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Introduction



Garlic is used in various parts of the world for its antimicrobial activity, ability to repel insects, and its characteristic aroma and flavor. In the ancient Middle East and in the earliest Chinese dynasties, garlic was consumed both as a food and a medicine. Although garlic has been praised for its medicinal properties since ancient times, its benefits may go beyond traditional uses.(1)

Garlic (*Allium sativum* Linn) belongs to *Allium* species, containing large amounts of potential chemopreventive compounds. It has been studied for its therapeutic uses as antibiotic, antidiabetic, antioxidant, antiatherogenic, anticancer and fibrinolytic effects. "The name *Allium* is derived from the Celtic word *all*, which means pungent, and it betrays the presence of a host of remarkable flavorants and odorants all having in common one element, sulfur."⁷

Its Relationship to Cancer

Garlic contains a great combination of sulfur amino acids and their derivatives, as well as variety of alkyl (e.g. methyl) and alkenyl (e.g. allyl) cysteine sulfoxides. These sulfoxides are the precursors for the formation of a variety host of volatile sulfides when garlic is sliced or crushed.(2) The intact cells of garlic contain alliin, an odorless, sulfur-containing amino acid derivative. When the cells are crushed, it gets introduced to the enzyme alliinase located in neighboring cells. This enzyme converts alliin to allicin (diallylthiosulfinate). Then, allicin can be converted easily to many other sulfurated compounds, including those found in aged garlic extract. Chewing also produces the conversion to allicin, which results in odor production. (3) When the garlic clove is cut allicin undergoes a series of decomposition reaction carried out by alliinase, yielding sulfenic acids, which are further degraded to various thiosulfinates. The thiosulfinates are further broken down to polysulfides, which form the odoriferous elements associated with the smell and taste of garlic.(9)

Garlic constituents (Table 1) have been shown to influence both initiation and promotion phases of cancer in several animal and cell culture models.(4) Although the biochemical mechanisms responsible for the observed antimutagenic and antitumorogenic effects of garlic and its constituents are not exactly known, several studies have shown that thioallyl derivatives can inhibit growth of transplantable tumors and have antipromotional activity on several mammalian tumor cell lines. "For example, treatment of human melanoma

cells with S-allylcysteine reduced expression of cell-surface gangliosides, tumor-associated markers of differentiation and transformation." S180 tumor cells that were exposed to a garlic extract displayed delayed progression to S phase. In skin exposed to 7,12-dimethylbenz[a]anthracene and phorbol ester, pretreatment with an ethanolic garlic extract hindered phosphorylation of phospholipids, an early event induced by tumor promoters. In a similar way, reduction in phosphorylation of G-protein and tyrosine phosphatase-1B was associated with the antiproliferative activity of garlic constituents on normal smooth muscle and endothelial cells. Therefore, garlic exerts antiproliferative activity on normal and malignant cells.(4)

Table 1. Some of the Important Sulfur Compounds Found in Garlic(1)

3,5-Diethyl-1,2,4-trithiolane Diallyl sulfide
Allyl 1-propenyl disulfide Diallyl trisulfide
Allyl 1-propenyl trisulfide Methyl allyl trisulfide
Allyl alcohol Methyl allyl disulfide
Diallyl disulfide (DADS) S-allyl cysteine (SAC)

In their study, Pinto et. al. demonstrated that a single treatment with S-allylmercaptocysteine (an S-cysteinyl derivative) compromises the growth of human prostate carcinoma cells within 4 days in culture. Interestingly enough, the antiproliferative effect of S-allylmercaptocysteine persists for more than 4 days after its removal from culture.(4)

Furthermore, exposure to N-nitroso compounds, a class of potential carcinogens, may be an important factor in determining human cancer risk. We synthesize N-nitroso compounds from precursors occurring in our daily diet. The ability of human liver cells to metabolize nitrosamines to compounds that have been known to produce DNA damage in animals supports the hypothesis that N-nitroso compounds are possible carcinogens for humans. The ability of garlic to block the synthesis of N-nitroso compounds may explain part of the protection that is observed in epidemiological investigation. Garlic effectively decreases the spontaneous and the microbial formation of nitrosamines. N-nitrosoproline is a nonmutagenic and noncarcinogenic compound, which is used as a biomarker of the body's potential to form carcinogenic nitrosamines. Adding 5 g of fresh crushed garlic to human subjects' diet was found to markedly inhibit urinary N-nitrosoproline excretion. This suggested that a decrease in nitrosation reactions had occurred. Therefore, there is a positive relationship between the sulfhydryl content of foods and their ability to block nitrosamine formation. Other Allium plants, like onion, leeks and chives, may have similar inhibitory effects against nitrosamine and possibly tumor formation.(1)

Other experimental research suggest an inhibitory role in colon carcinogenesis by certain sulfur containing compounds, such as diallyl sulfide, S-allylmercaptocystein and S-allylcystein, present in Allium Vegetables. Diallyl disulfide, a garlic constituent, has recently been shown to reduce the occurrence of invasive colon adenocarcinoma in experimental animals. Some of the potentially chemopreventive sulfur-containing compounds are also present in garlic supplements.(6)

Although a couple of studies have found no association between the consumption of onions, leeks, or garlic supplement and the incidence of lung carcinoma (10) and female breast carcinoma (11), work by others has shown that chemicals in garlic and onion prevent cancers at other sites in addition to the colon and esophagus. These include the skin, breast, lung and stomach. With the exception of the skin tumorigenesis studies, the Allium chemopreventives were found to be more active in the initiation phase of carcinogenesis than after the establishment of tumorigenesis. Some of these experiments are summarized in Table 2.(9)

Finally, John Milner, Ph.D., of Pennsylvania State University has recently found that a diet consisting of 2 to 4 percent garlic delayed the growth of breast cancer and reduced the number of tumors. "The total tumor number was reduced by 56% in rats fed the 2% garlic-powder diet throughout the 20 weeks feeding period compared to control-fed rats." (12) In a separate study, he found that garlic could dramatically reduce the number of "adducts" in deoxyribonucleic acid. Adducts are those chemicals that attach nitrosamines to DNA setting the stage for cancerous changes. He exposed a group of rats to nitrosamines, but some of the animals were also given large amounts of aged garlic powder. Depending on the amount of garlic they ate, the rats had a 40 to 80 percent reduction in the occurrence of adducts in the liver. In addition, garlic-eating rats benefited from 55 to 69 percent fewer mammary gland adducts.(13) Moreover, depressed cytochrome P450 activity or induced glutathione-S-transferase activity and an increase in glutathione concentration caused by garlic are consistent with a decrease in the potential of carcinogenic compounds. This decreased potential is evident from the reduced presence of DNA adducts resulting from treatment with several procarcinogens.1

Table 2. Experimental Chemoprevention with Allium-Derived Agents⁹

Organ Site	Colon	Esophagus	Lung	Breast
Carcinogen	Dimethylhydrazine	Nitrosomethylbenzylamine	Benzo[a]pyrene	
Dimethylbenzathracene				
Allium agent	DAS	DAS	Diallyl trisulfide	
High-selenium garlic				
Results	Strong inhibition	Complete inhibition	Strong inhibition	
Strong inhibition				

Cancer Prevention Using Garlic and Selenium

It is difficult to pursue the public to eat only those foods that are presumably good for their health, so an alternative is to enrich foods with known cancer preventive agents. The idea with the high-selenium garlic and onion may represent a viable strategy for achieving this goal. Ip and Lisk claim that high-selenium garlic and onion have good

anticancer activity and can be easily adapted for human consumption on a regular basis. They add that this does not result in an excessive accumulation of tissue selenium, a concern that is associated with the standard selenium compounds such as selenite and selenomethionine.(2)

Furthermore, Ip and Lisk demonstrated the feasibility of using selenium-enriched food products for cancer prevention. Both garlic and onion crops were cultivated with selenium fertilization and were produced strictly for their own research. It is of interest to note that the high-selenium onion contained only 28 p.p.m. Se, in contrast to a concentration of 112 p.p.m. found in the high-selenium garlic, even though they were grown in the same season and location and with the same schedule of selenium fertilization. The discrepancy suggests that onion may not have the same capacity to accumulate selenium as garlic.(2)

Other Benefits

Allicin, a constituent of garlic, is known as Russian Penicillin as it is active against many bacteria that are resistant to antibiotics. It has been reported that bacteria resistant to 8 major antibiotics have shown a high response towards garlic extract, which contain allicin as the main active principle.(7)

"Oxygen radical injury and lipid peroxidation have been suggested as major causes of atherosclerosis, cancer, liver disease, and the aging process. More specifically, oxidative modification of low-density lipoprotein (LDL) has been recognized as an important process of atherosclerosis." In their study, Ide et. al. determined the effects of aged garlic extract, four of its constituents, and a metabolite on Cu²⁺-induced oxidative modification of LDL using an in vitro system. All these compounds were shown to inhibit oxidative modification of LDL.(5)

Protection from radiation, free radical production, and stress conditions are some other effects of garlic products reported elsewhere.(7)

Negative Effects

Excessive intake of Allium species may interfere with hemoglobin production and may lead to lysis of red blood cells. Prolong feeding of high levels of raw garlic to rats has resulted in anemia, weight loss and failure to grow.(7)

Summary

Garlic has been touted for its medicinal properties in almost all ancient cultures. It belongs to the Allium family all members of which contain sulfur. Garlic contains an abundance of sulfur amino acids and their derivatives. The processing of these compounds through various preparations is what causes the odor of garlic. Interestingly, the same derivatives are found to have tremendous effect, through many different systems and pathways, on carcinogenesis and its prevention. Selenium is another

compound that can be concentrated in garlic, and it is found to be effective in cancer prevention. Garlic's benefits far outweigh its negative effects, and thus it tends to live up to its reputation.

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