Allium sativum, a potential phytopharmacological source of natural medicine for better health

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GSC Advanced Research and Reviews, 2021, 06(03), 202–232

Publication history: Received on 07 February 2021; revised on 13 March 2021; accepted on 15 March 2021

Article DOI: https://doi.org/10.30574/gscarr.2021.6.3.0049

Abstract

Allium sativum, is a perennial flowering bulb which has been consumed worldwide as a functional food and known from thousands of years for its medicinal and culinary properties. Therapeutic potential of garlic is attributed to presence of its vital phytoconstituents. In present review, a complete therapeutic profile of drug is summarized by discussing its potential benefits highlighting the bioactive constituents. Phytoconstituents of crude drugs are used as antiviral, antioxidant, anti-inflammatory, antibacterial, antifungal, immunomodulatory, cardioprotective, anticancer, hepatoprotective, anti-diabetic, anti-obesity, neuroprotective, etc. Thus, it could conclude that garlic is one of the superior natural sources of bioactive compounds and has promising applications in the development of functional foods and nutraceuticals to improve health, and to prevent chronic diseases in the human.

Keywords: Allium sativum; Phytochemistry; Phytoconstituents; Pharmacological Activities

1. Introduction

Since more than five thousand years, medicinal plants have been widely used as food supplements, condiments, prophylactic agents and as therapeutic agents in the treatment various diseases and disorders of human beings and animals. Without medicinal plants, we cannot imagine the existence of human life [1]. Even today in 21st century, the livelihood of tribal people are depend on daily use of plants as food or as medicine. Herbal plants wholly or parts thereof are commonly used in cooking. Along with vegetables, medicinal plants such as Allium sativum (garlic), Allium cepa (onion), Elettaria cardamomum (cardamom), Cuminum cyminum (cumin), Myristica fragrans (nutmeg), Piper nigrum (black pepper), Madhuca indica etc are also being used in the kitchen [2-7].

Almost 25 centuries ago, Hippocrates, father of medicine, said that let food be thy medicine and let medicine be thy food. Supporting this statement, Hippocrates prescribed garlic for a variety of conditions. In the light of COVID-19 situation, WHO encouraging the people across the world to use medicinal plants. Some of the medicinal plants that are commonly used are Withania somnifera (ashwagandha), Capsicum annuum (capsicum), Hypericum perforatum (St. John’s wort), Aloe barbadensis (Aloe vera), Oroxylum indicum, etc [8-16].

Allium sativum (Fig. 1) known by its common name Garlic has been used as condiment during cooking of foods. Garlic has become common ingredient of kitchen in India and Indian subcontinental countries. cousins’ as potential health benefits and food properties of Garlic [17,18]. It is one of the earliest examples of herb effective for the treatment of various diseases and maintenance of general health. It was found in Egyptian and ancient Greek temples. Therapeutic
applications of garlic have been recorded in ancient medical texts from Egypt, Greece, Rome, China and India. Garlic was administered to provide strength and increase work capacity for labourers in many cultures [19]. Garlic was consumed to provide strength and increase work capacity for labourers in many cultures. Perhaps, it was given as one of the earliest “performance enhancing” agents to the original Olympic athletes in Greece [20]. Avicenna, a Persian physician-philosopher wrote in his book Canon of Medicine that the garlic for the treatment of a wide variety of ailments including arthritis, snake and insect bites, parasites, chronic cough, and as antibiotic for infectious diseases [21].

![Garlic bulb with petals](image)

Figure 1 Allium sativum (garlic) bulb with petals

Clinically, garlic has been investigated for a variety of indications, namely, hypertension, hypercholesterolemia, diabetes and for the prevention of arteriosclerosis and cancer. Researchers have increasingly focused on black garlic, a processed garlic product with increased polyphenol and flavonoid contents, as well as better antioxidant properties, compared to the fresh garlic [22].

### 2. Potential bioactive compounds

Medicinal properties of the herb are attributed to their active chemical compounds (ACC). These compounds may be volatile or non-volatile. There are various analytical techniques by which active chemical compounds are determined. These methods can also be used for analysis of ACC in pharmaceutical formulations including ayurvedic products [23-42]. In order to justify the writing of Galen from second century “Garlic as the rustic’s theriac” means garlic possesses potential to cure all ailments, we searched high quality studies published in renowned journals, reviewed the therapeutic functions of garlic and the bioactive components responsible for it.

Bioactive compounds of garlic include organosulfur compounds, saponins, phenolic acids, flavonoids and polysaccharides [43-46]. It contains at least thirty three sulfur compounds, several enzymes and the minerals germanium, calcium, copper, iron, potassium, magnesium, selenium and zinc; vitamins A, B1 and C, fiber and water. Seventeen amino acids are found in garlic, lysine, histidine, arginine, aspartic acid threonine, swine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan and phenylalanine [47]. The major active components of garlic are organosulfur compounds which includes diallyl thiosulfate [allicin], diallyl sulfide [DAS], diallyl disulfide [DADS], diallyl trisulfide [DATS], E/Z-ajoene, S-allyl-cysteine [SAC] and S-allyl-cysteine sulfoxide [alliin] [48-52].

### 3. Pharmacological activities

Hundreds of successful clinical investigations have been carried out for estimation of broad-spectrum therapeutic benefits of garlic. Contemporary investigations are going on to confirm many of the beliefs of ancient cultures regarding garlic, defining mechanisms of action and exploring potential of garlic for disease prevention and treatment.

#### 3.1. Effects on cardiovascular diseases

Garlic has history of being used for treatment of cardiovascular diseases. A scientific literature review shows garlic consumption has significant effect on lowering blood pressure, prevention of atherosclerosis, reduction of serum cholesterol and triglyceride, inhibition of platelet aggregation and increasing fibrinolytic activity [55]. Garlic lower hypertension by reducing oxidative stress, increasing the production of nitric oxide and hydrogen sulphide and inhibiting the angiotensin converting enzyme [56-61]. In-vivo animal experiments on wistar rats demonstrated that garlic significantly alleviated isoproterenol induced myocardial necrosis [62]. In another study, when garlic powder was
given in addition to hydrochlorothiazide plus triamterene baseline therapy showed a mean reduction of systolic blood pressure by 10-11 mmHg and diastolic blood pressure by 6-8 mmHg versus placebo [63,64].

It has been demonstrated that the intake of garlic powder can effectively reduce blood pressure, total cholesterol, low-density lipoprotein cholesterol and other risk factors related to cardiovascular diseases [65]. Preparations of garlic including garlic paste, garlic oil, allicin, and ajoene have been found to significantly reduce cholesterol biosynthesis in rat hepatocytes via inhibiting 3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase and 14-a-demethylase [66,67]. In rabbits that were fed with a high-cholesterol diet and supplemented with garlic or allicin, it was found that hypercholesterolemia was significantly inhibited by 50% and showed a decrease in tissue cholesterol and low-density lipid [LDL] concentrations and raised high density lipid [HDL] concentrations along with reduced atheromatous changes [68]. It was reported that raw garlic possibly works via its active metabolite allicin action on coronary endothelial function and vaso reactivity [69].

The electrophysiological correlation to vasodilatation in human coronary arteries under the influence of garlic extract showed decrease in the isometric wall tension. Allicin and ajoene hyperpolarized the cell membrane and relaxed the vascular strips in a concentration dependent manner and suggested that garlic extract and its compounds can be classified as phytopharmacological K+ channel openers [70]. The studies have revealed that garlic might reduce platelet aggregation so that the patients who are on treatment of anticoagulant medication need to be warned about consuming garlic [71,72].

3.2. Antioxidant activity

Garlic and its active ingredients such as phenols and saponins have certain antioxidant effects. Whole garlic and aged garlic extract [AGE] exhibit direct antioxidant effects and enhance the serum levels of two antioxidant enzymes, catalase and glutathione peroxidase [73]. Garlic extract has shown efficiency in removal of hydroxyl radicals in a dose dependent fashion, but their effectiveness was reduced about 10% by heating to 100°C for 20 min. Other garlic constituents, such as S-allyl cysteine, also confirmed significant antioxidant effects. The sulfur compounds found in fresh garlic appear to be nearly 1000 times more potent as antioxidants than crude and aged garlic extract. Garlic was able to reduce the radicals present in cigarette smoke [74]. A study evaluated the antioxidant capacities of both raw and cooked garlic, and found that the raw garlic exhibited stronger antioxidant activity. Stir-fried garlic was also shown to have stronger antioxidant capacities indicating that the processing could affect the antioxidant property of garlic [75]. Different processing methods also affected the antioxidant activity of garlic. Usually, raw garlic had a stronger antioxidant activity than cooked garlic and the antioxidant activity of fermented garlic, such as black garlic, was stronger than that of crude garlic.

3.3. Antimicrobial activity

Garlic shows broad spectrum antimicrobial activities against many species of bacteria, viruses, parasites, protozoan and fungi [76]. Antimicrobial studies of essential oil obtained by steam distillation of garlic bulbs were found rich in diallyl disulphide, diallyl trisulphide and diallyl tetrasulphide and possesses potent antimicrobial activities, it inhibits the growth of Gram positive and Gram negative bacteria, such as *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Enterobacter*, *Escherichia*, *Klebsiella*, *Lactobacillus*, *Pseudomonas*, *Shigella*, *Salmonella*, *Proteus*, and *Helicobacter pylori* [77]. Garlic oil also showed antibacterial activities against *Staphylococcus aureus*, *Staphylococcus albus*, *Staphylococcus saprophyticus*, *Shigella flexneri*, *Shigella sonnei*, *Salmonella typhi* and *Escherichia coli* [78].

In a study of garlic oil with *Penicillium funiculosum* as a model strain inhibited the fungus probably by penetrating into hyphae cells and even their organelles, destroying the cell structure and inducing the leakage of cytoplasm and macromolecules [79]. Another study of garlic oil for its antifungal activity revealed that it could penetrate the cellular membrane of *C. albicans* as well as the membranes of organelles such as the mitochondria, resulting in organelle destruction and ultimately cell death [80]. Garlic might be promising in treatment of fungal diseases from important pathogenic genera *Candida*, *Malassezia* and the *Dermatophytes* and have shown to inhibit growth of fungal diseases as equally as the drug ketoconazole [81]. Allitrinin possesses anti-human cytomegalovirus activity [HCMV] activity and the mechanism is associated with suppression of i.e. gene transcription [82]. The above studies summarized that bioactive components present in garlic destroy the cell structure and the metabolic process of bacterial and fungal cells.

3.4. Anti-inflammatory activity

Garlic has been described as an anti-inflammatory agent of plant origin. Investigation revealed anti-inflammatory activity of garlic is equivalent to indomethacin [83]. Garlic was also recommended to be used as an adjuvant in various inflammatory disorders. A study with carrageein induced paw-edema animal model has shown anti-inflammatory
activity of garlic is as effective as piroxicam [84]. In another study, the ethyl linoleate in garlic reduced the production of nitric oxide [NO] and prostaglandin E-2 by down regulating the expression of inducible NO synthase [iNOS] and cyclooxygenase-2 [COX2] in lipopolysaccharide stimulated RAW 264.7 macrophages [85]. Garlic supplements are effective in osteoarthritis in obese or overweight patients as it reduces the pro-inflammatory adipocytokine and resistin [86]. Many studies have shown that anti-inflammatory effects of garlic are associated with inhibition of inflammatory mediators.

3.5. Immunomodulatory effects

In wake of novel viruses like Covid-19 and Ebola, boosting immunity is receiving new attention. Garlic has been suggested as a promising candidate for maintaining the homeostasis of the immune system. Sulfur containing amino acids and polysaccharides present in garlic are the main immune-modulating components [87]. A randomized, double-blind, placebo-controlled parallel intervention revealed that aged garlic extract has potential to improve both natural killer [NK] and γδ-T cell function and can reduce the severity of cold and flu symptoms [88]. In a study, the combination of garlic oil and levamisole have shown additive up regulatory effect on immunity by stimulating T-helper 1 and T-helper 2 [89]. AGE consumption was found to reduce the occurrence and severity of the cold and flu and improve the immune system functions in humans [90].

3.6. Antineoplastic activity

Cancer or malignant neoplasm is a broad group of diseases involving unregulated cell growth. Cancer is a primary cause of death in the world and accounts for approximately 8.8 million deaths per year [91]. Many herbs, fruits and rhizomes like berries, cruciferous vegetables, tomatoes, garlic and ginger are reported to have anticancer properties [92,93,94]. Some photochemical present in garlic are capable of selective killing of cancer cells[95]. A study revealed that garlic and its sulfur compounds have potential to decrease or abolish the activation of carcinogens, thus reducing the risk of cancer [96]. Carcinogenic nitrosamines produced during cooking are reported to be inhibited by organic allyl sulfides present in garlic [97,98]. Moreover, garlic allyl sulfides have shown activity to block DNA alkylation, which is a preliminary step of nitrosamine carcinogenesis. Biactive compounds present in garlic are capable to arrest cell cycle at the G0/G1 phase and G2/M phases in cancer cells, increase the expression of tumor suppressor genes, inhibit the angiogenesis process, induction of apoptosis and modulation of various other genetic pathways [99]. A case-control study on Chinese population in Taiyuan revealed raw garlic consumption is associated with reduced risk of lung cancer [100].

A study found that ethanol-based garlic extract [GE] suppressed the growth of multiple myeloma and prostate cancer cells in vitro. GE influenced hundreds of proteins involved in cellular signaling, including changes in vital cell signaling cascades regulating proliferation, apoptosis, and the cellular redox balance. The growth of mammary tumor cells was also suppressed in vivo by GE by increasing stress on the endoplasmic reticulum [101]. The intake of raw and crushed garlic upregulates apoptotic related genes and proto-oncogene which stimulates expression of genes related to immunity and cancer in the blood of human beings [102]. A study revealed that cisplatin induced renal, ultrastructural and biochemical changes such as hemorrhaging, glomerular atrophy, tubular necrosis and degeneration in adult male rats were improved by AGE therapy [103].

Thus, bioactive active components of garlic act as prophylactic to prevent and manage different malignancies. Antineoplastic mechanism of garlic includes regulation of carcinogen metabolism, inhibition of cell growth and proliferation, induction of apoptosis, suppression of angiogenesis and inhibition of invasion and migration. Garlic has shown potential to prevent or cure negative effects of antineoplastic therapies.

3.7. Hepatoprotective activity

Multiple studies have revealed that garlic has hepatoprotective effects [104,105,106]. In a study revealed reduction in lipid level by garlic oil [150 mg/kg bw/d] in ethanol and high lipid diet feeding induced significant fat accumulation in rat liver [107]. Another study have evaluated the therapeutic effects of raw garlic on alcoholic liver disease patients. In that study, 20 alcoholic patients were enrolled and received about 2.4 g raw garlic bulbs daily in the morning for 45 days. Results showed that raw garlic alleviated liver damage indicated by the decline of serum ALT, AST, ALP, gamma glutamyl transferase [GGT] and LDH activities [108]. In an in vitro study, the black garlic extract reduced the damage of tert-butyl hydroperoxide in rat clone-9 hepatocytes by inhibiting apoptosis, lipid peroxidation, oxidative stress, and inflammation [109].

In another study, garlic attenuated liver damage induced by alloxan in rats and improved the biochemical plasma factors of hepatic functions, such as urea, creatinine, aspartate transaminase, and alanine transaminase [110]. Also, it was reported that the active compounds such as DAS, DADS, and S-methyl-l-cysteine present in garlic, could prevent and
treat liver damage, such as acute and chronic ethanol-induced liver damage [111]. Compared with unfermented garlic extract, the fermented garlic extract by Lactobacillus plantarum was able to more effectively reduce liver lipid levels and improve hepatic steatosis in mice [112]. A study revealed that garlic with high dose has the potential ability to induce liver damage and low doses are safe doses of garlic [113]. The above studies revealed that garlic can effectively alleviate acute or chronic liver injury, but the side effects of excessive consumption of garlic also need to be considered. It is necessary to evaluate the safe dose and duration of garlic usage in humans.

3.8. Gastrointestinal tract effects

Garlic has been reported to have protective effects on digestive disorders. Raw garlic has reported to have anti-bacterial effects against \textit{H. pylori} residing in the stomach and may be prescribed along with routine drugs for the treatment of gastric \textit{H. pylori} infection [114]. Extract of black garlic effectively promoted gastrointestinal motility by increasing 5-HT\textsubscript{4} content effectively which stimulated the gastrointestinal peristalsis and enhanced its gastrointestinal tract emptying and promoted defecation [115]. Both the garlic and silymarin have shown the hepatoprotective effect against the isoniazid induced hepatotoxicity in rats [116]. AGE supplementation reversed the hepatic injury through its antioxidant activity in hepatotoxicity induced by ethephon in Wistar albino rat [117]. AGE was effective in preventing indomethacin-induced ulcers in rats by reducing oxidative stress and elevating prostaglandin E-2, glutathione, and NO in gastric tissue [118]. Overall, bioactive compounds present in garlic shows antibacterial effect against \textit{H. pylori}, improve gastrointestinal functions and alleviate colitis and gastric ulcers by reducing oxidative stress and inhibiting inflammation.

3.9. Anti-diabetic activity

Garlic is called as insulin secretagogue and insulin sensitizer based on its antioxidative, anti-inflammatory and antiglycative properties which are responsible for its role in preventing diabetes progression and the development of diabetes related complications [119]. Aqueous extract of garlic exhibited promising hypoglycemic and hypolipidemic activity in alloxan-induced diabetic rats [120]. A study revealed that oral administrations of the garlic extract significantly decreased serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels, while increased serum insulin in diabetic rats but not in normal rats [121]. AGE exhibits a dose-dependent ameliorative action on indicators of diabetes in streptozotocin-induced diabetic rats [122].

Garlic decreased pancreatic \(\beta\)-cell damage, hepatic injury and showed more promising effect in terms of reducing oxidative stress and pathological changes when compared to resveratrol and metformin groups [123]. In a study of streptozotocin induced diabetic retinopathy in rats, administration of an extract of raw garlic by gastric gavage for seven weeks showed marked decrease in body weight, significant increase in blood glucose and glycated hemoglobin levels and improved effects on the retina [124]. A lack of scientific evidence from human studies and inconsistent data from animal studies warrant large scale clinical studies with diabetic patients to confirm the usefulness of garlic in the treatment and prevention of diabetes.

3.10. Anti-obesity activity

Garlic and its constituents have been shown to possess potent regulatory activities on lipid metabolism. Garlic oil suppressed body weight gain and white adipose tissue mass in the rat model of high-fat diet-induced obesity by increasing UCP1 expression and by enhancing fat oxidation and energy expenditure [125]. Garlic oil has shown to counteract the influence of a high-fat diet on the weight of body and adipose tissue in hyperlipidemia rats [126]. Methanolic extract of black garlic was found to reduce the weight of rats fed with a high-fat diet. This treatment regulated lipid metabolism by up-regulating the expression of AMPK, fork head box protein O1, perilipin, and adiponectin in the adipose tissue of the rats and down-regulating the cluster of differentiation 36 [CD36], plasminogen activator inhibitor 1, resistin, and TNF-\(\alpha\) [127]. From studies it was seen that fermented garlic products have certain positive effects on obesity by inhibiting lipogenesis and regulating lipid metabolism.

3.11. Wound healing activity

Several animal studies have shown that garlic extracts increase the rate of wound healing and decrease the rate of infection. A study on rats showed that allicin acted on fibroblasts and treated the wounded site faster compared to Vaseline treated site. [128]. Another study on the chicken dorsum skin excision wound assay to investigate the influence of different concentrations of aged garlic solution [AGS] on wound healing revealed that a very highly significant increase in angiogenesis was observed among all groups treated with aged garlic solution and no significant change was observed among control and skin lotion-treated groups [129]. Overall, allicin appear to be the main wound healing components in garlic.
3.12. Neuroprotection

Investigations have revealed that garlic contains organic sulfur compounds which are effective in treatment of neurological diseases. Active component N-α-[1-deoxy-D-fructos-1-yl]-L-arginine [FruArg] from AGE alleviated neuroinflammation by inhibiting the production of NO and regulating the expression of multiple protein targets related to oxidative stress in lipopolysaccharide activated murine BV-2 microglial cells [130]. S-allyl-L-cysteine [SAC] exerts significant protective effects against endoplasmic reticulum stress-induced neurotoxicity in cultured rat hippocampal neurons and organotypic hippocampal slice cultures [131]. SAC and FruArg are prototype for developing novel therapeutic drugs for neurological diseases.

3.13. Renal Protection

Garlic was reported to possess renal protective effect [132]. A study revealed that garlic has regenerative potential after tubular injury induced by gentamicin in animal models [133]. In another gentamicin induced nephrotoxicity study in rats, administration of pulverized garlic supplemented diet showed nephron protective effect [134]. The aqueous extract of garlic was shown to reduce the oxidative stress in the kidneys of diabetic rats [135]. Another study revealed that allicin may play a role in chronic kidney disease, reducing hypertension, oxidative stress and improving renal dysfunction. Silico analysis suggested that allicin could have acted on angiotensin II receptor type 1. Allicin showed antihypertensive, antioxidant, and nephroprotective effects. The beneficial effects showed by allicin are similar, or even better, than those of losartan [136].

4. Conclusion

Therapeutic potential of garlic in treatment of diseases and preventing or reducing associated symptoms have been recognized worldwide. Microorganisms are getting resistant to allopathic antimicrobial medicines because of their vast use in treatment; however, intake of garlic is able to provide some level of anti-microbial activities and can boost the immune system. More clinical studies should be conducted to illustrate mechanisms of actions of the bioactive compounds present in garlic. In addition, the effects of the processing, such as fermentation and heat, on garlic should be further studied because they could impact the biological functions and safety of garlic. Furthermore, more clinic trials should be carried out to confirm the health benefits of garlic on humans, and special attention should be paid to the side effects and safety of garlic.

Compliance with ethical standards

Acknowledgments

Authors are thankful to Shri. Yogendraji Gode, President, IBSSs Dr. Rajendra Gode Institute of Pharmacy, Amravati and Dr.Rajendra Gode College of Pharmacy, Amravati for providing necessary facility to undertake this work.

Disclosure of conflict of interest

The author declares no conflict of interest.

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