The stinking rose: organosulfur compounds and cancer¹,²

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In this issue of the AJCN, Pinto et al (1) showed potentially important effects of aged garlic extract derivatives, S-allylcysteine and S-allylmethylcysteine, on LNCAp prostate cancer cell glutathione and polyamine concentrations in vitro. This work adds additional support to the body of work in animals and cells showing potent effects of garlic in the inhibition of tumorogenesis. Some studies showed inhibition of carcinogen-antiduct formation as an important mechanism of action using both garlic and selenium-enriched garlic (2–5). Another study showed that the rise in polyamines seen after colonic irradiation could be inhibited by pretreatment with diallyl sulfide, an organosulfur compound found in garlic. However, the ultimate interest in garlic is as a dietary constituent or supplement. S-Allylmethylcysteine is only found in garlic bulbs that have been aged for at least a year, and it is not clear whether the in vitro observations would translate into benefits for humans eating garlic. In fact, the epidemiologic studies examining garlic intake and cancer do not show a strong effect of garlic ingestion (6, 7).

Organosulfur compounds occur in a large number of different plants, including garlic, Chinese chive, Welsh onion, turred stone leek, and shallots. Garlic was consumed both as a food and a medicine in the ancient Middle East and in the earliest Chinese dynasties. It has been extensively investigated both scientifically and clinically. Well over a thousand papers on garlic and related alliums have been published in the past 20 y. There is a clear rationale for garlic developing its distinctive smell as a defense against predators. The intact cells of garlic contain an odorless, sulfur-containing amino acid derivative, alliin (S-allyl-l-cysteine sulfoxide). When the cells are crushed, it comes into contact with the enzyme alliinase located in neighboring cells. This enzyme converts alliin to alllicin (diallyl thiosulfinate). Alllicin can be converted easily to many other sulfurated compounds, including those found in aged garlic extract. The conversion to alllicin occurs when garlic is chewed, resulting in odor production, which reduces the acceptability to some individuals of eating large amounts of garlic. Other side effects are gastrointestinal flatulence and frequent bowel movements. A 2.5% garlic powder diet found effective in some animal studies is equivalent to a 4.76-g/m² dose in humans. This would be equivalent to a 70-kg man eating numerous average-sized cloves of garlic (4 g each). Because conversion of alliin to alllicin does not proceed in the acid environment of the stomach, enteric-coated capsules containing dried powdered garlic have been developed to deliver alliin and allliinase to the alkaline environment of the small intestine. Once released, the allicin reacts rapidly with the amino acid cysteine derived from protein in food consumed with the garlic. Much work remains to be done on the metabolism of naturally derived organosulfur compounds such as those found in garlic before we can be certain that the observations made in animals and in cell culture extend to humans.

Many different phytochemicals have potent activity on carcinogenesis, risk factors for cardiovascular disease, and aging in animals and humans. Why have plants evolved substances that have potent effects in animal systems? There are at least two hypotheses. One hypothesis is that phytochemicals such as digoxin from the foxglove plant fit the human cardiotonic receptor through some accident of evolution in plants and humans. An alternative hypothesis is one of coevolution. Insects, birds, and other predators clearly influenced the evolution of plants, and plants may have influenced the evolution of mammals and humans. Plants have been on this planet for one billion years compared with the relatively brief two million years that the human species has been on this planet. On the basis of this chronology, it may be that early humans were simply opportunists taking advantage of the rich bounty of phytochemicals in their environment. Early humans ingesting large amounts of certain phytochemicals, such as ascorbic acid, lost the ability to synthesize these substances as endogenous antioxidants. These phytochemicals would then take on the role of essential nutrients or vitamins. This argument applies to some extent to other phytochemicals such as the sulfur-containing compounds found in garlic and other allium species, inhibitors of cholesterol biosynthesis found in yeast and citrus fruits, and the isoflavonoids found in soybean protein isolate.

The ancient environment of humans was rich in plant-derived phytochemicals. With the advent of agriculture 10,000 y ago, humans began to influence the ecology of their food supply. This led to increased supplies of energy and nutrients, but in recent times has led to a decrease in the biodiversity of food intake. It has been estimated that humans currently eat only 150–200 of the 50,000–100,000 edible plant species on earth. Furthermore, only 20% of Americans eat the five servings per day of fruits and vegetables recommended by the National Cancer Institute.

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Clearly, additional human studies of metabolism and efficacy are needed using appropriate intermediate markers of the fate and effectiveness of garlic and its constituents. The other implication of this new realization is that nutritional interventions for cancer prevention may need to include multiple phytochemicals and micronutrients. Although ongoing studies of the effects of fat, energy, and individual micronutrients in cancer prevention trials are important, models of nutritional intervention that can incorporate some of the anticipated nutrient-nutrient interactions likely to occur are sorely needed.

REFERENCES


