**Review**

**Therapeutic Value of Garlic (Allium sativum): A Review**

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**ABSTRACT**

Garlic (*Allium sativum*) is a source of medicine in many ways in human beings in routine life as well as in animals and its leaves, flowers, and cloves have been used in traditional medicine for a long time. Research in recent decades has shown widespread pharmacological and therapeutic effects of *A. sativum* and its organosulfur compounds especially allicin. The most important chemical constituents of this plant are organosulfur compounds such as allicin, diallyl disulfide, S-allylcysteine, and diallyl trisulfide. These chemicals were used for the treatment of inflammation, cancer, blood pressure, atherosclerosis, and hyperlipidemia as praised by several authors. Additionally, extracts of garlic have been used to treat various diseases and have shown anti-viral, anti-bacterial, anti-fungal, anticoagulative and antioxidant effects. However, few adverse effects have been found with garlic are nausea and vomiting when high quantity consumed. To review the therapeutic values of garlic and its importance in human and veterinary practices. Garlic is safe and rich sources of biologically active compounds with low toxicity. Further studies are needed to confirm the safety and quality of the plants to be used by clinicians as therapeutic agents.

**Keywords**

*Allium sativum*; Therapeutic values; Antibacterial; Antifungal; Antiviral; Anticancer; Anticoagulative; Antioxidant; Anti-inflammatory.

**INTRODUCTION**

Traditional medicines occupy a valuable place amongst rural groups of developing countries for the provision of health care inside the absence of an efficient public health care scheme.¹ The use of traditional treatments is common in sub-Saharan Africa, and visits to traditional healers remain a prime live of care for many people because of preference, affordability, limitation of practitioners and modern hospitals.² Moreover, traditional medicines may be the supply of remedy for lots of health complications.³,⁴

Garlic, *Allium sativum* is a member of the Alliaceae family, has been widely recognized as a valuable spice and a popular medicine for various diseases and physiological disorders. The word garlic was originated from the Celtic word meaning pungent. Garlic is cultivated practically throughout the world and appears to have originated in central Asia and then spread to China, the Near East, and the Mediterranean region before moving west to Central and Southern Europe, Northern Africa (Egypt) and Mexico.⁵-⁷ Garlic has played an essential role for over 7,000-years in central Asia, Africa, Europe, and the Mediterranean region.⁸

Garlic is a bulb growing to 25-70 cm with hermaphrodite flowers where its leaves and cloves have been used in traditional medicine for a long time. Aged garlic is used to make aged garlic extract (AGE), a popular herbal supplement that has been proven to boost the immune system and possibly prevent cancer and cardiovascular disease. Additionally, as garlic ages, it loses its strong flavor, so there is no need to worry about breath odor. Garlic can be used for culinary and medicinal purposes. The culinary use includes spicy flavor that mellows and sweetens considerably with cooking. While its medicinal uses include treatment of whooping cough, lung disease, stomach complaint and disorder resulting from childbirth, cold, sore eyes, and earache as well as help in the prevention of heart disease.³,⁹,¹⁰ A study on Czech revealed that garlic oil especially dehydrated powder could help in reducing the accumulation of cholesterol in the vascular walls of animals.¹¹,¹²

Allicin (diallyl-dithiosulfinic acid) is the most important component of garlic and generally claimed to be responsible for its numerous beneficial effects including antibacterial, antiviral, anti-

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fungal and antioxidative effect. Nowadays, the alarming growth of the number of antibiotic-resistant bacteria and difficulties in the treatment of infections has initiated a search for new antibacterial compounds and develop new alternative strategies in combating bacterial infections. Medicinal plants such as garlic, with their long history of use in folk medicine for the treatment of infectious diseases, have become a promising new source of antibacterial agents. Besides, they exhibit a direct antimicrobial activity and/or an indirect activity through synergism with antibiotics that increase their effectiveness. Hence, this review was prepared with the aim of increasing awareness on the medicinal importance of *A. sativum* in human and veterinary medicine.

**ALLIUM SATIVUM**

**Biosynthesis**

Allicin (allyl 2-propenethiosulfinate or diallyl thiosulfinate) is the principal bioactive compound present in aqueous garlic extract or raw garlic homogenate. It is produced from the non-proteinogenic acid allin (S-allyl cysteine sulfoxide) upon tissue damage in a reaction that is catalyzed by the enzyme alliinase (Figure 1). Allicin enzyme is activated when garlic is chopped or crushed and acts on allin (present in raw garlic) to produce allicin. In addition, structurally analogous thiosulfimates are produced in nature by other *Allium* species.

![Figure 1. Biosynthesis of Allicin from S-allyl Cysteine Sulfoxide (alliin) (a). The Enzyme Alliinase Catalyzes the Formation of Allyl Sulfenic Acid and Dehydroalanine. (b). When Two Molecules of Allyl Sulfenic Acid Condense Spontaneously to Yield One Molecule of Allicin.](image1.png)

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Allyl methyl thiosulfonate, 1-propenyl allyl thiosulfonate, and γ-L-glutamyl-S-alkyl-L-cysteine are other sulfur-containing compounds present in garlic. The thiosulfimates are condensation products of two sulfenic acids to form disulfur-containing compounds present in garlic. Thiosulfimates are important constituents of the plant that is responsible for many of its medicinal effects and garlic's pungent odor. Besides, diallyl disulphide (DDS), S-allylcysteine (SAC) and diallyl trisulfide (DTS) are other sulfur compounds that have some roles in the therapeutic effects of the plant. DTS is a chemically stable final transformation product of allicin.

![Figure 2. Reaction Mechanism of a Thiol with a Thiosulfinate. (a). The Reaction Leads Directly, (b) Indirectly, to the Formation of a Mixed Disulfide, which Under Some Conditions may React Further with RSH in a Thiol-disulfide Exchange Reaction to form RSSR and R,SH.](image2.png)

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**Chemical Constituents of Allium sativum and its Nutritional Value**

*A. sativum* contains about 33 sulfur compounds, several enzymes, amino acids, and minerals such as selenium. Studies carried out on the chemical composition of the garlic show that sulfur compounds such as allicin are important constituents of the plant that is responsible for many of its medicinal effects and garlic's pungent odor. Besides, diallyl disulphide (DDS), S-allylcysteine (SAC) and diallyl trisulfide (DTS) are other sulfur compounds that have some roles in the therapeutic effects of the plant. DTS is a chemically stable final transformation product of allicin.

Garlic powder is a simply dehydrated and crushed garlic clove. Besides, the water extract of heat-treated garlic contains mainly alliin. Accordingly, enzymatic activity of alliinase of garlic powder is similar to that of fresh garlic. However, dehydration temperature should not exceed 60 °C, above which alliinase is inactivated. In contrast to fresh garlic and garlic powder, Garlic oil, and steam-distilled garlic do not have significant amounts of alliin or allicin, but instead, contain various products of allicin transformation. Garlic has been analyzed for moisture, carbohydrate, protein, fat, minerals, vitamins, energy, ash, pH, acidity and essential oil contents. Some of the nutritional and chemical properties of garlic bulbs are summarized in Table 1.

**Table 1. Nutritional Value and Properties of Allium Sativum; Values Expressed per 100 g of Raw Garlic (Allium sativum)**

| Properties          | Values | Minerals          | Values | Vitamins          | Values |
|---------------------|--------|-------------------|--------|-------------------|--------|
| Energy              | 119 Kcal| Potassium         | 446 mg | Thiamine          | 0.16 mg|
| Moisture            | 70%    | Phosphorus        | 134 mg | Riboflavin        | 0.02 mg|
| Protein             | 4.3 g  | Magnesium         | 24.1 mg| Niacin            | 1.02 mg|
| Carbohydrate        | 24.3 g | Sodium            | 19 mg  | Pyridoxine        | 0.32 mg|
| Fiber               | 1.2 g  | Calcium           | 17.8 mg| Folic acid        | 4.8 µg |
| Fat                 | 0.23 g | Iron              | 1.2 mg | Ascorbic acid     | 14 mg  |
| Alcohol             | 0 g    | Zinc              | 1.1 mg | Carotenoids       | 5 µg   |
| Ash                 | 2.3%   | Iodine            | 4.7 µg | Vitamin A         | Traces |
| PH                  | 6.05   | Selenium          | 2 µg   | Vitamin E         | 0.011 µg|
| Acidity             | 0.172% | Source: Pacurar et al |

Source: Pacurar et al

![Table 1](image3.png)
Historical Background and Traditional uses of *Allium Sativum*

The ancient Egyptians used garlic to treat diarrhea and its potential medical value was described on the walls of ancient temples and on papyrus dating to 1500 BC. It was used by Greek physicians Hippocrates and Galen to treat intestinal and extra-intestinal diseases; ancient Japanese and Chinese used it to treat headaches, flu, sore throat, and fever. In Africa, particularly in Nigeria, it is used to treat abdominal discomfort, diarrhea, otitis media, and respiratory tract infections.29,30

Garlic is nicknamed as Russian penicillin due to its widespread use as a topical and systemic antimicrobial agent; it is commonly used in many cultures as an excitement and reputation of healing power. Garlic was used to treat common colds, hay fever and asthma in Europe and other countries for a long time.31,32 In the pre-antibiotic era, alllicin can kill bacteria *via* the gas phase and was used to successfully treat many lung-pathogenic bacteria such as tuberculosis from crushed garlic preparations through breathing in the vapor.30

**MEDICINAL IMPORTANCE OF ALLIUM SATIVUM**

Therapeutic use of garlic has been recognized as a potential medicinal value for thousands of years to different microorganisms. Antifungal, antiviral, antibacterial, anthelmintic, anthelmintic, antiseptic medicinal value for thousands of years to different microorganisms. Antifungal, antiviral, antibacterial, anthelmintic, antiseptic, anti-inflammatory properties of garlic have been well documented. The extracts exhibited a pronounced activity against both gram-negative (*E. coli*, Salmonella species, and Citrobacter Enterobacter, *Pseudomonas klebsiella*) and gram-positive (*Staphylococcus aureus*, *S. pneumoniae* Group A streptococcus, and *Bacillus anthracis*) bacteria causing considerable morbidity worldwide.9,25

**Antimicrobial Activity**

Allicin and other sulfur compounds are thought to be the major compounds responsible for the antimicrobial effect of garlic. The antimicrobial properties of garlic were first described by Pasteur in 1858, and since then, many researchers have demonstrated its effectiveness and broad-spectrum antimicrobial activity against many species of bacteria, viruses, parasites, protozoan and fungi.30,31 Garlic is more effective with the least side effects as compared to alternative commercial antibiotics; as a result, they are used as an alternative remedy for the treatment of various infections.29,30 Out of the many medicinal plants, garlic has an antimicrobial property that protects the host from other pathogens highlighting the importance of search for natural antimicrobial drugs.28,29 Previously conducted researches confirmed that garlic is not only effective against Gram-positive and Gram-negative bacteria but also possesses antiviral and antifungal activities.28,30,31

**Anti-bacterial activity:** Garlic has been used for centuries in various societies to combat infectious disease. According to different research findings, garlic has been proven to be effective against a plethora of gram-positive, gram-negative, and acid-fast bacteria. These include Salmonella, *Escherichia coli*, *Pseudomonas*, *Proteus*, *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, Salmonella spp., Klebsiella spp., Micrococcus spp., Clostridium spp. and *Mycobacterium* spp.26,31,33,34

The gram-positive *Staphylococcus aureus* was more susceptible to the toxic effects of garlic than its gram-negative counterparts. It has been shown that Gram-negative diarrheagenic pathogens (*E. coli*, *Proteus mirabilis*, Shigella spp., and Salmonella spp.) from stool samples were highly sensitive to garlic.34 It has been shown that the aqueous extract of garlic can be used alongside conventional antibiotics to fight agents of nosocomial infections in hospitals.23 *In vitro* and *in vivo* study of garlic extract was also effective against *Streptococcus mutans* which is primary etiological organisms in dental caries.35,36

The cloves of garlic and rhizomes of ginger, extracted with 95% ethanol, suggested to have antibacterial activity against multi-drug clinical pathogens and can be used for prevention of drug resistant microbial diseases. *Pseudomonas aeruginosa* was the most sensitive germ to the mixture. Garlic also suggested as a treatment for multi-drug resistant tuberculosis. Besides, alllicin in its pure form was found to exhibit antibacterial activity against multidrug-resistant enterotoxigenic strains of *E. coli*.30,33,35 In a study by Lai and Roy, fresh extracts of *A. sativum* (garlic) and *Nigella sativum* (black cumin) had more antibacterial activity against the isolates of the urinary tract infection than cefalexin, cotrimoxazole, and nalidixic acid. Garlic, allyl methyl sulfide, has antibacterial activity against the pig pathogen *Actinobacillus pleuropneumoniae* serotype 9.9,24

**Anti-viral activity:** Garlic and its sulfur constituents verified anti-viral activity against Coxsackievirus species, Herpes simplex virus types 1 and 2, Influenza B, Para-influenza virus type 3, *Vaccinia* virus, Vesicular stomatitis virus, *Human immunodeficiency* virus type 1 and *Human rhinovirus* type 2. The order of compounds found in garlic for virucidal activity was, ajoene>alllicin>allyl methyl thiosulfate>allyl methyl thiosulfate; no activity was found for the polar fractions, alllin, deoxy allin, diallyl disulfide, or diallyl trisulfide. According to different research findings, garlic is an effectual treatment for both the influenza B virus and herpes simplex virus. Two independent researchers in Japan and Romania have found that garlic is able to protect living organisms from the influenza virus and enhanced the production of neutralizing antibodies when given the vaccine.24,36,37

Ajoene, isolated from extracts of garlic may inhibit adhesive interaction and fusion of leukocytes. In a study investigating the effect of allitridin (diallyl trisulfide) on the replication of human cytomegalovirus (HCMV) and the expression of viral immediate-early genes, it was revealed that this substance has anti-HCMV efficacy.38 In another study, it was supposed that the antiviral activity of garlic in humans may be secondary to a direct toxic effect on viruses. It also enhanced the NK-cell (Natural killer-cell) activity that destroys virus-infected cells.24 On, a double-blind placebo-controlled study has shown significant protection from the common cold virus and used for prevention, treatment and reduction of reinfection benefits from taking allimax powder capsules once daily.4,11,39
Anti-fungal activity: Different dilutions of extracts of *A. sativum* have been shown to possess fungistatic and fungicidal activity *in vitro* and *in vivo*. Ajoene is an active compound found in garlic which plays a great role as a topical antifungal agent. Garlic has been shown to inhibit the growth of fungal diseases as equally as the drug ketoconazole, when tested on the fungi *Malassezia furfur*, *Candida albicans*, *Aspergillus*, *Cryptococcus* and other Candida species. A report from a Chinese medical journal delineates the use of intravenous garlic to treat a potentially fatal fungal brain infection called *Cryptococcus meningitis*. Studies on the effect of amphotericin B (AmB) against Candida, albicans showed that allicin enhances significantly the effect of AmB against *Candida albicans*, *Saccharomyces cerevisiae* and against *Aspergillus fumigatus* *in vitro* and *in vivo*.30,40

An *in vivo* study showed that antibody-alliinase conjugates and allin are effective against murine pulmonary aspergillosis.31 An *in vitro* study showed both intrinsically antifungal activity of allicin and its synergy with the azoles group of drugs, in the treatment of candidiasis.32 One study showed that six different mixtures of garlic distilled oils containing DDS and DTS are active against a number of yeasts (*C. albicans*, *C. tropicalis*, and *Blastoschizomyces capitatus*).30 Saponins from *A. sativum* were shown to be effective against *Botrytis cinerea* and *Trichoderma harzianum*.43 Another antifungal protein, allivin, was isolated from *A. sativum* with antifungal activity against *Botrytis cinerea*, *Mycosphaerella arachidicola* and *Physalospor apiricola*.24

According to the study made in mice, liquid garlic extract was having a substantial effect in reducing the Candida colonies in mice through stimulating the body’s own defenses to enhance the phagocytic activity of the cells. Garlic oil can be used to treat ringworm, skin parasites and warts if it is applied externally. Lesions that were caused by skin fungi in rabbits and guinea pigs were treated with external applications of garlic extract and began to heal after seven days.21,44

Anti-Cancer Activity

Among the most prominent and favorable effects of garlic is its effect on the inhibition of the growth of cancer cells. Diallyl trisulfide (DATS) is one of the components of garlic that has a great effect on fighting cancer cells. The cytotoxicity caused by DATS is mediated by the generation of reactive oxygen species (ROS) and subsequent activation of the ROS-dependent caspase pathway in U937 leukemia cells. The action of garlic has been attributed to stimulating immune effector cells including T-cell and natural killer cells.23,44 Numerous epidemiological, clinical and laboratory studies have demonstrated that garlic has a great role in cancer prevention especially in relation to digestive tract cancers. Different studies on humans have shown that regular intake of garlic reduces the risk of esophageal, stomach and colon cancer. This was thought to be due to the antioxidant effect of allicin in reducing the formation of carcinogenic compounds in the gastrointestinal tract.27,46

Garlic has also a variety of anti-tumor effects, including tumor cell growth inhibition and chemopreventive effects. In rodents, garlic and its constituents have been reported to inhibit the development of chemically induced tumors in the liver, colon prostate, bladder, mammary gland, esophagus, lung, skin, and stomach in both rodent and human studies.26,46,48 DATS an organosulfur compound isolated from garlic has been shown anticancer activity both in *in vitro* and *in vivo* investigations. The cytotoxicity of DATS toward prostate epithelial cells reduced as opposed to PC-3 cancer cells.48

The toxic effect of garlic indirectly plays an important role in the death of cancer cells. Another key role in the prevention of cancers is garlic’s effect on the immune system. Macrophage activity, NK as well as the cytokine tumor necrosis factor (TNF), were all shown to have increased activity after administration of garlic and this resulted in an increase in antitumor response.49 Colorectal cancer is the third leading cause of cancer death in the world. In this respect, normal garlic cannot be administered and would need to be introduced as part of a strict diet. The garlic and low meat diet, however, show a decrease in colorectal tumor growth.6,41

According to different research findings, aged garlic extract such as S-allyl cysteine, and S-allylmercapto-L-cysteine exhibited radical scavenging activity. In addition, S-allyl cysteine and some organosulfur compounds derived from garlic have been found to retard the growth of chemically induced and transplantable tumors in several animal models. Therefore, the consumption of garlic may provide some kind of protection from cancer development.6,24

Anti-Helminthia Activity

Development of anthelmintic resistance in helminths reported in a number of countries gives a clear indication that control programs based exclusively on their use are not sustainable. The development of integrated programs to control helminths is vital, but such control programs require viable alternatives to the use of anthelmintic.49,50 Medicinal plants such as garlic have been used to treat parasitic infections in man and animals. A study showed that allicin is able to produce morphological changes in the male *Schistosoma mansoni*.51 The alcoholic extract of bulb of *A. sativum* has also shown moderate *in vitro* anthelmintic activity against human *Ascaris lumbricoides*. Garlic has been reported to be effective in the exposure of dysentery and possess anthelmintic activity against *Entamoeba histolytica* and *Giardia lamblia*.4,52

Diallyl trisulfide has *in vitro* activity against several important protozoan parasites. The results indicated that the compound has the potential to be used in the treatment of several human and animal parasitic diseases such as *Trypanosoma species*, *Entamoeba histolytica* and *Giardia lamblia*.13,32,24 Garlic oil is effective against a wide range of protozoan parasites including *Plasmodium species*, *Trypanosoma species*, *Leishmania species*, *Giardia species*, and *C. hominis* *planchonii*. Its aqueous extract has also been shown to be effective against hymenolepiasis and giardiasis. In an *in vitro* study, the extracts of *A. sativum* were shown to have anthelmintic
activity against Haemonchus contortus from sheep by decreasing larval count. The ethanol extract was the most effective in decreasing larval count. In another study, aqueous extract from garlic has good activity against nematodes such as Trichuris muris and Angiostrongylus cantonensis when followed by chloroform extract.6,22,33

Garlic with a mixture of the different extracts was tested in vivo and in vitro for its anthelmintic activity against cestodes (Hymenolepis diminuta, H. microstoma, and Taenia taeniaformis) and trematodes (Fasciola hepatica, Echinostoma caproni). In all in vitro tests, the target parasites died. In addition, the same composition was effective only against Echin. Caproni (intestinal fluke), while both worms were killed in vitro. The essential oil of A. sativum has a paralytic effect on F. gigantica.46 The extract of A. sativum also possesses mosquito larvicial properties. It is effective against filarial mosquito Culexquinque fasciatus (24-hour post-treatment), Culexquinque fasciatus and Anopheles stephensi.57 Essential oil from A. sativum has acaridical activity against Rhizophusphaeus (Boophilus) Microplus (Cestrinick) tick larvae.46 A. sativum has also been an insecticidal activity against larvae of Aedesalbopictus (Skuse), Lycoerilla inginuin, and Spodoptera litura at 1000 ppm.39,60

Anti-Inflammatory Activity

Garlic extracts have been shown to exert anti-inflammatory effects.43 In one study, garlic treatment significantly attenuated in vivo and in vitro for its anthelmintic activity against cestodes (Hymenolepis diminuta, H. microstoma, and Taenia taeniaformis) and trematodes (Fasciola hepatica, Echinostoma caproni). In all in vitro tests, the target parasites died. In addition, the same composition was effective only against Echin. Caproni (intestinal fluke), while both worms were killed in vitro. The essential oil of A. sativum has a paralytic effect on F. gigantica.46 The extract of A. sativum also possesses mosquito larvicial properties. It is effective against filarial mosquito Culexquinque fasciatus (24-hour post-treatment), Culexquinque fasciatus and Anopheles stephensi.57 Essential oil from A. sativum has acaridical activity against Rhizophusphaeus (Boophilus) Microplus (Cestrinick) tick larvae.46 A. sativum has also been an insecticidal activity against larvae of Aedesalbopictus (Skuse), Lycoerilla inginuin, and Spodoptera litura at 1000 ppm.39,60

Cytokines involved in inflammatory bowel disease (IBD) direct a predominantly cell-mediated T-helper-1 (Th1) immune response. Several compounds isolated from A. sativum modulate leukocyte cell proliferation and cytokine production. To investigate the possible therapeutic effects of garlic in the treatment of patients with IBD, whole blood and peripheral blood mononuclear cells (PBMCs) should be assessed. In the presence of various concentrations of garlic extract, in vitro, the effect of garlic extract on leukocyte cytokine production was determined using multiparameter flow cytometry. Accordingly, inflammation associated with IBD can be treated with garlic extract by inhibiting Th1 and inflammatory cytokines while upregulating IL-10 production. An in vitro animal model study needs to be undertaken to determine the significance of these in vitro findings.4,62,63

Other authors have shown the preventive effect and possible toxicity of garlic oil and its organosulfur compounds in endotoxin-induced systemic inflammation and intestinal damage.44 A lead compound derived from allin is shown to be a good starting point for the development of anti-inflammatory drugs with fewer side effects.65

Anti-Oxidative Activity

Whole garlic knob and aged garlic extract exhibit direct antioxidant effects and enhance the serum levels of two antioxidant enzymes, catalase, and glutathione peroxidase.66 Garlic extract, allicin is efficiently scavenged exogenously generated hydroxyl radicals in a dose-dependent fashion, but their effectiveness was reduced by about 10% by heating to 100 °C for 20 min. The sulfur compounds such as S-allyl cysteine, found in fresh garlic appear to be nearly 1000 times more potent as antioxidants than crude, aged garlic extract. Garlic (both the homogenate of 10% in physiological saline solution and its supernatant) was able to reduce the radicals present in cigarette smoke.66

In vivo, antioxidant effects of several garlic organosulfur compounds have been studied. In one study, two lipophilic organosulfur compounds, diallyl sulfide (DAS) and diallyl disulfide (DADS) and two hydrophilic organosulfur compounds, S-ethyl cysteine (SEC) and N-acetylcysteine (NAC), protected against lipid-related oxidations by activating associated antioxidant enzymes. The in vivo antioxidant effects of four test organosulfur compounds against lipid-associated oxidations have been studied by the researcher reported that these antioxidant effects were due to the activation and modification of several enzymes such as 3-hydroxy-3 methylglutaryl-CoA reductase, glutathione-s-transferase and catalase.31,67

Anti-Coagulant/Fibrinolytic Activity

Garlic and other species in the genus allium have played an important role as a prophylactic and therapeutic agent over centuries. Of these, the usefulness of garlic in preventing disease of the cardiovascular system is widely recognized. There are several reports on anticoagulants.68 In a study, blood anticoagulant substance was isolated from garlic and its physical and chemical properties were also studied. A half milligram of garlic extracts completely inhibited one milliliter of blood from coagulating. The inhibiting effect of garlic extract on blood clotting was almost the same as that of potassium oxalate.3,4,11

MECHANISMS OF ACTION AND SYNERGISTIC EFFECT OF ALLIUM SATIVUM

It is widely accepted that plant extracts, because of complex nature, possess multiple mechanisms of action. Garlic extracts and their main components may exhibit activity by: (i) inhibiting bacterial growth or viability, (ii) targeting bacterial virulence factors or (iii) potentiating the effectiveness of antibiotics as resistance modifying agents. The inhibition of bacterial growth occurs through several mechanisms: disruption of membrane function and structure (including the efflux system), interruption of deoxyribonucleic acid/ribonucleic acid (DNA/RNA) synthesis and function, interference with intermediary metabolism and induction of coagulation of cytoplasmic constituents (Table 2).13,40,70

Synergistic interaction between two agents, in which one agent enhances the effect of the other and together they act more efficiently than as individual agents. The mechanism of synergistic action is explained by (a) modification of active sites on bacterial cell, (b) inhibition of enzymes, which catalyze degradation or modification of antibiotics, (c) increase of membrane permeabil-
ity and (d) inhibition of efflux pumps.\textsuperscript{71}

Allicin, an antibacterial compound from garlic (\textit{A. sati-
vum}), potentiated the action of cefazolin (4 to 128-fold) and oxacillin (32 to 64-fold), against \textit{Staphylococcus} spp. and cefoperazone (8 to 16-fold) against \textit{P. aeruginosa}.\textsuperscript{72} The significant antibacterial activity of garlic extract on streptomycin-resistant strains (\textit{Staph. aureus} and \textit{E. coli}) solely and in synergism with streptomycin has also been proved.\textsuperscript{73}

It was found in another study that polymyxin B (PMB), is effective against various yeasts and filamentous fungi when used in combination with allicin. This combination increases the plasma membrane permeability in \textit{Saccharomyces cerevisiae}. The synergistic activity between PMB and allicin combinations resulted in the disappearance of the swollen spherical structure of the yeast as a result of structural alterations of its vacuole.\textsuperscript{74}

In addition, the synergism between ciprofloxacin and garlic extract has antibacterial activity against multi-drug clinical pathogens such as enterotoxigenic strains of \textit{E. coli} and mycobacteria.\textsuperscript{29,75}

**Drug Interaction and Pharmacokinetics of Garlic**

Glutathione is a compound necessary for the liver to facilitate the detoxification of substances. Organo-sulfur compounds found in garlic showed to prevent glutathione depletion. Patients who experience increases in reactive oxygen-induced stress on liver function may be protected by garlic ingestion.\textsuperscript{67} It was found in \textit{E. coli} cultures that aged garlic extract, S-allyl cysteine, diallyl sulfide, and diallyl disulfide do not interfere with the antibiotic activity of gentamycin but may improve gentamycin-induced nephrotoxicity.\textsuperscript{23,75} Aged garlic has also been shown to reverse the oxidant effects of nicotine toxicity in rat studies. More researches are required in future garlic may be a unique choice to help minimize

### Table 2. Mechanism of Action and Pharmacological Effects of \textit{Allium Sativum}

| Effect          | Pathogen                                      | MOA                                           | Preparation                        |
|-----------------|-----------------------------------------------|-----------------------------------------------|------------------------------------|
| **Antibacterial** |                                               |                                               |                                    |
|                 | \textit{Staphylococcus aureus}                | Inhibition of bacteria growth                 | Aqueous, ethanol, chloroform extract |
|                 | \textit{Escherichia coli, Salmonella typhi}   | Higher inhibitory effect with Ethanolic extract and potentiating antibiotics effect | Aqueous and ethanol extract        |
|                 | \textit{Bacillus subtilis, Klebsiella pneumonia} | Inhibition of bacteria growth with Ethanolic extract | Aqueous, methanol and ethanol extract |
|                 | \textit{Helicobacter pylori}                  | Higher inhibitory effect                      | Extract                            |
|                 | \textit{Salmonella enteritidis}               | Higher inhibitory effect                      | Extract                            |
|                 | \textit{Shigella spp, Proteus mirabilis}      |                                                | Extract                            |
|                 | \textit{Actinobacillus pleuropneumonia serotype 9} | Inhibition of bacteria growth                 | Extract                            |
|                 | \textit{Streptococcus mutan}                  |                                                | Extract                            |
| **Antiviral**    |                                               |                                               |                                    |
|                 | \textit{Human cytomegalovirus, Influenza B, Herpes simplex virus type 1-2, Parainfluenza virus type 3, vaccine virus, Vesicular stomatitis virus, Human rhinovirus type 2} | Boost antibody production                 | Not mentioned                      |
| **Antifungal**   |                                               |                                               |                                    |
|                 | \textit{Candida albicans, C. tropicalis, Blastoschizomyces capitatus} | Inhibition by Changing antioxidant metabolites | Extract, DADS                      |
|                 | \textit{Botrytis cinerea, Trichoderma harzianum} |                                                | Extract                            |
|                 | \textit{Ascosphaera apis}                     | Inhibition of fungal growth                   | Essential oil vapors               |
|                 | \textit{Parascodioctoides brasiliensis}       |                                                | Extract                            |
|                 | \textit{Aspergillus niger}                    | Potentiating antibiotics effect               | Extract, Ajoene                    |
|                 | \textit{Dermatophytes, Saprophytes, Candidia}  | Blockage of lipid synthesis                  | Ethanol extract                    |
|                 | \textit{Cryptococcus spp, Bot. cinerea, Mycosphaera arachidicola, Physalospar spirica} | Inhibition of fungal growth                  | Alcoholic extract                  |
| **Antiparasitic**|                                               |                                               |                                    |
|                 | \textit{Trypanosoma spp, Entamoeba hirloytica, Giardia lamblia} | Inhibition of glutathione reductase          | Extract                            |
|                 | \textit{Schistosoma mansoni}                  | Enhances morphological changes                | Extract                            |
|                 | \textit{Trypanosoma cruzi T. brucei, Plasmodium spp, Giardia spp} | Inhibition of Trypanothione reductase.       | Extract                            |
|                 | \textit{Leishmania spp, Cochlospermum planchom} | Inhibition of glutathione reductase          | Extract                            |
|                 | \textit{Hymenolepsiidae, Giardia}             | Muscular paralysis of the parasite            | Aqueous extract                    |
|                 | \textit{Haemonchus contortus}                 | Muscular paralysis of the parasite            | Ethanol, dichloromethane and water extract |
| **Other**       |                                               |                                               |                                    |
|                 | Anti-inflammatory effect                      | Inhibition of assembly-disassembly processes of the cytoskeleton | Extract                            |
|                 | Antioxidant properties                        | Protection against free radical damage in the body | Organo-sulfur compound in garlic   |
|                 | Anti-coagulant/ antithrombotic effect         | Suppresses the coagulation system and inhibition of platelet aggregation | Extract                            |
|                 | Anti-tumor/cancer                             | Enhances immune effector cells, growth inhibition, and chemopreventive effects | Extract                            |

Source: Mikaili et al\textsuperscript{24}
the toxic effects of therapeutic drugs.\textsuperscript{3,8}

One study indicated that those who use traditional/complementary/alternative medicines (TCAMs) in addition to antiretroviral (ARV) treatment may be at risk of experiencing clinically significant pharmacokinetic interactions, particularly between the traditional complementary alternative medicines and the protease inhibitors as well as non-nucleoside reverse transcriptase inhibitors (NNRTIs). Mechanisms of pharmacokinetic interactions include alterations to the normal functioning of drug efflux transporters, such as P-gp and/or Cytochromes P450 (CYP) isoenzymes, such a CYP3A4 that mediates the absorption and elimination of drugs in the small intestine and liver. Specific mechanisms of action include inhibition and activation of these proteins and induction via the pregnane X receptor also known as the steroid and xenobiotic sensing nuclear receptor (SXR). Garlic exhibited potentially significant interactions, each with protease inhibitors or non-nucleoside reverse transcriptase inhibitors.\textsuperscript{3,5,7}

**ADVERSE EFFECT OF GARLIC**

Nausea, vomiting and breath odor are major adverse effects especially when raw forms of the herb are used and care should be taken in consuming high quantities. Although garlic generally poses little in terms of safety issues, there are isolated cases of topical garlic burns and anaphylaxis.\textsuperscript{8,7,7}

According to Tattelman, garlic should be taken with great caution in patients taking anticoagulants. It seems prudent to stop taking high dosages of garlic seven to ten days before surgery because garlic can prolong bleeding time.\textsuperscript{7,8} One study indicated that garlic application usually results in local inflammation, but, if applied under a pressure bandage, or if there is great caution in patients taking anticoagulants. It seems prudent to stop taking high dosages of garlic seven to ten days before surgery because garlic can prolong bleeding time.\textsuperscript{7,8} A parallel study also highlighted the potential ability of a high dose of garlic to induce morphological changes in the liver and kidneys.\textsuperscript{7,8} Another study shows intraperitoneal (IP) administration of high doses of garlic (500 mg/kg) results in profound changes in lung and liver tissues of rats than oral administration. It is also shown that the adverse effect of high doses of garlic oil might further influence the hemostatic balance.\textsuperscript{7,8}

**CONCLUSION**

A recent increase in the popularity of alternative medicine and natural products has renewed interest in garlic and their derivatives as potential natural remedies. Garlic, from crushed to capsules, and is consumed throughout the world. Garlic has a lot of benefits and potential uses in preventing and curing different diseases. Fresh and powdered garlic are popular for food flavor and should continue to be used. Nowadays, the problem of bacterial resistance is growing, and the outlook for the use of antibacterial drugs in the future is still uncertain. Even through pharmaceutical industries have produced a number of new antibiotics in the last few decades, resistance to these drugs by bacteria has increased. Garlic is a valuable source of new and biologically active molecules possessing antibacterial properties through direct action against bacteria or synergism with antibiotics. Garlic's antifungal, antibiotic and perhaps anticancer effects are well-accepted world over because of the many scientific literature supporting these effects. Garlic also has hepatoprotective, antioxidant, and anthemimic effects as well as unidentified anti-malarial substances. In conclusion, a detailed study regarding the phytochemical assessment and pharmacological effect of garlic and more attention as well as researches regarding the anticoagulant, anti-inflammatory, immuno modulatory and wound-healing action. Besides, advances being made in analytical techniques, sophisticated bioassays, and biotechnological exploitation should provide the means by which these important plants continue to play a key role in the benefit of man and animals' health. Finally, medicinal plants are in danger due to marketing and using them for different activities, so every citizen should give care and conservation in their natural habitat, this can be achieved through public education to increase the awareness of the community about potential uses of medicinal plants.

**CONFLICT OF INTEREST**

The authors declare that they have no conflicts of interest.

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