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Recent Advances on the Nutritional Effects Associated with the Use of Garlic as a Supplement

The Influence of Heating on the Anticancer Properties of Garlic[1]

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ABSTRACT Allyl sulfur compounds are the major active constituents found in crushed garlic. Research has revealed that garlic and its lipid- or water-soluble components have many pharmacologic properties; however, studies also demonstrate that heating has a negative influence on these beneficial effects. We recently conducted several studies to investigate the influence of microwave or oven heating on the anticarcinogenesis property of garlic. Our studies showed that as little as 60 s of microwave heating or 45 min of oven heating can block garlic's ability to inhibit in vivo binding of mammary carcinogen [7,12-dimethylbenzene(a)anthracene (DMBA)] metabolites to rat mammary epithelial cell DNA. Allowing crushed garlic to "stand" for 10 min before microwave heating for 60 s prevented the total loss of anticarcinogenic activity. Our studies demonstrated that this blocking of the ability of garlic was consistent with inactivation of alliinase. These studies suggest that heating destroyed garlic's active allyl sulfur compound formation, which may relate to its anticancer properties. J. Nutr. 131: 1054S–1057S, 2001.

KEY WORDS: • *garlic* • *heating* • *DNA adducts*

Garlic (*Allium Sativum* L.) is cultivated worldwide and its potential medical properties have been recognized for thousands of years. Garlic has acquired a reputation in many cultures as a formidable prophylactic and therapeutic medical agent. Many recent studies have demonstrated garlic's pharmacologic effects, such as antibacterial, antifungal, hypolipidemic, hypoglycemic, antiothrombotic, antioxidant and anticancer properties (Bordia et al. 1975, Conner et al. 1984, Imai et al. 1994, Lawson et al. 1992, Mathew and Augusti 1973, Rees et al. 1993).

The evidence of an anticarcinogenic role for garlic comes from both epidemiologic and laboratory investigations. A decade ago, for example, a study from China indicated an inverse relationship in mortality between stomach cancer and garlic consumption (Wei et al. 1988), providing the first evidence of garlic's anticancer potential. The results of this study were corroborated by a study conducted in Italy (Buiatti et al. 1989). Similarly, a lower risk of colon cancer for American consumers of garlic was reported in the Iowa Woman's Health Study (Steinmetz et al. 1994). Although the minimum daily intake required to reduce cancer risk remains to be determined, garlic had been categorized as a dietary anticarcinogen (Lau et al. 1990).

Laboratory investigations have shown that both water- and lipid-soluble sulfur compounds from garlic provide its anticarcinogenic benefits (Hussain et al. 1990, Ip et al.1992, Liu et al. 1992, Perchellet et al. 1990, Rao et al. 1990, Reddy et al. 1993, Schaffer et al. 1997, Sumiyoshi and Wargovich, 1990). Animal research has demonstrated further that the protection offered by garlic is not limited to only a specific tissue or specific carcinogen, but can occur in several tissues and as a result of treatment of different types of carcinogens (Belman 1983, Dion et al. 1997, Hong et al. 1992, Sadhana et al. 1988, Schaffer et al. 1996, Shenoy and Choughuley 1992, Wargovich et al. 1988). Studies have also demonstrated that garlic powder and its associated allyl sulfur compounds are effective at both the initiation and promotion phases of the cancer process (Liu et al. 1992). Although Phase I and Phase II enzymes in liver and other target tissues affected by organosulfur compounds may be involved in carcinogen metabolism (Devasagayam et al. 1982, Ip and Lisk 1997, Schaffer et al. 1997, Sparnins et al. 1988), additional studies were required to explain the precise mechanism.

Garlic is a rich source of water- and lipid-soluble organosulfur compounds, but the constituents responsible for the health benefits of garlic may vary in type and concentration, depending on different processing, preparation and soil conditions. This paper briefly reviews organosulfur compounds found in garlic and the influence of heating on garlic's benefits, especially on its anticancer ability.

Organosulfur compounds in garlic and their roles. The remarkable, high sulfur content of garlic distinguishes it from many other vegetables. Evidence from laboratory research

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TABLE 1

Structure of allyl sulfur compounds[1]

Chemical	Structure
Alliin	$CH_2{=}CH{-}CH_2{-}S({=}O){-}CH_2{-}CH(NH_2){-}COOH$
Allicin	$CH_2{=}CH{-}CH_2{-}S({=}O){-}S{-}CH_2{-}CH{=}CH_2$
DADS	$CH_2{=}CH{-}CH_2{-}S{-}S{-}CH_2{-}CH{=}CH_2$
SAC	$CH_2{=}CH{-}CH_2{-}S{-}CH_2{-}CH(NH_2){-}COOH$

[1] DADS, diallyl disulfide; SAC, *S*-allylcysteine.

suggests that a large group of allyl sulfur compounds may be responsible for the biological and medical functions of garlic (Augusti 1974 and1975, Murthy and Amonkar 1974, Sparnins et al. 1988, Wargovich 1987, Wargovich et al. 1988, Yamada and Azuma 1977). The major representatives of these allyl sulfur compounds and their liaisons are shown in **Table 1** and **Figure 1**.

γ-Glutamylcysteines serve as important storage compounds in garlic cloves and have been shown to play a significant role in the production of additional alliin during the early developmental stages of the garlic plant (Lancaster and Shaw 1989). Although alliin has been reported to have antioxidant properties (Rabinkov et al. 1988), other studies have found that alliin is unable to inhibit in vitro cholesterol biosynthesis (Gebhardt 1993). Similarly, we found that alliin was ineffective in retarding 7,12-dimethylbenzene(a)anthracene (DMBA)[3] adducts in cancer prevention.

Chopping or crushing garlic releases alliinase, which rapidly converts alliin (*S*-alkyl-L-cysteine sulfoxide) to allicin (dialkly thiosulfinate) (Lawson 1993). Alliin is the parent compound of allicin, and allicin is the parent compound of diallyl disulfide (DADS). Allicin is the major thiosulfinate compound found in crushed garlic, but it is quite unstable and quickly converts into diallyl sulfide (DAS), DADS, diallyl trisulfide (DATS) and polysulfide compounds (Block 1985). Allicin is not only responsible for the characteristic odor of fresh garlic (Whitaker 1976), but is also considered one of the most important biologically active compounds found in crushed or homogenized garlic (Koch and Lawson 1994). A number of therapeutic applications of garlic involve allicin and compounds derived from it (Augusti 1974 and1975, Murthy and Amonkar 1974, Sparnins et al. 1988, Wargovich 1987, Wargovich et al. 1988, Yamada and Azuma 1977). Allicin and allicin potential have been used commercially as indices to evaluate and compare the medical value of commercially available prepared garlic. During the alcoholic fermentation of garlic, such as in some deodorized commercial preparations, *S*-allylcysteine (SAC) is converted from γ-glutamyl-*S*-allylcysteine, a precursor of alliin. Although experiments have shown SAC to be an active compound found in garlic, its presence in whole garlic cloves is variable and has been ignored by researchers.

[3] Abbreviations: DADS, diallyl disulfide; DAS, diallyl sulfide; DATS, diallyl trisulfide; DMBA, 7,12-dimethylbenz(a)anthracene; SAC, *S*-allylcysteine; TXB_2, thromboxane B_2.

Alliinase (EC 4.41.4), a glycoprotein, is responsible for the conversion of alliin to allicin. Alliinase can be activated only when garlic cloves are crushed or cut; like other enzymes, it is thermolabile (Jansen et al. 1989). When alliinase is inactivated by heating, the cascade of thiosulfinate formation is blocked from alliin, and allicin and its derivatives cannot be formed. Our research has shown that as little as 60 s of microwave heating can totally destroy alliinase enzyme activity, whereas microwave heating for 30 s inhibited 90% of alliinase activity compared with unheated garlic.

Heating and its negative effect on garlic's performance. Heating can have different effects on food component viability. Lycopene bioavailability, for example, has been shown to improve by heating tomato in oil (Stahl and Sies 1992). However, Chen et al. (1985) found that boiling garlic at 100°C for 20 min completely suppressed its antibacterial activities. Research also showed that increasing the temperature from 60 to 100°C produced a significant decrease in the inhibitory effect of garlic bulbs against the fungi tested (Yin and Cheng 1998). Although garlic has been suggested for many years by epidemiology and laboratory experiments to have cardiovascular benefits, these health effects are lost in heat-treated garlic. In a recent study (Bordia et al. 1996), a dose-dependent inhibition of serum thromboxane B_2 (TXB_2) concentration was observed in rats treated with aqueous extracts of raw garlic. However, boiled garlic extracts had little effect on TXB_2 synthesis, even at a high concentration. Ali (1995) also found that boiled garlic had little effect on inhibition of cyclooxygenase activity in rabbit tissue compared with raw garlic. Similarly, heating garlic to 100°C for 20, 40 or 60 min can reduce its antioxidant activity (Prasad et al. 1996). A more complete list of the effects of heating on garlic's functioning can be found in **Table 2**.

Heating blocks the anticancer ability of garlic. Research has revealed that garlic powder and its water- or lipid-soluble allyl sulfur compounds can protect against chemically induced experimental animal tumors (Amagase and Milner 1993, Amagase et al.1996). In our recent studies (**Fig. 2**), supplements with raw garlic given by gastric gavage reduced DMBA-induced DNA adduct formation by 64%. Microwave treatment of garlic for 30 s did not influence the degree of protection; however, garlic crushed or not crushed before microwave heating for 30 s resulted in a 62 and 61% reduction, respectively, in adduct formation. Microwaving uncrushed garlic for 60 s completely blocked the ability of garlic to suppress the adduct formation. Crushing and immediately microwaving for 60 s similarly blocked the protection offered by garlic. However, maintaining crushed garlic at room temperature for 10 min before 60 s of microwave heating partially restored the anticarcinogenic properties, although the protection was 30% less than that for unmicrowaved garlic. Similarly, oven-heated whole garlic (garlic without cutting the top) for 45 min thoroughly obstructed the anticarcinogenic benefit of garlic. If intact garlic was cut at the top and allowed

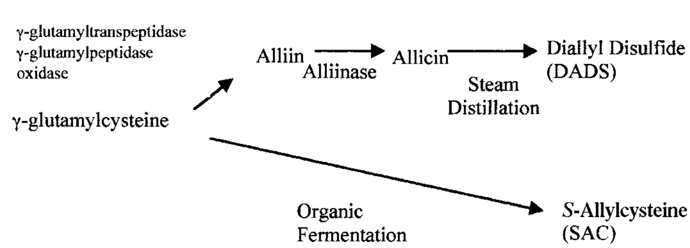

FIGURE 1 Major allyl sulfur compounds and their liaisons.

TABLE 2

Tests showing heating reduces the effects of garlic[1]

Garlic preparation	Temperature/Time	Testing	Reference
Garlic bulb	60–100°C	Fungal growth	Yin and Cheng 1998
Green garlic	60–80°C	Fungal growth	Yin and Cheng 1998
Garlic	Boiling	Bacterial growth	Cellini et al. 1996
Garlic	Boiling	TXB_2 level	Bordia et al. 1996
Garlic	100°C/20, 40 and 60 min	Oxygen free radical–scavenging activity	Prasad et al. 1996
Garlic	Boiling	Cyclooxygenase activity	Ali 1995
Garlic	Heating	Antioxidant	Imai et al. 1994
Garlic	Boiling	Prostaglandin synthesis	Ali et al. 1993
Garlic	Boiling	Bacteria growth	Chen et al. 1985

[1] TXB_2, thromboxane B_2.

to "stand" for 10 min before oven heating, it still maintained partial protection compared with unheated garlic. Additional study showed that SAC and DADS could decrease the formation of DNA adducts, whereas isomolar alliin did not alter the occurrence of adduct formation (**Fig. 3**).

Summary

These studies reveal that garlic's benefits are lost due to the heating process. According to Ali (1995), the reason that boiled garlic has little effect on cyclooxygenase activity may be related to the fact that the active component of raw garlic is destroyed upon heating. Our studies demonstrated that the loss of protection against DMBA-induced adducts due to heating may be related to a loss of alliinase activity. The present studies reveal that after garlic is heated for 30 s in a microwave oven, only ~10% of its original alliinase activity remained. It is possible that this residual alliinase was sufficient to convert alliin to active compounds and to continue garlic's ability to alter the occurrence of DNA adducts. However, 60 s of heating in a microwave not only resulted in almost undetectable alliinase activity but also eliminated garlic's ability to suppress DMBA-induced DNA-adduct formation. It remains to be determined whether there is a direct link between depression of alliinase activity and the loss of the ability to alter DMBA bioactivation. Furthermore, our studies give evidence that ~10 min "standing" time after crushing garlic is necessary for the biologically active generation of compounds to reduce the blunting effects of heating.

Although garlic is known for its many pharmaceutical effects, these abilities can be depressed by preparation or processing methods. The negative influence of heating may be related to suppression of the activity of the enzyme alliinase. Additionally, our studies suggest that the generation of biologically active allyl sulfur compounds is dependent not only on total alliinase activity, but also the time for which it is allowed to function.

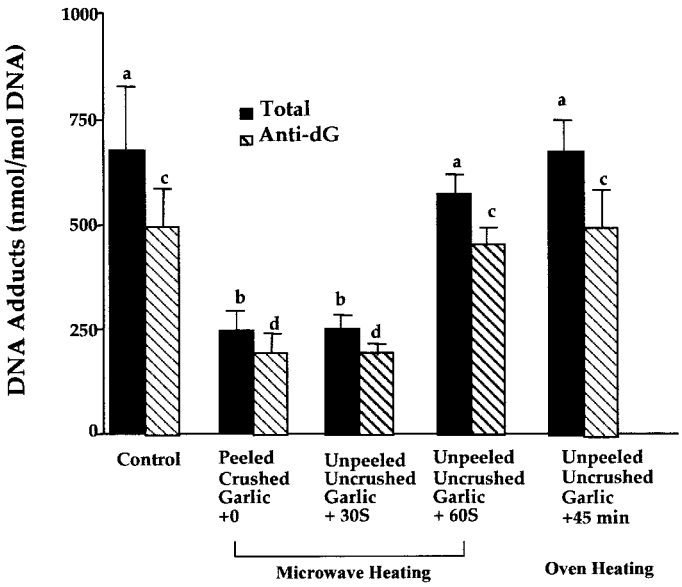

FIGURE 2 Effect of heating garlic for various times on the occurrence of 7,12-dimethylbenz(a)anthracene (DMBA)-induced DNA adducts total and anti-3,4-dihydrodiol-1,2-epoxide-deoxyguanosine (anti-dG) adducts. Rats were provided no supplemental garlic (controls), or a homogenized garlic/corn oil suspension prepared as follows: unheated peeled and crushed garlic (0S); unpeeled and uncrushed garlic heated in microwave for either 30 (30S) or 60 s (60S); or unpeeled and uncrushed garlic heated in an oven for 45 min (45 min). Bars not sharing a common superscript letter differ $P < 0.05$.

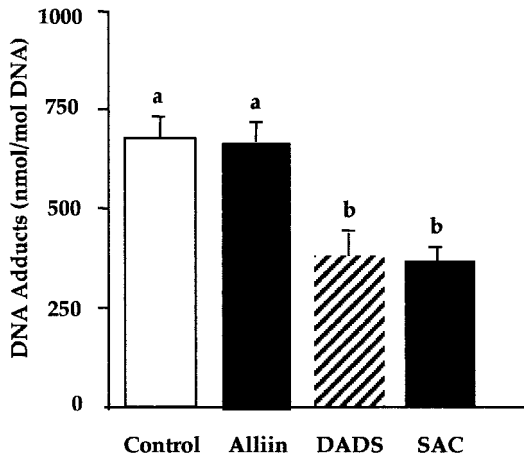

FIGURE 3 Influence of gastric gavage treatment of rats with 0.105 μmol alliin, diallyl disulfide (DADS), or S-allylcysteine (SAC) on 7,12-dimethylbenz(a)anthracene (DMBA)-induced DNA adducts in mammary tissue. Control rats were given double-distilled water because it was the carrier for alliin and SAC. Values are means ± SEM, $n = 5$. Bars not sharing a common superscript letter differ $P < 0.05$.

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