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Allium sativum L.: Therapeutic uses and pharmacological properties

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ABSTRACT. Garlic (*Allium sativum* L.) is known as bulb vegetable or spice that utilized as herb and flavoring agent in food in many different countries. These herbs contain biologically active components that contribute to their pharmacological properties, which have been used medicinally for over 5000 years. *Allium* species have been shown to help reduce the development of tumors, anticancer, cardiovascular disease, aging process, infections, antiallergy, and antibiotic properties. The pharmacological activities of *Allium* species, both cultivated and wild, were examined in this work. This study implemented a literary analysis of the various pharmacological activities of *A. sativum*. The data was collected from reputable journals and electronic database, then analyzed using pictures and described qualitatively. Numerous studies have praised the chemical components of garlic for their use in the treatment of Alzheimer's disease, cardiovascular disease, cancer, diabetes, nephroprotection, atherosclerosis, osteoporosis, and wound healing. As a result, this manuscript is expected to inform and inspire researchers about the medicinal value of garlic.

Keywords: *Allium sativum;* allicin; alliin; Alzheimer's disease; cardiovascular disease

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INTRODUCTION

For its therapeutic characteristics, onions, leeks, shallots, scallions, and chives, as well as other *Allium* species, have been utilized for ages. The Babylonians, Egyptians, Greeks, Phoenicians, and Romans used garlic as a treatment for worms, wounds, respiratory infections, skin conditions, skin infections, and tumors (Lanzotti *et al*., 2014). Originally from central Asia, the pungent bulbous crop known as garlic (*Allium sativum* L.) is used in both cuisine and traditional medicine to treat a number of illnesses (Prajapati *et al*., 2022). Garlic production is still rising, especially in Asia, the Mediterranean area, and North and South America. China is the largest manufacturer in the world. Spain produces the majority of the crop for Europe, with Castile-La Mancha having the most land devoted to it (Armentia *et al*., 2020). This family has over 700 species, which are dispersed widely throughout the globe and valued for their flavor, ease of cultivation, and lengthy storage duration (Marsic *et al*., 2019). Garlic has always been used in cooking as a digestive aid in addition to imparting flavor (Satyal *et al*., 2017). A range of garlic products, including garlic powder, harvested garlic, garlic vinegar, garlic paste, and garlic slices, have been available in grocery shops to satisfy consumers' growing expectations (Abdelrahman *et al*., 2021). For thousands of years, humans have relied on raw extracts from plants, animals, and microorganisms to cure and identify a variety of diseases (Hussain *et al*., 2022). Garlic is frequently referred to as lashun in most areas of Nepal and India (Shakya & Labh, 2014). Throughout human history, there has been a great deal of interest in garlic as a miracle cure. A number of microorganisms, including bacteria, protozoa, fungi, and viruses, have been shown to be harmful to compressed garlic formulations, as we detailed in our previous study (Yampolsky & Eliseeva, 2019; Samdani *et al*., 2021; Choudhary *et al*., 2022).

Several bioactive compounds, including phenolic compounds, organic sulfides, saponins, and polysaccharides, are present in the widely used spice *A. sativum* (Fufa, 2019). The father of medicine, Hippocrates, once said, "Let food be thy medicine, and medicine be thy nourishment." This was roughly 25 centuries ago. Hippocrates supported this assertion by recommending garlic as a treatment

for several illnesses. The World Health Organization (WHO) is advising people all around the world to use therapeutic herbs in light of the COVID-19 problem (Tiwary & Hussain, 2021).

In addition, garlic has a higher concentration of phenolic compounds than a number of popular vegetables (Marsic *et al*., 2019). The chemical allicin, which has physiological activity, is present in freshly smashed garlic cloves. It is caused by the interaction of the enzyme alliinase with the non-protein amino acid alliin (Rahman *et al*., 2012). Allicin is released when garlic cloves are crushed or chopped. Alliin, an odorless amino acid present in garlic cloves, is converted by the enzyme alliinase (a cysteine sulfoxide lyase) into allicin and other thiosulfates, which, in addition to having antibacterial qualities, give garlic its unique odor. Allicin totally blocks RNA synthesis while only marginally impairing DNA and protein synthesis, suggesting that RNA is the main target of allicin (Khodavandi *et al*., 2011; Mansor *et al*., 2016; Valenzuela-Gutiérrez *et al*., 2021). A single bulb of garlic represented the entire pharmacy sector at the time because of the wide range of effects at a period when antibiotics and other pharmaceuticals were not yet invented (Bhandari, 2012). It has received substantial research for its antibacterial properties and, more recently, for its active involvement in combating cancer and cardiovascular issues. Garlic has a great reputation for therapeutic efficacy among medicinal plant species (Hayat *et al*., 2018). According to research by Shahbazi (2019), garlic extract exhibits strong inhibitory effects on the growth of both gram-positive and gram-negative bacteria as well as antioxidant and antiradical properties. However, the mechanisms of action in these circumstances are unknown.

The active components of garlic are a variety of complex, sulfur-containing compounds that are simple to ingest, metabolize, and destroy. In multiple randomized experiments, garlic appears to alter the HDL/LDL ratio favorably and to reduce the chemical cholesterol content of total components by around 10%. Garlic has also been shown in randomized trials to be effective as a mild anti-hypertensive, resulting in a 5-7% reduction in blood pressure (Londhe *et al*., 2011). These properties have been proven in several *in vivo* and *in vitro* studies, and clinical trials have demonstrated the value of garlic in lowering the risk factors of serious contemporary diseases (Kaur *et al*., 2021). In 1957, Weisberger & Pensky provided the first description of garlic's anticancer effects. They found that both in vitro and in vivo, garlic extracts prevented the multiplication of cancer cells. Since then, much laboratory and epidemiological research has been done to both confirm the substance's chemopreventive and anti-carcinogenic properties and to further understand how they work (Najman *et al*., 2022). The garlic and its cloves are seen in Fig. 1.

This study employed a literary analysis of *A. sativum*'s various pharmacological activities. This work is regarded as the ancillary data for development of products containing garlic and its derivatives for the treatment of various health conditions.

MATERIALS AND METHODS

The different pharmacological activities of garlic (*Allium sativum*) were investigated by literate the reputable journals from different platforms online. Scientific names of the medicinal plant were searched in electronic databases including PubMed, Science Direct, and www.itis.gov. Along with the important keywords like *A. sativum*, allicin, alliin, are also searched in the electronic databases.

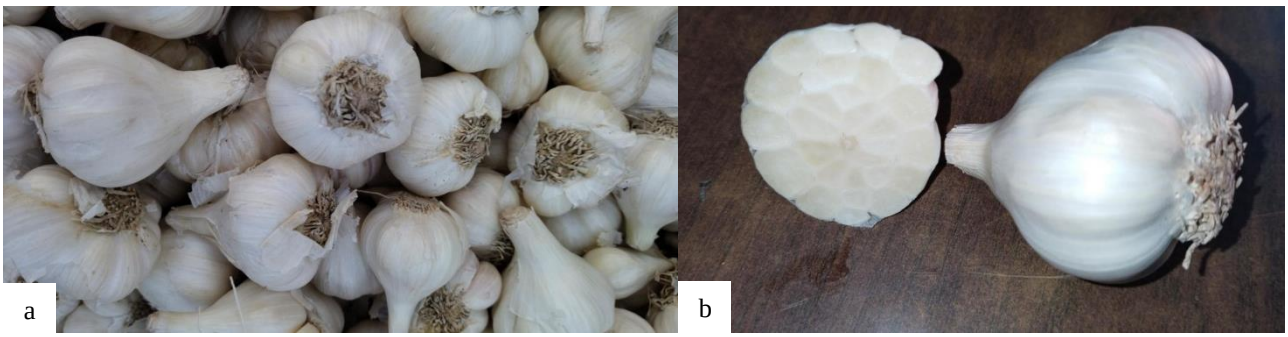

Fig. 1. a. The morphology of garlic (*Allium sativum* L.) bulbs; b. Cross section of garlic bulb

Data analysis. The authors made the images using the Microsoft PowerPoint, also couple of images were itself clicked by the authors for the purpose of this study only.

RESULTS AND DISCUSSION

Morphology. The leaves are 12–15 cm tall and have a green tint (but some species can reach a height of 60 cm). The fruit of the garlic plant is pale or barely yellowish and has a strong aroma. Depending on the cultivar, the tall leaves may grow from a softer pseudo-stem made of overlapping leaf sheaths or from tiny, hard stems above the bulb. Up to 20 edible bulblets known as cloves are contained in the membrane-skinned bulbs (Iciek *et al*., 2009). The bulb, an underground section, is made up of clove clusters. It has lengthy leaves with alternately arranged blade groups (Shinde *et al*., 2021).

The stem. The pseudo-stem, which is quite short, creates a tray at the base from which adventitious roots sprout. The leaves are connected by their sheaths to form a string (Saddique *et al*., 2015).

The root. Its adventitious root system is thick and sparsely branched, and it surrounds the central stele with an endoderm, a multicellular cortex, and an epidermis (So *et al*., 2021).

The leaves. The species' leaves range in number from 9 to 12 and are linear and alternate with a tubular sheath (Mann, 1952).

The bulb. With rounded, elliptical, or circular shapes, as well as transverse broad and transverse narrow elliptical shapes, it can be white, brown, light brown, violet, light violet, or dark violet (IPGRI *et al*., 2001; Kumar, 2015; Nasir *et al*., 2020).

Chemical constituents. At least 33 sulfur compounds, several enzymes, calcium, potassium, magnesium, copper, selenium, iron, and zinc are all present in garlic along with fibers, water, and vitamins A, B1, and C (Londhe *et al*., 2011; Jangam & Badole, 2014). It contains 17 different amino acids, including methionine, lysine, aspartic acid, histidine, arginine, threonine, swine, glycine, glutamine, alanine, cystine, proline, phenylalanine, valine, leucine, isoleucine, and tryptophan. The medicinal benefits of garlic as well as its strong smell are due to the higher concentration of sulfur compounds found in garlic compared to other Allium species (Shakya & Labh, 2014). The main components of garlic are depicted in Fig. 2. The enzyme alliinase is activated when garlic is minced or crushed, and allicin is created from alliin (found in intact garlic).

Fig. 2. Major constituents of garlic (*Allium sativum* L.)

Pharmacological properties. The advantages of garlic for the treatment and prevention of a number of ailments have been supported by more than 3000 publications in the past, validating and recognizing its traditional use (Rana *et al*., 2011). Due to its possible medical value, garlic has been

used for thousands of years to cure a variety of bacteria. Consider the antifungal, antibacterial, antiviral, antiseptic, anti-helmintic, and anti-inflammatory properties of garlic. Furthermore, garlic extracts showed activity against both gram-positive and gram-negative bacteria, which are all major global causes of morbidity (Daka, 2011).

Antioxidant. Numerous natural products, including fruits, vegetables, mushrooms, cereal, flowers, and wild fruits, have had their antioxidant activities thoroughly assessed (Shang *et al*., 2019). Garlic and chemicals produced from it have been shown to naturally activate enzymes involved in detoxification and antioxidant activity, hence lowering intracellular ROS (Patiño-Morales *et al*., 2022). Hazardous reactive oxygen species can be neutralized by many natural substances' innate enzymatic defense mechanisms. A large number of plant substances, including flavonoids, phenolic acid, and phenolic diterpenes, have potent antioxidant effects. Catalase and glutathione peroxidase levels in the serum are increased by the whole and aged garlic extracts' antioxidant capabilities. According to Shakya & Labh (2014), allicin and garlic extract are both capable of scavenging exogenously produced hydroxyl radicals in a dose-dependent manner. SAC, polyphenols, and flavonoids are just a few of the bioactive compounds found in black garlic. The three compounds are produced through heating. Black garlic has higher antioxidant compounds as a result of prolonged heating (Abderrahim *et al*., 2019; Tahir *et al*., 2022).

Anti-hypertensive. Garlic is most commonly used as a complementary medicine to decrease blood pressure. Hypertension (systolic blood pressure of 140 mmHg and diastolic blood pressure of 90 mmHg) is the most major risk factor for chronic cardiovascular disease and one of the primary risk factors for atherosclerosis, affecting an estimated 1 billion individuals globally. According to Saudagar & Waghulde (2018), the antihypertensive effects are mediated via prostaglandin-like activities that reduce peripheral vascular resistance. Despite the fact that its molecular mechanisms of action are yet unknown, garlic has been utilized to treat and prevent hypertension. It has been found that diallyl sulfide (DAS) and allyl methyl sulfide (AMS) inhibit angiotensin II-stimulated cell cycle progression and migration in aortic smooth muscle cells. They also found that both OSCs stopped ROS from being produced by angiotensin II. Their findings suggest that the compounds AMS and DAS, which are derived from garlic, may be effective antioxidants that target the arterial thickening associated with hypertension (Bhandari, 2012). A total of 26 hypertensive individuals were given two alliin tablets containing 4.75 gm of garlic concentrate (about 2375 gram of dried parsley and 0.31 gm of dehydrated garlic), three times daily for three days. Garlic has a hypoglycemic effect. About 85% of the patients saw a reduction in systolic and diastolic blood pressure of 12.3 mmHg and 6.5 mmHg, respectively. In 12 out of 13 patients, the dizziness had been resolved, and the condition of the final patient had improved. It was stated that 14 of the 17 patients who had complained of headaches had found alleviation (Singh & Singh, 2019).

Hyperlipidemia. One of the major cardiovascular risk factors for type 2 diabetes mellitus patients with dyslipidemia is examined (Alam *et al*., 2018). The findings show that garlic significantly lowered cholesterol levels (-28 mg/dl, -12.03% P=0.001) and LDL-C (-30 mg/dl, -17.99% P=0.001), compared to the nonrandomized group (n = 32), which only saw a non-significant decrease in total cholesterol (-2 mg/dl, -0.9% P= ns) and LDL-C (-3 Mg/dl, -1.6% P= ns). Patients receiving garlic therapy had significantly higher HDL cholesterol than those receiving a placebo (0.62, 1.6% P=n.s. vs. 3.35 mg/dl, 8.81% P=0.05), but there was no obvious difference in triglyceride levels between the two groups. According to the findings, garlic significantly reduced serum total cholesterol and LDL cholesterol compared to placebo, while slightly raising HDL cholesterol.

Antiplatelet and fibrinolytic effects. Platelet inhibition is another well-researched side effect of garlic use. Fresh garlic cloves, ajoene, and garlic oil have all been found to suppress platelets in several in vitro and animal studies. One of the mechanisms shown by in vitro studies is a dose-dependent inhibition of platelet aggregation through nearly complete suppression of thromboxane production. Other mechanisms include a dose-dependent inhibition of collagen-induced platelet aggregation and inhibition of adenosine diphosphate (ADP) and epinephrine-induced platelet

aggregation. There are numerous potential causes of garlic's impact on platelets. Lipoxygenase, not cyclooxygenase, inhibits the formation of thromboxane. Using garlic supplements dramatically lowers platelet aggregation. Garlic also reduces the epinephrine-induced platelet aggregation. One week prior to any surgical treatment, it is advisable to stop ingesting garlic (Paudel, 2014).

Respiratory tract infections. Because allicin vapor is antibacterial, the idea of using it to treat lung infections is appealing. Several cases of pulmonary tuberculosis have reportedly been successfully treated by inhaling the vapor from prepared garlic. To help hide the smell, patients were given face masks with pouches containing ethanol, ground-up eucalyptus oil, and garlic juice. The majority of the time, pulmonary TB was successfully treated by having them breath the fumes for two one-hour intervals each day (Borlinghaus *et al*., 2021).

Anti-diabetic. Oral injection of garlic extract led to notable decreases in total cholesterol, serum glucose, urea, uric acid, triglycerides, aspartate aminotransferase, and alanine aminotransferase levels, as well as a rise in blood insulin in diabetic mice but not in normal animals. Garlic had a stronger anti-diabetic impact than glibenclamide, according to a study comparing the effects of the two drugs (Singh *et al*., 2019).

Anti-inflammatory activity. The body's natural defense mechanism, which includes inflammation, is activated when multiple endogenous signaling molecules and outside pathogenic agents interact either directly or indirectly with different membrane receptor types. Garlic extracts effectively reduced inflammation in animal models of inflammation (Paudel, 2014). The sulfur compound thiochromone, which is derived from garlic, lowers NF-B activity, which decreases amyloid formation and neuroinflammation. As a result, it might be utilized to treat neurological diseases like Alzheimer's disease that are worse by inflammation (Hussein *et al*., 2017).

Anti-cancer activity. By altering cytokinesis and preventing NF-kB activity in the surrounding tissue, garlic reduces inflammation. The potential anticancer preventative benefits of garlic preparations and their respective ingredients have been shown in numerous in vivo and in vitro investigations. Apoptosis was shown to be induced by ajoene in malignant cells but not in healthy cells; this may be because peroxide generation takes place. Malignant cells' proliferation is halted during the cell cycle by organosulfur compounds such DAS, DADS, and DATS (Singh *et al*., 2018). Chemicals that induce cancer give rise to chemical species known as electrophiles. Any drug that promotes GST activity would therefore have a chemo-preventive effect. Garlic-derived OSC was investigated for its effects on the GST activity in the liver and other tissues. Garlic consumption and a lower risk of cancer appear to be related, according to more recent research. It is believed that sulfurous compounds stop the growth of cancerous cells in the liver and stomach (Palani *et al*., 2014). There have been several proposed mechanisms of action, but the precise mode of action is yet unknown.

Antifungal activity. Garlic extracts were successful in eradicating a number of fungal species, including *Torulopsis, Cryptococcus, Candida, Trichophyton, Trichosporon, Aspergillus,* and *Rhodotorula. Rhodotorula mucilaginosa* and *Meyerozyma guilliermondii*'s growth and germination have recently been shown to be inhibited by garlic extract (Mahi *et al*., 2021). Amphotericin B is still the treatment of choice for treating systemic fungal infections, however even this medication has detrimental side effects. In China, systemic antifungal medications made from the *A. sativum* are extensively used to treat fungi infections. Researchers were able to evaluate the scientific validity of employing chemicals derived from *A. sativum* as antifungal agents by studying a Chinese commercial product known as allitridum (Kamel & Saleh, 2000). The ethanol and water diluted garlic extract totally reduced *Botrytis cinerea* (100%) when given at large doses (60% and 80%, respectively). *Penicillium expansum* was shown to be removed by extracts diluted in ethanol and water at a concentration of 80% in 96.21% and 99.21%, respectively. With an 80% extract showing 79.63% inhibition, *Neofabraea alba* appeared to be more responsive to ethanol-diluted extracts (Hindi, 2013).

Antibacterial activity. *A. sativum* is known to be effective in treating a number of bacterial and fungal conditions. In 1858 and 1930, Louis Pasteur and Lehmann published the first modern scientific

data on the therapeutic and antibacterial effects of garlic extract (Singh & Singh, 2019). Garlic, also known as *A. sativum*, has antiviral, antifungal, and antibacterial properties. Although to varying degrees of susceptibility, the growth of harmful bacteria was stopped by garlic extracts in ethanol, chloroform, and aqueous (Fufa, 2019). The antibacterial effects of *A. sativum* were assessed using the diffusion method (Airaodion *et al*., 2020). Allicin activity in garlic is responsible for its antimicrobial properties (Borlinghaus *et al*., 2021), and also it is effective against a variety of microorganisms, including antibiotic-resistant, gram-negative and gram-positive bacteria like *Escherichia coli*, *Shigella* sp., *Pseudomonas aeruginosa, Staphylococcus aureus, S. faecalis*, *Klebsiella* sp., *S. pyogenes*, and *Salmonella enterica* (Sadeghian & Ghazvini, 2015; Ibrahim, 2017).

Antiviral activity. Garlic's ability to combat bacteria and viruses is the subject of more studies every year. Allicin and chemicals generated from it have been demonstrated to be effective against viruses, while alliin and S-allyl cysteine have not. According to research by Navidshad *et al.* (2018), garlic has been proven to have in vitro activity against HIV, herpes simplex types 1 and 2, CMV, rotavirus, and viral pneumonia. Ajoene, diallyl trisulfide, and allicin have all been shown to have activity, and the limited study suggests that garlic extract has in vitro action against CMV, HIV, rotavirus, rhinovirus, herpes simplex viruses 1 and 2, influenza A and B, and viral pneumonia. In the context of HIV, it is theorized that ajoene suppresses integrin-dependent functions.

Anti-Ulcer. Allicin (800 mg/day) was used to treat *H. pylori* infection for 14 days, although none of the patients had their illness totally cleared. On the other hand, according to Sharifi-Rad *et al.* (2019), providing 4.2 mg of allicin daily may be successful in getting rid of *H. pylori.*

The therapeutic benefits and pharmacological components of garlic, which have been briefly reviewed, will aid recent discoveries in the modernization of diagnostic and therapeutic approaches to the treatment of a variety of illnesses and disorders of the human body. It is intended that by serving as a fresh addition to the text, this publication would encourage researchers to consider the importance of exclusivity in diverse applications of garlic.

CONCLUSION

The explanation that follows emphasizes the notion that garlic is a gift from creation to humanity. By inhibiting the development of numerous types of bacteria, fungus, harmful viruses, bugs, and worms, a single garlic clove can treat a wide spectrum of illnesses. In traditional remedies, it has been shown to have a number of biological qualities, including anticarcinogenic, antioxidant, antidiabetic, renoprotective, anti-atherosclerotic, antibacterial, antifungal, and antihypertensive actions. The sulfur-containing phytoconstituents alliin, allicin, ajoenes, vinyldithiins, and flavonoids like quercetin are abundant in *A. sativum*. Various biological activities, including antibacterial, antiviral, antifungal, antiprotozoal, antioxidant, anti-inflammatory, and anticancer activities, have been assessed for extracts and isolated compounds of *A. sativum*. Garlic consumption is recommended in the battle against cardiovascular disease, according to numerous scientists. It is intended that this review study would offer a brief spectrum of applications of garlic in food and medicine.

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