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A review on garlic (*Allium sativum* L.) as a functional food

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Abstract
Garlic (*Allium sativum* L.) botanically a member of the Lillaceae family and Allium genus, is considered to be rich in medicinal properties. The undamaged bulbs contain allin which will be enzymatically converted to allicin during cutting. Allicin, is the major bioactive compound found in garlic followed by other organosulfur compounds. Preparation of garlic extractions can be done in liquid form and solid form. The composition and bioactivity of the extraction depend on the strain, age, method of preparation and consumption method. When extracted and isolated, the bioactive compounds of garlic show a wide range of beneficial health effects to treat various infectious diseases, non-communicable diseases as well as metabolic and genetic disorders. An overview is provided on the numerous clinical and experimental investigations done on the reduction of LDL cholesterol level, cardiovascular disease, blood glucose levels by garlic derivative compounds. Furthermore, anti-carcinogenic effect, anti-microbial effect and antioxidant property of garlic are also reviewed.

Keywords: Allicin, antioxidant, cardiovascular, functional food, garlic, organosulfur compounds

1. Introduction
Functional foods have begun a new era in food technology with the increasing global health threats as well as with the lack of nutritional food sources. According to European researches, food products can only be considered functional if together with the basic nutritional impact it has beneficial effects on one or more functions of the human organism thus either improving the general and physical conditions or/and decreasing the risk of the evolution of diseases [1,2].
There are numerous natural foods with functional properties. Garlic is claimed as one of the important element in daily diet which also acts as a functional food. Garlic is a widely grown crop around the world with a need of plenty of sunlight. It is used directly as a food or as a seasoning or as a spice. It has a pungent odor due to the odorous sulfur compounds.
Plants of genus Allium are considered to have rich medicinal properties to prevent different non-communicable diseases, metabolic disorders as well as genetic disorders. From the genus Allium, the frequently used plant by humans is garlic (*Allium sativum L.*). Chemical constituents of garlic such as organosulfur compounds are responsible for the functional properties in garlic. The principle bioactive compound present in garlic is called "Allicin" which is in higher percentage in raw form of garlic. Different processing methods like crushing or chopping activate the allinase enzyme which will convert allin into its bioactive form allicin.
Garlic can be prepared in solid form and liquid form. Solid form can be used as dry powder or soft heated mass. Liquid form could be prepared as a water formulation, oil or an extraction using solvents like alcohol [3]. However, the composition and the effect of its bioactivity depend on the garlic strain, age, storage condition, method of processing and consumption [4].
An animal experiment was done using normal rats which were treated orally and intraperitoneally with raw and boiled aqueous extracts of garlic for 4 weeks and their serum levels of glucose, cholesterol, and triglycerides were measured. It was found out that the raw garlic had a profound effect in reducing the glucose, cholesterol, and triglyceride levels, whereas boiled garlic had little effect in controlling these parameters (Thomson *et al*., 2006) [5]. Therefore, different factors in processing can affect the bioactivity of garlic extracts. Undamaged garlic bulbs have S-allyl-L-cysteine sulfoxide (allin) and γ-glutamyl cysteine derivatives as the main compounds while steam distilled oils are rich in sulfide family compounds. Dried garlic powder is rich in allin and diallyl disulfides. Macerates (ground garlic) are enriched extractions with sulfide family compounds, dithiines, and (E–Z)-ajoene compounds. And soaked, sliced, aged garlic extract in ethanol solution contains S-allyl-L-cysteine (SAC) and S-allyl mercaptocysteine [6]. Garlic is being used since ancient history for different therapeutic effects.

It is said that in early Olympics in Greece the athletes were fed garlic to increase their stamina levels [7]. The ancient China and India have used garlic to help respiration and digestion as well as to treat parasitic infections [8]. Furthermore, it had been recommended to treat arthritis, toothache, chronic cough, constipation, parasitic infestation, snake and insect bites, gynecologic diseases, as well as in infectious diseases [9].

2. Effect of garlic on lipid metabolism

There are four types of lipoproteins such as chylomicrons, high-density lipoproteins (HDL), low density lipoproteins (LDL) and triglycerides. A clinical investigation was done on the blood lipid profiles of 23 volunteer humans subjected with high blood cholesterol (>5.98 mmol/L). The subjects were treated with garlic extract supplementation for 4 months and the change in their blood lipid profiles were analyzed before and after treatment. Thus it was found out that their serum total cholesterol, low-density lipoprotein (LDL), very–low-density lipoprotein (VLDL) cholesterols and triglyceride levels were significantly lower after the treatment of extract. But an increased level of high-density lipoprotein cholesterol (HDL) level was observed after the extract use [10].

A study using mice has proved that the lyophilized garlic supplementation at 2% and 5% levels on a diet containing 1% cholesterol or 15% lard, decreases the low density lipoprotein (LDL) while increasing the high density lipoprotein cholesterol (HDL) and resulting in a similar effect on lipid metabolism as at 2% and 5% levels. It was further identified that the liver weight, total liver lipid and cholesterol levels were increased in rats fed with the cholesterol diet but a supplementation of garlic decreased those parameters by about 30% [11].

Aged garlic extract reduces cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl-CoA reductase and is additive with statins in its action [12]. Thus, garlic inhibits enzymes involved in lipid synthesis, decrease platelet aggregation, prevent lipid peroxidation of oxidized erythrocytes and LDL, increase antioxidant status, and inhibit angiotension-converting enzyme [13]. The effect of allicin in preventing atherosclerosis and hypercholesterolemia was investigated using male ICR mice. They were given oral administration of allicin with doses of 5, 10, or 20 mg/kg body weight, daily for 12 weeks. A decrease in daily food consumption was also noted in most of the treated animals. Meanwhile, allicin showed a favorable effect in reducing blood cholesterol, triglycerides, and glucose levels and caused a significant decrease in lowering the hepatic cholesterol storage [14].

3. Effect of garlic on cardiovascular diseases

Cardiovascular disease has been a major non-communicable disease in recent history. Allicin which is the main bioactive compound in garlic has the beneficial effects to the cardiovascular system. From the pharmacokinetic studies, allicin is known to be hydrophobic and can be readily absorbed through the cell membrane without inducing any damage to the phospholipid bilayer and then rapidly metabolized to exert pharmacological effects that are important to the cardiovascular system. It was found to provide cardio-protective effects by inducing vasorelaxation and alleviating various pathological conditions of CVD, including cardiac hypertrophy, angiogenesis, platelet aggregation, hyperlipidemia and hyperglycemia [15].

Cardiovascular diseases are resulted from high cholesterol, high homocysteine, hypertension and inflammation. This will also increase the risk of dementia and result in Alzheimer disease. Oxidative damage is a major factor in cardiovascular disease and dementia, diseases whose risk increases with age. Garlic, extracted and aged to form antioxidant-rich aged garlic extract (AGE or Kyolic), may help reduce the risk of these diseases [12]. A study investigated that allicin, the principle active ingredient in garlic has the antioxidant properties which help to prevent the oxidative stress induced cell injury or cell death. The antioxidant capacities of allicin were measured by using 1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assay and hydrogen peroxide (H_2O_2)-induced cell damage on H_9C_2 cardiomyoblasts. It is believed that the protective effect of allicin on H_9C_2 cells could inhibit intracellular ROS production instead of scavenging extracellular H_2O_2 or free radicals. For the observed protective effect on H_9C_2 cells, allicin might also be effective in reducing free radical-induced myocardial cell death in ischemic condition [16].

4. Antioxidant property of garlic

Garlic is claimed to be effective against diseases due to its scavenging property for oxygen free radicals. High pressure liquid chromatography method was used to investigate the ability of allicin which is the active ingredient in garlic to scavenge the hydroxyl radicals. The decrease in hydroxyl radicals has shown the effectiveness of the antioxidant property of allicin by preventing lipid peroxidation [17].

Reactive oxygen species make the most damage to cells through cell aging and making diseases including cardiovascular, cancer, neurodegenerative and inflammatory. Aged garlic extracts have unique water-soluble organosulfur compounds, lipid-soluble organosulfur components and flavonoids, notably allixin and selenium. Fresh extracts from garlic is aged over a prolonged period and aged garlic extract (AGE) is made. Long term extraction helps to create the antioxidant property by converting unstable molecules to a stable state such as allicin and highly bioavailable water-soluble organosulfur compounds, such as S-allylcysteine and S-allylmercaptocysteine. Thus it can scavenge the reactive oxygen species as well as activates the antioxidant enzymes in cells such a superoxide dismutase, catalase and glutathione peroxidase, and increase glutathione in the cells [18]. Free radicals can have an oxidative damage which implies the pathogenesis of vascular disease in diabetes and hypertension. The total serum antioxidant levels of both diabetic and hypertensive rats were measured before and after the treated with garlic for 3 weeks. The serum antioxidant levels of rats after 3 weeks of treatment were significantly higher ($P < .001$) than the pretreatment levels in both diabetic and hypertensive rats. The increased serum antioxidant levels were paralleled by a decrease in serum glucose in the garlic-treated diabetic rats and lowered systolic blood pressure in the garlic-treated hypertensive rats [19].

5. Antimicrobial effect of garlic

Anti-microbial activity is prevailed in allicin. Allicin was found to be effective in its antibacterial activity against a wide range of gram negative and positive bacteria. The anti-parasitic effect of allicin has been investigated against some major human intestinal protozoan parasites such as *Entamoeba histolytica* and *Giardia lamblia*. The main anti-parasitic effect is due to the chemical reaction with thiol groups of various enzymes, e.g. alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase, which can affect essential metabolism of cysteine proteinase activity involved

in the virulence of *E. histolytica* [20]. Essential oil of garlic is identified as a natural anti-microbial additive to be used in various food products [21].

Four diallyl-sulphides occurring naturally in garlic oil were studied *in vitro* for their anti-microbial activity. The magnitude of activity of the four diallyl sulphides followed the order diallyl tetrasulphide > diallyl trisulphide > diallyl disulphide > diallyl monosulphide. The results suggested that disulphide bonds are an important factor in determining the antimicrobial capabilities of these sulphides which naturally occur in garlic essential oils [22]. The exogenous addition of garlic-derived organosulfur compounds in ground beef has showed a greater antioxidant capacity than the α-tocopherol (P<0.05). It has significantly reduced total aerobes and inhibited the growth of five inoculated pathogenic bacteria, *Salmonella typhimurium*, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Staphylococcus aureus* and *Campylobacter jejuni* (P<0.05) [23].

6. Effect of garlic on blood glucose levels

Effect of garlic on blood glucose level is an area which is still being studied by scientists. The beneficial effect of garlic on diabetes mellitus 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. Garlic extracts have been reported to be effective in reducing insulin resistance [24]. Aged garlic extract (AGE) decreases homocysteine, lowers blood pressure, and increases microcirculation, which is important in diabetes [12]. Few studies have shown its positive effect on reducing the blood glucose levels of diabetes mellitus patients. A study was conducted on fasting blood glucose levels of diabetes patients for 12 weeks provided with a metformin and a garlic treatment. It was found out that the reduction in blood glucose was more substantial in the metformin with garlic treatment than the metformin treatment alone [25]. Diabetes type 2 patients with hyperlipidemia had shown a successful decrease in LDL cholesterol levels and increase in HDL cholesterol levels in females when treated with "gsarsin", a derivative of garlic present in Arabian countries [26].

7. Anti-carcinogenic effect of garlic

Garlic is considered to be a food with great anti carcinogenic properties. Garlic acts as an anti-carcinogen through different mechanisms including the scavenging of radicals, increasing glutathione levels, increasing the activities of enzymes such as glutathione S-transferase, catalase, inhibition of cytochrome p4502E1, DNA repair mechanisms, prevention of chromosomal damage etc [27]. Anti-proliferative action of garlic compounds to retard the tumor growth has been studied using the epidemiologic studies and animal experiments. Mice transplanted with mammary tumor cells were given supplements of protein extractions from garlic bulb and a significant decrease in the size of mouse mammary tumor was observed [28]. Different studies show that garlic rich in allicin compound inhibits proliferation of human mammary endometrial and colon cancer cells [29]. Linoleic acid is considered to be an enhancer of breast cancer risk. It was examined that the garlic compound increases the effect of eicosapentaenoic acid, a breast cancer suppressor while decreases the effect of linoleic acid [30]. Organosulfur compounds in garlic such as allyl-sulfides are responsible to decrease the risk of hormone responsive cancers. It has been proposed that the sulfhydryl-group hydrophobic portion of proteins, as well as estrogen receptors with cysteine residues in hormone-binding, could be a target of inhibition from organosulfur compounds of garlic, therefore prevents the hormone responsive cancers [31]. Several experiments were done on the ability of garlic and its organic allyl sulfur components inhibit the cancer process. It was revealed that the water soluble S- allyl cysteine was effective in reducing the risk of chemically induced tumors in animal models but had no effect on established tumors. However, oil-soluble compounds such as diallyl disulfide are effective in reducing the proliferation of neoplasms [32].

8. Conclusion

The main active chemical constituent in garlic is allicin. Allicin together with other organosulfur compounds have been tested positively for their antioxidant property, anti-carcinogenic property and antimicrobial property as well as their successful prevention of cardiovascular diseases, diabetes mellitus, high blood cholesterol (LDL, triglycerides, VLDL) levels.

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