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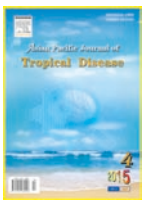

Document heading doi: 10.1016/S2222-1808(14)60782-9

Garlic (*Allium sativum*): diet based therapy of 21st century–a review

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PEER REVIEW

Comments

The present review explored the functional/nutraceutical role of garlic against various threats including dyslipidemia and hyperglycemia, cardiovascular disorders, antioxidant capacity and carcinogenic perspectives. It's looking good and comprehensive.

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ABSTRACT

Functional and nutraceutical foods provide an opportunity to improve one's health by reducing health care costs and to support economic development in rural communities. For this reason, various phyto-based functional foods are becoming popular worldwide owing to number of evidences for their safer therapeutic applications. Garlic (*Allium sativum* L.,) is an essential vegetable that has been widely utilized as seasoning, flavoring, culinary and in herbal remedies. The consumption of traditional plants especially garlic has progressively increased worldwide because of their great effectiveness, fewer side effects and relatively low cost. Garlic is well known to contain an array of phytochemicals. These bioactive molecules are playing pivotal role in maintaining human health and having potential to reduce various ailments. It has distinct nutritional profile with special reference to its various bioactive components that can be used in different diet based therapies to cure various life-style related disorders. The present review is an attempt to explore the functional/nutraceutical role of garlic against various threats including dyslipidemia and hyperglycemia, cardiovascular disorders, antioxidant capacity and carcinogenic perspectives.

KEYWORDS

Garlic, Functional food, Nutraceuticals food, Diet based therapy

1. Introduction

Functional and nutraceutical foods are becoming popular all over the world owing to their health promoting perspectives. There are several traditional plants, used as a therapeutic carrier for different physiological threats. Investigation through diet based therapies, elucidate the significance of these traditional plants including garlic, onion, black cumin, green tea, ginger, peanut *etc.*, however, several avenues are yet to be explored for researchers[1]. Pakistan being diverse in indigenous phphytocoenosium has such types of traditional plants that are contributing to health.

Functional foods are significant in this milieu owing to easy accessibility, low price and allied health promoting perspectives. In this circumstance, many fruit and vegetables, cereals, nuts and pulses *etc.* are vital because they possess therapeutic potential due to certain arrangement of biologically active chemical substances known as phytochemicals. These are the biologically important chemical molecules in plant food that are mainly concerned with modulation of various metabolic pathways, like free radical scavenging, antimicrobial properties and providing protection against diseases[2].

The diversity in human diet cannot be understood properly as socioeconomic and environmental factors lead to wide variations in the

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Article history:

Received 27 Oct 2014

Received in revised form 5 Nov 2014, 2nd revised form 15 Jan 2015

Accepted 6 Feb 2015

Available online 9 Feb 2015

dietary pattern of the global population. The abrupt increase in medical care costs and human's desire for maintenance of one's health result in greater attention for nutritionists and public health scientists to elucidate the diet-health linkages. Diet and health linkages are correlating as consumer thread is varied and now they are more conscious toward nutritional and functional attributes of food[3]. However, a number of strategies are needed, to explore nutrients dense sources, their potential utilization and applications, and especially their mode of actions[4]. Nevertheless, vegetables are one of the important segments of human diet since ancient times and hold unique position in all dietary guidance systems. The American Dietician Association recommended daily 4-5 servings of vegetables to meet the requirements of desired nutrients.

Vegetables are rich sources of bioactive molecules such as carotenoids, chlorophylls, anthocyanins and flavonoids[5]. These bioactive molecules have the ability to target at molecular level effectively by modulating enzyme kinetics, release of cytokines, and signal transduction[6]. Among the functional foods, use of garlic is mounting day by day because of its health promoting potential besides basic nutrition. The medicinal uses of various herbs have been proven experimentally as lifesaving entities, associated with health claims owing to their rich phytochemicals profile[7]. Health promoting aspects of garlic are mainly accredited to its sulfur containing compounds mainly allicin and *S*-allylcysteine ((SAC). Among organosulfur compounds, thiosulfinates, ajoenes and allicin (diallyl thiosulphate) are the chief bioactive components in garlic responsible for curing various ailments.

Links of crucial importance have been settled between dietetic components and human health safety[8]. There are lot of evidences that consumption of different vegetables are important for human health as they are very good sources of dietary fibers, antioxidants, carotenoids, sulfurcontaining compounds, vitamins, and minerals[9]. Epidemiological studies conducted worldwide have brought to light that liberal consumption of vegetables especially rich in nutraceuticals is associated with a guarantee of prevention and reduction of health related chronic disorders[10].

1.1. Garlic, an overview

Garlic (*Allium sativum* L.) is one of the most commonly used plants utilized both for medicinal purposes and culinary practices as providing flavor and taste to the final product. It is believed to be originated from Central Asia over 6 000 years ago and has been extended towards West, South and East. However, intact garlic as well as its components/ fractions is used since long time ago in Chinese medicines even 3 000 years while Egyptians fed garlic to pyramid crews to boost their immunity thereby render safe from various maladies and improve their performance[11].

Garlic health promoting perspectives have been proven and it is recommended worldwide as a dietary supplement. It is also cultivated for its medicinal value owing to an increase in its consumption both in cooking and curing. Lately, a wide range of its cooking related and medicinal preparations show their availability in market. In many countries, health potentials of garlic and its various products have been recognized and are useable as dietary supplementation. Dehydrated garlic as well as its extracted oil is gaining popularity and are being sold as dietary supplements[12].

Garlic is a rich source of sulfurous compounds, for example, diallyl sulfide, allicin (diallyl thiosulphate), -glutamyl-*S*-allyl-*L*-cysteines, and *S*-allyl-*L*-cysteine sulfoxides (alliin) and altogether they are called allium compounds. They are found efficacious in reduction of certain types of cancer as well as in management of cholesterol and eventually blood pressure[13,14]. The garlic organosulfur components are mainly responsible for its health promoting properties. Major research interventions have focused on its potency in prevention of ailments related to lifestyle related disorders for instance in case of sedentary lifestyle like hypercholesterolemia, dyslipidemia, and high blood pressure.

The nutritional composition of garlic bulb contains approximately 65% water, 28% carbohydrates 2.3% organosulfur compounds, 2% protein, 1.2% free amino acids and 1.5% fiber. Briefly, raw garlic contains water, carbohydrate, and proteins in the amounts of 58.58, 33.06, and 6.36 g/100 g, respectively. The consumption of 100 grams of garlic provides 149 kilocalories. Carbohydrates and proteins are the major components of garlic powder accounting for more than 80% while among vitamins, thiamin have special consideration with high bioavailability owing to some specific sulfur containing components. Regarding minerals, selenium needs special interest as its level is at least 9 ppm higher than almost all other plants. Main pharmacological effects of garlic are due to its featured organo-sulphur compounds[15]. Allicin (diallyl thiosulphate), which is the most important bioactive component in garlic holds the responsibility for its distinctive pungent smell and other remedial properties[16].

Table 1

Proximate analysis, vitamin contents and minerals present in 100 g of raw garlic (USDA).

Category	Content (per 100 g)	Amino acid	Content (mg/100 g)
Calorie	1109 KJ	Tryptophan	58
Water	53.6 g	Lysine	549
Protein	12.0 g	Threonine	376
Lipid	5.1 g	Valine	1040
Saccharide	41.4 g	Methionine	116
Dietary fibre	1.2 g	Phenylalanine	534
Ash content	2.3 g	Leucine	737
Sodium	53.9 mg	Isoleucine	404
Calcium	13.0 mg	Cystine	318
Iron	2.1 mg	Tyrosine	592
Vitamin B2	0.1 mg	Arginine	1964
Vitamin B6	10.7 mg	Histidine	318
Nicotinic acid	14.0 mg	Alanine	722
		Aspartate	1560
		Glutamate	2456
		Glycine	563
		Proline	318
		Serine	477

Table 2

Botanical classification of raw garlic

Kingdom	Plantae
Clade	Angiosperms
Clade	Monocots
Order	Asparagales
Family	Amaryllidaceae
Subfamily	Allioideae
Genus	*Allium*
Species	sativum

1.2. Chemistry of garlic

Garlic bioactive compounds are placed into categories as: sulfur-containing and non-sulfur compounds. Sulphur is chiefly found as alkylcysteine sulphoxides and gamma-glutamyl peptides which in combination constitute more than 70% of the total sulphur content in

garlic. The degradation of alkyl cysteine sulphoxides, alliin, methiin, and isoalliin is brought about by alliinase enzyme and result in a release of powerful smelling volatiles, provide particular odor and flavor to the *Allium* species. Alliin is converted into allicin by crushing the garlic clove within seconds. Garlic remains odorless unless it is mashed. Cross-section investigation has exhibited that location of the substrate alliin and the enzyme alliinase are separate compartments. In garlic the flavor precursor showing dominant characteristic is alliin having less concentrations of isoalliin, methiin and trace amounts of propiin[17]. The therapeutic effects of garlic are mainly attributed to a sulfur-containing compound known as allicin[18]. The garlic clove lack allicin content but contains its precursor, the non-protein amino acid alliin. Garlic bulbs contain alliin and alliinase at about 1.7 and 2.8% of their dry weight, respectively. By the crushing of garlic bulbs variable amounts of allicin is produced ranging from 1.6-13.0% of their dry mass[19].

The distinguishing flavor of fresh garlic is associated with thiosulfinates and various other volatile substances produced by alliinase (EC4.4.1.4) like *S*-alkyl-substituted cysteine sulfoxide derivatives, alkyl alkane thiosulfinates, pyruvic acid, and ammonia[20]. The enzyme action starts as soon as garlic tissues are disrupted. The major substrate in garlic is non protein amino acid alliin (*S*-allyl-*L*-cysteine sulfoxide). Allicin (diallylthiosulfinate) formed by enzymatic activity constitutes about 60 to 80% of total garlic thiosulfinates. Gene coding for the enzyme alliinase has disclosed that it is constituted of 448 amino acids having a molecular mass of 51.45 kDa and carbohydrate amount of 5.5–6.0% with 55 000 kDa. Alliinase enzyme contain 10 cysteine residues, all exist in S-S bridges which make the enzyme inactive by their reduction, or by removing pyridoxal coenzyme factor. Indeed, none other compound outside the thiosulfinates has been discovered to contribute for a fairly large portion of the pharmacological preparations of mashed garlic at similar levels. Allicin amount in fresh garlic varies to a large extent. According to British pharmacopoeia 1998, the minimum allicin content ensuring pharmaceutical and economic viability of garlic powder products is 4.5 mg/g. It is well observed that garlic allicin content varies with various geographical regions. Difference in allicin content among various ecotypes is directly related to genetic variations[19].

1.3. Characterization of garlic preparations

Estimation of garlic flavor components is important to the food industry since the quality of garlic and garlic products affects overall food quality. Similarly, chromatographic methods have been utilized by the dietary supplements industry to investigate garlic volatiles that may affect the overall acceptability of supplements to the consumer. Several sulfur components were investigated including allyl methyl sulfide, allyl mercaptan, 3,3'-thiobis-1-propene and diallyl disulfide. The diallyl disulfide appeared to be the more prominent component for all garlic preparations. The biological potentials of different components of garlic for example lectins (abundantly found proteins in garlic), prostaglandins, pectin, adenosine, fructan, vitamins B1, B2, B6, C and E, biotin, nicotinic acid, glycolipids, phospholipids, fatty acids and essential amino acids, have been investigated for years. Recently, the importance of pharmacological activities, including antifungal, antitumor, antithrombotic and hypocholesterolemic attributes[21] of definite sapogenins and steroid saponins, such as beta-chlorogenin has been discovered[22].

Some other distinctive chemical components include allicin and organo-selenium which show many biological influences, like lowering cholesterol level, preventing cancer *etc.* and most likely act synergistically. Flavonoids, abundant in many fruits especially onion, are almost not found in garlic, while a minimal quantity of non-volatile water-soluble sulphur containing compounds exist in garlic. These are SAC (enzyme induced transformation of gamma-glutamylcysteines during aqueous solution) which are also useful in the betterment of many health disorders[23]. The most important garlic preparations used as dietary supplements are the one containing the most safe and effective, high stability and odorless components. In accordance with various researches, aged garlic extract by dint of its extraction method, has more effectiveness and safety as compared to fresh garlic, garlic powder and related formulations[24].

Garlic oil mainly contains diallyl disulphide, diallyl trisulphide, allyl propyl disulphide, and disulphide, also containing a small amount of diallyl polysulphide[25]. It is considered to be more effective than aqueous extracts and reveals a wide range of pharmacological effects including antidiabetic and anticarcinogenic[26]. Conversely, its application in the food industry is very restricted due to its strong flavor and odor, water insolubility, and low physicochemical stability.

1.4. Life style related disorders

Poor dietary habits and changing lifestyle often lead to various physiological threats such as cardiovascular complications, immune dysfunctions and cancer[27-29]. It is estimated that 30-40% of different diseases are curable with a vigorous lifestyle and dietary modules[30-32]. Disease prevention stratagem should include nutritional and exercise guidelines; particular targeted dietary components could be a part of this approach. Diet and healthy foods have a significant impact on the antioxidant potential of the body and combat deficiency of nutrients, like tocopherols, polyphenols that reduce the risk of various maladies like diabetes mellitus, and atherosclerosis. Plants rich in phytochemicals profile have the ability to scavenge free radicals and ameliorate oxidative stress[33]. Among these phytochemicals, phytosterols, antioxidants and flavonoids have shown hypoglycemic and hypocholesterolemic potential[13]. Functional foods and their bioactive moieties have shown therapeutic potential against various biological threats including antioxidant, anti-cancer and immunomodulation[34]. Free radicals being reactive in nature, damage to macromolecules. Imbalance of these reactive oxygen species result in oxidative stress on different cells and tissues. Oxidative stress is a disturbance between the production of reactive oxygen species and antioxidant defense, resulting in tissue injury. Oxidative stress also leads to DNA damaging, cardiovascular and neuropathy disorders and cancers[35]. It is urged to utilize herbal products having better efficiency and safety, as a substitute for chemical therapy. Various herbal products that may be comprised of one or blend of different antioxidants have been investigated to protect against hepatic injury, having immune modulatory or antiviral properties[36].

2. Health claims of garlic

2.1. Diabetes mellitus

Diabetes is a metabolic syndrome that steadily affects different physiological systems of the human body. It is one of the leading causes of mortality worldwide and, if uncontrolled, can threat multi-organ systems[37]. Uncontrollable blood glucose is known to be the core feature in the inception of diabetes difficulties of Type 1 as well

as Type 2 (American Association of Diabetes Educators, 2002). Most common type is Type 2 category, while Type-1 diabetes develops mostly in early childhood. Kidneys play a significant role and become the target for investigation in studies of diabetic complications as many other factors involved in the development of diabetic nephropathy are the same as in other common diabetic complications, like retinopathy and microvascular diseases.

There is an estimate that in 2030, 376 million peoples worldwide will be affected with diabetes[38]. It is mainly characterized by relative deficiency in insulin secretion or insulin action associated with hyperglycemia and malfunctioning in the metabolism of carbohydrate, lipid, and protein. Diabetes may also lead to various other complications like, cardiovascular disorders, oxidative stress and immune dysfunction[39]. Cardiovascular diseases are the main cause of illness and death all over the world. By increasing the level of cholesterol and low density lipoprotein (LDL) oxidation triggers events that initiate atherosclerosis[40]. As a result of various health disparities there is an onset of autoimmune disorders and immune dysfunction. According to Nogichi[41], 33% of all the diabetic patients take various medications that may be considered effective, among them garlic is one of the most frequently used. Garlic and its preparations have shown varied biological activities, including antidiabetic, antiatherosclerotic, anticarcinogenic and antithrombotic actions[42]. However, these biological activities are well famous, only certain complications, like cardiovascular diseases and tumor development, have been widely studied[43]. It is also predicted that the number of studies related to garlic hypoglycemic perspectives is limited and the outcomes are also inconsistent.

It is investigated that the effect of garlic extract prepared with water or combination of other organic solvents are studied on normal as well as alloxan-induced diabetic rabbits. It is inferred that all those garlic preparations possess an intense hypoglycemia action, which was accomplished by employing ethyl ether extract with that of tolbutamide. Later on, the influence of garlic oil was studied on diabetic animals by Anwar[44], in order to verify the hypoglycemic perspectives of garlic. Lately, garlic juice was determined to cure hyperglycemia in diabetic rats, and it also eased out the oxidative pressure and harm in their liver and kidney. In addition to garlic extract and garlic oil, allyl sulfide, *S*-allyl-cysteine sulfoxide (alliin), was also found to be possessed with the same hypoglycemic effect as was in case of glibenclamide[45].

Recently, it is accounted that the hypoglycemic action of garlic, garlic oil and its organosulfur constituents especially di-allyl-trisulfide, result in higher insulin secretion and insulin sensitivity in streptozotocin-induced diabetic rats. However, there was not an appropriate hypoglycemic activity of garlic powder in diabetic animals induced with streptozotocin. It is concluded that incoherent results are partly due to different garlic preparations used in the different experimental observations. The chemical profile of garlic products mainly depend upon the processing and working conditions, like temperature, preparation time, and the type of solvents used for extraction[46].

2.2. Cholesterol lowering potential

Cardiovascular disorder is one of the leading causes of both mortality and morbidity all over the globe. Oxidation of cholesterol fractions, especially of LDLs, is playing a cardinal role in atherosclerosis development. Lipid peroxidation by toxic radicals increases the concentration of free radicals and causes certain diseases including atherosclerosis in humans. Management of plasma cholesterol level is a keystone element to protect cardiovascular disease disorders. Various medications have been applied in treatment but due to the long time therapy and their side effects, natural products may be considered as a suitable remedy. Garlic has been being used in traditional medicine to improve the lipid profile and its different supplementations hold remarkable effect on cholesterol level, LDL-cholesterol, and high density lipoprotein-cholesterol. Consumption of garlic and garlic preparations are very useful in regulating plasma lipid levels[47], plasma anticoagulant activity[48] and also contributed toward the prevention of the atherosclerosis process[49]. Garlic preparations have been reported owing to numerous remedial benefits, including decreasing plasma cholesterol levels and blood pressure, decreasing platelet aggregation, protecting LDL from oxidation. Various garlic preparations like garlic oil, garlic extract *etc.* are also effective in lowering blood pressure and oxidative stress in hypertensive persons. Ackermann *et al.*[50] estimated that garlic preparations have comparatively lower declines (1.2-17.3 and 12.4-25.4 mg/dL) in total cholesterol level as compared to whole garlic after 1 and 3 months correspondingly. Effect of garlic on lipid profile was elaborated that garlic significantly reduced total cholesterol and triglycerides level[51].

Aqueous garlic extracts has the ability to decrease cholesterol synthesis up to 75% without cellular toxicity mediated by sterol 4-alpha-methyl oxidase. It is also effective in reducing coronary calcium progression[52]. It was elaborated in one study that *S*-allyl cysteine sulfoxide decreased the activity of 3-hydroxy-3-methylglutaryl-CoA reductase enzyme while significantly increased the activity of lecithin acyl transferase in isoproterenol-induced myocardial ischaemia[49]. According to Yeh and Liu[52] observations, SAC, *S*-propylcysteine and *S*-ethylcysteine inhibited cholesterol synthesis up to 40-60% as compared to gamma-glutamyl-*S*-methylcysteine, gamma-glutamyl-*S*-allylcysteine and gamma-glutamyl-*S*-propylcysteine that contributed 20-35%. Moreover, only SAC appears to decrease the activity of 3-hydroxy-3-methylglutaryl-CoA reductase by enhancing sulfhydryl oxidation. There is no doubt that garlic and its various preparations possess anticoagulant perspectives[48], but still there is a lot of controversy with respect to the garlic lipid profile and its antioxidant status. As there is not an exact molecular mechanisms identified for garlic perspectives in the atherosclerosis, further establishment should be made to develop a relation among garlic extract, antioxidant status, and blood lipid profile.

2.3. Cardiovascular complications

Epidemiological studies have investigated various risk factors associated with atherosclerosis development such as elevation in serum lipid level (cholesterol and triglycerides), increase in plasma fibrinogen level, elevation in platelet activation, modification in metabolism of glucose and smoking[53]. One of the important cause in the atherosclerosis formation is oxidation of LDL[54]. It is revealed through various epidemiological studies that atherosclerosis-related conditions like coronary artery disease, ischemic stroke and peripheral artery disease increase with age. It usually happens in the muscular arteries such as aorta, coronary, carotid, femur, and ilium arteries.

Aging influences structural and functional attributes of the vessels that leads to various cardiovascular complications. By virtue of that the morbidity and mortality increase especially in hypertension conditions. Aging induces alleviation in endothelium-dependent, alteration in endothelial cells and vascular tone regulating, it also decreases endothelial synthesis and eventually releases nitric oxide. During aging

increased collagen-elastin ratio as well as sedimentation and sticking of calcium along with lipids inside the blood vessels leads to enhancement of the hardness of vascular wall[55]. In old age groups increase in oxidative pressure with respect to aging is significant factor in the occurrence of atherosclerosis. Both *in vitro* and *in vivo* studies exposed that an important stimulator of early atherosclerotic lesion is oxidative modification of LDL that contributes to continual rise in amount of LDL hydroxy fatty acids with the increasing age in healthy individuals. "Aging" may also occur in a condition when there is a delay in the removal of lipoprotein from the plasma, leads to a gradual "senescent" type of passing on lipoprotein that is particularly more exposed to oxidation as in oxygen radical-stimulated modification. Oxidized LDL have pro-atherogenic perspectives including increase in smooth muscle proliferation, smooth muscle cells and fibroblasts and cytotoxicity to vascular endothelial cells as well as the induction of apoptotic activity in vascular endothelial cells[56].

Garlic and its various preparations have been used to assess and cure various cardiovascular disorders for a long time. Studies on both rats and rabbits have shown that garlic extract has been used to alleviate diet-induced hypercholesterolemia[57]. It is clarified that garlic extract and aged garlic extract are efficacious in reduction of plasma cholesterol, triglyceride level and LDL-cholesterol in hyper-lipidemic persons however, no any effect in normolipidemic ones[49]. Preparations utilizing garlic powder have also been studied for reduction of plasma cholesterol levels in high cholesterol people[58], while a few objections have also been observed by Gardner *et al*[59]. It is clearly predicted that garlic and its various components have a potential to decrease plasma cholesterol and triglyceride level by inhabitation of important enzymes of cholesterol and fatty acid synthesis mechanism[52].

Platelet aggregation and gradual thrombus formation is reduced competently by utilizing garlic and its components whilst firbrinolysis increases as a result of dissolution of clot and thrombi. Daily ingestion of 2.4 g of garlic supplemented with aged garlic extract has high threshold level of collagen, epinephrine-induced platelet assemblage as well as platelet adherence to fibrinogen among healthy subjects[60]. It is also observed in one case study that high intake of age garlic extract (7.2-8.0 g per day) enhanced threshold values of ADP-stimulated platelet accumulation, platelet adhesiveness to collagen as well as von Willebrand factor. In addition suppression of the ADP-stimulated platelet aggregation has been observed in normolipidemic individuals with dietary intervention of aged garlic extract at the rate of 5 mL per day (equivalent to 1.5 g per day)[49]. Aged garlic extract prohibited both percentage as well as staring rate of platelet congregation up to 10 mol/L at concentrations of ADP. The *K*m value for ADP-induced platelet aggregation was nearly doubled after dietary modification with age garlic extract whilst the maximum rate of aggregation was unchanged.

Garlic oil is found to limit platelet accumulation particularly caused by adrenaline; arachidonic acid, collagen and calcium that alleviate the constitution of pro-aggregatory prostaglandin thromboxane-A2 known as thromboxane-B2 in heart patients. In animals, studies have revealed that fresh garlic extracts are effective against cyclooxygenase activity in cell culture[43]. *In vitro* studies have pointed out that use of aged garlic extract improved both blood properties and microcirculation controlling hemolysis in oxidized erythrocytes cells as well as lipid peroxidation rate[61]. This confirmation was made by another subsequent research in which chronic garlic powder ingestion inclines to rarefy aging in aortic hardness. This contributes in protecting the aorta elasticity in term of correlate to aging among humans. Studies on utilization of aqueous garlic extracts has confirmed that it not only assist in the constricting factor in pulmonary arteries as well as in producing and functioning of endothelial-derived relaxing factor (NO) [62], but could also decrease blood pressure in high cholesterolemic individuals. Oxidative pressure was related to preservation of enzymatic activities like glutathione peroxidase and superoxide dismutase[63]. Animal modeling has been utilized to describe the influence of garlic oil preparation on rats with nicotine-caused lipid peroxidation. Supplementation of garlic oil removes lipid peroxidation activity in all major organs of the rodents like heart, lung, liver and kidney. This reducing of lipid peroxidation activity was related to a rising antioxidant property of enzymes (super oxide dismutase, catalase, and glutathione peroxidase) as well as higher level of glutathione. If garlic and its preparations are recommended as an antioxidant tools, it is very important to prove its effectiveness in human clinical trials. However, the data revealed that garlic consumption may reduce oxidative stress and aging related diseases[18].

This was determined that the antioxidant condition in non-smoking people is twofold higher than smokers. Introduction of age garlic extract for nearly 14 days tend to reduce the plasma and urine concentration in non-smoking people by 29% and 37% respectively, whereas by 35 and 48% in smokers respectively. After fortnight in both groups plasma and urine concentrations becomes nearly equal to values as before dietary supplementation of age garlic extract while changes other than these were not noticed in other bio-chemical parameters[64]. Garlic consists of a complicated concoction of pytochemicals outlook that act in a synergistic way in order to provide beneficial effects and particularly its antioxidant potential. Flavonoid is high potency antioxidants and their utilization causes significant reduction in LDL to lipid peroxidation[65]. Ingestion of phytochemical especially flavonoids, for instance apigenin, myricetin, quercetin, is related to mortality in an inverse ratio because of cardiovascular disorders[66].

2.4. Antioxidant activity

Oxidation of DNA, lipid and protein by ROS plays an important role in wide range of diseases, including aging, cancer and cardiovascular disorders, inflammatory and neurodegenerative diseases. Research studies elucidated phytotherapy, potent source of antioxidant phytochemicals, like vitamins C and E, flavonoids, pigments and glutathione, protect against various cellular degradations[67]. Among garlic preparations, age garlic extracts have higher antioxidant potential than fresh garlic and commercial garlic supplementations. Water-soluble organo-sulphur compounds, such as SAC and *S*-allylmercaptocysteine (SAMC), have a great antioxidant potential[68]. The two constituents SAC and SAMC are the prime organo-sulphur constituents that are found in age garlic extract whereas some other components which possess an antioxidant potency include stable fat-soluble allyl sulphides as diallyl sulfide, diallyl disulfide, diallyl trisulfide and diallyl polisulphides[23]; some tetrahydro-b-carboline derivatives that formed during the natural aging process; flavonoids, saponins and some essential micronutrients like selenium and macronutrients, as lectins with antiperoxide perspectives are prominent in the kidney, liver and heart of rats. Phytochemical profile of age garlic extract may act as synergistically that exerts their antioxidant potential by scavenging ROS[69]. Age garlic extract owing to its antioxidant potential, reduces the risk of cardiovascular and cerebrovascular syndromes by preventing LDL oxidation as well as lipid peroxidation[47].

2.5. Cancer perspectives

Garlic is incepted to be utilized as an anticancer agent in 1950's and the findings depicted that thiosulfinate constituents of garlic had a subduing effect on the growth of tumor cells[70]. Based on these findings, many corresponding epidemiological and laboratory scale researches were conducted to assure the presence of chemo-preventive or anti-cancer effects in garlic and its closely related allium species like garlic and onion[71]. These research trails have been confirmed that intake of both garlic and onion reduces carcinoma as well as sarcoma risk in different tissues and body organs, like bladder, colon, prostate, lungs, oesophagus, stomach, skin, brain and liver[72]. These effects are not fully understood and their mode of action is not yet completely known. It is stated that garlic and onion exhibit indirect way of anti-carcinogen action by different mechanisms that inhibit carcinogen metabolism, increase the detoxification and facilitate its excretion from the body. Garlic may also effect on cytochrome P450 and inhibit the procarcinogens' activation, alter oxidative damage by their antioxidant action and further stop cell proliferation by inducing apoptosis that inhibit unnecessary cell division. It also helps in chromosomal abbreviation prevention (anticlastogenic effect)[73] and alteration of the cyclooxygenase as well as lipoxygenase activities (anti-inflammatory effects)[74].

It is also investigated from modern research that both water and fat-soluble sulphur containing compounds from garlic supply anti-carcinogenic advantages like diallyl sulfide, diallyl sulphoxide, diallyl disulfide, diallyl sulfone, diallyl trisulfide, and SAC. Other sulphur containing compounds, such as SAMC, methiin, ajoene, along with some diallyl disulfide and diallyl trisulfide, can change the mechanism of cell increase by stimulating apoptosis in various human cells like human leukaemic cells. Apart from some organo-sulphur containing compounds, eruboside-B is a crucial steroid saponin which is extracted from garlic bulb as well as some organo-Se containing compounds, and gives the anti-carcinogenic potency to garlic as well as onion. The pure Se containing compounds have been proved as superior anti-cancer agents than S-analogues, like diallyl selenide that has activity of about 300 times more as compared to diallyl sulfide for the treatment of mammal cancer[13].

The two major Se containing compounds having potential to cure cancer activity in garlic and onion are Se-methyl selenocysteine and g-glutamyl-Se-methyl selenocysteine, but Se-methyl selenocysteine and Se-allyl selenocysteine are the most promising chemo-preventive[75]. For quantification of Se-containing compounds, new analytical techniques are required[76]. Advancement in analysis of gene expression along with various functional assays elaborates the significant information on anti-carcinogenic capabilities of all active components. Facts from cDNA array studies explicate the anti-proliferative perspectives of diallyl disulfide that may be due to variation in gene expression of aggrecan 1, cadherin 5, tenascin R and vitronectin[77]. Similarly, it is reported that garlic and its active components response mainly depends on the consumer's genetic backgrounds (nutrigenetic effects), changes in cellular molecular weight within respect to dose (metabolomics effects), DNA methylation, and histone regulation (nutritional epigenetic effects). Identification biomarkers can also be used to determine the response of garlic or other allium foods on reducing cancer burden that is important to develop strategies for the functional food[78].

In addition, in recent days researchers have focused on anti-mutagenic view of garlic, which is an estimate that particular suphur containing compounds like diallyl sulfide, have a positive impact on DNA repair mechanisms[73]. It is concluded that daily recommended intake of garlic and onion provides protection against cancer insurgence. The United States National Cancer Institute accounted garlic is a potential food because of its various functional and nutraceutical aspects with special reference to cancer prevention.

3. Conclusions

Garlic (*Allium sativum* L.) is one of the most essential herbaceous vegetables that have been probed against various life sight related disorders. It is helpful in various biological functions due to array of phytochemicals. Garlic nutrition includes manganese, selenium, calcium, vitamins B1 and B6, tryptophan and protein. These components provide synergistic effect against various threats but still need further attention of the researchers. It is assumed that health promoting potential of garlic is mainly attributed to sulfur containing compounds like allicin, citral, geraniol, linalool, phellandrene, s-methyl-1-cysteine sulfoxide. However, pharmacological effectiveness is linked to organosulphur compounds, particularly cysteine sulfoxides and thiosulfinates. Globally, garlic and its various preparations like fresh garlic juice, garlic powder, garlic extract, and garlic oil are becoming popular against numerous physiological menaces. With their unique combination of bioactive moieties, allium vegetables should be in our diet on a regular basis. Both *in vivo* and *in vitro* studies have elucidated the potential of garlic against variety of metabolic syndromes. Garlic has wide applications as antioxidant, antifungal, antithrombotic, hypocholestrolemic and hypoglycemic agent. It reduces glucose metabolism in diabetics, slows the development of arteriosclerosis and lowers the risk of various cancers. Furthermore, it reduces the chance of heart attacks in myocardial infarct patients and could also improve the immune dysfunction.

Conflict of interest statement

We declare that we have no conflict of interest.

Comments

Background

Functional and nutraceutical foods are becoming popular in all over the world owing to their health promoting perspectives. There are various traditional plants that used as a therapeutic carrier for different physiological threats. Vegetables are enriched sources of these bioactive substances, such as carotenoids, chlorophylls, anthocyanins, and flavonoids. These bioactive molecules have the ability to target at molecular level effectively and their molecular aspects include enzyme kinetics, release of cytokines, and signal transduction. Among the functional foods, use of garlic is mounting day by day because of its health promoting potential besides basic nutrition. The medicinal uses of various herbs have been proven experimentally as lifesaving entities, associated with health claims owing to their rich phytochemicals profile. Health promoting aspects of garlic are mainly accredited to its sulfur containing compounds mainly allicin and SAC. Among organosulfur compounds, thiosulfinates, ajoenes and allicin (diallyl thiosulphate) are the chief bioactive components in garlic.

Applications

This review is helpful for further researcher related to garlic and health perspectives.

Peer review

The present review explored the functional/nutraceutical role of garlic against various threats including dyslipidemia and hyperglycemia, cardiovascular disorders, antioxidant capacity and carcinogenic perspectives. It's looking good and comprehensive.

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