Pulippu(Sour)	*Manbootham*(Earth)	*Theebotham* (Fire)	Promotes digestion, reduces *vatham*
Uppu(Salt)	*Neerbootham*(Water)	*Theebotham* (Fire)	Produces heat, hastens digestion
Kaippu(Bitter)	*Valibootham*(Air)	*Visumbu* (Ether)	Ease digestion, kills germs, reduces *kapam*
Kaarppu(Pungent)	*Valibootham* (Air)	T*heebotham* (Fire)	Normalize *kapam*
Thuvarppu(Astrigent)	*Valibootham*(Air)	*Manbootham (*Earth)	Normalize *pitham*

TASTE FORMATION AND ITS FUNCTIONS:

According to the concept of Siddha each and everything in the universe which is made up of the five basic elements such as earth, water, fire, air, space, reflects the nature of universe and is quoted by the above said lines, *Andathilullatheypindam*. Likewise, taste is also the combination of any two of the five basic elements and drugs for ailments are selected based on taste. Sometimes a single herb or mineral may have more than one taste but only one acts as the *muthanmaisuvai* (prime taste)[14]. Combination and properties of six tastes are described in the table.

1.Garlic:*(Allium sativum)*

Garlic has antihypertensive, antihypercholesterolaemic, cardioprotective,antiplatelet, hypoglycaemic activities due to the presence of alliin, allicin, diallyl disulphide, S-allylcysteine and diallyl trisulfide organosulfurcompounds [15-20]. Garlic significantly reduced serum total cholesterol and LDL cholesterol and moderately raised HDL cholesterol as compared to placebo in patients with type 2 diabetes mellitus [21].Consumption of dry garlic powder could be beneficial on the plasma lipid profile in hypercholesterolemia [22].Alcoholic extracts and aqueous extract of garlic had a significant hypolipidemic activity in hyperlipidemic guinea pigs[23]. Garlic inhibit hepatic cholesterol synthesis by water-soluble sulfur compounds, especially SAC (Sallylcysteine) [24].

Garlic can inhibit enzymes involved in lipid synthesis, decrease platelet aggregation, prevent lipid peroxidation of oxidized erythrocytes, inhibit angiotension-converting enzyme, reduce serum total cholesterol, platelet aggregation and hypertension. Clinical trials have indicated garlic's ability to reduce the ability of platelet aggregation, blood pressure and oxidative-stress reduction[25]. Garlic consumption reduces the activity of the enzyme-HMG-CoA reductase and may influence the level of cholesterol hydroxylase and other enzymes-fatty acid synthase. Garlic has specific anti-atherosclerotic effects, by reducing the mRNA expression of inducible nitric oxide synthase (iNOS) and inhibition of oxidized low-density lipoprotein (LDL) induced by lactate dedrogenase (LDH) and inhibition of oxidized LDL induced by depletion of glutathione [26].

Garlic may play an important role in the treatment of dyslipidemic patient by reducing both total cholesterol (TC) and triglycerides (TG)[27]. Garlic is a potential stimulant of lipase enzyme thereby, decreasing blood triglyceride level [28-30].

2.Fenugreek:*(Trigonella foenum)*

Fenugreek cold extract when given orally to test animals, improved the lipid profile by lowering serum total cholesterol, triglyceride and LDL cholesterol concentration but the HDL cholesterol concentration was significantly higher. The prepared herbal extract improved the HDL/ LDL ratio and was comparable to that of standard drug in maintaining the same in the normal range[31-34] and increased the excretion of cholesterol and total bile acids into the faeces [35].

3. Cardamom: *(Elletra cardamom)*

The extracts and its constituents of cardamom possess anti-hyperlipidemic and antioxidative effects[36-39]. The oral administration of cardamom extract has beneficial effects on blood cholesterol, triglyceride, VLDL, HDL and LDL levels in 18 adult male and female Wistar rat[40].A significant decrease in the fasting and postprandial blood glucose levels, decrease in the total cholesterol and triglyceride and increase in HDL levels were observed in the cardamom and pioglitazone-treated groups as compared to dexamethasone control group ($P < 0.01$)[41]. Cardamom in a dose of 3 g in 2 divided doses per day over 3 months reduced systolic, diastolic and mean blood pressure, increased fibrinolytic activity, antidiabetic and significant renal protective effect also enhanced antioxidant status in a study of newly diagnosed individuals with primary hypertension of stage I[42-45].

4.Malabar tamarind:*(Garcinia cambogia)*

The L-hydroxy citric acid in the fruit of Garcinia has lipid lowering action and hence used in obesity. Crude ethanolic extracts of G.cambogia (bitter kola) seeds showed dose-dependent decrease in the plasma level ofvery-low-density lipoprotein and a dosedependent increase of chylomicrons in adult male rats. G.cambogia extract effectively lowered the body weight gain, visceral fat accumulation, blood and hepatic lipid concentrations, and plasma insulin and leptin levels in a high-fat diet (HFD)-induced obesity mouse model [46].

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5. Arjun tree:*(Terminalia arjuna)*

The hypolipidemic activity of the 50% ethanol extract of bark of T. arjuna were evaluated in rats. The 50% v/v ethanol bark extract at the dose of 40mg/kg body weight, substantially reduced the plasma total cholesterol, triglycerides and LDL cholesterol while HDL cholesterol increased in experimental group in comparison with hypercholesterolemic animal group. The bark extract of Terminalia arjuna has excellent hypolipidemic activity. The effect of the extract seems to be mediated through increased hepatic clearance of cholesterol, down regulation of lipogenic enzymes and inhibition of HMG- CoA reductase [47].

6. Myrrh tree: *(Commiphora mukul)*

The plant sterol guggulsterone [4,17 (20)-pregnadiene3,16-dione] (GS) is the active substance inthe resin of the guggul tree (Commiphoramukul). It is used to treat a variety of disorders in humans, including dyslipidemia, obesity, and inflammation.GS is a highly e□cacious antagonist of the farnesoid X receptor (FXR), a nuclear hormone receptor that is activated by bile acids. GS treatment decreases hepatic cholesterol in wild-type mice fed a high-cholesterol diet but is not e□ective in FXR-null mice. Inhibition of FXR activation is proposed as the basis for cholesterol-lowering activity [48,49].

Co-administration of cloves showed enhanced activities ofantioxidant enzymes such as SOD, CAT, GPX and GST.Hypolipidemic efficacy of S. aromaticum is revealed by the attainment of near normal values in lipid profiles in rats fed with high fat diets. The hypolipidemic effect of S. aromaticum may be due to its ability to combat oxidative stress by quenching free radicals generated in the body as a result of HFD [50].

7.Turmeric: *(Curcuma longa)*

Curcumin a potent antioxidant and anti-inflammatory component of turmeric is found to increase LDL receptor (LXR), which plays a role in elimination of LDL from blood [51,52]**.** Tetrahydrocurcumin (THC) is one of the major metabolites of curcumin exert greater antioxidant activity in both in vitro and in vivo systems [53-56].Administration of THC and curcumin to diabetic rats reversed the level of serum total lipids, LDL,VLDL, triglycerides and phospholipids back toward normal level[57].THC and curcumin significantly reduce the levels of serum and liver lipids, in STZ and nicotinamide diabetes rats[58].

8. Cumin seeds*: (*Cuminum cyminum)

Ethanolic extract of seeds of *Cuminum cyminum* was found to have antidyslipidemic activity as evident by 21.04% ($P < 0.01$) decline in serum triglycerides, 22.7% ($P < 0.01$) decline in total serum cholesterol, and 16.9% of decline in serum LDL-C, respectively, along with 12.2% ($P < 0.05$) increase in serum HDL-C on high fat diet fed male Syrian golden hamster[59].

9.Onion:*(Allium cepa)*

The flavonoid of onion (quercetin, quercitrin, and rutin) and sulfuric compounds (allyl propyldisulfide, diallyl disulfide) has health improving effects and also decrease blood cholesterol levels, prevent cardiovascular diseases. S-methyl-L-cysteine sulphoxide in onioncan normalize lipid contents in blood[60-64]. Fermented onion extract shows antioxidative activity (ORAC), inhibitory effect on adipocytes differentiation and antihyperlipidemic activities. In addition, the inhibition activity of HMG-CoA reductase andCETP was increased 20% in the fermented onion-treated group at 100 mg/kg. Oral administration has a hypolipidemic effect on lipid metabolism due to the presence of quercetin [65].

10.Cinnamon tree: *(Cinnamom vera)*

The phytochemical screening of cinnamon revealed the presence of alkaloids, coumarins, flavonoids, saponins, carbohydrates, steroids, tannins and phenols. Blevins et al. (2007) reported that oral administration of cinnamon (20 mg/Kg body weight) significantly decreased serum total cholesterol, triglyceride levels and at the same time markedly increased plasma insulin. Treatment with cinnamon essential oil significantly decreased and improved the diabetic status including protection of DNA against oxidative damage and hypocholesterolemic effect in experimental rats [66].

DISCUSSION

The selected herbs have antihyperlipidemic activity which is clearly established through animal and clinical studies. In the above said herbs most of the herbs have pungent, bitter taste and some are astringent. Few of them has sweet taste but not as a prime taste. Sweet is considered as the natppu taste for salt. A basic property noted in the herbs possessing antihyperlidimeic activity is that they don't have sweet or salt taste which are formed by the combination of *neerbootham* with *manbootha-m*and *theebotham*. Among body constituents' blood, body fat and semen are formed by *Neerboootham*. Here aiyam is formed by the basic elements air and water, hence the bitter and astringent tastes are able to reduce the water-based body constituents like fat, cholesterol and triglycerides. Studies also shows that high preference to sweet taste increases the risk of developing hyperlipidemia compared to non -preference individuals as sweet is a source of high calorie levels [67,68]. High dietary salt intake is a known risk factor for the development of cardiovascular diseases.

CONCLUSION

The present study has used the data of clinical and animal trails using herbs with antihyperlipidemic activity. The findings of the studies suggest that herbs with bitter, pungent, astringent tastes are commonly used in lowering the lipid levels, whereas sweet and salt tend to promote hyperlipidaemia and its comorbidities. Considering these facts, it is suggested that herbs commonly used in Siddha Medicines with tastes other than sweet and salt could be a better choice in regulating the lipid profile towards normalcy.

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