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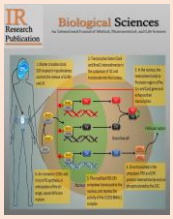

Pharmacological properties and phytoconstituents of garlic (*Allium sativum* L.): A review

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ABSTRACT

Medicinal plants have been used since ancient times for human healthcare in the form of traditional medicines, spices, and other food components. Throughout history, many different cultures have recognized the potential use of garlic for the prevention and treatment of different diseases. Garlic is a common bulb vegetable or spice that is used as an herb and to flavor food. The plant contains biologically active components that contribute to its pharmacological properties. The medicinal effects of garlic were known for 5,000 years. Garlic is recommended as a nutritive element in the treatment of various health problems and the prolongation of human life. The chemical constituents of garlic have also been investigated for the treatment of aging, Alzheimer's disease, anti-fungal/bacterial/viral/ Protozoans, atherosclerosis, blood pressure, cancer, cardiovascular disease, diabetes, neuro/ nephroprotection, osteoporosis, stress, hyperlipidemia, and, wound healing and highly praised by several authors. *A. sativum* is rich in several sulfur-containing phytoconstituents such as alliin, allicin, ajoenes, vinyldithiins, and flavonoids. Extracts and isolated compounds of garlic have been evaluated for various biological activities including antibacterial, antiviral, antifungal, antiprotozoal, antioxidant, anti-inflammatory, and anticancer activities among others. Therefore, this paper is reviewed show the potential health benefits of garlic and to inspire and impress young researchers about the medicinal values of garlic.

Introduction

Garlic (Allium sativum L.) is a pungent bulbous crop native to central Asia it is used in both food and as a traditional medicine to treat a variety of ailments [1]. Particularly in Asia, the Mediterranean region, and North and South America, garlic production is still booming. The biggest producer in the world is China. Most of Europe's production is in Spain, with Castile-La Mancha having the largest hectarage dedicated to the crop [2]. There are around 700 species in this family, which are widely scattered over the world and prized for their flavor, ease of growing, and extended storage period [3].

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In addition to adding flavor to food, garlic has overwhelmingly been used in cooking as a digestive aid [4]. To meet the expanding expectations of consumers, a variety of garlic goods, such as garlic paste, garlic powder, garlic vinegar, harvested garlic, and garlic slices, have become accessible in food stores [5]. Humans have been relying on plants, animals, and microbiological sources in their full glory such as crude extract to treat and diagnose a wide range of illnesses for thousands of years [6]. In Nepal and India, in most states, garlic is commonly called Lashun [7]. Garlic has sparked a lot of curiosity as a therapeutic panacea throughout human history. Compressed garlic preparations have been proven to be toxic to a variety of microbes, including bacteria, protozoa, fungi, and viruses [8].

Allium sativum is a widely used spice that includes several bioactive substances, such as phenolic compounds, saponins, organic sulfides, saponins, and polysaccharides [9]. Hippocrates, the father of medicine, remarked about 25 centuries ago, "Let food be thy medicine, and medicine be thy nourishment." Hippocrates backed up this claim by prescribing garlic for a range of ailments. Given the COVID-19 crisis, the World Health Organization (WHO) is urging people all around the world to use therapeutic plants [10].

Furthermore, garlic contains more phenolic chemicals than several well-known vegetables [3]. Freshly crushed garlic cloves contain the physiologically active compound allicin. The Interaction between the enzyme alliinase and the non-protein amino acid alliin is what causes it [11]. Crushing or chopping garlic cloves releases allicin. The enzyme Alliinase (a cysteine sulfoxide lyase) transforms alliin, an odorless amino acid found in garlic cloves, into allicin and other thiosulfates, which, in addition to their antibacterial properties, give garlic its distinct odor. Allicin inhibits RNA production completely while only slightly inhibiting DNA and protein synthesis, implying that RNA is allicin's major target [12]. Due to the vast spectrum of effects at a time when antibiotics and other pharmacy drugs did not exist, a single bulb of garlic represented an entire pharmacy industry [13]. Garlic has a stellar therapeutic reputation among medicinal plant species, and it has been extensively researched for its antibacterial characteristics and, more recently, for its active role in anticancer and cardiological problems [14]. Garlic extract has been demonstrated to have significant inhibitory effects on the development of both gram-positive and gram-negative bacteria, as well as antioxidant and antiradical characteristics [15]. Anti-atherosclerotic, anti-hypertensive, anti-microbial, hypoglycemic, hypolipidemic, anticancer, anti-coagulant, and hepatoprotective effects of garlic. However, the mechanisms of action in these situations are unknown [16]. Garlic's active ingredients are several complex sulfur-containing substances that are easily absorbed, processed, and degraded. Garlic appears to lower around 10% of total components' Chemical Cholesterol concentration and favorably modifies the HDL/LDL ratio in several randomized trials. In randomized trials, garlic has also been demonstrated to be efficient as a mild anti-hypertensive, thereby lowering blood pressure by around 5-7 percent [17]. These qualities have been established in several in vivo and in vitro research, with clinical trials showing garlic's usefulness in decreasing the risk factors of major modern diseases [18]. **Figure 1** shows the garlic and its cloves.

In 1958, Weisberger and Pensky described garlic's anticancer effects for the first time. They discovered that garlic extracts inhibited cancer cell proliferation both in vitro and in vivo. Since then, many laboratories and epidemiological research has been conducted to confirm its chemopreventive and anti-carcinogenic activities, as well as to understand the mechanisms of action [19]. This review summarizes the potential health benefits and chemical composition of Garlic.

Fig 1. Allium sativum (Garlic) bulbs.

Morphology

The leaves are green in color and grow to be 12-15 cm tall (some species can grow up to 60 cm tall). Garlic fruit has a pungent odor and is pale or slightly yellowish. Depending on the cultivar, the tall leaves may develop from small, rigid stems above the bulb or a softer pseudo stem consisting of overlapping leaf sheaths. The bulbs are covered with membrane skin and contain up to 20 edible bulblets known as cloves [20]. The clove clusters create the bulb, which is a subterranean portion. It has long leaves with blades grouped in an alternate arrangement [21].

The Stem

The stem, or pseudo-stem, is very short and forms a tray at the base where adventitious roots emerge. It Is constituted of a string of leaves joined together by their sheaths [22].

The Root

It has an adventitious root system, which is thick and sparsely branching, with an epidermis, a multicellular cortex, and an endoderm surrounding the central stele [23].

The leaves

The leaves are linear and alternating with a tubular sheath and their number varies from 9 to 12 in the species [24].

The Bulb

It can be white, brown, light brown, violet, light violet, or dark violet, with rounded, elliptical, or circular shapes, as well as transverse broad and transverse narrow elliptical shapes [25,26].

Chemical constituents

Garlic contains at least 33 Sulphur compounds, minerals germanium, many enzymes, potassium, copper, selenium, iron, calcium, magnesium, and zinc, as well as vitamins A, B1, and C, fibers, and water. Lysine, aspartic acid, histidine, arginine, threonine, swine, glycine, glutamine, alanine, cystine, proline, valine, leucine, methionine, phenylalanine, isoleucine, tryptophan are among the 17 amino acids included in it. Garlic contains more Sulphur compounds than other Allium species, which are responsible for garlic's pungent flavor as well as its therapeutic properties [6]. Figure 2 represents the major constituents of garlic. When garlic is minced or crushed, the enzyme alliinase is triggered, and allicin is produced from alliin (present in intact garlic). Other important compounds discovered in garlic homogenate include ally methyl thiosulfate and 1-propenyl ally thiosulfate. Garlic contains minerals including germanium and selenium, as well as enzymes and vitamins like peroxidase, alliinase, and tyrosinase [29]. **Table 1** includes the major pharmacological activity of garlic (Allium sativum) and its related compounds.

Pharmacological properties

More than 3,000 publications in the past have backed the benefits of garlic for the treatment and prevention of a variety of illnesses, validating and

Fig 2. Major constituents of Garlic.

recognizing its traditional use [33]. For thousands of years, diverse bacteria have been treated with garlic for therapeutic purposes due to its potential medicinal significance. Garlic, for instance, has been shown to have antifungal, antibacterial, antiviral, antiseptic, antihelmintic, and anti-inflammatory qualities. Additionally, garlic extracts demonstrated action against gram-negative and gram-positive bacteria, all of which are significant causes of morbidity, globally [34].

Antioxidant

The antioxidant activities of natural products have been widely evaluated, such as fruits, vegetables, mushrooms, cereal, flowers, and wild fruits [35]. It has been proven that natural substances like garlic and compounds derived from garlic can activate enzymes involved in detoxification and antioxidant activity, hence reducing intracellular ROS [36]. The endogenous enzymatic defense mechanism of many natural compounds can neutralize hazardous reactive oxygen species. Numerous plant compounds, such as flavonoids, phenolic acid, and phenolic diterpenes, have powerful antioxidant properties [37]. The antioxidant properties of the whole and aged garlic extracts augment serum levels of catalase and glutathione peroxidase. Garlic extract and allicin are effective at scavenging exogenously generated hydroxyl radicals in a dose-dependent manner [6].

Black garlic contains bioactive substances such as SAC, polyphenols, and flavonoids. Heating is used to create the three chemicals. The length of heating is what causes black garlic to contain more antioxidant chemicals [38,39].

Table 1. The major pharmacological activity of garlic (*Allium sativum*) and its related compounds.

Serial No.	Bioactive Compound	Medicinal Activity
1	Allicin	Antibacterial
2	DADS and DATS	Antifungal
3	Allicin and DATS	Antiviral
4	Allicin, DADS, and DATS	Antioxidant
5	Allicin and DATS	Anti-inflammatory
6	Allicin, alliin, DADS, and DAS	Anti-cancer
7	Allyl propyl disulfide, allicin, and cysteine sulfoxide, and Alliin	Antidiabetic

DAS: Diallyl sulfide, DATS: Diallyl trisulfide, DADS: Diallyl disulfide

Anti-hypertensive

Perhaps the most well-known use of garlic is as a supplementary treatment for lowering blood pressure. The most significant risk factor for chronic cardiovascular illness and one of the main risk factors for atherosclerosis, affecting an estimated 1 billion people worldwide, is hypertension (systolic blood pressure 140 mmHg and diastolic blood pressure 90 mmHg). The antihypertensive properties are mediated via prostaglandin-like actions that lower peripheral vascular resistance [40].

Garlic has been used to treat and prevent hypertension, although its molecular mechanisms of action are yet unknown. It is revealed that angiotensin II-stimulated cell cycle progression and migration in aortic smooth muscle cells were blocked by allyl methyl sulfide (AMS) and diallyl sulfide (DAS). They also discovered that both OSCs prevented angiotensin II's production of ROS. Therefore, their findings imply that chemicals derived from garlic called AMS and DAS may be efficient antioxidants that target the arterial thickening found in hypertension [41]. Garlic has a hypoglycemic activity, which Loeper & Debray identified in 1921. 26 hypertensive patients received two alliin tablets containing 4.75 gm of garlic concentrate (about 2.375 gm of desiccated parsley and 0.31 gm of dehydrated garlic), three times each day for three days. An average drop in systolic and diastolic blood pressure of 12.3 mmHg and 6.5 mmHg, respectively, was seen in 85% of the patients. He also stated that dizziness had been cured in 12 out of 13 patients and that the remaining patient had improved. Of the 17 patients who had complained of headaches, he reported that 14 had experienced relief [42].

Hyperlipidemia

The study assesses how garlic affects patients with type 2 diabetes mellitus who have dyslipidemia, one of the main cardiovascular risk factors. The results demonstrate that garlic reduced cholesterol levels (-28 mg/dl, -12.03% P=0.001) and LDL-C (-30 mg/dl, -17.99% P=0.001), whereas the nonrandomized group (n = 32) only noticed a non-significant decrease in the total cholesterol (-2 mg/dl, -0.9% P= ns) and LDL-C (-3 Mg/dl, -1.6% P= ns). Patients receiving garlic therapy had vastly greater HDL cholesterol (3.35 mg/dl, 8.81% P=0.05) compared to the placebo group (0.62, 1.6% P= n.s.), however, there was no discernible difference in triglyceride levels among the two groups. The results show that as compared to placebo, garlic dramatically decreased LDL cholesterol and serum total cholesterol and moderately increased HDL cholesterol [43].

Antiplatelet and fibrinolytic effects

Another well-studied consequence of garlic usage is platelet inhibition. Numerous in vitro and animal experiments using fresh garlic cloves, ajoene, and garlic oil, have shown that these substances inhibit platelets. A dose-dependent inhibition of platelet aggregation through nearly complete suppression of thromboxane production, dose-dependent inhibition of collagen-induced platelet aggregation, and inhibition of adenosine diphosphate (ADP) and epinephrine-induced platelet aggregation are among the mechanisms demonstrated by in vitro studies. 8 Garlic's effects on platelets may be caused by several different methods. It is believed that cyclooxygenase inhibition, but not lipoxygenase, is what prevents the synthesis of thromboxane [44]. According to studies, taking garlic remedies significantly reduces platelet aggregation. The epinephrine-induced platelet aggregation is likewise lessened by garlic. It is advised to cease taking garlic one week before any surgical procedure [45].

Respiratory tract infections

The prospect of using allicin vapor to treat lung infections is appealing because it is antibacterial. It has been claimed that inhaling the vapor from prepared garlic has successfully treated several people with pulmonary tuberculosis. Patients were given face masks with pouches containing ethanol, eucalyptus oil, and garlic juice that had been ground up to assist cover the odor. They inhaled the fumes for two one-hour intervals each day, and pulmonary TB was successfully treated in most cases [46].

Anti-diabetic

In diabetic mice, but not in normal mice, oral administration of garlic extract resulted in significant reductions in total cholesterol, serum glucose, urea, uric acid, triglycerides, aspartate aminotransferase, and alanine aminotransferase levels, as well as an increase in serum insulin. A comparison study between the effects of garlic extract and glibenclamide revealed that garlic had a more potent anti-diabetic effect than glibenclamide [47].

Anti-inflammatory activity

Inflammation, a crucial part of the body's natural defense system, is triggered when several endogenous signaling molecules and foreign pathogenic agents engage either indirectly or directly with various membrane receptor types [48]. In experimental models of inflammation, garlic extract has significantly reduced inflammation [49]. According to one study, thiochromone, a Sulphur molecule derived from garlic, reduces NF-B activity, which prevents neuroinflammation and amyloid genesis. As a result, it may be used to treat inflammation-related neurodegenerative illnesses like Alzheimer's disease [50].

Anti-cancer Activity

Garlic acts as an anti-inflammatory agent by altering cytokinesis and inhibiting NF-kB behavior in surrounding tissue. Numerous in vivo and in vitro studies have demonstrated the potential anticancer preventive effects of garlic preparations and their respective constituents. It was discovered that ajoene prompted apoptosis in cancerous cells but not in healthy ones; this may be because peroxide production occurs. Organosulfur substances like DAS, DADS, and DATS stop the growth of malignant cells during the cell cycle stage [51]. Chemical species known as electrophiles are created from chemicals that cause cancer. Therefore, any substance that encourages GST activity would have a chemopreventive effect. On the GST activity in the liver and other tissues, garlic-derived OSC was examined. By increasing GST activity in the liver, forestomach, small intestine, and lung 96 hours after oral administration, allyl methyl trisulphide (AMTS) decreased benzo(a)pyrene (BP)-induced forestomach cancers in mice [52]. More recent research appears to link garlic consumption to a reduction in cancer risk. Sulfurous substances are thought to prevent the growth of malignant cells in the stomach and liver. Numerous mechanisms of action have been postulated, while the precise mode of action is still unclear [53].

Antifungal Activity

A variety of fungus species including Torulopsis, Cryptococcus, Candida, Trichophyton, Trichosporon, Aspergillus, and Rhodotorula, were successfully eradicated by garlic extracts. Garlic extract has recently been discovered to prevent the growth and germination of Rhodotorula mucilaginosa and Meyerozyma guilliermondii [29].

The drug of choice for controlling systemic fungal infections is still amphotericin B, but even then, it is constrained by serious side effects. Commercial allium sativum-derived substances are frequently used in The People's Republic of China as a systemic antifungal medication to treat fungal infections. Studying Chinese commercial preparation called allitridum allowed researchers to assess the scientific merit of using compounds derived from allium sativum as antifungal agents [54]. When administered at significant concentrations (60%, and 80%, respectively), the ethanol and aqueous diluted garlic extract completely suppressed Botrytis cinerea (100%). Penicillium expansum was found 96.21% and 99.21% eliminated by extracts diluted in ethanol and water, respectively, at a concentration of 80%. Neofabraea alba appeared to be more susceptible to ethanol-diluted extracts, with 80% extract demonstrating 79.63% inhibition [55].

Antibacterial Activity

Allium sativum, or garlic, has a reputation for treating several bacterial and fungal illnesses. Louis Pasteur and Lehmann gave the first modern scientific data for the medicinal and antibacterial properties of garlic extract in 1858 and 1930, [42]. Allium sativum, or garlic, possesses antiviral, antifungal, and antibacterial effects. Garlic extracts in ethanol, chloroform, and aqueous, all stopped the growth of harmful bacteria, though to variable degrees of susceptibility [9]. Using the diffusion method, the antibacterial properties of Allium sativum were evaluated [56]. Garlic's antimicrobial properties are attributed to allicin activity, which is effective against a wide range of microorganisms,

including antibiotic-resistant, Gram-negative, and Gram-positive bacteria like *Escherichia coli*, Shigella, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *S. faecalis*, Klebs, *S. pyogenes*, *Salmonella enterica* [57].

Antiviral Activity

Comparatively few studies have been conducted on the antiviral and antibacterial effects of garlic. Alliin and S-allyl cysteine have not been shown to have any efficacy against viruses, even though allicin and compounds derived from allicin do. Garlic has been shown to have in vitro activity against HIV, herpes simplex virus types 1 and 2, cytomegalovirus, rotavirus, and viral pneumonia [58].

According to the limited research, garlic extract exhibits in vitro action against CMV, HIV, rotavirus, rhinovirus, herpes simplex viruses 1 and 2, influenza A and B, and viral pneumonia, Ajoene, diallyl trisulfide, and allicin have all been demonstrated to have activity. It is hypothesized that ajoene inhibits integrin-dependent activities in the HIV context. Diallyl disulfide and allyl alcohol have also demonstrated efficacy against HIV-infected cells [59].

Anti-Ulcer

H. pylori infection was treated with allicin (800 mg/day) for 14 days, but none of the patients had their infection completely eradicated. On the other hand, administering 4.2 mg of allicin daily may be effective in eliminating H. pylori [60]. Medicines obtained from plants have portrayed a crucial involvement in both cultures' health, ancient and modern times because of their inexpensive properties and the belief of the people that natural products have less or no side effects [61].

Conclusion

The preceding description underscores the idea that garlic is a gift from creation to humans. A mere garlic clove can cure a wide range of ailments by blocking the growth of many kinds of bacteria, fungi, dangerous viruses, bugs, and worms. It has been reported to possess several biological properties including anticarcinogenic, antioxidant, antidiabetic, Reno-protective, anti-atherosclerotic, antibacterial, antifungal, and antihypertensive activities in traditional medicines. *A. sativum* is rich in several sulfur-containing phytoconstituents such as alliin, allicin, ajoenes, vinyldithiins, and flavonoids such as quercetin. Extracts and isolated compounds of *A. sativum* have been evaluated for various biological activities including antibacterial, antiviral, antifungal, antiprotozoal, antioxidant, anti-inflammatory, and anticancer activities among others. Numerous scientists have called the consumption of garlic in the fight against cardiac complications. This review's investigation objective is to present a concise range of garlic in medications and cuisine.

Contribution of authors

The authors confirm their contribution to the paper as follows: Study conception and design: Md Sadique Hussain, Mudita Mishra, Swati Tyagi. Data collection: Sunvej Choudhary, Mohd Ubed Noor. Analysis and interpretation of results: Md Sadique Hussain. Draft manuscript preparation: Sunvej Choudhary, Mohd Ubed Noor, Md Sadique Hussain. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

None

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