

HEALTH BENEFITS OF ALLIUM VEGETABLES INTAKES

ANNOUNCEMENT



5-7 May 2010 - Brussels - Belgium

Social and Health Benefits of Balanced Diet: The role of Fruit and Vegetables

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Allium Foods: Mystical Functional Foods for Health Promotion

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There is little doubt that nutrition and health are intimately intertwined. For generations, people have believed that foods can do more than merely provide energy and nutrients for growth and development and thus contribute to overall health and disease prevention. Beliefs about the medicinal properties of foods have been highlighted in a number of the early writings. Hippocrates is frequently quoted to proclaim "Let food be thy medicine and medicine be thy food." Today, statements about the ability of foods and food components to reduce disease risks or enhance the quality of life are relatively commonplace and continue to captivate our lives.

Garlic and other allium foods (onions, leeks, chives, etc.) are commonly consumed foods which are often revered for their potential medicinal properties. This reverence has been promoted in recent years, especially for garlic, because of the emergence of data revealing that in addition to antimicrobial properties these foods may reduce human illnesses including that related to heart disease and cancer. The ability of garlic and its constituents to assist in maintaining normal immune-competence and possibly improve mental function suggests it, and possibly other allium foods, may have widespread health implications^{1, 2}. Unfortunately, while the interrelationship between garlic intake and health are intriguing, there remain a dearth of well-controlled clinical investigations with allium foods and the data that exist is often inconsistent. The current series of articles point to the potential benefits of garlic, and onions, in several health related conditions. The articles also provide evidence that it would be unwise, and inappropriate, to assume that all individuals will respond identically, if at all.

Many reasons may explain why a food, such as garlic, might be inconsistently related to a health outcome³. Dietary exposures, specific targets modified by the components in the food, and interactions with other nutrients in the diet or by the genomics of the consumer are likely key variables and fundamental to determining the direction or magnitude of the overall response. Foremost among these is the variation in the amount of the active agent(s) that arrives at the target site. Unfortunately, reliable tools for estimating intakes/exposures are unavailable, along with relative poor databases about the amount of these foods that is added to prepared foods. Questions about the use or non-use, or frequency are often so imprecise that it is difficult to draw strong conclusions. Likewise, our ability to assess the use of supplements remains in its infancy and contributes to uncertainty about the range of intakes and thus biological consequences. The use of standardized test to evaluate natural and commercial garlic preparations as suggested by Gonzales et al⁴ offers interesting possibilities for better defining true garlic exposures.

While there are problems in evaluating intake, there are even greater challenges in evaluating the content of specific bioactive constituents occurring in garlic that are being consumed. Undeniably there is more to garlic than the odor associated sulfur constituents. Variation in these other constituents including arginine rich proteins, fructooligosaccharides, and flavonoids, as well as the sulfur constituents, likely contribute to the variability in response. Growing conditions can influence the composition of many plants/herbs and thus likely accounts for some of the variation in response to garlic grown and processed throughout the world. Several years ago Lawson and Gardner⁵ highlighted the wide variation in the types of sulfur compounds that can occur in various garlic preparations and their

stability. Comparison of these variation preparations is sometimes similar to comparing apples and oranges in that they are within the same class of foods but can be exceeding different in the bioactive constituents they provide. Again, standardization methods may help shed light on what intakes are needed to bring about a desired response. Dr. Galeone (in this issue) concluded that onions were more beneficial in retarding myocardial infarction than garlic. Thus, it cannot be assumed that all allium foods are identical. Greater attention to the merits of individual foods for specific purposes needs, and deserves, greater attention.

Defining the molecular target for garlic and its active components is another important challenge. Based on epidemiological, preclinical and intervention data, multiple pathways appear to be influenced by the allyl sulfur compounds arising from garlic once eaten as a natural food or a commercially available preparation. The article by Reinhard (this publication) provides compelling evidence that garlic reduced blood pressure, but on those with baseline pressures greater than 140 mmHg. Thus, an insult (including excess calories, bacteria, viruses, etc.) might be needed to achieve benefits from the enhanced intake of allium foods. Understanding the cellular process that has been changed to account for the reduction in blood pressure is of paramount importance. One must ask if the response is specific to some type of insult or genotype that makes the individual vulnerable and thus determines the benefits from exaggerated garlic intake. It is important to note that this study suggests that the response to garlic may be equivalent to what is classically observed with drugs. Thus, opportunities exist for using it as a dietary component for optimizing health. Additionally the combination of agents (drugs and nutrients) may offer exciting opportunities for promoting health while minimizing adverse events and associated complications.

While there is a wealth of preclinical evidence linking allium foods intake, particularly garlic, with cancer risk and tumor behavior, the amount of clinical evidence is far less plentiful or compelling. The article by Kim and Kwon (in this series) highlights the challenges associated with unraveling the true relationship between garlic intake and cancer and how to convey the most appropriate message to consumers. While several cellular changes including oxidative stress, DNA repair, decreased cell division, apoptosis and immunocompetence may account for a response, the actual molecular event accounting for the decrease in cancer burden deserves far more attention^{1, 6}. Again, it should be noted that individuality in response to garlic is evident throughout the cancer research literature. This variation may be due to the ability to absorb, metabolize or secrete the active agents in garlic. It is most logical that genetic and epigenetic variation among individuals contributes to the response that is observed^{3, 7, 8}.

While exciting information exist about the health benefit of allium foods, and garlic in particular, the dearth of clinical information make strong recommendations challenging. Nevertheless, the information in this series of articles highlights their potential health benefits, while recognizing not all individuals will share the benefits equally. Since the ill-consequences are generally limited to halitosis, and remedial methods exist, there are few reasons to limit these foods in the diet. Maybe the old saying can be modified to "a clove" a day will keep the doctor away".

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Garlic supplements for patients with hypertension

— Kurt Reinhart —

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Background

Among its many qualities, garlic's ability to lower blood pressure is one of the most widely studied. Results from controlled trials however, have varied. Some studies have shown a modest reduction in blood pressure, while others have shown no effect. In addition, a garlic-induced reduction in blood pressure could be a safety concern for those who use it for other reasons. A recent meta-analysis was conducted to A) determine the actual effect of garlic supplements on blood pressure in patients with hypertension and B) determine if blood pressure reductions could occur in patients with normal blood pressure¹.

A meta-analysis

A systematic search of the literature was conducted to find randomized controlled trials of garlic compared to placebo which provided data on blood pressure changes. Two authors independently selected trials based on set criteria and extracted data from them including starting average blood pressure in garlic and placebo groups and ending blood pressure in both groups, as well as trial and patient characteristics. Studies were split into those with an average baseline systolic blood pressure (SBP) greater than 140 mmHg (referred to as the hypertensive group) and those with a lower average baseline SBP (referred to as the normotensive group). A random effects model was used to calculate a weighted mean difference in SBP and diastolic blood pressure (DBP) reduction for both sets of trials.

Blood pressure reduced by garlic supplements

Ten studies met the authors' pre-defined criteria and were included. Three studies were included in the hypertensive group and the other 7 were included in the normotensive group. In the hypertensive group studies, compared to placebo, garlic lowered SBP by 16.3 mmHg (95% confidence interval [CI], 6.2 to 26.5) and DBP by 9.3 mmHg (95% CI, 5.3 to 13.3). There was no such effect

in the studies in the normotensive group. An I² test, which evaluates how different the included studies were from each other, was less than 25% for both analyses indicating only minor differences between the studies.

Garlic supplements or anti-hypertensives prescription ?

Neither SBP nor DBP were reduced in those with a baseline DBP < 140 mmHg, indicating there is likely no safety issue with garlic in regards to blood pressure. These results however, show a rather robust reduction in blood pressure in subjects who have a baseline SBP greater than 140 mmHg. This level of reduction is similar to those of some prescription anti-hypertensives. These findings warrant further study of garlic in hypertensive patients.

While this data is compelling, there are a few limitations. First is the use of composite data. In the 3 studies included in the analysis of patients with SBP > 140 mmHg, the average SBP of the participants was >140 mmHg, however, it is possible that some participants had much lower baseline SBP. The opposite is true for studies included in the <140 mmHg analysis. Second was that blood pressure was not a primary endpoint for some of the included studies and may have not been obtained with scientific rigor. And finally, there are inherent limitations with the use of meta-analysis including the inability to control for biases of individual trials.

Although data is lacking to support using garlic supplements in place of standard anti-hypertensive medications, this information suggests it may be reasonable for those who refuse or don't tolerate prescription agents. Close monitoring of blood pressure should be completed on these patients. Garlic has also been found to improve cholesterol levels in some patients and patients who take garlic for this reason are not likely to suffer from hypotension².



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Allium vegetables intake and risk of acute myocardial infarction in Italy

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Background

Garlic (*Allium sativum*) and onion (*Allium cepa*) are a rich source of several phytonutrients recognized as important elements of the Mediterranean diet¹. Several in vitro studies and clinical trials on garlic supplementation suggested that garlic intake might protect from cardiovascular disease risk by reducing serum cholesterol concentration and blood pressure². However, only two epidemiological studies considered the relation between dietary intake of onions and cardiovascular diseases, and they both found an inverse association^{3, 4}.

To provide further information on the role of dietary intake of allium vegetables and risk of coronary heart disease, we analysed the relationship between onion and garlic intake and non-fatal Acute Myocardial Infarction (AMI), using data from a case-control study conducted in Italy.

A case-control study

Data was derived from a case-control study of non-fatal AMI, conducted in the greater Milan area, Italy, between 1995 and 2003. The cases were 760 patients with a first episode of non-fatal AMI. The controls were 682 patients from the same geographic area, admitted to the same hospitals as cases for a wide spectrum of acute conditions not related to known AMI risk factors or diet. Interviews were conducted in the hospital using a structured questionnaire, including information on socio-demographic factors, anthropometric variables, diet, smoking and alcohol consumption, physical activity, and many other variables. For onion intake, we asked for the weekly frequency of consumption and usual portion size (small, intermediate, and large). For garlic intake, we asked for the customary consumption as a qualitative variable, scored as 1 for non-use or low use (when garlic was used only for flavouring foods but it was not eaten), 2 for intermediate use (when garlic was used for flavouring foods and it was eaten occasionally) and 3 for high use (when garlic was used in many recipes and always eaten).

The odd ratios (OR) of AMI, and the corresponding 95% confidence intervals (CI), for different levels of allium vegetables were derived using unconditional multiple logistic regression models, including terms for age, sex, education, tobacco smoking, and other major confounding factors.

Onion intake decrease risk of AMI

Table 1 reports the distribution of cases of AMI and controls and the ORs and 95% CIs for subsequent levels of onion and garlic intake. Compared with nonusers, the ORs of AMI, adjusted for sex and age, for the subsequent categories of onion intake were 0.87 (95% CI: 0.67-1.13) for less than 1 portion of onion per week and 0.69 (95% CI: 0.54-0.90) for 1 or more portions per week, with a significant trend in risk. After allowance for major confounding factors, the corresponding ORs of AMI were 0.90 (95% CI: 0.69-1.21) and 0.78 (95% CI: 0.56-0.99) still, with a

significant trend in risk. For garlic, as compared to none or low use, the ORs were 0.84 (95% CI: 0.66-1.09) for intermediate and 0.94 (95% CI: 0.68-1.32) for high use.

A possible role of phenolic compounds

Several epidemiological studies indicated a protective effect of a variety of plant-based foods on the risk of cardiovascular disease⁵. Possible constituents in vegetables accounting for this protection are bioactive compounds such as phenolic and organosulfur compounds. Onions are particularly rich in both, while garlic is rich in organosulfur, but not in phenolic compounds⁶. Phenolic compounds, including their subcategory, flavonoids, have antithrombotic and endothelial protective activity⁷ which might explain the protective effect against coronary mortality found in several epidemiological studies^{4, 7}.

We found no significant inverse relation between garlic intake and AMI risk. Several trials suggested possible small short-term benefits of garlic on the lipid and antiplatelet factors⁸. Much variability has been observed between different studies because of differences in duration of treatment with garlic, the total quantity of garlic consumed, and lack of consistency when preparing garlic⁸.

Therefore, the current study, the first from Mediterranean countries, suggests that a diet rich in onion, and not in garlic, may have a favourable effect on the risk of AMI. However, additional epidemiological studies are needed to assess the association between allium vegetables intake and risk of cardiovascular diseases.

Table 1. Distribution of 760 cases of acute myocardial infarction (AMI) and 682 controls, with corresponding odds ratios (ORs) and 95% confidence intervals (CI), according to onion intake (portions/week) and garlic use. Milan, Italy, 1995-2003.

	Cases:Controls	OR (95%CI)*	OR (95%CI) †
Onion intake (portions per week)			
Nonusers	384:308	1‡	1‡
]0, 1[192:173	0.87 (0.67-1.13)	0.90 (0.69-1.21)
≥1	184:201	0.69 (0.54-0.90)	0.78 (0.56-0.99)
p for trend		0.006	0.05
Garlic use**			
None or low	290:252	1‡	1‡
Intermediate	330:315	0.90 (0.72-1.14)	0.84 (0.66-1.09)
High	139:114	1.10 (0.81-1.49)	0.94 (0.68-1.32)
p for trend		0.70	0.50

* Estimates from multiple logistic regression models, including terms for age and sex.

† Estimates from multiple logistic regression models, including terms for age, sex, education, tobacco smoking, coffee, alcohol drinking, total energy intake, fish intake, vegetable intake, body mass index, physical activity, cholesterol levels, history of hypertension, diabetes and family history of AMI in first-degree relatives.

‡ Reference category.

** The sum does not add up to the total because of some missing values.

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Evidence-based review for garlic and cancer in the perspective of food labeling

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The need for evaluating health claims

The increasing amount of information available regarding the health benefits of foods has resulted in consumer interest in health issues. This information has become a leading factor in purchasing decisions. Therefore, labeling and advertising should not be misleading. The requirement to protect consumers and ensure their right to accurate information on food functionality has led to the introduction of regulations about health claims throughout the world. In the United States, health claims were first authorized by FDA after enactment of the Nutrition Labeling and Education Act of 1990¹. The Codex Committee on Nutrition and Foods for Special Dietary Uses recently made new guidelines on the scientific substantiation for health claims². In Korea, the Health/Functional Food Act was signed into law in 2002 and a new regulatory framework for making health claims came into effect in 2004³. In order to protect consumers from false or misleading claims, many countries have been using an evidence-based review system for evaluating health claims⁴.

Concerning the garlic

Garlic is widely consumed as spices in Korea and belongs to the vegetables of the *Allium* genus that is characterized by a high content of organosulfur compounds and flavonoids. A variety of components, including nonsulfur compounds, work synergistically to provide various health benefits⁵. The major compound known to contribute to the pharmacological effect is the sulfur-containing compounds, such as diallyl⁶. Currently, there is no claim about garlic intake and cancer risk reduction in the area of food labeling. Thus the scientific evidence for garlic intake with respect to the risk of different types of cancer was evaluated using the US FDA's Evidence-Based Review System for the Scientific Evaluation of Health Claims⁷.

Garlic intake and cancer risk

There are numerous animal and in vitro studies that provide evidence for a relationship between garlic intake and risk reduction of cancers. Also, several studies have reported an inverse association in humans. Nineteen human studies were identified and reviewed for evaluating

the strength of the evidence supporting the relationship between garlic intake and the risk reduction of different cancers, based on the perspective for food labeling. On the basis of this evidence-based review, it was concluded that there was no credible evidence to support a relationship between garlic intake and a reduced risk of gastric, breast, lung, or endometrial cancer. Very limited evidence was found to support a relationship between garlic consumption and reduced risk of colon, prostate, esophageal, larynx, oral, ovary, and/or renal cell cancers. There are several other reviews that evaluated the association between garlic intake and reduction of cancer risk. In 2000, the Agency for Health Research Quality (AHRQ) reported that intake of garlic supplement might be associated with decreased odds of multiple cancers; however, the ability to interpret existing data was substantively limited by marked variability in types of garlic preparations that have been studied and inadequate definition of active constituents in the various preparations⁸. Recently, the American Institute for Cancer Research (AICR) published their review on the relationship between food, nutrition, physical activity and the prevention of cancer⁹. According to their review, only colon cancer risk reduction may be associated with garlic consumption. These results are very similar to our conclusions. Garlic is generally used in small amounts for seasoning, thus it is very difficult to analyze the quantity of garlic consumption through the food frequency questionnaire. Moreover, there are too many variables that can affect the chemical composition, such as the preparation, from raw garlic or cooked to extracted products or whole garlic, and the conditions of cultivation. For these reasons, most systematic review results indicated that the effects of garlic are very limited in reducing the risk of cancer.

Further research are needed...

Considering the large base of basic research published until recently, garlic must have a lot of beneficial effects in human health. However, for delivering the information to the average consumer, more systematically designed research is needed. We anticipate that this research will enable the beneficial health effect of garlic to be further confirmed.



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