

Pharmacological Potentials of Garlic (*Allium sativum* L.) and its Chemical Constituents

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Abstract

Garlic (*Allium sativum*) is an herb used widely as a flavoring in cooking has also been used as a medicine throughout ancient and modern history to prevent and treat wide range of conditions and diseases. It is found that Garlic is one of the most known traditional herbal remedy for a wide range of ailments. It's used to improve blood circulation to reduce the risk of heart disease. Garlic also thought to help reduce high cholesterol and elevated blood pressure. Antioxidants help to contains and remove those harm full substances before they can accumulate and damage the body. The oils that extracted from the species and herbs are found to be effective in killing bacteria, viruses and others. Garlic is used for many conditions related to heart and blood system these conditions include high blood pressure, high cholesterol coronary heart disease and hardening of arteries.

Keywords: *Allium sativum*, Garlic, Phytochemistry, Anti-Cancer, Bioactive Compounds.

Introduction

Allium sativum, a member of the Alliaceae family, is known for being a valuable spice and a well-liked treatment for a variety of diseases and physiological conditions.(1) Traditional nutritional and therapeutic uses of garlic (*Allium sativum*) as an anti-infective agent exist. These applications are supported by in vitro evidence of the antibacterial activity of fresh and freeze-dried garlic extracts against human pathogenic bacteria, fungi, and viruses.(2) A persistent perennial member of the onion family is garlic. It may have originated in Asia, according to studies, but it has since spread to Europe, North Africa, Mexico, and other parts of the world. Alliaceae is the family that includes garlic.(3) The name “*Allium sativum*” is derived from the Celtic word “all”, meaning burning or stinging, and the Latin “sativum” meaning planted or cultivated. The use of higher plants and their extracts to treat infections is an ancient practice in traditional medicine.(4) Because of their antibacterial properties, which are mostly synthesized during secondary metabolism of the plants, many plants have been employed.(5) The herbal medicine might appear in the form of powders, liquids, or combinations that can be steamed, rubbed into incisions, or applied topically. Traditional medicine is the synthesis of all the knowledge, abilities, and procedures based on the theories, convictions, and life-experiences peculiar to many cultural groups that are employed to uphold health as well as to prevent, identify, and cure physical and mental sickness.(6) A significant section of the population in many developing nations depend on traditional healers and their arsenal of medicinal plants to address their healthcare needs. Garlic (*Allium sativum*) is one of those plants that were seriously investigated over several years and used for century to light infectious disease brown in Gebresalama and Mehratu.(7) According to Wayne and his colleagues, the growth of garlic requires on even, consistent supply of water. Too much water causes wet feel and many causes bulb rots to occurs according to the rain fail garlic may need extra moisture is in spring and early summer.(8) Naturally occurring plants have played an important role in the discovery of new therapeutic agents. The therapeutic uses include beneficial effects on the cardiovascular system, antibiotics, anticancer, anti-inflammatory, and hypoglycemic and hormone-like effects. But improper perception and use of herbal remedies result in adverse condition on our health.(9)(10) According to Georgiana V and her collogues, the understanding of consumer and physician on the toxicities, contradiction and drug interaction as well as side effects of herbal remedies is poor.(8) Due to this, several cardio vascular conditions, CNS bleeding, mouth ulcer, dermatitis is

observable. Adverse reactions attend because of improper use of garlic, including gastro bleeding and spontaneous epidural hematoma. Medicinal plants have been a good source of new pharmacologically active molecules.(11) For example, natural products could be a potential alternative for controlling the pathogen associated with diseases. Recently, antibiotics and most drugs on the market have shown unwanted symptoms and the emergence of resistant pathogenic microorganisms, toxic effects related to these drugs, and withdrawal issues restricting their use in many countries, therefore, much attention has been paid to the herbal extracts and pharmacologically active molecules extracted from different plant species that are used previously in the traditional medicine.(12)(13) Many plant species have been reported to exert pharmacological properties due to their phytoconstituents such as glycosides, alkaloids, saponins, steroids, flavonoids, tannins, and terpenoids (e.g., monoterpenes, diterpenes, and sesquiterpenes).(14) Nowadays, eighty percent of the world's populations depend on traditional medicines as an essential source of their primary health care. Medicinal plant extracts and their constituents also possess various biological activities including virucidal, bactericidal, fungicidal, anti-inflammatory, analgesic, sedative, spasmolytic, and local anesthetic activities among others.(15) Garlic (*Allium sativum* L.; Family: Amaryllidaceae) is an aromatic herbaceous annual spice and one of the oldest authenticated and most important herbs that have been used from ancient times as traditional medicine. It is considered the second broadly used *Allium* species with onion (*Allium cepa* L.), which is used as a remedy against several common diseases such as cold, influenza, snake bites, and hypertension.(16) *Allium* species and their active components are reported to reduce the risk of diabetes and cardiovascular diseases, protect against infections by activating the immune system and have antimicrobial, antifungal, anti-aging as well as anti-cancer properties which confirmed by epidemiological data from human clinical studies.(17) Garlic has been used for cooking purposes as a spice that can flavor foods during the cooking process.(18) As well, it possesses therapeutic purposes including the treatment of lung disorders, whooping cough, stomach disorders, cold, earache, and assists in preventing cardiovascular disease. While aged garlic extract (AGE), prepared from aged garlic is a folk herbal remedy that has been shown to enhance the immune system and thus inhibit cancer and heart disorders. Raw garlic and its transformed products have been reported to contain various sulfur compounds that have been included in several types of preparations.(19)(9) Moreover, quercetin, the major flavonoid isolated from garlic, was found to interact with some

medications such as vitamin E and C and modify the in vitro as well as the in vivo transferases and cytochrome P450 isozymes activity, however, the in vivo studies revealed that garlic oil and its three allyl sulfide components increase the CYP3A1, 2B1, and 1A1 expression in the hepatic detoxification system. Allicin [S-(2-propenyl)-2-propene-1-sulfinothioate], the most biologically active sulfur-containing compound of garlic, is responsible for its smell and taste. Alliin (S-allyl-L-cysteine sulfoxide) is the main precursor of allicin, which represents about 70% of total thiosulfinates existing in the crushed cloves.(20)(21) Allyl mercaptan is the odorant molecule responsible for the garlic breath and results from the interaction of allicin or diallyl disulfide with cysteine in the presence of S-ally-mercapto cysteine. Allicin is a lipid-soluble sulfur compound, which can be easily damaged by cooking and has the ability to provoke intolerance, allergic reactions, and gastrointestinal disorders. Various pharmacological activities have also been reported for the extracts and isolated compounds from garlic.(22)(11)

Geographical distribution of *Allium sativum*

Garlic, or *A. sativum* L. (Figure 1), is a member of the Amaryllidaceae family. The perennial herbaceous plant is huge, with tall blooming stems that can reach a height of 1 m, and the bulb is typically used to treat diseases.(11) The leaf blades are strong, linear, flattened, and between 0.5 and 1.0 inches (1.25 and 2.5 cm) long. Sanskrit literature from around 5,000 years ago describe its therapeutic properties, while traditional Chinese medicine (TCM) originally used it at least 3,000 years ago.(12) Nowadays, there are more than 300 different types of garlic that are planted practically everywhere. Nowadays, *A. sativum* is grown all over the world. A perennial herb, garlic may be cultivated all year and blooms in warm climates.(23)

Phytochemistry of *Allium sativum*

According to reports, *A. sativum* bulbs contain a variety of bioactive substances, many of which include sulphur.(24) These substances include thiosulfinates (allicin), sulphides (diallyl disulfide (DADS)), vinyl dithiins (2-vinyl-(4H)-1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), ajoenes (E-ajoen) the primary toxic substances are allicin, S-methyl cysteine sulfoxide (MCSO), and S-propylcysteine sulfoxide (PCSO), with allicin being the predominant cysteine sulfoxide. As other enzymes interact with allicin, MCSO, and PCSO, additional compounds are produced, such as allyl methane thiosulfinates, methyl methanethiosulfonate, and other thiosulfinates.(25)(26)



Figure 1: Different parts of garlic (A, B) habit; (C, D) bulb.

Ethnobotanical uses of *Allium sativum*

Due to the pungent scent of garlic, which is related to organosulfur compounds like allicin and DADS, it is a popular culinary ingredient and condiment. The potential therapeutic benefits of garlic in traditional medicine include its use for treating conditions such as diabetes, hypertension, pneumonia, hair loss, snakebite, wounds, cough, paralysis, scabies, malaria, haemorrhoids, carbuncles, respiratory illnesses, influenza, female infertility, etc.(27) These benefits are primarily due to its diuretic, aphrodisiac, sedative, and cardioprotective properties.(26)

Chemical Constituents of Garlic

Several phytochemicals, including those containing sulphur, have been found in the bulbs of *A. sativum* (Figure 1), including ajoenes (E-ajoene, Z-ajoene), thiosulfinates (allicin), and vinylthiins, Dialyl disulfide (DADS), diallyl trisulfide (DATS), and other sulphides

represented for 82% of the total sulphur content of garlic.(28) They also included 2-vinyl-(4H)-1,3-dithiin and 3-vinyl-(4H)-1,2-dithiin. After chopping the garlic and dissolving the parenchyma, the enzyme allinase converts alliin, the primary cysteine sulfoxide, to allicin.(29)

The major odoriferous compounds in freshly milled garlic homogenates are S-propyl-cysteine-sulfoxide (PCSO), allicin, and S-methyl cysteine-sulfoxide (MCSO).(30) The enzyme allinase can act on a mixture of MCSO, PCSO, and alliin to produce other molecules, such as allyl methane thiosulfinates, methyl methanethiosulfonate, and further corresponding thiosulfinates (R-S-S-R'), where R and R' are allyl, propyl, and methyls groups.(31)

Alliin (allyl thiosulfinate), is a sulfenic acid thioester and its pharmacological effect is attributed to its antioxidant activity as well as its interaction with thiol-containing proteins. In the allicin biosynthesis, cysteine is transformed to alliin that is hydrolyzed by the allinase enzyme.(31) This enzyme composed of pyridoxal phosphate (PLP) which splits alliin and produces ammonium, pyruvate, and allyl sulfenic acid that are highly reactive and unstable at room temperature, where two molecules were combined to form allicin.(32)

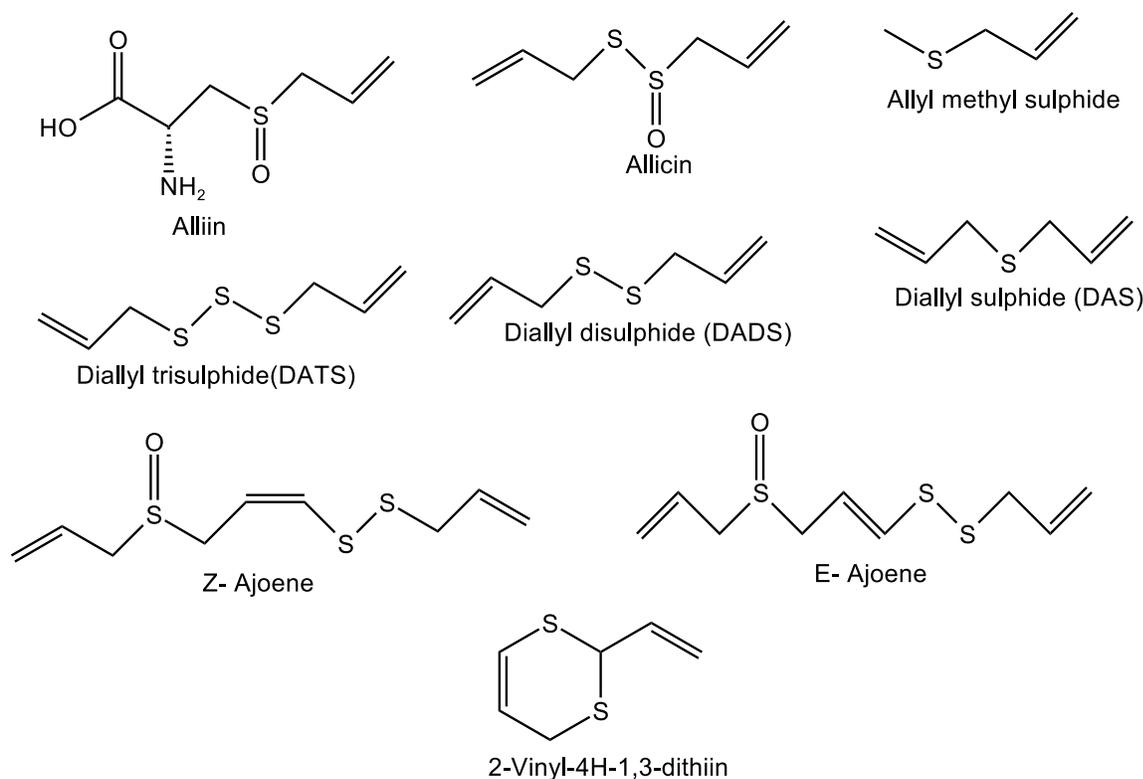


Figure 2: Structures of some of the sulphur-containing compounds isolated from *Allium sativum*.

Traditional Uses of Garlic

One of the most significant bulb vegetables, garlic is used as a spice and flavouring all over the globe. It has a strong flavor.(24) Its pungent effects and spicy scent are mostly brought on by organosulfur compounds like allicin and DADS, and A number of biological effects, including anticarcinogenic, antioxidant, antidiabetic, renoprotective, anti-atherosclerotic, antibacterial, antifungal, and antihypertensive actions, have historically been attributed to garlic and its associated components.(33) Garlic also exhibits carminative, antipyretic, sedative, aphrodisiac, and diuretic actions and has been used in traditional medicine to treat indigestion, respiratory and urinary tract infections, and heart diseases.(34)

Pharmacological activity of plant extracts

Antibacterial activity

Garlic extracts have high range of anti-bacterial effect against both gram negative and gram-positive bacteria and were also effective against anti-biotic resistant bacteria and their toxic product. Garlic extract also showed remarkable efficiency with different effectiveness rate on gram negative bacteria such as *Salmonella*, *Shigella*, *S. aureus* and *E.coli*, *Streptococcus*(*Streptococcus faecalis*, *Streptococcus mutans*, *Streptococcus pyogenes*), *Klebsiella aerogenes*, *Pseudomonas aeruginosa*, *Proteus vulgaris*. Fungi susceptible to allicin are *Candida albicans* and *Aspergillus Niger*.(8)(35) The allicin affect the growth of bacteria by inhibiting their DNA and proteins synthesis partially and also by inhibiting RNA synthesis as primary target. The yield potential is the ability of solvents to extract the high amount of bioactive compound from the plant.(36) The type of solvent affects the amount of extract can be obtained. So, the polar solvents extract the polar compounds. Similarly, the non-polar solvents extract the non-polar compounds. This also used to determine the higher compound content of the plant is either polar or non-polar. So, we can generalize that the polarity of solvent can have effect on the amount of compound that can be obtained.(37) The Gram positive and gram-negative bacteria were found to be sensitive for all the extracts, which is in contrast to the findings of other workers. As revealed from aqueous extract is the most effective one in terms of stopping the growth of bacterial growth.(38) The second most efficient solvent to extract so successful extract was chloroform against both strains and concentrations. Chloroform had been

better solvent than ethanol and there is significant statistical difference among these two solvents. The susceptibility of bacteria to antibiotic chemical is expressed in MIC or high zone of inhibition.(39) The susceptibility of bacterial strains depends on their structural composition, particularly *S. aureus* contain only 2% lipid. So that lipid content of the membranes will have an effect on the permeability of hydrophobic and volatile bioactive substances in garlic. Additionally other to be considered is that using garlic with alcohol will not affect us.(40)(16)

Antifungal Activity

Garlic extracts showed a broad-spectrum fungicidal effect against a wide range of fungi including *Candida*, *Torulopsis*, *Trichophyton*, *Cryptococcus*, *Aspergillus*, *Trichosporon*, and *Rhodotorula* species.(41) Recently, garlic extract was found to inhibit the *Meyerozyma guilliermondii* and *Rhodotorula mucilaginosa* germination and growth.(42) Another study reported the antifungal activity of various *A. sativum* extracts namely aqueous, ethanolic, methanolic, and petroleum ether against human pathogenic fungi such are *Trichophyton verrucosum*, *T. mentagrophytes*, *T. rubrum*, *Botrytis cinerea*, *Candida* species, *Epidermophyton floccosum*, *Aspergillus niger*, *A. flavus*, *Rhizopus stolonifera*, *Microsporum gypseum*, *M. audouinii*, *Alternaria alternate*, *Neofabraea alba*, and *Penicillium expansum*.(41) The garlic extract acted by affecting the fungal cell wall and causing irreversible ultrastructural changes in the fungal cells, which lead to loss of structural integrity and affected the germination ability.(43) These changes in the cytoplasmic content led to nucleus and cell organelles damage that ultimately leads to cell death.(44) Moreover, allicin and garlic oil showed potent antifungal effects against *Candida albicans*, *Ascosphaera apisin*, and *A. niger* and they acted by penetrating the cellular membrane as well as organelles membranes like the mitochondria and leading to organelles destruction and cell death.(35)

Anti-Protozoal Activity

Several studies have found that the garlic extract have antiprotozoal activity against variety of protozoan parasites. It is found that aqueous, ethanolic and dichloromethane *A. sativum* extract had anthelmintic activity against *Haemonchus contortus*, with the ethanolic extract being the most effective while aqueous garlic extract had potent activity against *Trichuris muris* and *angiostromylus cantonensis*.(45) Garlic extract also inhibit the growth of *Blastocystis* species.

Garlic was also tested against *Taenia taeniaeformis*, *Hymenolepis microstoma*, *H. diminuta*, *Echinostoma caproni*, and *Fasciola hepatica* *in vivo* and *in vitro*.(46) The alcoholic extract of bulb of *A. sativum* has also shown moderate *in vitro* anthelmintic activity against human *Ascaris lumbricoides*. *A. sativum* has been reported to be effective in the exposure of dysentery and also act as vermifuge.(47) Oil of *A. sativum* has also been reported to possess anthelmintic activity and discards all injurious parasites in the intestine. Garlic is the best-known source of selenium. The sulfur compound allicin, produced by crushing or chewing fresh garlic, in turn produces other sulfur compounds: ajoene, allyl sulfides, and vinyldithiols.(5)

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

Activities	Extract/ Plant parts	Bioactive Compound	Mechanism of Action	References
Antibacterial	Ethanollic extract	Allicin	Chemical interaction with enzymes containing thiol	(48)(49)
Antifungal	Crude garlic extract	DADS DATS	Irreversible ultrastructural changes in the fungal cells, loss of structural integrity and affected the germination ability	(50)(49)
Anti-Protozoal Activity	Ethanollic bulb extract	Allicin, DATS, Ajoene	Preventing the parasite's RNA, DNA and protein synthesis.	(51)(49)
Antiviral	Aged garlic extract	Allicin, DATS	Chemical interaction with enzymes containing thiol, Enhancing Natural killer-cell (NK-cell) activity that destroys virus-infected cells	(51) (52)(53)
Antioxidant	Raw garlic samples Ethanollic extract	Allicin, DADS, and DATS, DAS	Modulation of ROS, increasing glutathione and cellular antioxidant enzymes. Controlling ROS generation and preventing mitogen-activated protein	(48)(54)(55) (56)

			kinase (MAPK). Suppressing the enzymatic activity of cytochrome P450-2E1, reducing the generation of reactive oxygen and nitrogen species	
Anti-Inflammatory Activity	Aged garlic extract	Allicin, DAS, Thiacremonone	Reducing the level of TNF- α and interleukin IL-1 β receptor-associated kinase 4, increasing AMPK activity in the liver. Diminishing the expression of the inflammatory cytokines (e.g., NF- κ B, IL-1 β , and TNF- α and ROS generation by suppressing CYP-2E1 hepatic enzyme Blocking the NF- κ B activity	(57)(52)(58)
Anti-Alzheimer's	Crude garlic extract	Allicin, Diallyl sulfide (DAS), Diallyl trisulfide (DATS)	Reducing the anticancer agent's negative effects inhibited MCF-7 cell growth and cell cycle progression at the G0-G1 phase	(58)(59)(60)
Anticancer activity	Crude garlic extract Aqueous extract Ethanollic bulb extract	Allicin, alliin, DADS, DAS, Z-Ajoene	Enhancing p38 expression and cleaved caspase 3. Stimulating apoptosis in human leukemic cells, promoting the peroxide production, caspase-3-like, and caspase-8 activities	(61)(16)(62)
Antihypertensive	Crude garlic extract	Gamma-glutamylcysteine	Inhibiting the angiotensin-converting enzyme	(16)(53)

Antiviral Activity

Garlic extracts have been tested for antiviral activity against influenza B, human rhinovirus, human cytomegalovirus (HCMV), parainfluenza virus, herpes simplex type 1 and 2, vaccinia virus, and vesicular stomatitis virus.(63) *In vivo* experiments revealed that garlic extract had antiviral activity against influenza viruses by improving the production of neutralizing antibodies when given to mice, and this activity was based on the presence of several phytochemicals, including ajoene, allicin, allyl methyl thiosulfinate, and methyl allyl thiosulfinate.(51)(53) Allicin works by inhibiting several thiol enzymes, whereas ajoene antiviral activity is due to the inhibition of leukocyte adhesive interaction and fusion. DATS was also effective against HCMV replication and viral early gene expression, and it works by increasing natural killer-cell (NK-cell) activity, which destroys virus-infected cells.(52)(64)

Antioxidant Activity

It has been reported that consuming garlic on a regular basis boosts internal antioxidant activity and reduces oxidative stress by either increasing endogenous antioxidant synthesis or decreasing the production of oxidizers such as oxygen-free radical species. Gentamycin is an antibiotic that has been used to treat a variety of bacterial infections.(65) It has been linked to hepatic damage by increasing aspartate transaminase and alanine aminotransferase enzymes and decreasing plasma albumin levels. Garlic has been shown to protect against gentamycin- and acetaminophen-induced hepatotoxicity by improving antioxidant status and regulating oxidative stress.(66) Garlic's antioxidant effect is thought to be due to ROS modulation, increased glutathione, and cellular antioxidant enzymes. Furthermore, garlic extract was found to increase the activities of some antioxidant enzymes (e.g., SOD) and decrease glutathione peroxidase (GSH-Px) in rat hepatic tissues.(66) Notably, several reports indicated that AGE rich in flavonoid, phenol, and different Sulphur compounds e.g., SAC shows high radical scavenging activity. Furthermore, AGE acted by increasing the expression of antioxidant enzymes such as glutamate-cysteine ligase modifier (GCLM) and heme oxygenase-1 (HO-1) subunits via the nuclear factor erythroid-2 related factor 2 (Nrf2)-antioxidant response element (ARE) pathway, which is responsible for human endothelial cell protection against oxidative stress.(67) Alliin, the main compound isolated from AGE, exhibits broad-spectrum antioxidant activity by regulating ROS production and inhibiting mitogen-activated protein kinase (MAPK).(68) Furthermore, it

has been reported to inhibit ROS production by inhibiting NADPH oxidase 1, thereby inhibiting osteoclast fusion caused by receptor activator of nuclear factor-kappa B ligand (RANKL). Allicin, DADS, and DATS are the main antioxidative compounds that demonstrated an antioxidant effect at physiological doses.(56)(49)

Anti-Inflammatory Activity

Garlic extracts and related phytochemicals have been shown to have anti-inflammatory properties. According to one study, garlic extracts significantly reduced the liver inflammation and damage caused by *Eimeria papillate* infections.(69) Garlic's anti-inflammatory activity is caused by inhibiting the emigration of neutrophilic granulocytes into epithelia. Aged black garlic (ABG) demonstrated potent antioxidant activity, which may be responsible for its anti-inflammatory activity. TNF-induced NF-B activation in human umbilical vein endothelial cells is inhibited by the ABG chloroform extract (TNF). Furthermore, we found that ABG extract may act via another mechanism by inhibiting NOS and COX-2 expression, preventing NO, IL-6, and TNF- formation in LPS-activated RAW264.7 cells and TPA-mediated dermatitis in mice. Allicin demonstrated a defensive mechanism against pathogens by increasing immune cell activity and influencing biochemical reactions associated with these immune cells.(70) Furthermore, allicin inhibits T-cell lymphocytes by inhibiting the SDF1 chemokine, which is associated with the weakness of the dynamic structure of the actin cytoskeleton and it also inhibits neutrophil trans endothelial migration.(68)(71) DAS anti-inflammatory activity was induced by decreasing the expression of inflammatory cytokines (NF-B, IL-1, and TNF) and ROS generation by suppressing the CYP-2E1 hepatic enzyme.(53) Another study found that thiacremonone (a sulphur compound isolated from garlic) prevents neuro inflammation and amyloidogenesis by inhibiting NF-B activity, and thus can be used to treat neurodegenerative disorders associated with inflammation (e.g., Alzheimer's disease).(49)

Anti-Alzheimer's Disease Activity

Alzheimer's disease (AD) is the main cause of dementia in the elderly with neurodegenerative and cerebrovascular disorders.(72) Acetylcholinesterase (AChE) is the main enzyme that Raw garlic extract was found to be the most effective and highly specific anticancer drug against different cancer cells without affecting non-cancerous cells reported that garlic extracts'

anticancer mechanisms include inhibition of cell growth and proliferation, regulation of carcinogen metabolism, stimulation of apoptosis, prevention of angiogenesis, invasion, and migration, and thus reducing the anticancer agent's negative effects.(73) Although no mechanisms were reported, aqueous garlic extract was found to reduce the viability of estrogen receptor (ER)-positive MCF-7 human breast cancer cell line in one of the earliest in vitro studies.(49) Similarly, crude garlic extract inhibited MCF-7 cell proliferation via unknown mechanisms. Fresh garlic extract inhibited MCF-7 cell growth and cell cycle progression at the G0-G1 phase by downregulating the expression of PCNA, cyclin D1, phosphorylated-ERK1 (p-ERK1), E-cadherin, -catenin, heat-shock protein 27 (hsp27), and Src-associated in mitosis of 68 kDa (sam68). Fresh garlic extract also increased eukaryotic initiation factor2- (p-eIF2-) phosphorylation, Rb levels, and cell cycle inhibitors (p21 and p27), while decreasing cytokeratin 8 and cytokeratin 18.(74)

Anticancer activity

A number of studies have demonstrated the chemo preventive activity of garlic by using different garlic preparations including fresh garlic extract, aged garlic, garlic oil and a number of organosulfur compounds derived from garlic. The chemo preventive activity has been attributed to the presence of organosulfur compounds in garlic.(75) The exact mode of action was not fully understood, but several modes of action have been proposed. These include its effect on drug metabolizing enzymes, antioxidant properties and tumor growth inhibition.(49)

Oral cancer

SAC was investigated for its ability to inhibit CAL-27 oral squamous cell cancer cells.(15) 24h treatment with 2-20 mM SAC inhibited cell viability via E-cadherin restoration (with increased E-cadherin/-catenin complex), decreased p-ERK1/2, downregulated the MAPK/ERK signaling pathway, and decreased SLUG.(18)

Gastric cancer cells

It is investigated that cytotoxic effect of fresh garlic extract on the AGS gastric carcinoma cell line. The results showed that AGS cells were cytotoxic; however, the mechanisms of such

effects were not investigated.(76) Aged black garlic extract has also been shown to inhibit cell growth and increase apoptosis in SGC-7901 gastric cancer cells.(77)

Colorectal cancer

A crude garlic extract was found to induce cytotoxicity against colo205 colon cancer cells, as well as an increase in apoptosis and mitochondrial membrane potential, as well as an increase in Bax, cyt.c, and caspase-3 expression.(78) However, the mechanisms underlying such an effect were not described. Garlic extract was found to inhibit proliferation by increasing apoptosis, which was associated with increased caspase-3 and caspase-7 activity. An additional experiment investigated the mechanisms underlying AGE's antiproliferative effects in colon cancer.(79)

Pancreatic cancer

The anticancer properties of garlic oil were investigated in human pancreatic carcinoma cell lines (AsPC-1, Mia PaCa-2, and PANC-1).(80) Following garlic oil treatment, the results revealed morphological changes, with the majority of cells becoming rounded, as well as inhibition of cell proliferation. Early-stage apoptosis was observed in AsPC-1 cells using a transmission electron microscope.(81) Garlic oil treatment reduced the number of AsPC-1 cells in a concentration-dependent manner while also arresting the cell cycle at the G2/M phase, as evidenced by a decrease in the G1 phase and an increase in the G2/M phase percentages.(82)

Leukemia

Garlic constituents have shown promising anticancer effects in murine and human leukemia in vitro models. Hodge et al. discovered that treating leukemia cells with fresh garlic extract (GE) significantly reduced viability in patients with childhood precursor-B acute lymphoblastic leukemia (ALL). Nearly all CD34-positive ALL cells stained positively for both Annexin V FITC and 7-amino-actinomycin D (7-AAD), but only a few CD34-negative lymphocytes did. While GE caused selective apoptosis in ALL cells, it had no effect on CD3-positive, CD25, or CD69 lymphocyte viability or T-cell immune function (because GE treatment had no effect on IFN, IL-2, or TNF- α production). In contrast, the chemotherapy drugs tested (daunorubicin, vincristine, L-asparaginase, and prednisolone) increased CD25 and CD69 cytokines while decreasing T-cell function significantly.(83) These findings are clinically significant because

garlic showed promising effects in sparing T-cell function, whereas chemotherapeutic agents decreased total immune system function non-selectively.(84) Furthermore, Z-ajoene has anti-proliferative properties against various cancers, inhibiting the growth of human breast cancer cells and glioblastoma multiforme cancer stem cells (GBM CSC). It was discovered to promote apoptosis in human leukemic cells by increasing peroxide production, caspase-3-like, and caspase-8 activity.(68)(85)

Antihypertensive Potential

Hypertension (systolic blood pressure (SBP) \geq 140 mm Hg; diastolic blood pressure (DBP) \geq 90 mm Hg) is a known risk factor for cardiovascular morbidity and mortality, affecting an estimated 1 billion individuals worldwide. Garlic (*Allium sativum*) has played an important dietary as well as medicinal role in human history.(11) Blood pressure reducing properties of garlic have been linked to its hydrogen sulphide production and allicin content – liberated from alliin and the enzyme allinase which has angiotensin II inhibiting and vasodilating effects, as shown in animal and human cell studies.(86) Studies concerning the effect of garlic consumption on blood pressure are not as numerous as the effect of garlic on serum lipids. Again, inconsistent results of the effect of garlic on blood pressure are abounding. In diabetic patients, it was reported that garlic oil can correct hyperglycemia. In addition, a precursor of various allyl sulfide constituents of garlic oil, S-allyl-cysteine sulfoxide (allin), was shown to have a hypoglycemic effect similar to that of glibenclamide.(87) Garlic has been found to be effective in lowering serum glucose levels in STZ-induced as well as alloxan-induced diabetic rats and mice.(49) The hypoglycaemic action of garlic could possibly be due to an increase in pancreatic secretion of insulin from β -cells, release of bound insulin or enhancement of insulin sensitivity.(68) It has been previously suggested that garlic (allicin) can enhance serum insulin by effectively combining with compounds like cysteine, which would spare insulin from SH group reactions which are a common cause of insulin inactivation.(88) Another mechanism proposed by researcher states that the antioxidant effect of S-allyl cysteine sulfoxide, an isolated product from garlic, may contribute to its beneficial effect in diabetes.(89) Research postulate garlic may act as an antidiabetic agent by increasing either the pancreatic secretion of insulin from the β -cells or release of bound insulin.(49)(88)

CONCLUSION

The active compounds and pharmacological properties of *A. sativum* were the main topics of this review. The primary components identified from *A. sativum* extracts include sulfur-containing substances such as alliin, allicin, ajoenes, vinyldithiols, and sulphides. Many biological qualities, including anticarcinogenic, antioxidant, antidiabetic, renoprotective, anti-atherosclerotic, antibacterial, antifungal, antiprotozoal, and antihypertensive activity, have been identified for extracts and isolated compounds from *A. sativum*. Moreover, the immunomodulatory and anti-inflammatory properties of garlic are well established. Garlic's main ingredient, allicin, can cause stomach disturbance, especially if taken in large dosages. Because of this, care should be taken while utilizing garlic as a medication to cure various diseases.

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