Medicinal Uses of Garlic - a mini review

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Abstract

Nature is serving as an abundant source of medicinal herbs and plants. Garlic is a medicinal herb with potential nutritional values. It has been used as a potential medicinal herb. Since time immemorial, garlic is a remedy for various physiological disorders. This review focuses on the medicinal uses of garlic in treatment and prevention of several chronic and acute diseases including infection of multidrug resistant Shigella infection.

Key Words: Garlic, Allicin, Anti-diabetic, Cardiovascular disease, shigellosis

Introduction

For thousands of years, nature has been serving as an abundant source of medicinal herbs and plants. A magnificent number of diverse bioactive compounds with potential biological activities have been isolated from plant origin[1]. Medicinal plants are mostly used by the non-industrialized societies due to their availability and relatively lower cost than modern medicines[2]. Garlic astonishingly is a miraculous medicinal herb with potential nutritional values. Garlic or *Allium sativum* is a member of Alliaceae family which is regarded as the oldest of all cultivated plants. For more than 5000 years, it has been used both as a valuable spice and food. It is the most extensively studied herb which was used by the ancient scholars as medicine. Considering as the blessing to mankind, it has been used as a potential medicinal herb as well as a remedy for various physiological disorders since time immemorial. Back in 3000B.C, garlic was used by various ancient civilizations covering Babylonian, Egyptian, Greek, and Chinese in the treatment of diseases such as pulmonary complaints, arthritis, heart disease, respiratory infections, diarrhea, aging symptomps, skin disease, headache, and tumors etc[3-5]. Evidence suggests that garlic has the property to lower cholesterol and triglyceride levels in blood[6].

Chemical composition of garlic

The active principle of garlic was found to be allicin which is assumed to be responsible for its pungent odor[7]. Studies suggest that Garlic contains at least 33 sulfur compounds[8] including alliin, allicin, diallyl trisulfide, S-allylcysteine, vinyldithiins, S-allylmercaptocysteine, allylpropyl disulfide etc. It also contains various minerals such as calcium, potassium, magnesium, and zinc, several enzymes including allinase, peroxidase, myrosinase, catalases, superoxide dismutases, arginases, and lipases. Moreover, it contains vitamins, for instance, B vitamins (B_1, B_2, B_3, B_6, B_7), Ascorbic acid and Tocopherols. Lysine, arginine, threonine, glutamine, proline, histidine, glycine, aspartic acid, cysteine, valine, methionine, isoleucine are some of the amino acids present in garlic. Furthermore, it contains lipids, prostaglandins, fructan, pectin, adenosine, and fiber [9-12].

Garlic as an anti-diabetic agent

Diabetes mellitus is a common endocrine disorder characterized by an excessive amount of glucose circulating in the blood stream, affecting the eyes, nerves, blood vessels, skin and kidneys with long-term complications. A number of studies have been conducted on animal models (mice, rat, rabbit) to investigate anti-diabetic potential of garlic and most of these studies showed significant results[13-17]. Thomson *et al* investigated anti-diabetic effects of garlic extract at 3 incremental doses in streptozotocin-induced diabetic rats. A significant anti

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diabetic potential including reduction of serum glucose, serum cholesterol, triglycerides and urinary protein levels by 57%, 40%, 35% and 50% respectively compared to the diabetic controls has been reported[18]. Another study reported that oral glucose tolerance and renal function can be improved with long term treatment with garlic oil[19]. Saravanan et al noticed that S-allylcysteine, a major bioactive component of garlic, decreased blood glucose and increased serum insulin. Therefore, it might be suggested that S-allylcysteine might be the active component to exert the anti-diabetic effect of the garlic extract[20]. Eidi et al reported garlic to be more effective than glibenclamide[21], while Sheela et al reported similar effectiveness[22]. However, some researchers found garlic extract ineffective on decreasing blood glucose[23-26]. A number of experimental and clinical studies supported anti-diabetic potential of garlic in animal model and human subjects. In preventing diabetes worldwide, garlic being safe and effective can play a major role. However, further studies are an important need to have clinical data in finding the ideal dose, safety and efficacy, formulation of garlic product.

Garlic in preventing cardiovascular disease

Cardiovascular disease involving the heart, blood and blood vessels is a complex multifactorial disease, which is characterized by hypercholesterolemia, hypertension, reduced fibrinolysis or thrombolysis, increased blood-clotting and platelet aggregation[27]. Cardiovascular disease (CVD) as well as blood stream disorders are the primary cause of death every year. CVDs are the number 1 cause of death globally, taking an estimated 17.9 million lives each year. It is a group of disorders of the heart and blood vessels and include coronary heart disease, cerebrovascular disease, rheumatic heart disease and other condition, and comprises high blood cholesterol level, coronary artery diseases, increased platelet activity, stroke, rheumatic heart disease, elevated triglycerides levels, cardiomyopathy, heart arrhythmia, congenital heart disease, hypertension, valvular heart disease, carditis, venous thrombosis, aortic aneurysms, peripheral artery disease[9, 28].

In recent years, Garlic being a focus of attention has been extensively used as the treatment in prevention of various aspects of CVDs. Epidemiological studies suggest that consumption of garlic and its preparations significantly benefits to prevent atherosclerosis, to reduce serum cholesterol and triglyceride, to inhibit platelet aggregation , lowering blood pressure, and to increase fibrinolytic activity[29]. Various studies indicated that garlic consumption prevents high-fat meal inducing hypercholesterolemia[30-33]. A study conducted on 432 coronary artery patients in India and half of them being administered garlic juice in milk revealed a significant benefit in reducing the complication within 3 years, compared to those who were not with garlic juice[34]. In another study it was reported that long term use of garlic in reducing atheromatous lesions to almost 50%, particularly in the aorta[35]. However, numerous studies indicated no lipid lowering effects of garlic[(36-44)] and revealed negative effects on hypertension[45-46].

Garlic in prevention of hypercholesterolemia

Hypercholesterolemia is the prime cause of atherosclerosis, which is thought to be the major cause of death and disability[47]. Increased serum cholesterol level is mainly responsible for the development of coronary artery dysfunctions. Various studies showed that garlic has significant role in cholesterol management. In a meta-analysis, Reid et al reported that garlic has a significant effect on total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides. Clinical relevance is associated with a reduction in 38% of coronary events at 50 years of age, if total serum cholesterol level is reduced by 8%[48]. In another study, it has been noticed that serum cholesterol level was remarkably decreased by 12% from 265 ± 16.75 mg/dL to 232.72 ± 11.23 mg/dL within 90 days with the use of garlic[49]. In an investigation, Rizwan et al observed reduction in total cholesterol level (28 mg/dl,

12.03 %), LDL (30 mg/dl, 17.99 %) and an increase of HDL (3.35 mg/dl, 8.81%) in patients treated with garlic[50]. However, Steiner et al reported a decrease in 6.1%, while Tohidi and Rahbani suggested 9% of the total cholesterol[51,52]. Alder and Holub also showed positive lipid-lowering effects of garlic on total cholesterol, which accounts for 11.5 %[53].

Garlic as antihypertensive

Approximately 1 billion individuals are suffering from hypertension worldwide[54]. It is the leading risk factor in developing chronic cardiac diseases and atherosclerosis[55]. Garlic has become the most popular complementary therapy for controlling blood pressure[56]. Garlic exerts prostaglandin-like effects that decrease peripheral vascular resistance[57]. Garlic is associated with the activation of nitric oxide synthesis, a potent endogenous vasodilator[58]. Castro et al reported that allyl methyl sulphide and diallyl sulphide, two important bioactive compounds derived from garlic, have antioxidant potential targeting at the arterial remodeling in hypertension[59]. Garlic extract activates sodium pump in the kidneys, which is associated with reduction of intracellular Na^+ concentration and normalizes blood pressure[60].

Garlic as a natural blood thinner

The function of platelets and fibrin is incredible in blood clotting and increase in the amount of fibrin in blood may cause cardiac arrest. The bioactive compounds in garlic significantly decrease fibrin formation as well as help reducing the existing fibrin in the blood[61]. Study demonstrated that garlic helps the rate of fibrin breakdown from 24-30% in people[62]. In an in-vitro study, aqueous extracts of garlic, garlic oil and onion were used to demonstrate their efficacy on blood coagulation process and fibrinolysis, and revealed garlic and garlic oil prevented blood coagulation or fibrinolysis[63].

Garlic in multidrug resistant Shigella infection

Major cause of diarrhoeal diseases are bacterial, viral and protozoal[64-66]. Of all the diarrhoeal cases, shigellosis (also known as bacillary dysentery) is predominant, which is increasingly recognised as a major diarrhoeal disease[67-69]. Shigellosis results in dehydration, electrolyte imbalance, hypoproteinemia and malnutrition. In addition, severe complications such as haemolytic-uraemic, toxic megacolon, septicamia, intestinal performation etc have been frequently observed during epidemics[68-71]. Shigellosis is endemic in Bangladesh and occasionally causes epidemic outbreak[72]. It is most prevalent among young children. In Bangladesh, infection caused by *Shigella* flexneri is most common, which is aquired by faecal-oral route and mostly spread by person to person contact[73,74]. Commonly used antibiotics and chemotherapeutic agents are becoming ineffective or resistant to *Shigella* strains[75,76]. The resistant pattern appears to be related to the type of antibiotics to which they are exposed[74]. By 1952, 80% of Shigella strains were resistant to sulphonamide[77]. In 1955, multiple drug resistant *Shigella* strains were first recognised[74]. Since that time, multiple drug resistant strains has been reported as an emergency throughout the world [74,78,79].

In Bangladesh, *Shigella* strains became resistant to tetracycline, chloramphenicol, streptomycin, sulphonamide during 1970s[80]. Ampicillin was then the drug of choice[74,77]. In 1970, the first ampicillin-resistant strains of *Shigella dysenteriae type1* was isolated[81]. Co-trimoxazole was found very effective even in the areas where ampicillin-resistant strains had become predominant. Resistance of Shigella to co-trimoxazole was reported in 1977[82] and in the following years and in mid-1984 most strains became resistant to this drug[80]. During 1982-84, 99% of *Shigella dysenteriae type 1* and 66% of Shigella flexneri were reported to be multiple drug resistant[80]. In 1987, *Shigella dysenteriae type1* became 100% resistant to ampicillin, chloramphenicol and cotrimoxazole[73]. Most of the strains of Shigella developed resistance to multiple antibiotics[83-86]. Resistance to tetracycline with ampicillin or with streptomycin are most frequent. It is also common to

four to seven antibiotics like ampicillin, tetracycline, chloramphenicol, streptomycin, erythromycin, carbenicillin and co-trimoxazole[84,89,87]. Resistant development is very extensive causing nalidixic acid to loose its efficacy rapidly[77,88]. Development of resistance to ciprofloxacin[80] and nalidixic acid has been reported by several researchers[87,90-95]. Resistance to gentamicin, which was reported sensitive to most of the multiple resistant strains of *Shigella*, was also recorded[96].

In search of newer drugs of natural origin, enormous research were being carried out, which may find effective against these resistant strains. Some of the in-vivo and in-vitro experiments were found successful[97-124]. The aqueous extract of garlic *(Allium sativum)* and its active constituent allicin were found effective against a wide range of multiple drug resistant strains. Studies revealed multiple drug resistant strains of *Shigella dysenteriae type 1*, *Shigella flexneri, Shigella boydii*. and *Shigella sonnei* were found to be strongly sensitive to the allicin and aqueous extract[97-100]. Comparing the anti-shigella activity of allicin and aqueous extract of garlic with those of five standard antibiotics (ampicillin, tetracycline, gentamycin, cotrimoxazole and nalidixic acid). Ineffectiveness of nalidixic acid was also noticed, which was the drug of choice for treatmenting shigellosis[100]. Even, resistance has now been developed against fluoroquinolones, cephalosporins and azithromycin.

Garlic as anti-inflammatory agent

Several studies documented about the antiinflammatory potential of garlic. Bose et al reported that the anti inflammatory potential of allicin to be the highest against carrageenan-induced inflammation in rat paw[125]. Antiinflammatory activity of garlic on mice has alsobeen reported [126]. Potential antiinflammatory effect of methanolic extract of garlic was observed, which recorded as 61% as compared to the standard drug diclofenac sodium suspension in 0.1% Tween 80[127]. Lee et al revealed Z- and E-ajoene and their sulfonyl analogs obtained from garlic indicating antiinflammatory activity, which showed inhibiting the production of nitric oxide (NO) and prostaglandin E_2 (PGE_2)[128]. A lead compound which was synthesized from allicin can also be a good starting point for developing antiinflammatory drugs with fewer side effects[129].

Garlic as natural antioxidant

Reactive oxygen species (ROS) are small oxygen containing molecules, which are naturally generated in the body during metabolic reactions, especially in aerobic respiration. DNA, proteins and fats may be damaged by ROS and free radicals. Various fetal diseases may arise due to high level of free radicals. Garlic extract can prevent the oxidative damage[130]. In two different studies, Rahman et al and Prasad et al reported antioxidant potential of garlic extract[131,132]. Torok et al revealed that antioxidant activity of the sulfur compounds obtained from fresh garlic extract is 1000 times more potent compared to crude aged garlic extract[133]. Allicin, an important bioactive constituent of garlic, was found to inhibit superoxide radical production as well as lipid peroxidation[134,135]. Besides, garlic exhibits inhibitory effect on nitric oxide formation[136,137]. It is also able to scavenge hydroxyl radicals[131,138]. However, Chung et al claimed allicin did not scavenge hydroxyl radicals rather allyl disulfide, allyl cystein and alliin did it[135]. At the time of cooking, the stability of garlic flavor can be increased by using soyabean oil[139] and garlic inhibits the oxidation reaction induced by soyabean oil[140].

The present review attempted to illustrate the effect of garlic and its preparation on Diabetes, hypercholesterolemia, hypertension and cardiovascular disorders. In addition, it also addressed the antiinflammatory and antioxidant potential of garlic based on numerous scientific studies. Garlic is nature treasure trove full of super nutrients and potential bioactive compounds. It's a source of never ending possibilities. However, extensive research should carry out to explore its hidden properties.

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