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# Pharmacological Properties of A Magical Shrub of Allium Sativum

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#### Abstract

Pakistan is rich in medicinal plants used for medicine for over a thousand years. Garlic is an essential vegetable, most consumed as spice and flavor during cooking food, which makes the food more digestible all over the world. Garlic has a tremendous pharmacological and therapeutic effect due to its biologically active compounds. The chemical composition of the plant are allicin, diallyl trisulfide, diallyl disulphide and S-allylcysteine contribute an important role in its nutraceutical/therapeutic applications. Garlic is a good source of several vitamins, minerals, and other nutrients that are useful for human health. It possesses high macro and micro nutritive molecules such as carbohydrates, protein, fat, calcium, sulfur potassium, iodine, phosphorous, fiber and silicon in addition to vitamins. Furthermore, garlic has pharmacological effects and is used to cure enormous conditions including, Antibacterial, antiviral, antifungal, antiparasitic, anthelmintic antiatherosclerotic, anti-inflammatory, antihyperlipidemic, immunomodulatory, anti-tumor, antidiabetic, diuretic, hepatoprotective, digestive effect and toxicological effects were observed invivo and invitro.

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#### Introduction

Pakistan is rich in medicinal plants used of plants for medicine for over a thousand years. Nowadays scientists have been gaining attention to medicinal plants for therapeutic purposes (Iqbal *et al.*, 2021). Among the different medicinal herbs garlic has played an important role as a medicinal herb for thousands of years. Garlic is a significant food and medicinal herb which is commonly found in Central Asia and widely grown all over Pakistan. It is grown in the southeast and on the Indus River as an irrigated crop. It is cultivated in Sindh and Panjab on a large scale (Varshney *et al.*, 2016). It is a 60 cm height perennial herb. The white sheath or skin that covers each individual clove makes up the garlic bulb. The garlic bulb is used as a spice or medicinal herb, whether it is fresh or dried. The lower half of the stem is sheathed by long, flat, sharp leaves; the scape is thin, smooth, and glossy; the long, beaked spathes enclose the heads bearing solid bulbils. White, small blossoms with leafy edges protruded from the plant (Tsai *et al.*, 2012).

Garlic (*Allium sativum*) a natural plant, is a member of Lilliceae (onion family) that has multipurpose medicinal applications (Labu *et al.*, 2019). Garlic is used as a flavoring agent in cooking and utilized as medicine since ancient times to treat and prevent a variety of conditions (Sharifi-rad *et al.*, 2016). Garlic can be prepared in various forms i.e., powder, oil, extracts, and raw juice. It has been described that the oil- and water-soluble organo-sulfur components of garlic are widely known for antimicrobial therapeutic properties (Bisen *et al.*, 2016). Garlic contains the typical odor and flavor (Saif*et al.*, 2020).

Garlic bulbs can be eaten alone or combined with food to produce desirable therapeutic effects (Londhæ*t al.*, 2011; Petrovska *et al.*, 2012; Suleria *et al.*, 2015). It is currently used in 22 forms of folk medicine to treat a wide range of infections. Many clinicians have used garlic for ages to fight infectious diseases all over the world (Londhe *et al.*, 2011). Garlic can be given as dietary supplements in the form of capsules and powders, making it different from traditional foods (Dureja *et al.*, 2003). The word garlic originated from Celtic means pungent.

Indian literature reported that garlic plays a valuable role in the nutritional and therapeutic activities in the medicinal history (Singh *et al.*, 2008). Clinical uses of garlic include cough, abdominal pain, loss of appetite, hemorrhoids, dermatitis, rheumatism, and loss of weight (Harris *et al.*, 2001; Kunnumakara *et al.*, 2009). The Father of Medicine Hippocrates, noticed that garlic is an effective diuretic and was excellent for curing tumors (Rivlin *et al.*, 2001). Aristotle attributed garlic as effective for the treatment of rabies, and it was recommended by Prophet Mohammad for the treatment of scorpion stings (Palani *et al.*, 2014; Mohammad *et al.*, 2017). It has been reported that treated dog and snake bites garlic was recommended (Sharifi-Rad *et al.*, 2016).

Table 1. Nutritive valves of Garlic.

S. No.	One clove of garlic (3 grams)	Quantity
1	Water	58.68%
2	Energy	623 kJ (150 kcal)
3	Carbohydrates	1 gram
4	Protein	6.39g
5	Fat	0.5g
6	Dietary fiber	2.1 g
7.	Potassium	12 mgs
8	Calcium	5 mgs
9	Sodium	1 mg
10	Calories	4

## History of garlic

Garlic is cultivated practically all over the world, mostly in central Asia, China, Mediterranean region, Southern, West to Central Europe, Northern Africa and Mexico (Londhe *et al.*, 2011). Garlic is mentioned as being helpful in treating several diseases, an ancient Egyptian medicine from 1550 BC. The Bible mentioned the cultivation of garlic one of the earliest plants in literature of Ancient Israel, India and Egypt. Asian people have been using this plant for at least 3,000 years, and some of the latest references were found approximately 5,000 years ago. Chinese strongly have faith that garlic crop is an extended longevity crop (Papu *et al.*, 2014; Walia *et al.*, 2016).

#### Macroscopic character of garlic

The plant can be found as a whole bulb with isolated cloves (bulblets); a diameter 4-6 cm of the sub-globular, and each bulb contains 8-20 cloves (Chanda *et al.*, 2011). It is attached 3-5 papery whitish membranous scales and a short woody disc stem attached to a bulb with numerous, wiry rootlets on the underside (Kadam *et al.*, 2013). Each clove is tapering, ovoid and irregularly upper end 2-3 cm long, 0.5-0.9 cm wide of dorsal convex surface, with yellowish-green folded leaves wrapped within two white fleshy, modified leaf bases or scales, each is covered by two very thin papery, white, and brittle scales. The odor is strong, unpleasant and the taste is bitter (Jayapraash *et al.*, 2014).

#### Garlic oil

Garlic oil has been proven to have antibacterial characteristics and to inhibit the growth of different microbes, including *Penicillium funiculosum, S. aureus, E. coli, and B. subtilism*(Bhatwalkar *et al.,* 2021). Most likely through invading cells and organelles, disrupting cell structure, cytoplasm, and macromolecules of the microorganisms. Additionally, garlic oil has also been found to be effective against bacterial cell metabolism, which is linked to the expression of gene mutations

that are involved in the cell cycle, oxidative phosphorylation, and protein synthesis in the endoplasmic reticulum. Furthermore, raw garlic treatment reduced *Helicobacter pylori* in the stomach of patients with*H. pylori* infection. The antibacterial activity of garlic oil has been found to be dependent on the variety of processing methods utilized (Zardast *et al.*, 2016). Garlic oil extracted through steam distillation showed antimicrobial properties. Garlic oil is composed of diallylsulphides (57%), allyl methyl sulfides (37%), and dimethyl mono to hexasulfides after steam distillation of garlic bulbs (6%) (Sendl *et al.*, 1995). Fresh garlic bulbs have an essential oil concentration of 0.09 to 0.35%. The chemical structures of garlic's key phytoconstituents (Ezeorba *et al.*, 2022).

## Chemical composition of garlic

Garlic is found to include at least 33 sulphur compounds, many micro and macro minerals like zinc, copper, potassium, iron, germanium, magnesium, selenium, calcium, water-soluble and fat-soluble vitamins such as A, B1, B2 and E, C, fibers, and water (Casado *et al.*, 2004). Amino acids such as arginine, threonine, lysine, histidine, aspartic acid, proline, cysteine, swine, glutamine, alanine, methionine, and valine are among seventeen most effective amino acids contained in garlic (Rauf *et al.*, 2022). Allicin is one of the most physiologically active substances in garlic, along with phenylalanine (diallyl thiosulfinateor diallyldisulfide), leucine, tryptophan (serotonin), methionine, and isoleucine. Allicin (S-allylcysteine sulfoxide) is the most prevalent sulphur component in garlic, with 12 and 32 mg/gm in fresh and dry garlic, respectively. During food preparation garlic used by different methods such as crushing, chopping and mincing, disrupt S-allyl cysteine sulfoxide, exposing it to allinase enzymes, which swiftly convert it to diallyl thiosulfinate, which gives garlic its distinctive scent (Kopec *et al.*, 2013). The enzyme allinase, which converts diallyl thiosulfanate, is rendered inactive below a pH of 3.5 or under heat. Molecular pharmacological, such as polar compounds of phenolic and steroidal origin, without odor and are also heat stable, allicin plays a significant role as an antioxidant and scavenging compound (Mohammed *et al.*, 2018).



Figure 1. Chemical structure of garlic oil compounds (Shang et al., 2019)

# Pharmacological activities of garlic

Allicin and its active biological derivatives compounds are present in garlic, historically garlic has been utilized as a medicine to treat different conditions and diseases related to the blood system and heart including high cholesterol, heart attack, coronary heart disease and thickening of the arteries (atherosclerosis), antilipemic, anti-hypertensive, anti-atherosclerotic (Mikaili *et al.*, 2013).

Garlic extract is used to prevent different types of cancer, such as lung, breast, prostate, stomach, colon, and rectal cancer. It is also most effective in conditions like hay fever (allergic rhinitis), osteoarthritis, diabetes, traveler's diarrhea, and late pregnancy. Garlic is used to build up the immune system, effective in bacterial and fungal infections (Corz-Martinez *et al.*, 2007).





Furthermore, Tesfaye and Mengesha, (2015) reported the pharmacological and therapeutic uses in daily routine infections to treat sinus congestion, cough, headache, fever, stomach pain, gout, rheumatism, hemorrhoids, shortness of breath, bronchitis, asthma, low blood sugar, low blood pressure, high blood sugar, and snakebites. It is also used for maintaining liver functions and stress and fatigue (Sanie-Jahromi *et al.*, 2023). In addition, garlic is also used for promising effects against sciatica, arthritis, lumbago, skin diseases, leprosy, discoloration of the skin, leukoderma, chronic fever, tuberculosis, rhinitis, malaria, obstinate skin diseases, itches, anemia, indigestion, piles, colic pain, enlargement of spleen, fistula, fracture of a bone, gout, urinary diseases, kidney stone, epilepsy, cataract and night blindness (Yoneska *et al.*, 2023). Garlic plays a crucial role as pharmacologically defined below:

#### Antibacterial activity of garlic

The Sulphur components present in garlic are responsible for both its strong odor and medicinal properties. Alliin is found

in the whole plant (S-allyl-Lcysteine sulfoxide). Allicin is an aromatic, soluble crystal compound. It has antibacterial properties and is a cysteine analog. Slight damage to garlic cloves causes changes in alliin, which is broken down into lactic acid and 2-propenyl-sulfonic acid by the enzyme allinase. This acid dimers quickly, forming allicin-diallyl sulphate or diallyl disulfide (Strika *et al.*, 2017) showed in Figure 1. Allicin is a labile molecule that may be easily altered to a variety of stable lipid-soluble allylsulfides, including ajoene (4,5,9-trithiadodeca-1,6,11-triene-9-oxide), one of the important natural compounds formed from garlic through an alliinase-induced cleavage of alliin into allicin. The pharmacological effect is attributed to oil- and water-soluble organo-sulfur compounds (allicin), which are responsible for the odor and taste of garlic. When the thiosulfinates (allicin) and diallyl disulfide are removed from the extract, it may be reduced due to antibacterial action of garlic. Additionally, the antibacterial activity of allicin is diminished by converting it to diallyl disulfide. Allicin's antimicrobial activity is primarily seen as an instantaneous and effective inhibition of synthesis of RNA, while DNA and synthesis of proteins are also suppressed to some extent, indicating that RNA is the principal target of allicin action. The role of bacterial strain structural variations may potentially have a susceptible to garlic metabolites. Because the active allicin molecule has a short half-life, the defense mechanism remains rapid and concentrated, preserving the remaining allicin in the clove for future attacks (Kamal, 2019).



Figure 3. Chemotherapeutic properties of Allium sativum

#### Antiviral activity of garlic

By protecting the influenza virus from the infection administered intranasally to mice by enhancing the development of neutralizing antibodies when given with influenza vaccination, Garlic shows an in vivo antiviral activity in mice infected by the infection of the influenza virus intranasally. Additionally, when combined with the influenza vaccination, the garlic

extract increases the formation of eliminating antibodies (Mehrbod *et al.*, 2009). Cobstituents of the garlic such as ajoene, allicin, allyl methyl thiosulfinate, and methyl allyl thiosulfinate, are potent virucides, according to research on the in vitro activity of garlic against several viruses, including herpes simplex virus types 1 and 2, parainfluenza virus type 3, vaccinia virus, 1, and 2, and human rhinovirus type 2. It has been suggested that an allicin-containing supplement can stop the spread of the common cold virus based on studies involving 146 volunteers. Diallyl trisulfide, found in garlic bulbs, has antihuman cytomegalovirus (anti-HCMV) activity, and the mechanism is related to the suppression of, for example, gene transcription (Guo *et al.*, 1993).

#### Antifungal activity of garlic

In vitro and in vivo tests showed substantial antifungal efficacy. Garlic extract has been shown to have anti-fungal efficacy against 40 species of zoopathogenic fungi, with growth inhibition in 8 of 16 examined genera. Garlic demonstrated a broad-spectrum action against 17 species of fungus, including Penicillium, dermatophytes, Aspergillus and yeasts when its efficacy was compared to the antifungal effects of nystatin, griseofulvin, and amphotericin. Nystatin was less efficient than garlic at slowing the growth of the fungus. Allicin was shown to be the primary anti-candida constituent in the aqueous extract of garlic bulbs, according to studies. Numerous strains of Cryptococcus neoformans are inhibited by aqueous extract of garlic (Singh *et al.*, 2019).

#### Anti-parasitic activity of garlic

An ultrastructural analysis shows that Allicin can alter the morphology of the *Schistosoma mansoni* male species. Allicin has shown activity against *Trypanosoma brucei, Trypanosoma cruzi* and *Plasmodium falciparum.* The intestinal protozoan parasites present in humans and animals, such as *Entamoeba histolytica* and *Giardia lamblia* are effective against Allicin (Papu *et al.*, 2014). The final chemical product of stable diallyl trisulfide is allicin. It was noticed that in vitro activity of diallyl trisulfide was considered against several important protozoan parasites. The results indicated that the substance has the potential to be effective in several parasite disorders in animals and humans, including those caused by Trypanosoma sp., *Ent. histolytica*, and *Giardia lamblia*. Human glutathione reductase and trypanothione reductase are both inhibited by ajoene, a compound isolated from *A. sativum*. Ajoene's multiple effects on important enzymes involved in the antioxidant thiol metabolism may contribute, at least in part, to its antiparasitic and cytostatic properties (Mikaili *et al.*, 2013).

#### Anthelmintic activity of garlic

The treatment for intestinal worms with garlic is very effective. Garlic has sulphurous components that are effective in eliminating tapeworms (*Taenia saginat, Taenia solium* and *Taenia asiatica*) and cestodes (*Hymenolepis, Microstoma,* and *H. Diminuta*) and is also identified for its anthelmintic activity and trematodes (*Echinostoma Caproni* and *Fasciola*)

*hepatica*). The target parasite killed in vitro test. It is confirmed in vitro study that both worms were killed due to the presence of the Sulphurous component of garlic and was also effective against the intestinal fluke *Echnio capronic* but effective against the liver fluke (Marufatuzzahan *et al.*, 2022). Paralytic effect on *Fasciola gigantica* due to the essential oil of *A. sativum*. At dosages of 1 and 3 mg/ml, the essential oil significantly reduced the frequency and intensity of the whole fluke's spontaneous muscle contractions. Additionally, A. sativum extract has larvicidal effects on mosquito larvae. It responds well against *Anopheles stephensi, Culex quinquefasciatus*, and *Culex quinquefasciatus*, *filarial* mosquitoes. *Rhipicephalus (Boophilus) and microplus (Canestrini)* tick larvae are susceptible to the acaricidal effects of A. sativum essential oil. *A. sativum*'s insecticidal effects on *Aedes albopictus (Skuse)*, *Lycoriella ingenue*, and *Spodoptera litura* larvae (Kavindra and Shalina, 2000). Additionally, both parasites' relative activity of acid and alkaline phosphomonoesterases, as well as their uptake of glucose and glycogen as well as their oxygen consumption, were all significantly decreased by garlic oil. There is a discussion on its potential manner of operation. The metabolism of host intestinal or caecal tissue was unaffected considerably (lqbal *et al.*, 2001).

#### Antiatherosclerotic activity of garlic

Garlic produces both antiatherogenic (preventive) and antiatherosclerotic (therapeutic) effects on atherosclerosis. It prevents the growth of atherosclerotic cells and other cell types, such as the production and buildup of collagen in the aorta (Duan *et al.*, 2023). The direct antiatherosclerotic effect of garlic may be explained by the tendency for all the major atherosclerotic symptoms (lipidosis, proliferation, and fibrosis) to decrease and normalize. ADP (adenosine diphosphate) pathway is inhibited by garlic extracts. Their mechanisms of action are similar to that of the clinically used drug clopidogrel (Johny *et al.*, 2023). In the garlic extract, pharmacologically active components were found to be lipophilic rather than hydrophilic. Allicin and thiosulfinates are responsible for the in-vitro activity of antiaggregatory activity (IVAA). Additionally, it was found that consuming more crushed garlic could compensate for the reduced activity and partial loss of its antithrombotic effect (Yuristo, 2023).

# Anti-inflammatory activity of garlic

Garlic extracts have anti-inflammatory properties. The use of garlic significantly reduced inflammation and liver damage caused by *Eimeria papillata* infections. Garlic oil primarily inhibits the cytoskeleton's assembly and disassembly processes to produce its anti-inflammatory effect (Linoj *et al.*, 2023). The thiacremonone, a sulphur compound derived from garlic, inhibits NF-B activity, which prevents neuroinflammation and amyloidogenesis. As a result, it may be used to treat inflammation-related neurodegenerative illnesses like Alzheimer's disease (Monika *et al.*, 2023). When applied, garlic often causes localized irritation, but if it is done so while wearing a pressure bandage, or if there is poor wound care or a secondary infection, it may result in a severe skin reaction and a deep chemical burn (Uddin *et al.*, 2022).

# Antihyperlipidemic activity of garlic

Garlic can prevent lipid peroxidation of low-density lipoprotein (LDL) and damaged erythrocytes, boost antioxidant levels, and inhibit the angiotensin-converting enzyme. Additionally, it may also inhibit enzymes involved in lipid synthesis (Xie *et al.*, 2023). Without exhibiting any cellular toxicity, garlic extract decreased cholesterol synthesis by up to 75%, and the inhibition is most likely due to sterol 4-alpha-methyl oxidase. Garlic has anti-clotting properties and speeds up the process by which blood clots break. Garlic powder and oil greatly decreased cholesterol production by inhibiting 14-alpha-demethylase and HMG-CoA reductase enzymes (Varade *et al.*, 2023).

#### Immunomodulatory activity of garlic

*Allium sativum* has a wide range of biological functions, including immunomodulation. It has been shown that mature garlic extract has better immunomodulatory effects than raw garlic extract. The influenced organosulfur chemicals in garlic are responsible for this chemical reaction. Mature garlic has immunomodulatory properties in vitro (Song et al., 2023). The proliferation of interleukin (IL)-2 and interferon (INF)- gene expression of activated lymphocytes can be affected by the concentration of garlic extract. Invitro Nitric oxide (NO) production is enhanced by garlic extracts to inhibit macrophage infection (Hamad, 2023). Allicin can prevent immune-mediated liver damage in mice. This is probably due to its immunomodulatory effects on T cells, adhesion molecules, and the inhibition of NF-kappa B activation (Yun *et al.,* 2023).

#### Anti-tumor effects of garlic

Garlic extracts are used to inhibit cancer growth in the presence of tumor promoters and sulphurous components. It can prevent the development of carcinogenic cells in the stomach, liver, and other organs (Huang *et al.*, 2023). Garlic has been reported as a significant amount of powerful bioactive chemicals (particularly allylsulfide derivatives) with anticancer activities in various in vitro and in vivo studies (Sahidur *et al.*, 2023). Garlic was used externally for the treatment of tumors by the ancient Egyptians and internally by Hippocrates and some Indian physicians (Rani *et al.*, 2023). Garlic is one of the excellent natural sources of germanium. It is interesting that this trace metal has also been associated with cancer prevention and treatment (Johny *et al.*, 2023). Besides that, garlic is a rich source of selenium, which may be useful in the treatment of cancer. The main seleno-compound in garlic bulbs is semethyl selenocysteine (Oravetz *et al.*, 2023).

#### Antidiabetic activity of garlic

Garlic has a strong hypoglycemic effect due to the presence of allicin, and this effect is thought to increase insulin release insulin sparing, and hepatic metabolism (Nasir *et al.*, 2020). Both streptozotocin and alloxan-induced diabetes mellitus in rats and mice could be treated with garlic to lower blood sugar levels (Ranjan *et al.*, 2020). Numerous in vivo actions of alliin include diabetes prevention, Because of its antidiabetic, hypotensive, and hypolipidemic characteristics, garlic and its components have shown potential in the treatment of metabolic syndrome. Garlic in lowering blood sugar in both human and animal models of type 1 and type 2 diabetes. These researchers hypothesized that the chemicals in garlic juice that

include sulphur are principally responsible for the hypoglycemic impact of garlic. Diallyl disulfide in high doses may make the worse metabolic disturbances in diabetic patients (Saikat *et al.*, 2021).

#### Diuretic effect of garlic

Garlic is helpful for the removal of liquid waste from the body so it acts as a diuretic. In the case of rheumatism, arthritis, gout, and edemas, garlic performs effective results (Sanjay *et al.*, 2019). The diuretic effects of *Allium sativum* on anesthetized dogs and rabbits. The natriuretic and diuretic responses were dose-dependent when garlic powder was administered to dogs under anesthesia. To induce diuretic-natriuretic responses in anesthetized rabbits, chromatographically separated fractions of garlic targeting allicin are administered intravenously. The purified component had a biphasic diuretic and inhibitory impact on kidney Na, K-ATPase when administered intravenously to anesthetized dogs (Tiwaei *et al.*, 2012).

## Hepatoprotective activity of garlic

Garlic can protect the liver cells from many toxic substances (Chidinma*et al.*, 2019). Garlic powder in the diet of rat's boosts antioxidant status, modulates oxidative stress, and protects rats from gentamycin-induced hepatotoxicity. Mature garlic extract protects the liver. It has been proved in vivo study of the liver toxins bromobenzene, paracetamol (acetaminophen) and carbon tetrachloride. It has been demonstrated to inhibit the production and bioactivation of liver carcinogenic nitrosamines and prevent the mutagenic effects of aflatoxin B1 (Singh *et al.*, 2019). A high dose of garlic causes liver toxicity and a pro-oxidative state characterized by increased malondialdehyde and decreased antioxidant enzyme functions such as catalase, peroxidase, and superoxide dismutase (Bar *et al.*, 2022). Excessive doses of garlic may cause liver damage. The soft tissues (lungs and liver) of Rats are more severely damaged by intraperitoneal administration of a high dose of garlic than by oral administration. The hemostatic equilibrium may become even more impacted by the negative effects of excessive dosages of garlic oil (Lamponi *et al.*, 2021).

# Digestive effect of garlic

Garlic improves digestion by stimulating enzymes from the liver, gall bladder, and pancreas, but its use should be avoided when the stomach suffering from acidity and has a frail stomach, so it can be mashed or raw and combined with butter (Sarvizadeh *et al.*, 2021). According to research, garlic contains allicin, which has positive effects on the microbes in the gut and can promote digestion and energy utilization. Additionally, garlic can help with bile acid secretion to control digestion, and garlic oil may help Japanese seabass digest better (Xu *et al.*, 2020). The consumption of a high dose of garlic oil causes intestinal mucosal damage in addition it increases peripheral proinflammatory cytokines (Dorrigiv *et al.*, 2020).

#### Clinical trials of garlic

Garlic has been utilized clinically to produce desired pharmacological and therapeutic activity. For instance, the pre and post-transplant period in patients with hepatopulmonary syndrome can be improved using garlic (Tudu *et al.*, 2022) In atherosclerotic patients, daily use of allicin may reduce the risk of fatal cardiovascular problems Although there is a potential that garlic could be used clinically to treat some diseases, care should be taken combining it with other medications because of possible drug interactions that might occur (Panyad *et al.*, 2022).

#### Conclusion

It was concluded from the present data, that this review provides proof that other researchers can use garlic, along with their active components, as a safe and effective therapeutic, A single clove of garlic has the capability to protect against several diseases by reducing the number of harmful microorganism (bacteria, viruses and fungus), parasites and helminths. Garlic prevention against atherosclerotic, inflammatory, hyperlipidemic, immunomodulatory, tumor, diabetic, diuretic, hepatoprotection and digestion. As a result, agriculturists and public health experts should give more attention to garlic. To fully explore its potential for the well-being of humanity, additional research is still needed in the fields of experimentation, clinical practice, and epidemiology.

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