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Garlic (*Allium sativum L.*): A mini review on its multiple pharmacological benefits for human health

Manisha.[a], Khushboo.[a], Aman Malik[b], Neera Raghav[c],Nitika Mor[a,*]

[a] *Baba Mastnath University, Asthal Bohar, Rohtak, 124021, India*
[b] *Pt. Bhagwat Dayal Sharma University of Health Sciences, Rohtak, India*
[c] *Kurukshetra University, Kurukshetra, 136119, India*
Email:mor.nitika@rediffmail.com[a],nraghav@kuk.ac.in,raomansi444@gmail.com, khushboo.15yadav1996@gmail.com, lakshaymalik8491st@gmail.com*
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Abstract: One of the most important bulbs crops farmed in India is garlic (*Allium sativum L.*). It is a rich source of bioactive substances that satisfy a person's daily nutritional demands for well-being. Allicin is the most prominent bioactive compound in garlic that exhibits various pharmacological properties including highly antioxidant, anticancer, anti-inflammatory, cardioprotective, neuroprotective, anti-diabetic, antimicrobial, anti-aging, and anti-hyperlipidemic effects. It offers defense against a variety of malignancies such as asthma, bronchitis, hemorrhoids, fever, cough, headache, stomach discomfort, low and high blood sugar, and snakebites can all be treated with garlic. Raw garlic has been proven the 'Panacea' for cardiovascular and heart-related diseases since earlier ago. This review emphasizes the biological role of this wonderful medicinal plant in the treatment of various ailments. The medicinal effects of different constituents of this plant have been also addressed.

Keywords: Allicin, anti-oxidant, cardioprotective,garlic, pharmacological.

Introduction

A tiny crop of subterranean bulbs is garlic. It belongs to the *Alliaceae* or *Liliaceae* family and is known by the botanical name *Allium sativum*[1]. Garlic is often referred to as a "stinking rose" because of its pungent odor. The first herb to be cultivated was garlic. Central Asia is associated with its origin[2]. The active ingredient in garlic is allicin[3]. Garlic's strong flavours and a plethora of health advantages are both attributed to allicin. Proteins, calcium, magnesium, iron, potassium, zinc, arginine, saponins, polyphenols, and selenium are all abundant in garlic[4]. It is also used as a food, spice, and traditional medication for the treatment of several illnesses. In traditional remedies, it has been shown several biological properties, including anticarcinogenic, antioxidant, antidiabetic, neuroprotective, anti-atherosclerotic, antibacterial, antifungal, and antihypertensive actions[5].

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*[6]. This review examines the phytochemical composition, pharmacokinetics, and pharmacological activities of *A. sativum* extracts as well as its main active constituent, allicin.

Additionally, it is a rich source of several vitamins, including vitamin A, vitamin B6, vitamin B1, and vitamin C. In Asian, French, and Italian cooking, it is a necessary ingredient used as a spice[5]. In the plains of India, garlic is grown from October to March. It is grown in the southern hills from May to October, whereas it is grown in the northern highlands from September to June. It only reproduces vegetatively and also acts as the natural wonder medicine and health promoter in nature[7]. It has anti-viral, anti-oxidant, anti-cancer, and anti-inflammatory properties, along with lowering cholesterol and treating cardiovascular illnesses are the thriving uses of garlic[8-9]. It is extremely helpful for conditions including cataracts, gout, arthritis, and stroke. Therefore, it has earned the moniker "super food."

Physical properties of garlic

Allium sativum, is a member of the *Alliaceae* or *Liliaceae* family. It is a 1.2 m (4 ft) tall perennial bulb that grows underground. Head or knobs are the two parts of the entire bulb of garlic[10-11]. However, the discrete component which measures 1 g (approx), is referred to as the garlic clove/bulblets. A clove on a plantation develops into a bulb. As a result, garlic is a plant with bulbs[11]. The 4–20 cloves make up each bulb[12]. The only part of the compound bulb that is consumed and utilized medicinally is the bulb itself. A thin layer of white, mauve, or purple skin surrounds them and holds them in a sac; they are gathered together between the membrane scales. Garlic has elongated compressed and flat leaves.

Their flowers are naturally hermaphrodite. They are located at the end of a stalk that rises directly from the bulb and is pale in color. The flowers of garlic are arranged in a globular head (umbel), which is surrounded by a specific type of leaf called a spathae. They include tiny bulbils. Bees and various other insects carry out pollination. The size, pungency, and color of garlic vary depending on the variety[13].

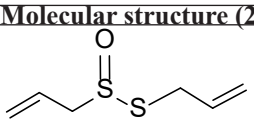
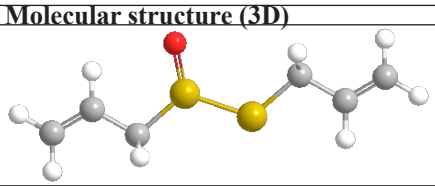
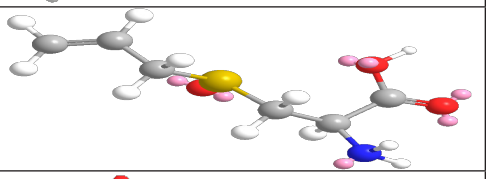
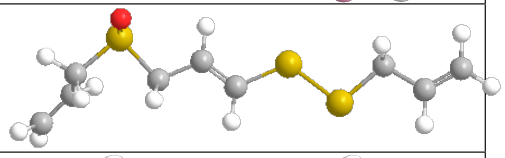
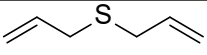
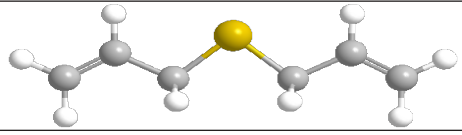
Chemical properties of garlic

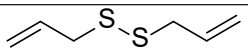
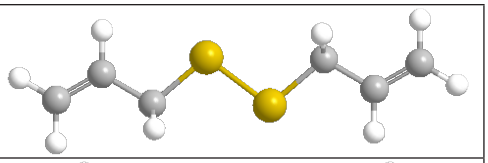
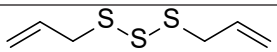
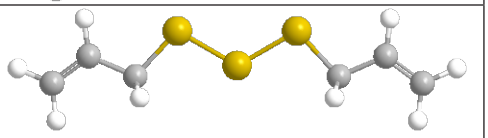
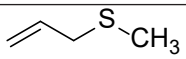
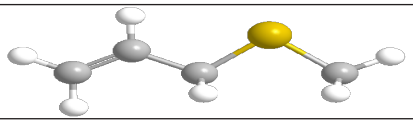
Sulfur is the good abundant in garlic and about 0.1 % of the volatile is found in garlic oil. This oil lacks oxygen yet good content of sulphur. Diallyl disulfide makes up the majority of the oil's composition, followed by diallyl trisulfide (20%), allyl propyl disulfide (6%), a negligible amount of diethyl disulfide, and maybe diallyl polysulfide[14]. These sulfur molecules are the responsible for garlic taste and smell good. Moreover, this strong volatile oil exhibits medicinal and therapeutic effects. The components of a garlic bulb include 84.09% water, 13.38% organic material, and 1.53% inorganic material. Garlic has been found to contain 20 different types of sulfur compounds, including allicin, methyl allyl trisulfide, diallyl trisulfide, and others depicted in Table 1. Seven other

organosulfur compounds, including gamma-l-glutamyl-S-methyl-l-cysteine, methiin, cycloalliin, and alliin, were also identified in it[15].

The biologically active component of garlic is Allicin. It cannot be generated from cooked garlic; it can only be released when raw garlic is crushed[16]. It is a component that dissolves in water and has no color or smell. The searing sensation of heat in raw garlic is caused by allicin opening the Thermo transient receptor potential channel (TRPA1) and TRPV1 (Transient receptor potential vanilliod1)[17].Allicin(diallylthiosulfinate) is produced when the enzyme alliinase, found in garlic, is activated as sulfur components of the garlic interact with the enzyme and generate allyl methyl sulphide. It immediately enters the blood and is expelled through the skin and lungs. Garlic has a non-sulfur chemical called phytoalexin (allixin), which may be useful in preventing cancer[18]. Garlic that had been fermented contained more riboflavin and α-tocopherol but less thiamin than garlic that had not been fermented[19]. The fermentation destroyed the ascorbic acid. The *Helicobacter pylori* bacteria, which causes gastric or duodenal ulcers, are successfully combated by the iso-E-10-devinylajoene, Z-10-devinylajoene, and three or five thiosulfinates found in garlic oil macerate. Enzymes, vitamins (Vit-B1, B2, B3, B5, B6, B9, and C), and other health-promoting substances are also found in garlic. minerals (calcium, iron, magnesium, manganese, phosphorus, potassium, sodium, zinc, selenium), saponins, oligosaccharides, dietary fibers, and flavonoids are among the substances that are high in arginine[20]. To produce pain signals, neurons in the spinal cord release neurotransmitters. Neuropeptides cause vasodilatation and inflammation at the location of sensory neuron activation[21]. Sulfenic acid is created during digestion in the body, and it reacts with harmful free radicals more quickly than any other chemical.

Table 1. List of the major compounds isolated from Allium sativum.

S.No.	Phytoconstituent	Molecular structure (2D)	Molecular structure (3D)
	Allicin ($C_6H_{10}OS_{2)}$		
	Alliin ($C_6H_{11}NO_3S$)		
	Ajoene ($C_9H_{14}OS_3$)		
	Diallyl sulfide (DAS) ($C_6H_{10}S$)		

	Diallyl disulfide (DADS) ($C_6H_{10}S_2$)		
	Diallyl trisulfide (DATS) ($C_6H_{10}S_3$)		
	Allyl methyl sulfide (AMS) (C_4H_8S)		

Biological effects

Garlic has been used to cure many ailments since ancient times such as blood pressure, atherosclerosis, high cholesterol, heart attacks, aphthous ulcer recurrence, and coronary heart disease (fig.1.). It has also been shown to have anti-aging and anti-hyperlipidemic effects[22]. Treatment of lung cancer, prostate cancer, breast cancer, stomach cancer, and colorectal cancer is successful with garlic.

When compared to fresh garlic, aged garlic exhibits more immunomodulatory effects. Garlic is also known to treat a variety of illnesses, including gout, rheumatoid arthritis, osteoarthritis, diabetes, allergic rhinitis, traveler's diarrhea, pre-eclampsia, bacterial and fungal infections, common cold & flu. Garlic is also used to cure hemorrhoids, psoriasis, hair loss, whooping cough, headaches, stomachaches, and sinus congestion[23]. A very valuable treatment for persistent asthma, garlic syrup is available in the market[24]. Moreover, it is used for fighting stress and fatigue. Further, it is found to be effective in preventing beriberi and scurvy[25].

Chemotherapeutic effect

By varying cytokinesis and preventing NF-kB activity in the surrounding tissue, garlic can reduce inflammation[26]. The potential anticancer effects of garlic supplements and their respective ingredients have been shown in numerous *in-vivo* and *in-vitro* investigations[27]. Apoptosis was shown to be induced by ajoene in malignant cells but not in healthy cells for the reason that peroxide generation takes place[28]. The other componentsof garlic like DAS, DADS, and DATSare examples of organosulfur compounds that inhibit the development of cancer cells during the cell cycle[29]. Any drug that promotes Glutathione S-Transferase (GST)activity would therefore have a chemopreventive effect. Garlic-derived organosulfur compounds have been investigated for their effects on GST activity in the liver and other tissues[30]. Recently, garlic consumption has been found to lower the risk of cancer[31].

It is believed that sulphurous compounds stop the growth of cancerous cells in the liver and stomach. Many mechanisms of action have been hypothesized; however, the particular mode of action is yet unknown[32].

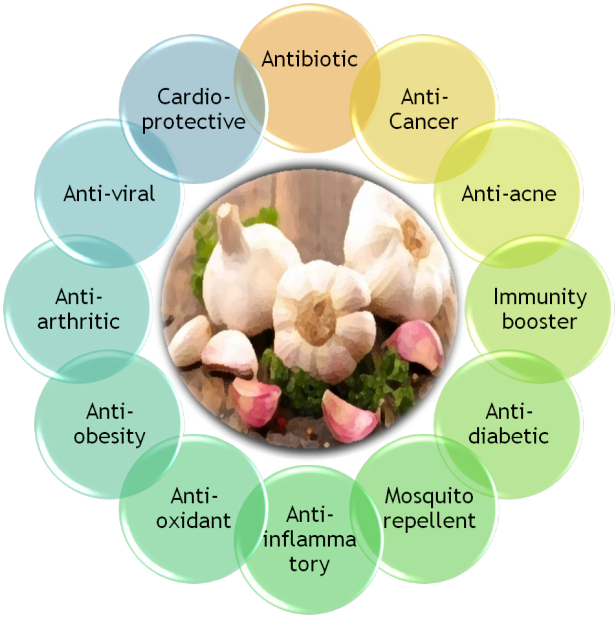


Figure 1: Biological Properties of Garlic

Antioxidant effect

Garlic and chemicals generated from it can activate enzymes involved in detoxification and antioxidant activity, hence lowering intracellular reactive oxygen species ROS[33]. Hazardous ROS can be neutralized by several natural substances' inherent enzymatic defense mechanisms. Likewise, many plant substances including flavonoids, phenolic acid, and phenolic diterpenes, possess potent antioxidant effects[1].

Catalase and glutathione peroxidase levels in the serum are increased by the whole and aged garlic extracts which indicates the strong antioxidant capabilities[34]. In a dose-dependent manner, allicin and garlic extract are both capable of scavenging exogenously produced hydroxyl radicals. S-allyl-L-cysteine, polyphenols, and flavonoids are just a few of the bioactive compounds found in black garlic[35]. Black garlic exhibits higher antioxidant activities as a result of production through longer heating.

Anti-microbial effect

- ***Anti-fungal Activity***

Garlic extracts have been proven to be a potential herb to eliminate several fungal species, including *Torulopsis, Cryptococcus, Candida, Trichophyton, Trichosporon, Aspergillus, and Rhodotorula*[36]. Recently researchers have shown that *Rhodotorula mucilaginosa* and *Meyerozyma guilliermondii* cannot grow or germinate when treated with garlic extract. Amphotericin B is still the treatment of choice for treating systemic fungal infections, however, even this medication has detrimental side effects[37]. In the People's Republic of China, systemic antifungal medications made from the *allium sativum* plant are extensively used to treat fungi infections. The ethanol and water-diluted garlic extract reduced *Botrytis cinerea* (100%) when given at large doses (60% and 80%, respectively). Penicillium expansum was shown to be removed by garlic extracts diluted in ethanol and water at a concentration of 80% in 96.21% and 99.21%, respectively. Neofabraea Alba showed greater sensitivity to ethanol-diluted extracts, with 79.63% inhibition seen with an 80% extract[38].

- ***Anti-bacterial Activity***

Garlic has been proven to be effective in treating many bacterial and fungal conditions[1]. In 1858 and 1930, Louis Pasteur and Lehmann respectively provided the first contemporary scientific evidence for the therapeutic

and bactericidal effects of garlic extract.

It has antiviral, antifungal, and antibacterial properties. Despite varying degrees of susceptibility, garlic extracts in ethanol, chloroform, and water all prevented the growth of dangerous bacteria[12]. The bactericidal abilities of *Allium sativum* were assessed using the diffusion method. Allicin activity, which is responsible for garlic's antimicrobial properties, is effective against a variety of microorganisms, including antibiotic-resistant Gram-positive and Gram-negative bacteria like *Salmonella enterica, Escherichia coli, Shigella, Pseudomonas aeruginosa, Staphylococcus aureus, S. faecalis,etc*[37].

- ***Respiratory tract infections***

Allicin vapors are used to treat lung infections[39]. Allicin is used as a defense against pests and pathogens because it is a natural antibiotic produced by garlic. Allicin is active against several multidrug-resistant (MDR). Several cases of pulmonary tuberculosis have reportedly been effectively cured by inhaling the vapors from cooked garlic[40]. To mitigate the smell of garlic, patients were given face masks with pouches containing ethanol, ground-up eucalyptus oil, and garlic juice. In many clinical trials, pulmonary TB was successfully treated by garlic extracts having them breath the fumes for two one-hour intervals each day[41].

Anti-inflammatory effect

The body's natural defense mechanism, which includes inflammation, is activated when multiple endogenous signaling molecules and outside pathogenic agents interact directly or indirectly with different membrane receptor types. Garlic extracts dramatically decreased inflammation in experimental models of inflammation[42]. According to one study, the sulfur compound thiochromone, which is derived from garlic, lowers NF-B activity, which decreases amyloid formation and neuroinflammation. As a result, inflammation-related neurodegenerative diseases like Alzheimer's disease may be treated with it[43]. It contains a compound diallyl disulfide, due to the presence of this compound garlic shows anti-inflammatory properties. This diallyl disulfide limits the effect of pro-inflammatory cytokines. Inflamed joints or muscles get relief by rubbing oil[44]. Garlic contains biological activities in its raw form. A lead compound derived from allicin was shown to be a good starting point for the development of anti-inflammatory drugs with lesser side effects. Garlic is a vital food item that is important in Respiratory Virus Infections (RVI) and it shows cholesterol lowering, antioxidant, and anti-inflammatory properties[45].

Anti-Hyperlipidemic effect

In this study, one of the major cardiovascular risk factors for type 2 diabetes mellitus patients with dyslipidemia is examined. 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), but the nonrandomized group (n = 32) only showed a non-significant decrease in total cholesterol (-2 mg/dl, -0.9% P= ns) and LDL-C (-3 Mg/dl, -1.6% P= ns)[46]. Patients undergoing 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 change in triglyceride levels between the two groups. According to these findings, garlic significantly reduced serum total cholesterol and LDL cholesterol compared to placebo, while slightly raising HDL cholesterol[1, 23]. 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 an increase in blood insulin in diabetic mice but not in normal animals. Garlic had a more potent anti-diabetic impact than glibenclamide, according to a study comparing the effects of the two drugs[18].

Anti-hypertensive effect

Their findings suggest that the compounds AMS and DAS, which are produced from garlic, may be effective antioxidants that work to reduce arterial thickness associated with hypertension[47]. Elkayam et. al (2001) reportedgarlic's hypoglycemic action; in which 26 hypertension patients received two alliin pills, three times daily for three days, comprising 4.75 gm of garlic concentrate (about 2.4 gm of dried parsley and 0.31 gm of dehydrated garlic). 85% of the patients were shown a reduction in systolic and diastolic blood pressure of 12.3 mmHg and 6.5 mmHg, respectively. The authors reported that 12 out of 13 patients had recovered from their vertigo, and the finally patients had improved. They noted that 17 patients who had complained of headaches, out of them 14 patients had experienced relief [48,49].

Antiplatelet and fibrinolytic effects

Fresh garlic cloves, ajoene, and garlic oil have been found to suppress platelets in several *in-vitro* and animal studies[14,50]. One of the mechanisms shown by *in-vitro* studies is a dose-dependent inhibition of platelet aggregation through nearly complete suppression of thromboxane production[51]. Other mechanisms include a dose-dependent inhibition of collagen-induced platelet aggregation and inhibition of adenosine diphosphate (ADP) and epinephrine-induced platelet aggregation[52]. There are numerous potential causes of garlic's impact on platelets. For instance, it helps to prevent the formation of thromboxane by cyclooxygenase inhibition rather than lipoxygenase. Studies show that using garlic supplements dramatically lowers platelet aggregation. It also reduces the epinephrine-induced platelet aggregation. It is advised to cease taking garlic one week before any surgical procedure[1,53].

Anti-Ulcer effect

Allicin (800 mg/day) was used to treat H. pylori infection for 14 days, although none of the patients had their illness cleared. On the other hand, treating H. pylori with 4.2 mg of allicin daily may be successful[54]. Due to their low cost and widespread assumption that natural goods have few if any, side effects, medicines made from plants have played a significant role in the health of both ancient and modern societies[1, 54].

Immunity Booster

Garlic contains a lot of sulfur-containing amino acids and other substances that tend to stimulate the immune system's function. It is one of the amazing

immune system's conductors, activating macrophages or killer cells to promote immunological function[55,56]. We are assaulted daily by poor nutrition, cigarette smoke, physical harm, stress, and chemical pollution. Garlic is needed as a supplement because of the extreme stress that our immune systems endure. Its exceptional germanium content alone provides good immunological activation. Garlic also includes thiamine, sulfur, niacin, phosphorus, and selenium in addition to germanium [57,58].

Anti-Parkinson effect

In various Parkinson's disease (PD) models, garlic (*Allium sativum*), which is renowned across the world for its flavor- and taste-enhancing qualities, has demonstrated preventive action[2]. Garlic has a variety of chemical components, mostly organosulfur compounds[59, 60], which have been demonstrated to have anti-Parkinson effects by focusing on oxidativestress, mitochondrial dysfunction, and neuroinflammation-related signaling.

Anti –Depressive effect

In rats with diabetes caused by streptozotocin (STZ), the effects of garlic on behaviors associated with anxiety, sadness, and brain oxidative indicators were investigated[61]. For ten days, animals were given garlic homogenate at doses of 0.1, 0.25, and 0.5 g/kg. This study's conclusion demonstrated that garlic reduces anxiety and depressive symptoms in diabetic rats, presumably by reducing oxidative stress in the brain[61,62].

Improvement in Metabolic Syndrome

A group of metabolic diseases known as metabolic syndrome include abdominal obesity, hypertension, atherogenic dyslipidemia, prothrombotic, and proinflammatory conditions. Patients with type 2 diabetes mellitus and cardiovascular disease have an increased risk of metabolic syndrome by about a factor of five and two, respectively. In this context, consuming 100 mg of raw, crushed garlic twice daily for four weeks dramatically reduced many metabolic syndrome risk indicators, such as blood pressure, triglyceride levels, and fasting blood glucose, and improved serum high-density lipoprotein cholesterol[63]. In addition, a double-blind, placebo-controlled study found that treatment with the garlic tablet Allicor at a dose of 300 mg twice daily for four weeks along with or in combination with sulfonylurea medications resulted in excellent metabolic control by lowering fasting blood glucose, serum fructosamine, and serum triglyceride levels in patients with type 2 diabetes mellitus, as well as lowering cardiovascular risk. Additionally, giving a garlic clove to type 2 diabetes individuals for 30 days decreased blood glucose and lipid metabolism and decreased serum lipids like cholesterol, TG, and LDL while increasing HDL fraction. Similar to this, giving diabetic patients 100 mg of garlic daily for five months and 300 mg twice daily for 24weeks reduced blood sugar, cholesterol, and TG [64].

Another study found that aged garlic extract (AGE) enhanced plasma adiponectin levels in patients without causing any negative side effects, reducing the risk factors of metabolic syndrome at a dose of 1.2 g per day for 24 weeks[65]. After consuming 2.4 g of AGE daily, low attenuation plaque in coronary arteries of patients with metabolic syndrome

was consequently reduced, indicating the anti-diabetic, anti-lipidic, and antioxidant characteristics of AGE. 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[66]. Garlic has been found a more potent anti-diabetic agent than glibenclamide, when comparing the effects of the two drugs [67,68].

Treatment of Osteoarthritis

Adipocytokines, resistin, and proinflammatory indicators play a specific role in the etiology of osteoarthritis (OA), a widespread degenerative disease of the bone joints that is associated with chronic and incapacitating pain [69]. After 12 weeks of treatment, a 1g/day dosage of garlic has been proven to be beneficial in alleviating symptoms in overweight or obese women with knee osteoarthritis.

Additionally, taking a garlic tablet twice a day for 12 weeks had analgesic and anti-inflammatory effects by lowering serum resistance and TNF- concentrations and the degree of pain in obese or overweight women with knee OA[70].Another randomized clinical trial revealed that garlic tablet acts as an antioxidant in postmenopausal osteoporotic women. In this study, a significant decrease in advanced oxidation protein products and plasma protein carbonyl plasma levels and a concomitant increase in TAC, as well as a reduction of oxidative stress and osteoporosis, were found after administration of garlic tablets at a dosage of 2 tablets (equivalent 2g fresh garlic) per day for 12 months [71].

Skin Illness

The use of garlic in traditional and alternative medicine dates back many years, and numerous clinical research studies have shown that it is effective in treating symptoms related to warts, denture stomatitis, venous ulcers, and skin wounds[72-74]. In a preclinical trial, after six days of treatment, aged garlic extract demonstrated dose-dependent wound healing capability[74].

Therefore, garlic is a crucial Indian spice or medicinal plant that plays an important role in the health benefits. This review compiles the various pharmacological effects of it and its other components and may provide a compendium of enriched information on garlic. Table 2 also helps to explain the biological role of garlic with different parameters.

Table 2. Table depicting biological properties of compounds isolated from *Allium sativum.*

Compound	Concentration used	Biological property	Employed	Response	Reference
Allicin	10-20 µM	Antioxidant	Cultured endothelial cells	Increased cellular glutathione levels	[75]Horev-Azaria et al., 2009.

Diallyl disulfide (DADS)	100 µM	Protection against liver injury	Human liver cell LO2	Activation of HO-1/ Nrf-2 pathway	[76]Zeng et al., 2013
Diallyl trisulfide (DATS)	10 µM	Protection against Apoptosis	H9c2 cells	Upregulation of the PI3K/Akt/Nrf2 pathway	[77]Tsai et al., 2013
aged garlic extract (AGE)	4mg/ml	Antioxidant	human umbilical vein endothelial cells	activation of the Nrf2-ARE signaling pathway	[78]Hiramatsu et al., 2016
S-allylcysteine (SAC)	25 mg/kg BW (i.p)	Reno-protective	male adult Wistar rats	Scavenge ROS and increase the activity of antioxidant enzymes (CAT, GPx, and GR)	[79]Gómez-Sierra et al., 2014
S-allylcysteine (SAC)	50 µM	neuroprotective effect	Primary cortical neuron cultures	activation of the Nrf2 antioxidant	[80]Shi et al., 2016
Garlic (whole clove)	2 g (oral)	Anti-viral Anti-proliferative	Normal Human Volunteers	stimulated synthesis of NO maintain IFN-α	[81]Bhattacharyya et al., 2007
DAS and DADS	DADS 200 µM DATS 20 µM	Anti-Artherosclerosis	Human Blood samples	Restore NOS–caveolin complex formation and PKB-dependent eNOS activation	[82]Lei et al., 2010

Conclusion

Since ancient times, medicinal plants have been utilized to make traditional remedies, spices, and other food items. In many different cultures, garlic has a long history of use in both the prevention and treatment of disease. The physiologically active components of the plant are sulfur-containing phytoconstituents including alliin, allicin, ajoenes, vinyldithiins, and flavonoids that are responsible for its pharmacological properties. People have been aware of the healing powers of garlic since at least 5,000 years ago. Thus, it is recommended to include garlic in the diet to treat a variety of illnesses and lengthen your life.

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