



Review Article

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Therapeutic Effects of Garlic: A Review

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Abstract

The therapeutic use of plants can be traced back to history as different cultures from time immemorial have been using plants and plant product for the prevention and treatment of diseases. Garlic, a plant of genus *Allium* has long outlived its years of being used just as a food spice. Research has illuminated its broad- spectrum of therapeutic properties against microbial activity. The anti- fungal potency of garlic has been established given the rise in resistance for synthetic pharmaceuticals. Due to the wide range of compounds inherent in Garlic like allicin, ajoene and s-allyl cysteine, scientist has suggested its potency in the treatment of diabetes, immune depression, cardiovascular diseases and more. However, the mechanism of action of some of these constituents of garlic has not been established, creating a niche that many scientists are working tirelessly to fill.

Keywords: Anti-Fungal potency; Synthetic pharmaceuticals; Microbial activity; Immune depression; Niche; Allicin; Ajoene; S-allyl cysteine

Introduction

Garlic (*Allium sativum*) is a perennial bulb that belongs to the genus, *Allium* and is closely related to onion, shallot, leek, chive, [1]. Natural products of animals, plants and microbial sources have been used by many cultures in ancient times including Babylonians, Chinese, Egyptians, Greeks, Hindus, Phoenicians, Romans, and Vikings, either in the pure forms or crude extracts to treat many diseases such as flatulence, intestinal disorders, respiratory infections, skin diseases, wounds, and many other ailments [2].

Garlic was in use at the beginning of recorded history and was found in Egyptian pyramids and ancient Greek temples. Its usefulness was known to ancient Egyptians, both as food flavoring and traditional medicine. In addition, garlic is one of the earliest documented examples of plants employed for treatment of disease and maintenance of health. Medical applications of garlic have been documented in ancient medical texts from Egypt, Greece, Rome, China and India. Almost 25 centuries ago, Hippocrates, the Father of Medicine, stated "let food be thy medicine and let medicine be thy food". Supporting this statement, Hippocrates prescribed garlic for a variety of conditions. Garlic was administered to provide strength and increase work capacity for labourers in many cultures. It was given as perhaps one of the earliest "performance enhancing" agents to the original Olympic athletes in Greece.

The therapeutic and preventive roles of garlic have been demonstrated through appreciable epidemiologic evidence. Several experimental and clinical investigations suggest many favorable

effects of garlic and its preparations. These effects have been largely attributed to

- reduction of risk factors for cardiovascular diseases,
- reduction of cancer risk,
- antioxidant effect,
- antimicrobial effect, and
- enhancement of detoxification foreign compound and hepatoprotection [3,4].

Today, the discovery of effective natural products and alternative medicines which is able to detoxify environmental toxicants is an important scientific issue that is popular amongst people concerned about potential adverse effects of conventional medicines. Garlic (*Allium sativum* L) is one of those plants that were seriously investigated over several years and used as a prophylactic as well as a therapeutic medicinal plant [5], known for its anticancer, anti-diabetic, antioxidant and immune modulation activities. In this review, a survey on current experimental as well as clinical state of knowledge about the preventive and therapeutic effects of garlic in different diseases is given.

Antimicrobial effects

Pasteur (1958), first described the anti- microbial properties of garlic and since then, many researches have demonstrated the effectiveness and broad-spectrum antimicrobial activity of garlic

against many species of bacteria, viruses, parasites, protozoan and fungi [6]. According to [7,8] garlic, amongst many other medicinal plants, has an antimicrobial property which protects the host from other pathogens highlighting the importance of search for natural antimicrobial drugs. Previously conducted researches by Tsao and Yin [9], confirmed that garlic is not only effective against Gram positive and Gram-negative bacteria but also possess antiviral and antifungal activities.

Antibacterial effects

According to Nervi [10] more recent studies have shown garlic to be effective against a group of gram-positive, gram-negative, and acid-fast bacteria. Garlic extract 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 [9].

Nervi [10] also documented that garlic exerts a differential inhibition between beneficial intestinal microflora and potentially harmful enterobacteria [11]. Its antibacterial activity is mainly due to the presence of allicin produced by the enzymatic activity of allinase on alliin. Allicin is considered to be the most potent antibacterial agent in crushed garlic extracts, but it can be unstable, breaking down within 16 h at 23°C [12]. Cysteine and glutathione counteract the thiolation activity of allicin. It is thought that allicin modifies the sulfhydryl groups on the enzymes of the TN1546 transposon, which encodes vancomycin resistance, enhancing susceptibility to vancomycin [13].

Antifungi effects

Ajoene is an active compound found in garlic which plays a great role as topical antifungal agent [14,15]. According to Shams Ghahfarokhi, et al. [16], garlic has been shown to inhibit 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 by Lemar, et al. [17], delineates the use of intravenous garlic to treat a potentially fatal and rare fungal infection of the brain called *Cryptococcus meningitis*. In the report, the Chinese compared the effectiveness of the garlic with standard medical treatment which involved a very toxic antibiotic called Amphotericin-B. The study revealed that, intravenous garlic was more effective than the drug and was not toxic regardless of its dosage. Lanzotti, et al. [18] also reported that garlic exhibited antifungal effects on two species, the air-borne pathogen *Botrytis cinerea* and *Trichoderma harzianum*. Greater satisfaction with the use of garlic rather than nystatin was reported by the patients with denture stomatitis [19].

Antiviral effects

Very little work has been done to investigate the antiviral properties of garlic. There are insufficient clinical trials regarding the effects of garlic in preventing or treating the common cold. A

single trial suggested that garlic may prevent occurrences of the common cold, but more studies are needed to validate this finding. This trial randomly assigned 146 participants to either a daily garlic supplement (with 180 mg of allicin content) or a placebo for 12 weeks.

An investigation by Lissiman, et al. [20] revealed 24 occurrences of the common cold in the garlic group compared with 65 in the placebo group, resulting in fewer days of illness in the garlic group compared with the placebo group. However, claims of effectiveness of garlic on common cold appear to rely largely on poor quality evidence.

Anti-protozoal properties

Several studies have shown that the extract was effective against a host of protozoa including *Candida albicans* [21], *Scedosporium prolificans* [15], *tinea pedis* [14], *Opalina ranarum*, *Balantidium* entozoon, *Entamoeba histolytica*, *Trypanosomes*, *Leishmania*, *Leptomonas*, and *Crithidia* [10].

Due to the occurrence of unpleasant side effects and increasing resistance to the synthetic pharmaceuticals, garlic was recommended for the treatment of giardiasis. Inhibitory activity of garlic on giardia was noted with crude extract at 25 µg/mL and the lethal dosage was established as approximately 50 µg/mL. Encouraged by these results, a clinical trial was carried out on patients that had giardiasis [22]. Garlic was established as an anti-giardial, removing the symptoms from all patients within 24 h and completely removing any indication of giardiasis from the stool within 72 h at a dosage of 1 mg/mL twice daily aqueous extract or 0.6 mg/mL commercially prepared garlic capsules. No in vitro calculations were possible, as the workers could not culture the protozoa in vitro. It was suggested that allicin, ajoene, and organosulfides from garlic are effective antiprotozoal compounds [21].

Effect of garlic on hypertension

Garlic has probably been most popularized as a complementary therapy for blood pressure control. A recent study conducted in vitro by Benavides has confirmed that, the vasoactive ability of garlic sulfur compounds whereby red blood cells convert garlic organic polysulfides into hydrogen sulfide, a known endogenous cardio-protective vascular cell signaling molecule. Although, as of 2015, clinical research conducted by Rohner, et al. [23] to determine the possible effects of consuming garlic on hypertension has found no clear effect [24]. A 2016 meta-analysis by Sahebkar, et al. [25] indicated there was no effect of garlic consumption on blood levels of lipoprotein(a), a biomarker of atherosclerosis. Because garlic might reduce platelet aggregation, people taking anticoagulant medication are cautioned about consuming garlic [26,27].

Anticancer

Garlic preparations and their respective constituents have suggested possible cancer-preventive effects in many in vitro and in vivo studies conducted by Kyo, et al. [28]. One of the most prominent

actions of garlic is the prevention of the growth of cancer, due to a large number of potent bioactive compounds with anti-tumor properties, largely allylsulfide derivatives. The action of different garlic derivatives has been reported by Capasso, [29] to modulate immune response through a series of molecular mechanisms in carcinogenesis, such as DNA adduct formation, mutagenesis, cell proliferation and differentiation, scavenging of free radicals as well as angiogenesis. Garlic exhibits a variety of anti-tumor effects, including inhibition of tumor cell growth and chemo preventive effects. In both rodents and humans, garlic and its constituents have been found to inhibit the development of chemically induced tumors in the liver [30], colon [31], prostate etc. [32].

Garlic reduces the growth rate of cancer cells, with cell cycle blockade that occurs in the G2/M phase [29] and also the antioxidant effect of allicin in reducing the formation of carcinogenic compounds in the gastro-intestinal tract [33]. The risk of patients with prostate cancer is reduced by garlic and was found to be independent of body size, intake of other foods and total calorie intake and was more pronounced for men with localized prostate cancer than with advanced prostate cancer. Men in the higher of two intake categories of total *Allium* vegetables (>10.0 g/day) had a statistically significant lower risk of prostate cancer than those in the lowest category (<2.2 g/day) [32].

Borkowska, et al. [34] investigations on the anticancer activity of garlic both in vitro and in vivo has been shown to be due to the presence of Diallyl trisulfide (DATS), an organosulfur compound isolated from garlic. The cytotoxicity of DATS toward prostate epithelial cells is reduced as opposed to PC-3 cancer cell. DATS reduces mitosis in tumors by decreased histone deacetylase activity, increased acetylation of H3 and H4, inhibition of cell cycle progression, and decreased activity of pro-tumor markers (survivin, Bcl-2, c-Myc, mTOR, EGFR, VEGF) [35].

Certain components of garlic have been found to block covalent bond formation of carcinogens to DNA, stimulate degradation of carcinogens, have anti-oxidative and free radical scavenging properties, and modulate immune responses, cell proliferation, and apoptosis. Ajoene, a garlic stable oil soluble sulfur rich compound and garlic-derived natural compound has been shown to induce apoptosis in human leukemic cells via stimulation of peroxide production, activation of caspase-3-like and caspase-8 activity. Garlic promotes the effect of eicosapentaenoic acid, a breast cancer suppressor, and opposes the effect of linoleic acid, a breast cancer enhancer [36]. Furthermore, allicin is also responsible for the anti-proliferative effect of garlic derivatives on human colon cancer cells.

Anti-diabetes

Studies conducted by Ohaeri [37], have shown the effectiveness of garlic in reducing blood glucose level in diabetic animals such as alloxan-induced diabetes mellitus in rats and mice. Garlic significantly reduced serum total cholesterol and LDL cholesterol and moderately raised HDL cholesterol as compared with placebo in diabetic patients [38]. S-allyl cysteine, a bioactive component

derived from garlic, restored erectile function in diabetic rats by preventing reactive oxygen species formation through modulation of NADPH oxidase subunit expression [39].

Garlic extract was administered orally for 14 days in a study conducted by Eidi, et al. [40] to evaluate the level of serum glucose, total cholesterol, triglycerides, urea and uric acid, in normal and streptozotocin-induced diabetic mice. The result of the study showed a significant decrease ($p < 0.05$) in serum glucose, total cholesterol, triglycerides, urea, uric acid, while serum insulin level increased in diabetic mice, but not in normal mice. The anti-diabetic effect of garlic is mainly attributed to the presence of volatile sulfur compounds, such as alliin, allicin, diallyl disulfide, diallyl trisulfide, diallyl sulfide, S-allyl cysteine, ajoene, and allyl mercaptan. The reduction in insulin resistance has been reported by Padiya and Banerjee [41], to be due to the presence of garlic extract. However, although experimental studies demonstrated a clear hypoglycemic effect of garlic, the effect of garlic on human blood glucose is still controversial.

Immune modulation

With the arrival of frightening viral diseases like HIV/AIDS, boosting immunity system is receiving a new attention. Due to the absence of an effective cure to these types of diseases have, strengthening the body's ability to fight off infection has become even more important.

Garlic contains certain that promote an immune response to germs/antigen [28,42]. When garlic is chewed or crushed, the compound alliin turns into allicin the main active ingredient in garlic [43]. The distinctive smell and taste of garlic is because of the presence of sulphur in allicin. However, due to its instability, it is quickly converted to other sulphur-containing compounds believed to give garlic its therapeutic properties [42].

According to Nantz, et al. [44], garlic has abundant sulfur containing amino acids and other compounds that have been shown to boost the activity of the immune system against viruses such as the viruses that cause common cold. Furthermore, studies conducted by Josling [45], have shown that garlic can reduce the risk of becoming sick, as well as the duration of the illness. It can also reduce the severity of symptoms.

Effect of garlic on hepatotoxicity

Detoxification of substances is facilitated by the liver in the presence of glutathione. It has been hypothesized that garlic organo-sulfur compounds may protect the liver cells from some toxic agents by preventing glutathione depletion. For this reason, it has been demonstrated that garlic protects against acetaminophen-induced hepatotoxicity. An elevated damage of the liver's marker enzymes (aspartate transaminase and alanine aminotransferase) and reduction in plasma albumin level is revealed to have been associated to gentamycin. Studies conducted by Ademiluyi, et al. [46] have shown that the dietary inclusion of garlic powder protects rats against gentamycin-induced hepatotoxicity, improves antioxidant status, and modulates oxidative stress. In addition, Garlic extract

may reduce lipid peroxidation and enhance antioxidant defense system [47].

Antioxidant

The antioxidant property exhibited by whole garlic and aged garlic extract also enhances the serum levels of two antioxidant enzymes, catalase and glutathione peroxidase [48]. S-allyl cysteine, a component of garlic also confirmed significant antioxidant effects. The sulfur compounds 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 [49]. Furthermore, allicin being another component that is abundant in dried garlic and is formed when garlic is crushed. According to recent studies, allicin decomposes to form sulfenic acid, a potent antioxidant [50-56].

Adverse effect of garlic

The most common side effect of garlic is bad breath (halitosis) and body odor especially when raw form of the herbs are taken, this is because allyl methyl sulfide (AMS) absorbed into the blood during the metabolism of garlic-derived sulfur compounds; it travels from the blood to the lungs [1] (and from there to the mouth, causing bad breath) and skin, where it is released through pores. As such it is considered safe to ingest one to two cloves of raw garlic per day in adults. Rare garlic allergy has been attributed to the protein allinase, which has induced immunoglobulin E (IgE) mediated hypersensitivity responses from skin prick testing.

Conclusion

The consumption of garlic for its therapeutic potential in curing and preventing/reducing the symptoms of disease has proven to be of clinical importance throughout the world. However, due to the ever-growing resistance of microbes, intake of garlic is able to provide some level of anti-fungal, anti-microbial activities. As such, more studies need to be conducted to refine the use and efficacy of garlic.

Acknowledgment

None.

Conflict of Interest

No conflict of interest.

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