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Review article

Role of garlic in dyslipidemia: an evidence based review

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ABSTRACT

Rapidly growing morbidity and mortality due to heart disease is a great concern for scientists. Among the etiology of atherosclerosis, dyslipidemia is a major risk factor. Garlic has active ingredients of *Allium sativum* used in high blood pressure management. Garlic has been used as a therapeutic agent for many illnesses such as hypertension, dyslipidemia and cardiovascular diseases. Evidence from various studies and clinical trials proved the efficacy of garlic to reduce lipid level. However, some contradictory results are also reported. This review was undertaken to assess the role of garlic therapy in dyslipidemia. Major databases including Google, PubMed, MEDLINE, and Cochrane library view were used for literature search. Clinical trials conducted on humans assessing the role of garlic therapy in dyslipidemia and the possible mechanisms responsible for such therapeutic actions were assessed. Several trials and meta-analyses have suggested a positive effect of garlic on total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides (TG). This review on garlic therapy in dyslipidemia suggests that it reduces elevated cholesterol to a modest extent.

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1. Introduction

Atherosclerosis, diabetes and hypertension are the major risk factors along with smoking, obesity and sedentary life styles leading to cardiac disease[1]. Atherosclerosis is a systemic diffuse disease in which fatty deposits called plaque buildup in the arteries over time that may manifest as a localized coronary, cerebral, mesenteric, renal, and/or peripheral arterial stenosis or as diffuse atherosclerosis; it causes heart disease, heart attack, peripheral artery disease and stroke[2]. It is critically important to recognize the need for treatment of dyslipidemia and to institute necessary therapies the long-term risks of disease recurrence or modify the metabolic derangements that promote atherosclerosis [3-4]. Drugs used in dyslipidemia may cause adverse effects if used for longer duration. There are various other alternate medicines used to reduce lipids without any major side effect [5]. Garlic is reported to prevent cardiovascular disease by multiple effects, one of which is the inhibition of platelet aggregation and its ability to do this has been extensively investigated [6-7].

Garlic (*Allium sativum*), belongs to the onion genus *Allium* an herb used widely as a flavoring in cooking, has also been used as a medicine throughout ancient and modern history to prevent and treat a wide range of conditions and diseases[8-9]. It has been used by humans for thousands of years; Hippocrates promoted the use of garlic for treating respiratory problems, parasites, poor digestion and fatigue. The original Olympic athletes in Ancient Greece were given garlic - possibly the earliest example of "performance enhancing" agents used in sports.

Cholesterol is essential for normal body function and chemical actions that include preserving the integrity of cell membranes, maintaining myelin sheath and synthesizing steroid hormones, co enzymes and vitamin D. On the other hand high levels of lipid increase the morbidity and mortality by increasing the risk of heart disease and stroke Studies have shown significant but modest lipid-lowering effects and antiplatelet activity[10-11].

Earlier reviews had strongly provided evidence that garlic was effective as a lipid-lowering agent [12- 13]. However, recent reviews have suggested contrasting results claiming that garlic has a modest role in dyslipidemia[14-15]. Therefore, this review will critically examine role of garlic therapy in dyslipidemia with regard to the current scientific and the possible mechanisms responsible for such therapeutic actions.

Forms of Garlic:

Garlic powder: It is primarily used as a flavoring agent for processed foods. They can be sliced or crushed, dried, and ground into powder.

Garlic oil: It is another important preparation and is produced as a result of distillation process of raw garlic.

Aged Garlic Extract: Another extensively studied garlic preparation is aged garlic extract (AGE). This process of storage leads to alteration in composition of the garlic extract and the compounds in garlic are converted naturally into stable and safe sulfur compounds with substantial loss of allicin activity and increased activity of new compound.

2. Methodology

This paper is based on a literature search of clinical trials, research article, systematic reviews and meta-analyses published to find out the effect of Garlic on Dyslipidemia. For this purpose a systematic literature search was performed by using multiple data search engines such as; MEDLINE, PubMed, Google Scholar, and Cochrane library. We limited our search for published articles from 1990 to November 2013. We used the following medical subject headings (MESH) and key words: garlic, *allium sativum*, allicin, cholesterol, hyperlipidemia, lipid and dyslipidemia. Reference list of published studies and review articles were also searched manually.

2.1. Study selection

2.1.1. Inclusion criteria

All human studies (clinical trials, parallel trials, cross-over trials) in English assessing the effect of garlic on cardiovascular disease prevention and reported TC, LDL, HDL or TAG endpoints among patients with dyslipidemia or cardiovascular disease were included.

2.1.2. Exclusion criteria

Studies were excluded if they combined garlic with other nutraceuticals or products with lipid altering effects, were conducted on animals were excluded. Theses, dissertations, unpublished data, and letter to editor were also excluded.

Two authors (F.J and K.N) independently reviewed abstracts and full articles of all citations to evaluate them for the inclusion and exclusion criteria. Disagreements were resolved by either discussion or evaluation by other investigators (W.Q).

3. Results and discussion

3.1. Garlic used in dyslipidemia

Concerning length of therapy and vast majority of side effects, herbal medication may be suitable substitute for these drugs. Garlic (*Allium Sativum*) has been used in herbal medicine for centuries for various diseases. In recent years garlic has been the focus of serious medical and clinical attention because of beneficial effects on several cardiovascular risk factors like reduction of serum lipids, blood pressure and plasma viscosity [16-19].

The cardiovascular-protective effects of garlic have been evaluated extensively in recent years, a number of intervention studies have similarly shown that garlic significantly reduced plasma lipids, especially total cholesterol and Low Density Lipoprotein (LDL) cholesterol in humans. Role of garlic in the treatment of hypercholesterolemia through inhibition of cholesterol bio-synthesis in the liver and also by inhibition of oxidation of low density lipoproteins is proven [20-23].

Table 1
Effect of garlic on lipid level.

Study	Type	Target	Duration of Rx	Dose	Intervention /control	Outcome
Steiner et al., (1996) [49]	Double-blind crossover trial	Hyperlipidemia	11 months	7.2 g aged garlic	20/21	Dec T. chol 6.1%, dec LDL
Ried K, 2013	Meta-analysis	Hyperlipidemia	2 months	39 primary trial		Dec in total chol 17+6 mg/dl, LDL 9+6mg/dl
Isaacsohn et al., (1998) [54]	Randomized, double-blind, placebo-control trial	Hyperlipidemia	12 weeks	900mg garlic powder	28/22	No change in lipid
Ashraf et al., (2005) [42]	Randomized, single-blind, placebo controlled study	dyslipidemia	12 weeks	300 mg garlic tablets twice daily	33/32	T.chol 12% dec, HDL 8.1% dec
Kojuri et al., (2007) [46]	Randomized, single-blind, placebo controlled study	Hyperlipidemia	12 weeks	garlic powder tablet (400 mg garlic, 1 mg allicin) twice daily	50/50/50 (in 3 arms)	T.chol 12.1% dec, LDL 17.3% dec,
Sobenin et al., (2008) [55]	Double blinded placebo controlled	Hyperlipidemia	12 weeks	Allicor (600mg daily)	21/21	T. chol 7.6% dec, LDL 11.8%, and HDL inc 11.5%

T. chol: total cholesterol, HDL: high-density lipoprotein, TG: triglyceride, LDL: low-density lipoprotein, Dec=decrease.

Studies indicate that garlic prevents inhibition of platelet aggregation by inhibiting cyclooxygenase activity and thus thromboxane A2 formation, by suppressing mobilization of intraplatelet Ca²⁺, and by increasing levels of cAMP and cGMP. Garlic also displays strong antioxidant properties and activates nitric oxide synthase. Garlic inhibits platelet aggregation by multiple mechanisms and may have a role in preventing cardiovascular disease

Several meta-analyses have shown very promising results. There was an overall reduction in cholesterol level seen that is, 8% with powdered form while 15% with non-powder preparations. Significant lowering of serum triglyceride was also noticed, while HDL level remains unchanged. Silagy and Neil concluded from the analysis of 17 human studies that plasma cholesterol concentrations of the subjects treated with garlic were 12% lower than

those receiving placebo. Furthermore, the two analyses detected a wide range of decrease in mean plasma cholesterol concentrations [24].

A recent meta-analysis conducted by Zeng et al. clearly illustrated that garlic therapy is more effective if used for a long term with higher baseline total cholesterol levels; they also concluded that garlic powder and aged garlic extract were more effective in reducing serum TC levels, while garlic oil was more effective in lowering serum TG levels[25].

Garlic produces its effects on endothelium and vascular dilatation through inhibition of oxidation process. Allicin as the main active ingredient with prospect to provide beneficial effects on cardiovascular system, garlic prevents from cardiovascular disease through inhibition of LDL oxidation thus inhibiting atherosclerosis of vessels, important risk factors for cardiovascular disease. Use of garlic in lowering the lipid levels and prevention of cardiac diseases were investigated thoroughly in literature, it is proven that garlic can reduce the total cholesterol thus improving some of the risk factors. Garlic has active ingredients of *Allium sativum* used in high blood pressure, blood pressure management and has long been the focus of experimental and clinical attentions due to its promising lipid-lowering effects[26]. Effect of short term garlic supplementation has also shown good result, garlic can be used as a tentative treatment along with antihypertensive drug because of its positive effect on lipid levels and antioxidant properties. Another meta-analysis done concluded that garlic reduces mean supine systolic and diastolic blood pressure to prevent cardiovascular morbidity and mortality in hypertensive patients. Ashraf and his colleagues have done one study shown promising effect of garlic on dyslipidemia in patients with type 2 diabetes mellitus[27]. Garlic extract contains antioxidant compounds and increase nitric oxide production and decreases the output of inflammatory cytokines from cultured cells. After 12 weeks the garlic treated group in this study had a significant reduction in total cholesterol. These data suggest that garlic may improve impaired endothelial function in men with coronary disease treated with aspirin and statin.

Ried has done one meta-analysis, the most comprehensive to date, includes 39 primary trials of the effect of garlic preparations on total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides. The findings suggest garlic to be effective in reducing total serum cholesterol and low-density lipoprotein cholesterol in individuals with elevated total cholesterol levels (>200 mg/dl), provided garlic is used for longer than 2 months. An 8% reduction in total serum cholesterol is of clinical relevance and is associated with a 38% reduction in risk of coronary events at 50 years of age [28].

Considerable evidence from the literature supports the invaluable role of garlic in the treatment of hypercholesterolemia through inhibition of cholesterol biosynthesis in the liver and also by inhibition of oxidation of low-density lipoproteins. Beneficial effect of garlic preparations on lipids and blood pressure extends also to platelet function, thus providing a wider potential protection of the cardiovascular system [29].

A single-blind, placebo controlled trial by Kojuri et al, on 150 hyperlipidemic patients showed that when patients were given enteric-coated garlic powder tablet (equal to 400 mg garlic, 1 mg allicin) twice daily, the total cholesterol decreased by 26.82 mg/dl and showed 12.1% reduction, and LDL-cholesterol decreased by 22.18 mg/dl, 17.3% reduction). Although triglyceride dropped by 13.72 mg/dl (6.3%) but it was not statistically significant [30].

Numerous animal studies as well as in vitro ones have demonstrated the hypolipidemic effects of garlic. The type of the garlic products may be another important factor responsible for the conflicting outcomes, as different garlic products are composed of different organosulfur compounds. Some studies indicated that different people might have a different response to garlic, and thus garlic may be more beneficial for some specific groups [31-32].

Some clinical investigations have demonstrated somewhat controversial results. These discrepancies may be due to the differences of the composition of garlic preparations and the biological response of garlic on individuals. [33]. Clinical studies have shown change in response have resulted due to the differences of the composition of garlic preparations and the response they may induce. This fact was well proven by a study done by Sobenin et al. using time released garlic powder tablets in their study [34].

Alternative therapeutic approaches with complementary therapies are becoming increasingly popular among patients. It is important for healthcare providers to be familiar with the safety and efficacy of these agents to facilitate optimal outcomes for patients with dyslipidemia. Literature has reported variable results in human models. The possible reason for these results are may be the difference in preparations with diverse composition, variations in sulphur content present in different garlic preparations used as mentioned in different studies.

A study conducted by Gardner et al on 192 adults found that any form of garlic, including raw garlic, when given at an approximate dose of a 4-g clove per day for 6 months, had statistically or clinically significant effects on

LDL-C or other plasma lipid concentrations in adults with moderate hypercholesterolemia. Based on meta-regression analysis of these trials, there was a significant positive relationship between reduction in LDL-C and reduction in the risk for major cardiovascular events. Higher baseline line TC levels and the use of dietary modification may alter the effect of garlic on these parameters [35].

The effect of garlic on cholesterol has been investigated in numerous trials and summarized in several meta-analyses, with variable results. Clinical trials using different types of garlic preparations in hypercholesterolemia patients have demonstrated debatable results and it was assumed that these discrepancies may have resulted due to the differences of the composition of garlic preparations and the response they may induce[36-37].

There are inherent limitations in this review. Firstly, the studies included had variety of garlic preparations, the different baseline risks and the different study procedures that increase the chances of heterogeneous effects and are difficult to compare. Secondly, we have covered limited studies in this review as our focus was newer studies being published from 1990 to 2013.

3.2. Adverse effects of garlic

Some case reports have reported that there are various adverse effects of garlic ingestion, such as allergic dermatitis in patient taking raw garlic [32]. Another report found that the antithrombotic activity of garlic might interact with oral anticoagulants (warfarin); therefore, caution must be taken when garlic is used with oral anticoagulants [32].

4. Conclusion

This review on garlic therapy in dyslipidemia suggests that it reduces elevated cholesterol to a modest extent. Garlic has high safety profile as it has very limited side effects. Various studies exploring the effects of garlic in dyslipidemia have demonstrated some contradictory results. The diverse composition and amount of active sulfur compounds of different garlic preparations used in various trials might be responsible for the inconsistent findings. Standardization of garlic preparations, duration of study as well as diet and life style modification may exhibit positive response. Further reviews are warranted to observe the effects of adjunctive garlic therapy with statins on TAG concentration.

Declaration of interest: The author has no relevant interest to declare.

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