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Review Article

Therapeutic Effect of Garlic Containing S-allyl Cysteine and Diallyl-di-Sulfide on Improving Blood Lipid Profile

Ayesha Siddiqa[1*], Shahnai Basharat[1], Fizza Mubarik[1], Fatima Farooq[1] and Muhammad Ali[2]

[1]University Institute of Diet & Nutritional Sciences, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan
[2] New foundland University, Canada

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***Corresponding Author:**
Ayesha Siddiqa
University Institute of Diet & Nutritional Sciences, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan
siddiqa_7@hotmail.com

ABSTRACT

Cardiovascular-related diseases are considered as the major risk for health and may lead to many illnesses. Hyperlipidemia is the highest common cause of diseases related to heart known as Coronary Heart Disease (CHD). Since ancient times, innumerable herbs and organic foods are used to treat diseases among which garlic has been shown beneficial for treating hyperlipidemia and normalizing lipid profile levels. Garlic may be used in different forms like powder, tablets, extracts or after ageing. Its sulfur containing compounds like allicin, S-allylcysteine, alliin, ajoene, diallyl disulfide are proven to have the pharmacological benefits. The main aim of the current review is to analyze and evaluate the studies regarding anti-hyperlipidemic effects of garlic and its supplements on normalizing lipid profile among hyperlipidemic subjects. After analyzing different studies being carried out earlier, it is concluded that garlic is effective in managing lipid profile including total cholesterol, triglycerides, LDL, HDL levels among people with hyperlipidemia ranging from mild to moderate intensity.

INTRODUCTION

At present, disorders associated with heart and arteries are considered one of the major cause of illness and death [1]. About 17 million people die from heart-related diseases like Cardiovascular Disease (CVD) each year and it is estimated that there will be 24.8 million people by 2030 worldwide [2]. Accumulation of low-density lipoprotein in inner layer of blood vessels, oxidation of low-density lipoprotein, utilization of oxidized low-density lipoprotein by macrophage scavenger receptors, the effect of macrophages on foam cells and the stability of plaque are the main reasons for the formation of atherosclerotic plaque. Inflammatory cytokines are involved in all stages of atherosclerosis, and as a result make this activity an incurable inflammatory disease [3]. Hyperlipidemia is said to be one of the major risk causing factor for coronary heart disease (CHD) and is found in the majority of adults in their young age. It was reported by the National Health and Nutrition Examination Survey, that 11.7% of adults with age from 20 to 39 years and 41.2% of adults from 40 to 64 years had elevated levels of low-density lipoprotein cholesterol (LDL-C) and 10.6% of 20 to 39 years of age adults and 47.7% of aged 40 to 64 years of age adults with hyperlipidemia receive treatment [4]. Unusually high levels of lipids in the blood are medically termed as hyperlipidemia. There are two major forms of lipids which are present in the blood i.e. triglycerides and cholesterol [5]. Triglycerides are produced when the body stores and saves calories that are not required for energy. The major food sources of triglycerides include red meat and whole-fat milk and foods that raise triglyceride levels include foods high in sugars, fructose and alcohol [6]. Like triglycerides, food sources of cholesterol also include fatty foods such as eggs, red meat, and cheese [7]. Hyperlipidemia is subcategorized into two broad categories: primary (genetical) or secondary (acquired)

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hyperlipidemia. Primary hyperlipidemia is caused by profusion of genetic diseases that a patient may have at birth carrying in genes, while secondary hyperlipidemia is usually caused by a totally another etiology, such as unhealthy food routine, different medications (amiodarone, glucocorticoids), uncontrolled diabetes, hypothyroidism or poor lifestyle [8].In both developing and developed countries, the usage of herbs and plant derivatives has recently been increased significantly [9]. Herbs are an extraordinary source of natural medicine so they have been used since ancient times for beneficial remedies for the treatment of diseases. Currently they are used not only as a medicine but also for dietary well-being [10,11]. The World Health Organization (WHO) states that these traditional medicines acquire preventive, early, therapeutic and regenerative roles [12]. Garlic (Allium sativum) is considered among the most widely studied herbal remedies. Traditionally, it has been utilized for the treatment of different ailments and certain infections like rheumatism, diabetes mellitus, heart disease, and many more. It has been proven to possess different properties like anti-hypertensive, anti-bacterial and hypoglycemic actions according to different experimental trials [13]. Supplements prepared from Garlic are thought to be the beneficial agents for highest risk reduction, because of the variety of cardio-protective effects possessed by the active ingredients of garlic, such as lowering the values of LDL, total cholesterol and blood pressure in people with mild high blood pressure, elevating HDL cholesterol, increasing fibrinolysis and preventing platelet aggregation etc [14,15]. The class of chemicals containing sulfur (including S-allylcysteine, ajoene,alliin, diallyl disulfide) present in garlic acquire the medicinal effects [16].Garlic is extensively used as a traditional medicine in many cultures of world because of many organic compounds present in it [17]. Aged black garlic is produced by ageing or maturing garlic at high temperatures and high humidity during a heating process. During processing, the unstable andodor-causing compounds of fresh garlic are converted into stable and odor free compounds S allyl cysteine (SAC) or broken down into organosulfur compounds including diallyl sulphide (DAS), diallyl disulphide (DADS), diallyl trisulphide (DATS), dithiins and ajoene [18]. As a result, ABG acquire a sweet and sour taste and gel-like texture. The dark brown color of garlic in thermal process is due to the Maillard reaction, which also produces antioxidant compounds [19,20]. It is also suggested that antioxidant activity and polyphenol content is much higher in aged black garlic than fresh garlic [21]. Aged black garlic causes heart-protective effects because it is high in SAC and polyphenols (ABG10+)[22].

Mechanism of action: The ability of garlic to lower the lipid concentration in the arterial wall results in the protective effect in atherosclerosis. Garlic as a therapeutic food, causes inhibition at the level of the arterial walls which is also called direct antiatherogenic and cause retreating effects also called anti-atherosclerotic [23]. The activities of lipogenic and cholesterogenic enzymes in the liver, which include malic enzyme, glucose-6 phosphate dehydrogenase, fatty acid synthase and 3-hydroxy-3-methyl-glutaryl-CoA (HMG CoA) reductase are repressed by garlic [24]. LDLsample which is isolated from human subjects which were given aged garlic extract (AGE) were found to be highly oxidation resistant [25]. This data suggests that suppression of oxidation of LDL may be considered as one of the most important mechanisms shown for the benefits of garlic during atherosclerosis [26]. Allicin was a compound which was originally identified as an active compound that possess the anti-atherosclerotic property. However, current in-vitro studies have shown that organosulfur compounds that are water-soluble, especially S-allyl cysteine (SAC), which is found during the extraction of aged garlic and the diallyl-di-sulfide (DADS), which is a part of garlic oil composition also have the potential to retard synthesis of cholesterol [24].

Studies showing positive effects of garlic on hyperlipidemia: Innumerable researches have been carried out to study the role and consequences of garlic and its constituents on lowering blood lipid profile. In a double-blind placebo-controlled arbitrary study of intervention, visible decrease in cholesterol and low-density lipoprotein was shown after taking garlic pills for the duration of twelve weeks. 46 patients having high blood cholesterol levels were given the garlic intervention. In this clinical trial, after receiving garlic supplement intervention (n=22) for the duration of twelve weeks the total serum cholesterol and low-density lipoprotein (LDL) cholesterol levels showed to be reduced significantly. On the other hand, in the placebo group (n=24), the same parameters were not changed. There were no significant differences recorded in triglycerides or in ratio of low-density-lipoprotein and high-density-lipoprotein among two different groups in this study. It was observed and resulted that enteric-coated garlic supplements, having releasing value of allicin equivalent to 9.6 mg, along with low-fat diet has possibility to improve the lipid profile of mild to moderate hypercholesterolemic patients. Provided the other research evidences, it is thought that the ability of garlic extract for reduction of hypercholesterolemia might be because of greater bioavailability of allicin, which in turn means, higher anti-hypercholesterolemic effect might be significantly visible at a higher level of allicin [27]. In another randomized single-blind, placebo-controlled study of intervention, total 172 subjects were selected randomly having coronary heart disease paired with recently diagnosed hyperlipidemia from

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cardiology outdoor of Shiraz University of Medical Sciences. After following the criteria of exclusion, 22 cases were excluded. Rest of the 150 patients were tested after 10 hours of fasting and found to have total cholesterol and LDL-cholesterol level equivalent or greater than 200 mg/dl and 100 mg/dl respectively. Rest of the patients were further distributed into 3 groups and selection was carried out randomly. Of all 3 groups, each group composed of 50 participants. Among all three groups, one group was introduced garlic powder tablet (enteric coated) two times a day daily. Other two groups received anethum tablet and placebo treatment respectively. All patients were prescribed National Cholesterol Education Program (NCEP) type Π, which means one should have about 0.6 g/kg of ideal body weight protein in a day, 55% calories of the total calories in a day through carbohydrate and total energy intake should not be greater than 30% obtained from dietary fat and quantity of polyunsaturated fats should be less than 10%. It was found, at the end of interventional study for six-weeks, that there were notably different values of triglyceride, total cholesterol, low-density-lipoprotein and high-density-lipoprotein in all of the three groups of intervention. In the group who received garlic intervention, the total cholesterol concentration and low-density-lipoprotein cholesterol was reduced by 26.82 mg/dl and 22.18 mg/dl respectively with both having p values as 0.000. On the other hand, there was a significant elevation in the levels of high-density-lipoprotein cholesterol by 10.02 mg/dl (P-value: .000). Hence it was concluded that there were visible and cholesterol, triacylglycerol concentrations, LDL-C and the ratios among total cholesterol to HDL-C and LDL-C to HDL-C [31].

Study Type	Subjects	Duration	Dosage	Effect of intervention
Double -blind randomized placebo-22 controlled[27]		12 weeks	9.6mg allicin	↓ total cholesterol ↓ LDL -cholesterol
Single-blind randomized placebo - controlled[28]	50	6 weeks	800mg garlic	↓ total cholesterol ↓ LDL cholesterol ↑ HDL cholesterol
Double -blind, randomized placebo-controlled[29]	28	12 weeks	6g	↓ alipoprotein B ↑ ratio of LDL-cholesterol/alipoprotein B ↑ HDL cholesterol
Double -blind, randomized placebo-controlled[30]	133	8 weeks	250mg garlic oil	↓ LDL ↓ triglycerides ↓ total cholesterol ↑ HDL
Randomized placebo-controlled[31]	50	12 weeks	900mg	↓ LDL ↓ratio of total cholesterol /HDL- cholesterol ↓ total cholesterol
Double -blind, randomized placebo-controlled[32]	51	12 months	300mg	↓ LDL
Clinical trial (before and after)[33]	50	6 weeks	900mg	↓ LDL ↑ total cholesterol ↑ HDL
Double -blind, crossover[34]	41	6 months	7.2g	↓ LDL ↓ total cholesterol

Table 1: Human Studies showing difference in lipid levels with garlic

CONCLUSION

Garlic has been playing a pivotal role as a traditional medicine especially for treating and Garlic has been playing a pivotal role as a traditional medicine especially for treating and managing hyperlipidemia. Due to its high organic sulfur compound content, it possesses antihyperlipidemic and cardioprotective properties. On the basis of previous clinical trials, this study concluded that normalization in abnormal levels of lipid profile can be achieved by adding garlic or garlic-based supplements in hyperlipidemic patient's diet. Since no side effect is being reported, hence garlic can be used safely as a traditional medicine for hyperlipidemia and decreasing risk of CVD.

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