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Garlic: A spice with wide medicinal actions

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Abstract

A member of the Liliaceae family, garlic (*Allium sativum*) is highly regarded throughout the world for both its medicinal and culinary value. Garlic (leaves, flowers, and cloves) is probably one of the earliest known medicinal plants, which used from ancient time to cure different disease in human. The key significance of present research is the medicinal value of garlic is its broad-spectrum therapeutic effect with minimal toxicity. Most active constituents of this plant are organosulfur compounds such as allicin, diallyl disulphide, S-allylcysteine, and diallyl trisulfide that are quickly absorbed and metabolized. Allicin is one of the most studied among these naturally arising compounds. Garlic and its compounds have been used to treat several diseases viz: antidiabetic, antioxidant, antiinflammatory, hepatoprotective, anthelmintics, antibacterial, antiviral, antifungal and wound healing. Diseases that may also be suppressed by garlic's medicinal actions include Alzheimer's disease, cancer, cardiovascular disease (Including atherosclerosis, hypertension, thrombosis and hyperlipidaemias) dermatologic applications, stress, and infections. The purpose of this article reviews the pharmacological effects and traditional uses of garlic and its active constituents. It can be further used as probable natural sources for the advancement of new drugs.

Keywords: garlic, allicin, herbal medicine, pharmacological activities

Introduction

Garlic (*Allium sativum* L.), is a member of the Alliaceae family, is one of the best essential vegetables all over the world. The importance of garlic is due to its use not only for culinary but also for therapeutic and medicinal resolves in both traditional and modern medicine. All parts of the plant, inflorescence, leaves, and cloves have been used from earliest time as a condiment or spice for flavouring soup, sausages and salads ^[1].

Garlic contains a higher concentration of sulfur compounds (Such as allicin, diallyl disulphide, S-allylcysteine, and diallyl trisulfide) which are responsible for its various kinds of medicinal effects. It is eaten up either as raw vegetable (fresh leaves or dried cloves), or after processing in the form of garlic oil, garlic extracts and garlic powder with changes in chemical composition and bioactive compounds content between the various forms. It has been widely recognized as a valuable spice and a popular remedy for many ailments and physiological disorders. Babylonians, Egyptians, Phoenicians, Greeks and Romans used garlic as a remedy for intestinal disorders, respiratory infections, skin diseases, bacterial infections, worms, wounds and tumours. Before the outcome of antibiotics, garlic has been used against amoebic dysentery and epidemic diseases such as cholera, diphtheria, and tuberculosis. Garlic was largely used during the World War II to treat wounds of soldiers and used directly to wounds to prevent the spread of infection ^[2].

Description

The garlic is a perennial plant with fine leaves and a compound bulb consisting of several small bulb-lets or cloves, varying from 10-50 which are surrounded by a thin, white or pinkish sheath, short and embedded roots. The cloves are asymmetric in shape, except for those near the centre. Garlic produces hermaphrodite flowers and grows up to 1.2 m (4ft) in height. The plant produces both seeds and bulb-lets ^[3]. Garlic and the other *Allium* species have been identified since ancient times for their health benefits. Garlic cultivated almost all over the world, 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. 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 ^[1].

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Table 1: Vernacularnames [3].

Language/Country	Vernacular names
Arabic	Saum
Chinese	Suan, Da Suan
French	Ail
Italian	Aglio
Spanish	Ajo
Hindi	Lahsun, Lahsan, Lissan
Assami	Naharu
Bengali	Rashuna
Gujrathi	Lasana
Kannada	Bellulli
Kashmir	Ruhan
Marathi	Lasuna
Malayalam	Velluli
Punjabi	Lasana, Tuma
Tamil	Puntu
Telugu	Vellulli, Tellagadda
Tibetan	Gokpas
Urdu	Lehsan

Classification

Kingdom - Plantae

Division - Angiosperm

Class - Monocotyledoneae

Order - Liliales

Family - Liliaceae

Genus - Allium

Species - *A. sativum***Table 2:** Phytochemical Compounds [4, 5].

Plant part	Compounds
Garlic bulb	<ul style="list-style-type: none"> 33 sulfur compounds (alliin, allicin, ajoene, allylpropyl, diallyl, trisulfide, sallylcysteine, vinylidithiines, S-allylmercaptocystein and others), several enzymes (allinase, peroxidases, myrosinase), minerals (germanium, calcium, copper, iron, phosphorus, potassium, magnesium, selenium and zinc), vitamins A, B1 and C, fiber and water. It also contains 17 amino acids: lysine, histidine, arginine, aspartic acid, threonine, swine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan and phenylalanine. Oligosaccharides, peptides, steroids, terpenoids, flavonoids, and phenols carbohydrates (sucrose and glucose). Essential oil:-DAS, DADS, diallyl trisulfide, methylallyl disulfide, methylallyl trisulfide, 2-vinyl-4H-1, 3-dithiin, 3-vinyl-4H-1, 2-dithiin, and ajoenes

Pharmacological Activities**1. Antidiabetic activity**

Oral administration of garlic extract revealed significant decrease in serum glucose, total cholesterol, triglycerides, urea, uric acid, aspartate amino transferase and alanine amino transferase levels, while increased serum insulin in diabetic mice, but not in normal mice. From a comparison study made between the action of garlic extract and glibenclamide, it was shown that the antidiabetic effect of the garlic was more effective than the glibenclamide [6]. It is reported that garlic oil can precise hyperglycemia in diabetic patients. Garlic has been found to be effective in lowering serum glucose levels in STZ-induced as well as alloxan-induced diabetic rabbits, rats and mice. In alloxan-induced diabetic male rabbits, dose of aqueous garlic extract resulted in better utilization of glucose

during glucose tolerance tests performed, with allicin at a dose of 1% solution of garlic/kg body weight. It expressively lowered serum glucose level (38.88%) and serum cholesterol level (57%), possibly by stimulating β cells [7]. The antidiabetic effects of garlic are mainly due to the volatile sulphur compounds. Garlic has been shown to be effective in reducing insulin resistance as well [8].

2. Antioxidant activity

It was observed that 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 these four organosulfur compounds against lipid-associated oxidations were due to the activation and modification of several enzymes such as 3-hydroxy-3 methylglutaryl- CoA reductase, glutathione-s-transferase and catalase [9]. In the fructose-induced metabolic syndrome, aqueous garlic extract reduces oxidative stress and inhibits vascular remodelling by suppressing NAD (P) H-oxidase [10]. The aged extracts obtained from the leaves showed the best antioxidant activity as comparison to flowers and bulbs. Garlic is rich in antioxidants which help destroy free radical particles that can damage cell membranes and DNA, and may contribute to the aging process [11].

3. Hepatoprotective activity

Excess intake of alcohol affected the production of oxygen radicals which leads to lowering the body's normal defence mechanism so changed enzyme action, decreased DNA repair and reduced consumption of oxygen, lipid peroxidation and protein oxidation. Oral administration of raw garlic protects tissue damage by increasing the antioxidant status against oxidative stress. Garlic plays an important role in antioxidant and it can be considered as ineffective drug for the cure of alcoholic disorders. Liver enzymes such as ALT, AST and ALP are marker enzymes for liver function and integrity. Administration of lead showed significant increase in plasma ALT and ALP activities, and equally decrease plasma AST activity level. Post-lead treatment with garlic significantly reduced the activities of ALT and ALP, and increased the activity of AST [12, 13]. Aged garlic and garlic's diallyl sulfur compounds protected against acute chemically induced hepatotoxicity in rats. Aged Garlic Extract have liver protective effects and It has been shown to inhibit both the formation and bio activation of liver carcinogenic nitrosamines and has prevented the mutagenic effects of aflatoxin B1 [14].

4. Anti-inflammatory activity

Cytokines involved in inflammatory bowel disease (IBD) direct a predominantly cell-mediated T helper- 1 (Th1) immune response. Numerous compounds isolated from garlic moderate leukocyte cell proliferation and cytokine production. 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 different concentrations of garlic extract and the effect on leukocyte cytokine production was determined *in vitro*. By inhibiting Th1 and inflammatory cytokines while up regulating IL-10 production, treatment with garlic extract may

help to resolve inflammation related with IBD [15]. The anti-inflammatory activity of garlic oil was due to the suppressed expression and production of pro-inflammatory cytokines TNF- α and IL-1 β . These regulations of colonic pro-inflammatory and anti-inflammatory cytokine levels by garlic oil treatment could be defined by the presence of the bioactive components such as diallyl sulfide, which showed to inhibit pro-inflammatory cytokines, TNF- α and IL-1 β secretion, and allyl methyl sulfide, which known to stimulate, anti-inflammatory cytokine, IL-10 production [16].

5. Cardiovascular activity

Garlic is well reported to scavenge oxidants, increase superoxide dismutase, catalase, glutathione peroxidase, and glutathione levels, as well as prevent lipid peroxidation and inflammatory prostaglandins. Garlic also reduces cholesterol synthesis by preventing 3-hydroxy-3 methylglutaryl-CoA. Garlic has been shown to prevent LDL oxidation, platelet aggregation, and arterial plaque formation, reduce homocysteine, lower blood pressure, and increase microcirculation, which is main in diabetes. Garlic may also help prevent cognitive decline by protecting neurons from neurotoxicity and apoptosis, thereby preventing ischemia- or reperfusion related neuronal death and by improving learning and memory retention [17]. Cardiovascular diseases include high blood cholesterol, and triglycerides level; raised platelet activity, which can give rise to arteriosclerotic plaques formation; high blood homocysteine; alteration on glucose metabolism; hypertension and obesity. Garlic and its compounds have been widely recognized as agents for prevention and treatment of cardiovascular diseases. Garlic consumption have significant effects on lowering blood pressure, inhibition of atherosclerosis, reduction of serum cholesterol and triglyceride, inhibition of platelet aggregation, and increasing fibrinolytic activity [18].

6. Hyperlipidaemia

Garlic depressed the activity of hepatic lipogenesis and cholesterologenic enzyme such as malic enzyme, fatty acid synthetase, glucose 6 -phosphate dehydrogenase and 3-hydroxyl 3-methyl glutaryl CoA (HMG-CoA) reductase. *In vitro* studies shown that water soluble organosulfur compounds especially S-allyl cysteine (SAC) present in aged garlic extract and diallyl disulphide (DADS) present in garlic oil are also effective inhibitors of cholesterol synthesis [19]. Garlic has universal ability to lower cholesterol level and reduce lipid peroxidation in order to prevent plaque formation. *In vitro* studies clearly have revealed that, it has a capacity to suppress low density lipoprotein (LDL) and an increased resistance of LDL to oxidation [20]. A material formed from garlic fermented with the mold *Monascus pilosu*, reduced serum total cholesterol and LDL cholesterol levels. The level of triglycerides had an affinity towards reduction in hyper-triglyceridemic patients, whereas high density lipoprotein cholesterol (HDL-C) was unaffected [21].

7. Immunomodulatory Potential

Garlican essential medicinal plant having immunomodulatory effects. Three proteins showing immunomodulatory effect were isolated from raw garlic extract. All these proteins show the mitogenic action towards human peripheral blood lymphocytes, murine splenocytes and thymocytes. These

immunomodulatory proteins were isolated from raw garlic, and observe 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, known in present study as the lectins or agglutinins ASA II and ASA I, was found to be effective mitogenic action having reliable value in therapeutic immunomodulation. Garlic has been shown to be a possible biological response modifier. Aged garlic extract (AGE) has been reported to have an array of pharmacologic effects, with immunomodulation [22].

8. Antibacterial activity

In rabbits, aqueous garlic extract and allicin had significant antibacterial activity against *Shigella flexneri*, fully curing the infected rabbits [23]. Antibacterial activity of garlic is mainly due to the presence of allicin produced by the enzymatic activity of allinase on alliin. Allicin is considered to be the most potent antibacterial agent in crushed garlic extracts, but it can be unstable, breaking down within 16 h at 23°C. However, the use of a water-based extract of allicin stabilizes the allicin molecule due to the hydrogen bonding of water to the reactive oxygen atom in allicin or there may be water soluble components in crushed garlic that destabilize the molecule [24]. Infection with *H. pylori* was a significant risk factor for the development of gastric lesions, gastric dysplasia and gastric cancer; garlic intake was inversely associated with *H. pylori* infection and gastric pathology [25]. Garlic extract inhibits the growth of Gram positive and Gram negative bacteria, such as *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Enterobacter*, *Escherichia*, *Klebsiella*, *Lactobacillus*, *Pseudomonas*, *Shigella*, *Salmonella*, *Proteus*, and *Helicobacter pylori* [26].

9. Antiviral activity

An *in vitro* study of Garlic and its sulfur constituents demonstrated antiviral activity against Coxsackie virus spp, Herpes Simplex Virus types 1 & 2, Influenza B, Parainfluenza Virus type 3, Vaccinia Virus, Vesicular Stomatitis Virus, Human Immunodeficiency Virus type 1 and Human Rhinovirus type 2. The order for virucidal activity generally was: ajoene>allicin>allyl methyl thiosulfinate> methyl allylthiosulfinate. Several studies have shown that garlic is an effectual treatment for both the influenza B virus and herpes simplex virus [27].

Garlic extract exhibited a dose dependent inhibitory effect against human cytomegalo virus in tissue culture. The anti-viral effect of garlic extract (GE) persisted long in infected cells and the strongest anti-viral effect of GE was demonstrated when it was applied continuously [28].

10. Antifungal activity

Aqueous garlic extract and concentrated garlic oil showed inhibitory effects against *Aspergillus* [29]. Allicin demonstrated fungicidal activity against numerous yeast and fungi, including *Candida albicans*, *Cryptococcus*, *Trichophyton*, *Histoplasma capsulatum* and *Cryptococcus neoformans* [30]. A study found that *Candida* colonies were substantially reduced in mice that had been treated using liquid garlic extract. The study also revealed that garlic stimulated phagocytic activity. Garlic oil can be used to treat ring-worm, skin parasites and warts if it is applied externally. Lesions that were caused by

skin fungi in rabbits and guinea pigs were treated with external applications of garlic extract began to heal after seven days [31]. Garlic has been shown to inhibit growth of fungal diseases as equally as the drug ketoconazole, when tested on the fungi *Malassezia furfur*, *Candida albicans*, *Aspergillus*, *Cryptococcus* and other *Candida* species [32].

11. Anticancer activity

The research evaluating the use of garlic in leukemic [33], melanoma [34] and neuroblastoma [35] cell lines. Allyl sulfides (sulphur compound) are characteristic flavor components of garlic. These compounds inhibit both initiation and promotion stages of tumorigenesis in experimental carcinogenesis for various types of cancer [36]. Pancreatic cancer risk was 54 % lower in individuals who consumed larger amounts of garlic compared with those who ate lower amounts [37]. The chemopreventive activity of garlic has been shown by using different garlic preparations including fresh garlic extract, aged garlic, garlic oil and a number of organosulphur compounds derived from garlic. The chemopreventive activity has been attributed to the presence of organosulphur compounds in garlic. 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 animals [38].

12. Antihypertensive activity

The gamma-glutamylcysteines are the compounds in garlic that may lower blood pressure, as indicated by their ability to inhibit angiotensin-converting enzyme in *in vitro*. Garlic pearls at a dose of 250mg/d for 2 months of supplementation; there was also a significant decline in both systolic and diastolic blood pressures. Dietary supplementation of garlic may be beneficial in reducing blood pressure and oxidative stress in hypertensive individuals [39]. An *in vitro* study has confirmed that, the vasoactive ability of garlic sulphur compounds where by red blood cells convert garlic organic polysulfides into hydrogen sulphide, a known endogenous cardio-protective vascular cell signaling molecule [40]. An experimental study was conducted to show the effects of two garlic sources AGE and raw garlic on systolic blood pressure (SBP) with spontaneously hypertensive (SHR) rats. Both the AGE and raw garlic showed a lowering effect in increased SBP where as raw garlic indicated to cause harmful effects such as anemia, the generation of papilloma in the fore stomach and a decline of body weight. In spontaneously hypertensive rats (SHR), processed garlic (with a dose of 500 mg capsules) can significantly reduce the blood pressure [41].

13. Antiplatelet effect

The daily consumption of 1 clove of fresh garlic for 6 months resulted in an 80% decrease in serum thromboxane B2 in middle-aged men [42]. According to a meta-analysis, consumption of garlic preparations led to inhibition of platelet aggregation in human. Garlic preparations have demonstrated antiplatelet effects by obstructing cyclooxygenase activity and thromboxane A2 formation [43]. A dose dependent inhibition

of platelet aggregation (induced by ADP, epinephrine and collagen) was first demonstrated in garlic oil (0.5 mg/day). Platelet aggregation control by garlic is observed in both *in vitro* and *in vivo* study. In *in situ* study overall antithrombotic effects of garlic by modulation of fibrinolytic activity through increased plasminogen activation and by inhibiting thrombin formation [44].

14. Anthelmintic activity

The alcoholic extract of bulb of Garlic has also shown moderate *in vitro* anthelmintic activity against human *Ascaris lumbricoides*. Garlic has been reported to be effective in the exposure of dysentery and also act as vermifuge. Oil of Garlic has also been reported to possess anthelmintic activity and discards all injurious parasites in the intestine [45]. Garlic is useful in the treatment of intestinal worms. Sulfurous components of garlic may be useful to eliminate tapeworms [14]. Garlic has anthelmintic activity against *Ascaridia galli* in chicken due to its allicin component (the main active component of garlic). Garlic oil caused mortality in *A. galli* and in *Heterakis gallinarum*. Garlic extract significantly reduced the glucose uptake, glycogen content and oxygen consumption in both parasites [46].

15. Reduces stress

Aged garlic extract is also effective to prevent adrenal hypertrophy, hyperglycemia and elevation of corticosterone in hyperglycemic mice induced by immobilization stress. After the exposure to immobilization stress, the adrenal glands hypertrophied, and their serum glucose level and corticosterone secretion became elevated, but insulin secretion did not change. The elevation of serum glucose was probably due to the stimulation of the pituitary-adrenocortical axis by the stress. Pre-treatment of aged garlic extract (AGE) (5 and 10 ml/kg, p.o.) significantly prevented adrenal hypertrophy, hyperglycemia and elevation of corticosterone, but did not alter serum insulin level [47].

Garlic, appears to have the capacity for protecting against the negative effects of stress that affects the autonomic nervous and neuroendocrine system. In rats exposed to psychologically stressful situations, aged garlic extracts significantly prevented the decreases in spleen weight seen in control animals. Additionally, the garlic significantly prevented the reduction of haemolytic plaque forming cells in spleen cells. Garlic was able to block the lipopolysaccharide induced immune cytokine and plasma corticosterone and catecholamine changes after cold water immersion stress [48].

16. Sickle Cell Anaemia

Sickle cell anaemia is a genetic disease caused by abnormal haemoglobin. Dense cells, which have an elevated density and possess an abnormal membrane, have a tendency to adhere to blood components such as neutrophils, platelets, and endothelial cells, which line blood vessels. Aged garlic extract (AGE) and other components of AGE, such as S-allylcysteine (SAC) and fructosyl arginine, could inhibit the formation of dense cells because AGE and SAC have been known to have antioxidant activity either Fructosyl arginine does not contain sulfur molecules like many other garlic components, yet it was found to have antioxidant activity. Aged Garlic Extract (4.0 mg/ml) could inhibit dense cell formation by 50% along with other effective nutrients like black tea extract, green tea

extract, pycnogenol, α -lipoic acid, vitamin E, co-enzyme Q10, and β -carotene [49].

17. Adverse effects of garlic

Common side effects of oral and intravenous garlic use are malodorous breath, body odour, nausea, vomiting, flatulence, weight loss, facial flushing, tachycardia, dizziness, insomnia and allergic reactions. Based on human studies, administration of intravenous garlic more than one month causes liver, kidney and bone marrow damage [19]. Rare garlic allergy has been attributed to the protein allinase, which has induced immunoglobulin E (IgE) mediated hypersensitivity responses from skin prick testing [50]. An entire bulb produces little juice; it is potent and can act as a strong emetic, even in small quantities. Although garlic generally poses little in terms of safety issues, there are isolated cases of topical garlic burns [51] and anaphylaxis after ingestion of young garlic [52].

18. Vaginal infections

Garlic is one of the best antibiotics. It has bactericidal and fungicidal properties, able to kill or inhibit the growth of microorganisms that could be responsible for infections that cause vaginal irritation, vaginitis or vaginal flow. For the cure of this disease plenty of garlic has been eaten. It can also be used to fight scabies [42]. Bacterial Vaginosis (BV) is one of the most common causes of vaginal discharge in women of reproductive ages. Garlic, can be used as an alternative herbal medication for BV. Garlic extract inhibited the growth of Gram-positive and Gram negative bacterial strains *in vitro*. Tea tree oil, garlic boric acid douching, and yogurt can be used as alternative herbal treatments for BV and yeast vaginitis. Great discharge was the most common complaint among the BV patients. Both treatments (garlic vaginal cream and metronidazole vaginal gel) had the same effect on reducing the discharges [53]. Garlic is a very common spice used in most food, allicin, one of the active compounds, have a variety of antimicrobial properties and block the growth of bacteria to prevent urinary tract infections (UTIs). The pure form of allicin has been found to exhibit antibacterial activity against a wide range of bacteria, including multi-drug-resistant strains of *E. coli* [54].

Conclusion

Garlic is safe and rich sources of biologically active compounds with low toxicity. All parts of the plant have been used from earliest time as a condiment or spice for flavouring soup, sausages and salads and also used in folk-and traditional medicine. Higher concentration of sulfur compounds of garlic is responsible for its medicinal effects. This review paper demonstrated some of the benefits of garlic for its potential uses in preventing and curing different diseases with its sulfur containing compounds, high trace mineral content, and enzymes, garlic has shown antidiabetic, antioxidant, hepatoprotective, anti-viral, anti-bacterial, anti-fungal and antioxidant abilities. The other pharmacological effect which required more attention i.e. anticoagulant, anti-inflammatory, immunomodulatory and wound healing action of garlic.

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