

## REVIEW

**ROLE OF GARLIC (*ALLIUM SATIVUM*) IN VARIOUS DISEASES: AN OVERVIEW**

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Pune-44, Maharashtra, India.[vikaslondhe2011@rediffmail.com](mailto:vikaslondhe2011@rediffmail.com)**KeyWords:** Garlic, Allicin,  
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## ABSTRACT

Garlic is probably one of the earliest known medicinal plants, which used from ancient time to cure different disease conditions in human. Garlic's principal medicinal uses are to lower blood pressure and cholesterol, fight infections, and prevent cancer. The active constituents are sulfur-containing compounds that are rapidly absorbed and metabolized. Numerous studies suggest that garlic lowers total cholesterol concentrations by approximately 10%, favorably altering HDL/LDL ratios. Literature survey support garlic's effectiveness as a mild antihypertensive, lowering blood pressure by 5-7%. Garlic inhibits platelet aggregation and enhances fibrinolytic activity, reducing clots on damaged endothelium. Another important use of garlic is as antidiabetic. Garlic controls the blood sugar level by different types of mechanisms. *In vitro* studies and animal data suggest that garlic may help to prevent some solid tumors. Therefore garlic is also effective in the cancer prevention. There are no studies evaluating its effectiveness in treating children or pregnant or nursing women. The other proposed uses of garlic include the hepatoprotective, antihelmentics, anti-inflammatory, antioxidant, antifungal and wound healing.

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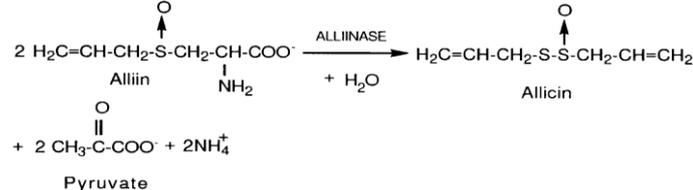
## INTRODUCTION

Garlic, *Allium sativum* L. is a member of the Alliaceae family, has been widely recognized as a valuable spice and a popular remedy for various ailments and physiological disorders. The name garlic may have originated from the Celtic word 'all' meaning pungent. Cultivated practically throughout the world, garlic appears to have originated in central Asia and then spread to China, the Near East, and the Mediterranean region before moving west to Central and Southern Europe, Northern Africa (Egypt) and Mexico <sup>(1)</sup>. Garlic has been used for thousands of years for medicinal purposes. Sanskrit records show its medicinal use about 5,000 years ago, and it has been used for at least 3,000 years in Chinese medicine. The Egyptians, Babylonians, Greeks, and Romans used garlic for healing purposes. In 1858, Pasteur noted garlic's antibacterial activity, and it was used as an antiseptic to prevent gangrene during World War I and World War II. Garlic's current principal medicinal uses are to prevent and treat cardiovascular disease by lowering blood pressure and cholesterol, as an antimicrobial, and as a preventive agent for cancer. The active constituents are several complex sulfur-containing compounds that are rapidly absorbed, transformed and metabolized. Pooled data from numerous randomized trials suggest that garlic lowers total cholesterol concentrations by approximately 10% and favorably alters HDL/LDL ratios. Randomized trials also support garlic's effectiveness as a mild antihypertensive

which lowers blood pressure by 5-7%. Garlic also inhibits platelet aggregation and enhances fibrinolytic activity, reducing clots on damaged endothelium. *In vitro* data suggest antibacterial effects, but these have not been evaluated in controlled trials in humans <sup>(2)</sup>.

## CHEMISTRY OF GARLIC

Garlic contains at least 33 sulfur compounds, several enzymes, 17 amino acids, and minerals such as selenium. It contains a higher concentration of sulfur compounds than any other *Allium* species. The sulfur compounds are responsible both for garlic's pungent odor and many of its medicinal effects. Dried, powdered garlic contains approximately 1% *alliin* (S-allyl cysteine sulfoxide). One of the most biologically active compounds, *allicin* (diallyl thiosulfinate or diallyl disulfide) does not exist in garlic until it is crushed or cut; injury to the garlic bulb activates the enzyme allinase, which metabolizes alliin to allicin. Allicin is further metabolized to vinyldithiines. This breakdown occurs within hours at room temperature and within minutes during cooking. Allicin, which was first chemically isolated in the 1940's, has antimicrobial effects against many viruses, bacteria, fungi and parasites. Garlic oil, aged garlic and steam-distilled garlic do not contain significant amounts of alliin or allicin, but instead contain various products of allicin transformation; none appears to have as much physiologic activity as fresh garlic or garlic powder <sup>(3)</sup>.

**Figure 1. Generation of allicin in a garlic clove.**


## ROLE OF GARLIC IN VARIOUS DISEASES

### Antihypertensive Potential

Hypertension (systolic blood pressure (SBP)  $\geq$  140 mm Hg; diastolic blood pressure (DBP)  $\geq$  90 mm Hg) is a known risk factor for cardiovascular morbidity and mortality, affecting an estimated 1 billion individuals worldwide. Garlic (*Allium sativum*) has played an important dietary as well as medicinal role in human history. Blood pressure reducing properties of garlic have been linked to its hydrogen sulphide production and allicin content – liberated from alliin and the enzyme alliinase which has angiotensin II inhibiting and vasodilating effects, as shown in animal and human cell studies. Studies concerning the effect of garlic consumption on blood pressure are not as numerous as the effect of garlic on serum lipids. Again, inconsistent results of the effect of garlic on blood pressure are abounding. For example, intake of about 900 mg, day<sup>-1</sup> garlic powder in hypercholesterolemic, mild hypertension patients, and normotensive subjects resulted in lower diastolic blood pressures as compared to the non-garlic consuming groups. In another study, there was a 5.5% decrease in systolic blood pressure and a modest reduction of diastolic blood pressure in response to 900 mg, day<sup>-1</sup> aged garlic consumption. In contrast to the above mentioned studies, consumption of 900 mg, day<sup>-1</sup> garlic powder in 42 healthy adults was of no effect on blood pressure. Studies on animal models to determine the effects of garlic on blood pressure are few but all of these reports indicate a blood pressure lowering ability of garlic. For example, consumption of 2% wild garlic leaves powder for 8 weeks was effective in lowering the blood pressure in normotensive rats'. The antihypertensive effects of garlic extract in the rat, two-kidney one-clip Goldblatt model has been reported by the researcher. Garlic gavage (100 mg, kg<sup>-1</sup> body wt) in rats has also been shown to block hypoxic pulmonary hypertension. Allicin is known to be a systemic vasodilator; moreover it acts as a pulmonary vasodilator in anesthetized intact-chest cat and isolated lung of the rat under constant flow conditions (4-11).

### Wound Healing Potential

Successful wound healing depends upon angiogenesis, and impaired angiogenesis is a hallmark of the chronic wounds encountered with diabetes and venous or arterial insufficiency. To intervene and improve wound closure, it is essential to investigate the effects of different natural remedies in wound healing. Study was done on the chicken dorsum skin excision wound assay to investigate the influence of different concentrations of aged garlic solution (AGS) on wound healing. Gross, histopathology, scanning electron microscopy (SEM) and computer-based three-dimensional (3D) image-probing techniques were utilized to determine the effects of AGS on wound closure, re-epithelialization, dermal matrix regeneration, and angiogenesis (12,13).

### Antidiabetic Potential

Diabetes is a metabolic disturbance that gradually affects the function of various systems in the body. Poorly

controlled blood glucose is believed to be the most important factor in the development of diabetic complications in both type 1 and type 2 diabetes. Based on report of WHO, garlic can be used for helping treatment of hyperglycemia. According to a report by Ryan et al. (2001), one-third of diabetic patients take alternative medications that they consider efficacious, of which garlic is the most commonly used. Garlic and garlic constituents prepared by various means have been shown to have antidiabetic actions.

In diabetic patients, it was reported that garlic oil can correct hyperglycemia. In addition, a precursor of various allyl sulfide constituents of garlic oil, S-allyl-cysteine sulfoxide (alliin), was shown to have a hypoglycemic effect similar to that of glibenclamide. Garlic has been found to be effective in lowering serum glucose levels in STZ-induced as well as alloxan-induced diabetic rats and mice. Most of the studies showed that garlic can reduce blood glucose levels in diabetic mice, rats and rabbits. It is not clear how garlic actually works in alleviating hyperglycaemia. The hypoglycaemic action of garlic could possibly be due to an increase in pancreatic secretion of insulin from  $\beta$ -cells, release of bound insulin or enhancement of insulin sensitivity. It has been previously suggested that garlic (allicin) can enhance serum insulin by effectively combining with compounds like cysteine, which would spare insulin from SH group reactions which are a common cause of insulin inactivation. Another mechanism proposed by researcher states that the antioxidant effect of S-allyl cysteine sulfoxide, an isolated product from garlic, may contribute to its beneficial effect in diabetes. Research postulate garlic may act as an antidiabetic agent by increasing either the pancreatic secretion of insulin from the  $\beta$ -cells or release of bound insulin (14-18).

### Anticancer Potential

A number of studies have demonstrated the chemopreventive activity of garlic by using different garlic preparations including fresh garlic extract, aged garlic, garlic oil and a number of organosulfur compounds derived from garlic. The chemopreventive activity has been attributed to the presence of organosulfur compounds in garlic. The exact mode of action was not fully understood, but several modes of action have been proposed. These include its effect on drug metabolizing enzymes, antioxidant properties and tumor growth inhibition. Most of these studies were carried out in the animal models. Also, recent research has focused on the antimutagenic activity of garlic. Recently, it has been observed that aged garlic extract, but not the fresh garlic extract, exhibited radical scavenging activity. The two major compounds in aged garlic, S-allylcysteine and S-allylmercapto-L-cysteine, had the highest radical scavenging activity. In addition, some organosulfur compounds derived from garlic, including S-allylcysteine, have been found to retard the growth of chemically induced and transplantable tumors in several animal models. Therefore, the consumption of garlic may provide some kind of protection from cancer development (19-21).

### Antiatherosclerosis and Hypolipidemic Potential

Atherosclerosis, the complex interaction of serum cholesterol with the cellular components of the arterial wall, the pathogenic substratum of many cardiovascular diseases, continues to be the leading cause of death in developed countries. However, the mechanism of the onset and development of atherosclerotic lesions is not

completely understood. Nevertheless, in recent years, remarkable progress has been made in the prevention and treatment of atherosclerosis. Atherosclerotic diseases such as ischaemic heart disease, stroke, and peripheral arterial disease are associated with high serum cholesterol, male gender, age, hypertension, cigarette smoking, diabetes. The direct influence of garlic in preventing onset and development of atherosclerotic lesions and inducing regression of the lesions on the artery wall can be divided into antiatherogenic or preventive and antiatherosclerotic or therapeutic, respectively. Thus, garlic produces both antiatherosclerotic (therapeutic) and antiatherogenic (preventive) effects on experimental atherosclerosis. Garlic's antiatherosclerotic activity is probably due to its direct effect on the processes occurring in the vascular wall as it does not depend on blood cholesterol lowering. The direct antiatherosclerotic effect of garlic can be explained by its action at the level of arterial cells. The earliest manifestation of atherosclerosis is an accumulation of intra and extracellular lipids. Accumulation of intracellular lipids, primarily cholesterol, in the subendothelial intimal cells is accompanied by stimulation of cell proliferation and the extracellular matrix productions Lipid accumulation (lipidosis), enhanced proliferation and accumulation of extracellular connective tissue matrix (fibrosis) are the major manifestations of atherosclerosis at different stages of plaque formation. It has been recently demonstrated that garlic lowers the contents of free cholesterol and cholesteryl esters in lipid-overloaded arterial cells. After 24 h of incubation in a primary culture of smooth muscle cells derived from atherosclerotic plaque of human aorta, aqueous extract from garlic powder decreased free cholesterol by 30%, cholesteryl esters by 30-40%, and triglycerides by 20%. The mechanisms of garlic's direct effect on intracellular lipids can be explained by its ability to suppress lipid synthesis as garlic powder extract inhibits biosynthesis of cholesteryl esters and triglycerides in atherosclerotic cells. In addition, garlic extract inhibits the activity of acyl-CoA:cholesterol acyltransferase (ACAT), the enzyme involved in the formation of cholesteryl esters, the main component of the excessive fat accumulated by cells. In atherosclerotic cells overloaded with cholesteryl esters ACAT activity is 3-fold higher than in normal cells; aqueous extract of garlic powder decreases this enzyme activity to normal levels. On the other hand, garlic extract stimulates cholesteryl ester hydrolase that degrades cholesteryl esters in atherosclerotic cells. The influence of garlic on both enzyme activities may explain cholesteryl ester reduction. Garlic inhibits proliferation of atherosclerotic cells and other cell types, h0.h2 as well as collagen synthesis and accumulation in the aorta thus, all the major manifestations of atherosclerosis (lipidosis, proliferation, and fibrosis) show a tendency toward a decrease and normalization under the action of garlic, which may account for the direct antiatherosclerotic effect (22-24, 9, 10, 16).

#### **Antimicrobial Potential**

The antibacterial properties of crushed garlic have been known for a long time. Various garlic preparations have been shown to exhibit a wide spectrum of antibacterial activity against Gram-negative and Gram-positive bacteria including species of *Escherichia*, *Salmonella*, *Staphylococcus*, *Streptococcus*, *Klebsiella*, *Proteus*, *Bacillus*, and *Clostridium*. Even acid-fast bacteria such as *Mycobacterium tuberculosis* are sensitive to garlic. Analysis of steam distillations of crushed garlic cloves

performed over a century ago showed a variety of allyl Sulfides isolated and identified the component responsible for the remarkable antibacterial activity of crushed garlic cloves. The compound turned out to be an oxygenated sulfur compound which they termed allicin from the Latin name of the garlic plant, *Allium sativum* (25-28).

#### **Antifungal Potential**

Garlic (*Allium sativum*) is an intriguing herb with alleged powers ranging from warding off vampires to the more recently reported power of curing fungal infections. Fungal infections have become an important aspect of modern infectious disease practice. The prominence of fungi as pathogens may be due to the longer survival of immunocompromised patients, the recent development and usage of broader-spectrum antibiotics, or the wider use of immunosuppressive and cancer chemotherapeutic agents. High dilutions of extracts of *Allium sativum*, or garlic, have been shown to possess fungistatic and fungicidal activity in vitro and in vivo. In the People's commercial *A. sativum* extracts are widely used to treat patients with systemic fungal infections. In support of the use of *A. sativum* to treat cryptococcal meningitis, researcher found anti-Cryptococcus neoformans activity in plasma and cerebrospinal fluid (CSF) following intravenous (I.V.) administration of a commercial *A. sativum* extract. *Allium sativum*, had the best activity against the three *Candida albicans*. The antifungal activity of six fractions derived from garlic was investigated in an in vitro system. Ajoene had the strongest activity in these fractions (29-32).

#### **Immunomodulatory Potential**

*Allium sativum* an important medicinal plant having immunomodulatory effects. Three proteins showing immunomodulatory were separated from garlic by Q-Sepharose chromatography of 30 kD ultrafiltrate of raw garlic extract. All these proteins exhibit the mitogenic activity towards human peripheral blood lymphocytes, murine splenocytes and thymocytes. P.Venkatesh *et al.*, was isolated these immunomodulatory proteins from raw garlic, and examine their effects on the immune system (lymphocytes, mast cells and basophils) in relation to mitogenicity and hypersensitivity. The richly present garlic ImPs, QR-1 and QR-2, identified in present study as the lectins or agglutinins ASA II and ASA I, was found to be potent mitogenic activity having potential utility in therapeutic immunomodulation. Garlic has been shown to be a possible biological response modifier. First reported the augmentation of tumor immunity by garlic; subsequently a variety of immunostimulatory effects of garlic were reported. Because certain diseases can be caused by immune dysfunction, modification of immune functions by garlic may contribute to the treatment and prevention of diseases. Thus, some pharmacologic effects of garlic might be mediated through immunomodification. A unique garlic preparation, called aged garlic extract (AGE) has been reported to have an array of pharmacologic effects, including immunomodulation. (33-35)

#### **Antioxidant Potential**

In vivo antioxidant effects of several organosulfur compounds derived from garlic have been studied. In one study, two lipophilic organosulfur compounds, diallyl sulfide (DAS) and diallyl disulfide (DADS) and two hydrophilic organosulfur compounds, s-ethyl cysteine (SEC) and n-acetyl cysteine (NAC), protected against lipid-related oxidations by activating associated antioxidant enzymes. The in vivo antioxidant effects of four test

organosulfur compounds against lipid-associated oxidations have been studied by researcher reported that these antioxidant effects were due to the activation and modification of several enzymes such as 3-hydroxy-3 methylglutaryl- CoA reductase, glutathione-s-transferase and catalase <sup>(36, 26)</sup>.

#### **Antiinflammatory Potential**

Cytokines involved in inflammatory bowel disease (IBD) direct a predominantly cell-mediated T helper- 1 (Th1) immune response. The nonspecific anti-inflammatory treatment being used in the management of patients with IBD has not changed much since the 1970s and new therapeutic agents are keenly sought. Several compounds isolated from *Allium sativum* (garlic) modulate leukocyte cell proliferation and cytokine production. To investigate the possible therapeutic effects of garlic in the treatment of patients with IBD, whole blood and peripheral blood mononuclear cells (PBMCs) were stimulated in the presence of various concentrations of garlic extract and the effect on leukocyte cytokine production was determined in vitro using multiparameter flow cytometry. By inhibiting Th1 and inflammatory cytokines while upregulating IL-10 production, treatment with garlic extract may help to resolve inflammation associated with IBD. An in vivo animal model study needs to be undertaken to determine the significance of these in vitro findings <sup>(37, 36)</sup>.

#### **Anthelmintic Potential**

Development of anthelmintic resistance in helminthes reported in a number of countries, gives a clear indication that control programs based exclusively on their use are not sustainable. The development of integrated programs to control helminths is vital, but such control programs require viable alternatives to the use of anthelmintics. Medicinal plants have served through ages, as a constant source of medicaments for the exposure of a variety of diseases. The history of herbal medicine is almost as old as human civilization. The plants are known to provide a rich source of botanical anthelmintics, antibacterials and insecticides. A number of medicinal plants have been used to treat parasitic infections in man and animals. The alcoholic extract of bulb of *A. sativum* has also shown moderate *in vitro* anthelmintic activity against human *Ascaris lumbricoides*. *A. sativum* has been reported to be effective in the exposure of dysentery and also act as vermifuge. Oil of *A. sativum* has also been reported to possess anthelmintic activity and discards all injurious parasites in the intestine. Garlic is the best known source of selenium. The sulfur compound allicin, produced by crushing or chewing fresh garlic, in turn produces other sulfur compounds: ajoene, allyl sulfides, and vinyldithiins <sup>(38, 39)</sup>.

#### **Anticoagulant and Fibrinolytic Potential**

Over the century garlic (*allium sativum*) and other species in the genus *allium* have enjoyed an important reputation as the prophylactic and therapeutic agent. Of these, the usefulness of garlic in preventing disease of cardiovascular system is widely recognized. There are several report on anticoagulant. Song et al (1960) have isolated blood anticoagulant substance from garlic and studied its physical and chemical properties. A half mg of garlic extract completely inhibited one ml of blood from coagulating. The inhibiting effect of garlic extract on blood clotting was almost the same as that of potassium oxalate <sup>(40, 41)</sup>.

#### **Hepatoprotective Potential**

Alcoholic liver disease is one of the most serious consequences of chronic alcohol abuse. The disease is often progressive and is considered to be a major cause of morbidity and mortality. Free radicals and oxidative stress have been implicated in the pathogenesis of ethanol induced liver injury in humans and experimental animals. Basically, ethanol is metabolized into cytotoxic acetaldehyde by alcohol dehydrogenase in the liver and acetaldehyde is oxidized to acetate by aldehyde oxidase or xanthine oxidase giving rise to Reactive oxygen species (ROS) via Cytp450. Thus, excess intake of alcohol resulted in the production of oxygen radicals which leads to lowering the body's normal defense mechanism thereby altered enzyme activity, decreased DNA repair and impaired utilization of oxygen, lipid peroxidation and protein oxidation. Oral administration of raw garlic protects tissue damage by increasing the antioxidant status against oxidative stress. Hence, garlic plays a promising role in antioxidant and it can be considered as a potent drug for the treatment of alcoholic disorders. Lead has been known to be environmental pollutant and its toxicity has also been associated with some health hazards. Liver enzymes such as ALT, AST and ALP are marker enzymes for liver function and integrity. These enzymes are usually raised in acute hepatotoxicity or mild hepatocellular injury, but tend to decrease with prolonged intoxication due to damage to the liver. Administration of lead showed significant increase in plasma ALT and ALP activities, and conversely decrease plasma AST activity level. Post-lead treatment with *A. sativum* significantly reduced the activities of ALT and ALP, and increased the activity of AST when compared to the rats treated with lead alone. The reduced serum ALT and ALP activities may generally be attributed to decreased production of these enzymes from these sources hence denotes the reversing effect of lead toxicity in rats <sup>(42-44)</sup>.

#### **CONCLUSION**

A single clove of garlic has the potential of curing a man from a large number of diseases by inhibiting the population of different strains of bacteria and fungi. Garlic (*Allium sativum*) use in cardiovascular therapeutics has an even longer history back over 3000 years to ancient time. Numerous animal studies have shown garlic to have a cholesterol lowering effect. The active chemical in garlic is allicin, which is produced when raw garlic is crushed, allowing the enzyme alliinase to act on the stable precursor allin. Garlic's antidiabetic, antibiotic and perhaps anticancer effects are well-accepted world over because of the many of scientific literature supporting these effects. Garlic also has hepatoprotective, antioxidant, and anthelmintic effect. The other pharmacological effect which required more attention of researcher includes the anticoagulant, anti inflammatory, immunomodulatory and wound healing action of garlic.

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