



The consumption of garlic as a preventive measure against the development of metabolic disorders

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Article History	Abstract
Received: 30/09/2023 Revised: 15/10/2023 Accepted: 30/10/2023 CC License CC-BY-NC-SA 4.0	Garlic is a perennial medicinal plant which is commonly used as a household spice. The medicinal use of garlic back to historical times and it was used to build stamina, treat diarrhea, to cure intestinal diseases, to treat headache, flu, sore throat and many more. Another form of processed garlic, black garlic, is a newer form of garlic and can be called as a functional food. Black garlic has a black colour, sweet taste, and absence of pungent odour. S-allyl cysteine (SAC) has been found to be one of the most predominant antioxidants presents in black garlic. The black colour of black garlic is due to the presence of the anti-oxidant Hydroxymethylfurfural (HMF). The functional properties of garlic are due to the presence of organosulfur compounds namely allin, allicin (diallyl thiosulfonate), diallyl trisulfide (DATS), allylpropyl disulfide, ajoene, vinyl dithiins, S-allylcysteine (SAC), S-allylmercaptocysteine. Due to the presence of these organosulfur compounds, garlic plays a major role in the treatment and prevention of various metabolic disorders like cardiovascular diseases, diabetes mellitus and cancer. This literature review reveals the effect of garlic over the prevention and health promotion for several metabolic disorders. Keywords: allylpropyl disulfide, atherosclerosis, cardiovascular disorders, cancer, diabetes mellitus, diallyl trisulfide, Hydroxymethylfurfural, vitamin C and minerals, S-allyl cysteine.

1. Introduction

Garlic (*Allium sativum* L.), is a compelling medicinal plant with a characteristic odor and a pungent taste. It is a bulbous perennial plant that grows upto 1.2m in height (Morales-González *et al.*, 2019). Garlic is known to belong to the *Alliaceae* family and is also widely known as a very valuable spice and a medicinal food, used for the prevention of various diseases and lifestyle disorders. The word garlic implies pungent. It has been

found that, garlic was originated in Central Asia, spreading to China, the Near East, and the Mediterranean Region. The cultivation of garlic was then moved to the west to Central and Southern Europe, Northern Africa (Egypt) and Mexico (Fesseha and Goa, 2019). The practice of using garlic as a medicine in the prevention of diseases dates back to ancient historical times. Evidences suggest that garlic had been fed to the athletes during the earliest Olympids in Greece in order to increase their stamina (Koulivand and Gorji, 2014). The Early Egyptians had used garlic in order to treat diarrhea and this medicinal power of garlic had been described on papyrus and on the walls of ancient temples dating back to the 1500 BC. Another ancient use of garlic was seen by the Greek physician Hippocrates and Galen to cure intestinal and extra-intestinal diseases. In ancient times, Japanese and Chinese used garlic to treat headache, flu, fever and sore throat. Another example of using garlic as a medicine was seen in Nigeria, Africa, where it was used to treat abdominal discomfort, diarrhea, otitis media and respiratory tract infection. In India and Europe, it was found that garlic was used in the treatment of common cold, hay fever and asthma. Thus, for all these healing properties of garlic, it was also known as Russian penicillin (Gebreyohannes and Gebreyohannes, 2013). This popular medicinal plant is also a well-known popular household spice which has carved its name in the enhancement of culinary, spiritual and medicinal purposes. Garlic is still widely known for its common medicinal uses such as an antibiotic, anti-thrombotic and antineoplastic agent (Rana *et al.*, 2011).

1.1. Black Garlic, a processed form of fresh garlic

Black garlic, a newer form of fresh garlic had been developed in Japan by aging the regular fresh garlic under controlled conditions without the use of any additives. During this process the final products that were developed were black in color, had a non-pungent odour, a fruity sweetness and could be eaten easily by peeling (Wang *et al.*, 2010). Black garlic, has now emerged as a prominent functional food in the market. Black garlic can be typically distinguished from raw garlic by the presence of its black colour, sweet taste, a chewy texture and the absence of the pungent odour. Apart from these, black garlic also possesses many therapeutic benefits like anti-cancer, anti-obesity, anti-oxidant and has neuro-protective properties (Tran *et al.*, 2020).

Production of black garlic takes place through the process of fermentation, carried out under specific controlled conditions, that is high temperature and relative humidity. The temperature required for garlic ranges from 40-degree Celcius to 90-degree Celcius. The relative humidity ranges from 70%-90% and the aging period reported is 8-69 days. It has been recorded that the pre-treatment of fresh garlic could affect the final product of black garlic (Afzaal *et al.*, 2021). Many chemical reactions such as caramelization and Millard reaction might take place because of these thermal processes. The development of black colour in garlic is due to a non-enzymatic browning reaction called Millard reaction. In addition to this, some new biological compounds are also formed which were previously not found in fresh garlic (Xiaoming *et al.*, 2018).

Fresh garlic contains 36% carbohydrate, 0.6% fat and 6% protein. Compared to this, in black garlic there was a 28-47% increase in the carbohydrate content. During the process of thermal processing, fructans of fresh garlic were found to progressively disintegrate into monosaccharaides (namely glucose and fructose), disaccharides and oligosaccharides. Monosaccharaides were found to be predominant in black garlic. During the conversion of fresh garlic to black garlic, protein denaturation is seen. Due to the high temperatures involved, few free amino acids like tyrosine and cysteine participate in the Millard reaction. Thus, their concentration decreases. Some studies have shown that the concentrations of branched chain amino acids (leucine, isoleucine and valine) were found to be increased in the black garlic as compared to fresh garlic. The polyphenol and anti-oxidant activities of black garlic were enhanced by 2.8%. One of the most predominant antioxidant of black garlic was found to be S-allyl cysteine (SAC), a molecule containing amino acid. Hydroxymethylfurfural (HMF) is another anti-oxidant present in black garlic, which could also be related to the formation of black color in black garlic. Due to the thermal processing, studies have found that black garlic contains a higher content of water-soluble antioxidants like S-allyl cysteine and S-allyl-mercapto cysteine, organosulfur compounds, products of millard reaction and volatile compounds as opposed to fresh garlic (Ahmed *et al.*, 2021).

1.2. Types of Garlic preparations

Garlic Oil: This is prepared by the method of steam distillation. It consists of a diverse group of sulfides like diallyl disulfide (DADS) and diallyl trisulfide (DAT). This fractionated oil is obtained by grounding whole garlic cloves in water and then they are either distilled by heat or taken out by an organic solvent (like hexane).

This process totally eliminated the water-soluble compounds present in garlic. This process also completely eliminates alliin from the garlic oil (Mathew and Biju, 2008).

Garlic powder: In order to prepare garlic powder, it was found that garlic cloves were crushed or sliced, then dried and eventually ground into powder. Due to the instability of alliin, it was thus found that garlic powder contained no alliin. The principal sulfur compound present in garlic was found to be alliin (Mathew and Biju, 2008).

Aged garlic extract: This garlic preparation was prepared by storing raw garlic in 15-20% ethanol for a period of 20 months. It was found that this entire process had encountered a huge loss of the compound alliin. On the other hand, there was found to be an increased productivity of some other compounds like S-allylcysteine (SAC), S-allyl mercaptocysteine, allixin, saponins and selenium. These compounds were found to be more bioavailable, had more antioxidant properties and were found to have more stability. The active compound of AGE was found to be SAC (Mathew and Biju, 2008).

1.3 Bioactive Compounds present in garlic

It has been found that garlic contains about 65% water, 28% carbohydrates, 2.3% organosulfur compounds, 2% proteins, 1.3% free amino acids and 1.5% fibre. Apart from these, garlic also contains fat soluble vitamins like vitamin A, E and K and water-soluble vitamins like B complex vitamins including vitamins B1, B2, B3, B6 and B8 and vitamin C. It also contains minerals like calcium, iron, magnesium, phosphorus, potassium, sodium and zinc (Melguizo-Rodríguez *et al.*, 2022).

1.4 Carbohydrate and Protein content of Garlic

The polysaccharides present in garlic are found to be one of its most effective compounds as they have hepatoprotective, immune enhancing, and anti-oxidant properties. These polysaccharides are made up of monosaccharides like fructans, galactose and glucose (Jiang *et al.*, 2022).

There are 17 amino acids present in garlic. These amino acids are histidine, arginine, lysine, threonine, glutamine, aspartic acid, glycine, serine, proline, alanine, methionine, cysteine, phenylalanine, tryptophan, valine, leucine and isoleucine (Lidiková *et al.*, 2023). Enzymes such as allinase, myrosinase and peroxidases are also present in garlic (Tsfaye, 2021).

1.5 Sulfur compounds present in garlic

At least 33 sulfur compounds are present in garlic. These organosulfur compounds are known for their effective scavenging potential of the free radicals isoleucine (Lidiková *et al.*, 2023). The major organosulfur compounds present in garlic are alliin, alliin (diallyl thiosulfonate), diallyl trisulfide (DATS), allylpropyl disulfide, ajoene, vinylthiols, S-allylcysteine (SAC), S-allylmercaptocysteine (Rana *et al.*, 2011).

Garlic's typical pungent smell is due to the presence of the compound alliin (diallyl thiosulphate). When the garlic is crushed or cut or there's injury to the garlic bulb, the enzyme allinase is activated and this converts alliin to alliin. This alliin when metabolized further produces compounds such as diallyl sulphide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATs), allyl methyl trisulfide, dithiols and ajoene and vinylthiols (Omar *et al.*, 2010). It has been found that the organosulfur compounds present in garlic had a higher digestibility in the raw state than in the cooked state (Shang *et al.*, 2019).

Apart from the organosulfur compounds, garlic also contains a variety of phenolic compounds and other compounds like saponins. It has been found that garlic contains about more than 20 phenolic compounds. The major phenolic compounds found were β -resorcylic acid, pyrogallol, protocatechuic acid, rutin, gallic acid and quercetin (Shang *et al.*, 2019).

2. Role of garlic in various metabolic disorders

2.1. Cardiovascular Diseases

Cardiovascular diseases refer to a group of diseases revolving around the heart and the blood vessels. Some of the diseases under the CVD group of diseases are hypertension, stroke, coronary artery disease (CAD), myocardial infarction, cardiomyopathy, peripheral artery disease, venous thrombosis, atherosclerosis and some other. All these diseases can be attributed to smoking, high blood pressure, lack of adequate exercise, poor dietary habits and uncontrolled alcohol consumption. It has also been estimated that by reducing the risk factors 90% of the CVD cases can be prevented (Ugwu and Suru, 2016). It has been found out through studies that

the component mostly responsible for the creation of a proinflammatory state in the body is RLP or remnant lipoprotein cholesterol. These RLP are found to be extremely arrhythmogenic (referred to a state where the normal heart muscle has been replaced by fatty fibrous tissue). RLPs are formed by the partial catabolization of chylomicrons and very low-density lipoprotein. Studies have revealed these remnant lipoproteins were found to be a well-established risk factor for Coronary Artery Disease (CAD) (Paul, 2017).

Hypertension: Garlic was found to have a role in treating hypertension (Paul, 2017). Studies reported that garlic extracts were found to be anti-hypertensive and vasorelaxant. These extracts were found to increase the synthesis of Nitric Oxide (NO), were found to induce vasodilation through hydrogen sulphide and inhibit the activity of angiotensin converting enzyme. It has been found through studies that allicin along with ajoene, cisetane and some other organosulfur compounds present in garlic could display hypotensive properties. It was also found out that aged garlic extract which contained 1.2mg of S-allyl cysteine was greatly instrumental in lowering the peripheral and central blood pressure persisting in patients with unconstrained hypertension (Ugwu & Suru, 2016).

Coronary Atherosclerosis: Garlic was also found to have a role in curing and treating coronary atherosclerosis. It was found that aged garlic extract (AGE) when supplemented with L-arginine, B vitamins and folic acid played a positive role in reducing atherosclerosis as well as improved the vascular function and oxidative biomarkers (Paul, 2017). Allicin, the bioactive constituent of garlic, positively reduced two risk factors of atherosclerosis. (i) It prevented the breakdown of macrophages and the LDL uptake. (ii) It was also found that aged garlic extract prevented the oxidation of lipid and oxidative modification of LDL, thus it reduces the amount of circulating oxidized LDL in the blood thereby eventually decreasing the build-up of cholesterol in smooth muscles, blood vessels and macrophages which ultimately leads to the formation of fatty streaks (Ugwu & Suru, 2016).

Anti-thrombotic property: It was found that Diallyl trisulfide (DATS) compound present in garlic has anti-thrombotic property (Ugwu & Suru, 2016).

Anti-platelet property: Methyl allyl trisulfide (MATs) found in garlic possesses anti-platelet property (Ugwu & Suru, 2016).

Anti-aggregatory property: Ajoene, found in garlic possess anti-aggregatory property (Ugwu & Suru, 2016).

2.2. Diabetes Mellitus

Diabetes mellitus can be defined as a class of metabolic disorders marked by persistent hyperglycemia which results either from the inadequate secretion of insulin or from the inadequate action of insulin (Kharroubi and Darwish, 2015). Thus, the benefits of consumption of garlic in diabetes mellitus can be attributed to the reduction in the blood sugar levels, improving the insulin sensitivity and providing cardiovascular protection (Kalhotra *et al.*, 2020). These beneficial effects of garlic were primarily due to the presence of its volatile active sulfur compounds, such as allicin, alliin, S-allyl cysteine, allyl mercaptan, ajoene, diallyl disulfide, diallyl sulfide and diallyl trisulfide (Ota & Ulrih, 2017).

In this regard several studies had been conducted. In one such study, it was concluded that a lower serum glucose level was achieved when aged garlic extract was administered orally. In this experimental research, it was found that there was a significant reduction in the blood glucose levels of diabetic rats who were given 300-600 mg/kg of aged garlic extract (AGE) while there was found to be a constant increase in the blood glucose level of the untreated control rats. There was also a considerable reduction found in the ranges of the glycosylated hemoglobin (GHb) after the administration of 300 and 600 mg/kg doses of aged garlic extract (Sanie-Jahromi *et al.*, 2023).

In another study it was demonstrated that the clinical supplementation of garlic along with the conventional anti-diabetic drugs could provide a significant diabetic control in type 2 diabetes. Additionally clinical trials had also stated that garlic and its derivatives could effectively induce a reduction in the insulin resistance. Garlic and its components further act as donors of hydrogen sulfur that further controls type 2 diabetes. Another study had concluded that in diabetic patients, garlic could reduce the fasting glucose levels and the hemoglobin A1c (HbA1C) levels as well as the lipid profile levels (Yedjou *et al.*, 2023).

2.3. Cancer

Cancer can be said to be the second leading cause of global death. The existence of cancer has also been found to have increased thereby making it a serious problem impacting the health of human societies (Hassanpour and Dehghani, 2017).

Therefore, taking some dietary preventive measures against cancer are a necessity. The allylsulfide derivatives present in garlic has been found to possess anti-cancer properties. Garlic was found to reduce the growth rate of cancer cells by producing blockage in the cell cycle. Garlic was also found to possess anti-tumour effects and chemo-preventive effects. The compound ajoene present in garlic waxes found to demonstrate anti-proliferative activity. Allicin, another compound present in garlic, was found to have inhibitory effect against the proliferation of cells of colon cancer and the endometrial of the human mammary glands. Diallyl sulfide and diallyl disulfide also had inhibitory effects against arylamine N-acetyltransferase activity as well as 2-aminofluorene-DNA found in the human promyelocytic leukemia cells. The inhibitory action on the cell growth of the human melanoma A375 cells was found to be caused by the DATS present in garlic (Bayan *et al.*, 2014).

It was found that the anti-cancer properties present in garlic were majorly due to the following reasons:

- i. Garlic was found to subdue the mutagenesis of cancer cells
- ii. Garlic contains potent anti-oxidant properties; therefore, it can help to scavenge and neutralize the free radicals and reactive oxygen species. Contradictorily, garlic was found to enhance the activity of glutathione reductase. In a study, it was seen that by orally administering garlic in mice, there was an increase in the circulatory antioxidants like vitamin E and superoxide dismutase.
- iii. Garlic was found to regulate the activities of enzymes. It was found to stimulate the enzymes involved in carcinogen detoxification like glutathione S-transferases (GSTs) and cytochrome P450 s (CYPs). DAS oxidant derivatives of garlic was found to reduce the enzymatic activity of CYP2E, thereby decreasing the toxic products of some common carcinogens, like carbon tetrachloride, N-nitrosodimethylamine and acetoaminophen.
- iv. Garlic compounds were also found to inhibit the protein folding observed in the endoplasmic reticulum (Zhang *et al.*, 2020).
- v. In a study it was found that intake of garlic had a positive impact on the colorectal cancer (Zhang *et al.*, 2020).

3. Conclusion

Allicin, the main active ingredient presents in garlic along with its derivatives play an important role in preventing the onset of various metabolic diseases like cardiovascular diseases, cancer, diabetes and displays a wide range of medicinal use across the world. This medicinal use of garlic dates back to the ancient times and can be attributed to the presence of high concentration of organosulfur compounds. However, more research is needed to better understand the nutraceutical benefits of garlic.

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