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DIETARY SPICES AS ANTI-HYPERLIPIDEMIC AGENTS WITH THEIR BIOACTIVE COMPOUNDS FOR CARDIOVASCULAR HEALTH: A REVIEW

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ABSTRACT

Hyperlipidemia is associated with elevated cholesterol and triglyceride levels which is a risk factor for atherosclerosis. Spices being an integral part of culinary culture around the world are known to possess anti-cholesterol compounds and increase the high density lipoprotein cholesterol. This review presents a comprehensive scientific data on the anti-cholesterol/hypolipidemic activities of various spices used in traditional medicine and cuisine. Bioactive compounds from spices with anti-hyperlipidemic activities and their mode of action are summarized. The findings reaffirm the importance of spices by suggesting their anti-hyperlipdemic/anti-cholesterol activities to prevent cardiovascular diseases.

***Keywords*:** Spices, Anti-cholesterol, anti-hyperlipidemic, hypocholestrolemia, hypolipidemic.

INTRODUCTION

Hyperlipidemia is ranked as one of the greatest risk factors contributing to the prevalence and severity of coronary heart diseases. Hyperlipidemia involves an imbalance of cholesterol levels, including low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) in the blood. LDL-C and HDL-C regulate the amount of cholesterol in the body and an imbalance can increase the risk of cardiovascular events, including myocardial infarction and stroke. An increase in high density lipoprotein cholesterol and a decrease in total cholesterol, low density lipoprotein cholesterol and triglycerides are associated with a decreased risk of heart diseases.

Spices imparting flavor, color, pungency and are also known to possess several medicinal properties. Spices have been an integral part of culinary culture around the world and have a long history of use for flavoring, coloring, and preserving food, as well as for medicinal purposes (Jiang, 2019). The long historical use of spices for their medicinal benefits is fully acknowledged, and there is a growing amount of literature concerning the potential/ purported benefits of spices from a health perspective. India with its wide climatic conditions and topographical features naturally possesses wide variety of spices which are being used in the diet. The health promoting properties of spices are related to their phytochemicals composition. There is, however, no updated compilation of anti-cholesterol activities of spices to provide a complete knowledge while using spices to control cholesterol levels. This review endeavors to systematically review scientific data on the anti-cholesterol/hypolipidemic activities of various spices used in traditional medicine and cuisine.

Methods

Systematic literature searches were carried out in the terms: spices and anti-cholesterol. Information was collected via search and studies in electronic databases including Web of Science, Pub. Med, Science Direct and Scopus.

Black pepper

Piper nigrum L., most commonly known as pepper is well renowned in folk medicine in several countries. The main odorants identified from the fruit of *P. nigrum* were α- and β-pinene, myrcene, a-phellandrene, limonene, linalool, methylpropanal, 2- and 3-methylbutanal, butyric acid and 3-methylbutyric acid. One of the major active components (5–9 %) in black pepper is an alkaloid amide called piperine (Madhavi *et al.*, 2009). Black pepper also contains alkamides, piptigrine, wisanine, and dipiperamide (Kapoor *et al.*, 2009). Black pepper reduces total cholesterol, free fatty acids, phospholipids and triglycerides in plasma and tissue of rats on a high-fat diet (Vijayakumar *et al.*, 2002). Piperine also enhances energy metabolism in the body; upon oral administration it was shown to markedly decrease the free cholesterol/esterified cholesterol ratio and phospholipid fractions level in rat testis (Malini *et al.*, 1999). Supplementation of black pepper to daily diet can promote absorption of nutrients and modulate lipid profile and obesogenic marker expression in high-fat-diet (HFD)-treated rats (Vijayakumar and Nalini, 2006). Duangjai *et al.*, (2013) found piperine lowers blood lipids in vivo and inhibits cholesterol uptake in vitro. The mechanism of this effect was not due to the interference of either the size of lipid micelles or the cholesterol efflux pathway, nor changing of solubility of lipid micelles, but translocation of cholesterol transporter NPC1L1 and SR-BI proteins to the cytosol.

Piperine has been shown to inhibit lipid droplet accumulation in mouse macrophages that are converted to foam cells in an animal study, suggesting it may help retard the progression in which fatty deposits build up in the arterial wall (Matsuda *et al*., 2008). Piperine also reduced plasma lipid and lipoprotein levels in rats (Vijayakumar and Nalini, 2006), inhibited platelet-derived growth factor-BB-induced proliferation and migration of vascular smooth muscle cells in blood vessels (Lee *et al*., 2015), and lowered blood pressure in animals (Taqvi *et al*., 2008).

Cinnamon

Cinnamomum, a tropical evergreen plant that has two main varieties; *Cinnamomum zeylanicum* and *Cinnamon cassia*. Cinnamon has been used as a spice in several cultures for centuries. Cinnamon's key components are essential oils and other derivatives such cinnamaldehyde, cinnamic acid and cinnamate, eugenol and water soluble polyphenols. Cinnamon supplementation significantly reduced blood triglycerides and total cholesterol concentrations without any significant effect on LDL-cholesterol and HDL-cholesterol (Maierean *et al*., 2017). Kim *et al*. (2006) demonstrated the effect of *Cinnamon* extract on blood lipids in an in vivo study. HDL-cholesterol concentrations were significantly higher ($p < 0.01$) in mice fed with cinnamon extract, and the concentrations of triglyceride were significantly lower. Khan *et al*. (2003) determined that after 40 days, 1, 3, or 6 g of cinnamon daily reduced triglyceride (23–30%), LDL cholesterol (7–27%), and total cholesterol (12–26%) levels. Similar hypocholesterolemic effects of *C. zeylanicum* were reported by Subash Babu *et al*. (2007). Javed *et al*. (2012) suggested that *C. zeylanicum* bark powder at the rate of 0.50 g/kg, 0.75 g/kg and methanol extract equivalent to 0.75 g/kg powder produced respective percent reductions in total lipids by 45, 49 and 64; triglycerides by 38, 53 and 60; total cholesterol by 53, 64 and 69 and LDL-cholesterol by 50, 59 and 62. Hassan *et al*. (2012) demonstrated that *C. zeylanicum* reduced total cholesterol, LDL cholesterol and triglycerides while increasing HDL-cholesterol in diabetic rats.

Clove

Syzygium aromaticum, also known as clove contains eugenol as the major bioactive molecule along with hidroxibenzoic acids, flavonoids, hidroxiphenyl propens, hidroxicinamic acids and gallic acid derivatives. *S. aromaticum* leaf meal had reduced the broiler's meat cholesterol level and lipid oxidation as reported by Adu *et al*. (2020). Another study reported the in vitro and in vivo experiments have documented the antiobesity efficacy of *S. aromaticum* extracts by reducing the serum triglycerides and cholesterol levels (Jung *et al*., 2012). *S. aromaticum* also reduced formation of cholesterol micelle as investigated by Sompong *et al*. (2016)

Coriander seeds

Coriandrum sativum (Coriander) has been documented as a traditional treatment for cholesterol The level of low density lipoprotein, very low density lipoprotein cholesterol decreased while that of high density lipoprotein cholesterol increased in the experimental group of rats fed with coriander seeds Dhanapakiam *et al*. (2008). Chithra and Leelammma (1997) reported the levels of total cholesterol and triglycerides decreased significantly in the tissues of rats which received coriander seeds. Significant increases in beta-hydroxy, beta-methyl glutaryl CoA reductase and plasma lecithin cholesterol acyl transferase activity were noted in the experimental group. The level of LDL + VLDL cholesterol decreased while that of HDL cholesterol increased. Similar studies were carried out by Sreelatha and Inbavalli (2012) where the levels of serum total cholesterol, triglycerides, and low-density lipoprotein cholesterol were lower in the extract-treated group and high-density lipoprotein cholesterol was higher. Another study reported *C. sativum* at a dose of 1g/kg body weight reduced cholesterol and triglycerides levels in both synthesis and excretory phases in rats (Lal *et al*., 2004). Aisssaoui *et al*. (2011) found that aqueous extract of *C. sativum* seeds had reduced the levels of total cholesterol, LDL-cholesterol, and triglycerides.

Fenugreek

Fenugreek (*Trigonella foenum-graecum*) is a good source of soluble dietary fiber and its consumption has been shown earlier to bring about a significant reduction in serum and liver cholesterol levels. The chemical components of fenugreek seeds include a large carbohydrate fraction (mucilaginous fiber, galactomannan), steroidal saponins (e.g., diosgenin and trigogenin), free amino acids (e.g., hydroxyisoleucine and lysine), flavonoids and alkaloids (e.g., gentianine and trigonelline). An animal study indicated that fenugreek fractions rich in steroid saponins decreased total plasma cholesterol but did not change triglyceride levels (Petit *et al*., 1995). The fiber content of fenugreek extract helped moderate the metabolism of lipids in the digestive tracts of rats (Boban *et al*; 2006; Srichamroen *et al*., 2008). In a hamster model of diabetes, a fenugreek-active compound (4-hydroxyisoleucine) decreased elevated plasma triglyceride by 33% and total cholesterol levels by 22% (Narendar *et al*., 2006). Human data suggest that higher intakes may be required for lipid-lowing activity to become significant. An open label clinical trial using a daily dose of 12.5–18 g seed powder in healthy volunteers demonstrated significant reductions in total cholesterol and LDL-C levels (Sowmya and Rajalakshmi, 1999). Another clinical trial study also showed that serum levels of triglycerides and VLDL-C were decreased significantly (30 and 30.6%, respectively) after taking 10 grams/day powdered fenugreek seeds soaked in hot water for 8 weeks in type 2 diabetic patients (Chevassus *et al*., 2010). In other studies, fenugreek seeds treatment decreased the levels of LDL, triglycerides, total cholesterol and/or blood lipids in hypercholesterolemic rats (Belguith-Hadriche *et al*., 2013; Knott *et al*., 2017). Similarly, hypocholesterolaemic potential of fenugreek seeds was assessed in vitro by measuring the reduction in micellar solubility of cholesterol and inhibition of lipase activity (Hozzein *et al*., 2019). The fenugreek cultivars studied showed considerable reductions in the micellar solubility of cholesterol, ranged from 50 to 55%.

Foeniculum vulgare Mill commonly called fennel has been used in traditional medicine and contains fatty acids, phenolic components, hydrocarbons and volatile components. Afiat *et al*. (2018) assesses the effects of fennel (*Foeniculum vulgare* Mill.) on lipid profiles in postmenopausal women. The results revealed a very slight positive change in LDL-C, triglyceride and HDL-C. Helal *et* *al*. (2011) concluded that the fennel might shift liver total lipid value to normal level in rats. Fatiha *et al*. (2014) observed administration of methanol extract of fennel showed 35%, 50% and 50% decrease in the total cholesterol, triglycerides and LDL-C, respectively in rats thus indicating its hyperlipidemic effects. Aqueous extract of fennel causes significant reduction of cholesterol, triglycerides, LDL-cholesterol, and apolipoprotein-B decreased by 40%, 23%, 61% and 61%, respectively, and increase in HDL-cholesterol and apolipoprotein A1 by 85% and 58%, respectively (Oulmouden *et al*., 2011).

Garlic

Garlic (*Allium sativum)*, a perennial herb, plays an important medicinal and dietary role throughout the history. Garlic is used in numerous forms such as extracted oil, powdered garlic tablets, or raw garlic (Negar *et al*., 2016). Many of the biological effects of garlic are attributed to the allicin, ajoene and other organosulfur constituents such as S-allyl-L-cysteine. Alliin, which is found predominantly in garlic, is cleaved by alliinase to form allicin when garlic is crushed or chopped. Evidence from in vitro, animal, and human research has shown that taking garlic may slow the development of atherosclerotic process by beneficially reducing fatty streak formation in blood vessels and atherosclerotic plaque size (Ferri *et al*., 2003; Durak *et al*., 2002), inhibiting oxidation of LDL-C. Garlic may reduce blood lipids levels via inhibition of HMG-CoA reductase (similar to the mechanism by which statins work) or other key enzymes involved in cholesterol and fatty acid synthesis (Rai *et al*., 2009).

Garlic can reduce the level of total cholesterol and LDL instead of HDL and triglycerides, indicating the ability of anti-hyperlipidemia (Sun *et al*., 2018). Allicin showed a favorable effect in reducing blood cholesterol, triglycerides and caused a significant decrease in lowering the hepatic cholesterol storage (Lu *et al*., 2012). Yang *et al*. (2018) reported that garlic oil improved the lipid profile by lowering serum TC, TG and LDL-C concentrations and the atherogenic index.

Ginger

Zingiber officinale Roscoe known as ginger is widely used in foods as a spice around the world. Ginger contains non-volatile pungent components such as gingerols, shogaols, paradols, and zingerone. Zingerone and shogaol are found in small amounts in fresh ginger and in large amounts in stored products. Ginger had markedly lowered blood levels of triglyceride, cholesterol, and LDL, with increased HDL, when compared with a placebo control (Alizadeh-Navaei *et al*., 2008). It significantly reduces plasma cholesterol in animals (Fuhrman *et al*., 2000). In addition, a study with rats indicated that ginger may prevent fat storage and reduce body weight (Han *et al*., 2008). Thomson *et al.* (2002) observed a significant reduction in the serum cholesterol when ginger was administered at 50 mg/kg concentration.

Nut meg

Nutmeg (*Myristica fragrans*) seeds contain myristic acid, trymiristin and fatty acid glycerides. Nut meg elicited a significant reduction in serum TC, TG and LDL-C levels while there was concomitant increase in HDL-C of hypercholesterolemic rats (Onyenibe *et al*., 2015). In a study by Kareem *et al*., (2009), increased levels of lipids induced by isoproterenol were decreased following pretreatment with nutmeg indicated it anti-hyperlipidemic effects in rats. Arulmozhi *et al*. (2006) found that in rats fed a high-cholesterol diet, *M. fragrans* extract significantly reduced the elevated TG (47% reduction at 450 mg) and cholesterol (66.7% reduction at 450 mg).

Turmeric

Turmeric (*Curcuma longa*) is a spice with a strong yellow pigment known for its medicinal properties in Ayurvedic medicine. The major active constituents of turmeric are curcuminoids including curcumin (diferuloylmethane), demethoxycurcumin, bisdemethoxycurcumin, and tetrahydrocurcumin (Jiang, 2019). A 12% decrease in total serum cholesterol levels and a 29% increase in HDL-C levels (Soni and Kuttan, 1992). Curcumin also reduced cholesterol levels in acute coronary syndrome patients in a clinical trial in which curcumin was administered in various doses (45, 90, or 180 mg/day). It appeared that lower doses of curcumin were more effective than higher doses in this regard, in which 45 mg/day of curcumin reduced LDL and total cholesterol levels with increased HDL concentrations (Alwi *et al*., 2008). Einbond *et al*. (2020) reported that curcumin alters the cholesterol biosynthetic pathway thereby prevent lipid disorders.

CONCLUSION

Spices with their anti-cholesterol activities are proven to increase the high density lipoprotein cholesterol and decreases the low density lipoprotein cholesterol, triglycerides thereby reducing the risk of heart diseases. Various bioactive compounds have been identified from spices with anti-hyperlipidemic activities and their mode of action is reported elsewhere. Use of spices in traditional medicine is well known and the inclusion of dietary spices in cuisines helps in reducing the cholesterol levels.

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