SCIENTIFIC STATUS SUMMARY

Functional Foods:
Their role in disease prevention and health promotion

NOVEMBER 1998

A PUBLICATION OF
THE INSTITUTE OF FOOD TECHNOLOGISTS'
EXPERT PANEL ON FOOD SAFETY AND NUTRITION

Functional Foods: Their role in disease prevention and health promotion

This Scientific Status Summary addresses the primary plant and animal foods that have been linked with physiological benefits

CLARE M. HASLER, PH.D.
Executive Director, Functional Foods for Health Program, University of Illinois, Dept. of Food Science and Human Nutrition, 103 ABL (M/C 640), 1302 W. Pennsylvania Ave., Urbana, IL 61801.

A PUBLICATION OF THE INSTITUTE OF FOOD TECHNOLOGISTS' EXPERT PANEL ON FOOD SAFETY AND NUTRITION

The tenet "Let food be thy medicine and medicine be thy food," espoused by Hippocrates nearly 2,500 years ago, is receiving renewed interest. In particular, there has been an explosion of consumer interest in the health enhancing role of specific foods or physiologically-active food components, so-called functional foods (Hasler, 1998). Clearly, all foods are functional, as they provide taste, aroma, or nutritive value. Within the last decade, however, the term functional as it applies to food has adopted a different connotation—that of providing an *additional* physiological benefit beyond that of meeting basic nutritional needs. This Scientific Status Summary reviews the literature for the primary plant and animal foods that have been linked with physiological benefits. Although a plethora of biologically-active compounds have been identified in this regard (Kuhn, 1998), this review focuses on foods, rather than specific compounds isolated from foods.

Defining Functional Foods

The term functional foods was first introduced in Japan in the mid-1980s and refers to processed foods containing ingredients that aid specific bodily functions in addition to being nutritious. To date, Japan is the only country that has formulated a specific regulatory approval process for functional foods. Known as *Foods for Specified Health Use* (FOSHU), these foods are eligible to bear a seal of approval from the Japanese Ministry of Health and Welfare (Arai, 1996). Currently, 100 products are licensed as FOSHU foods in Japan.

In the United States, the functional foods category is not recognized legally. Irrespective of this, many organizations have proposed definitions for this new and emerging area of the food and nutrition sciences. The Institute of Medicine's Food and Nutrition Board (IOM/FNB, 1994) defined functional foods as "any food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains."

Health-conscious baby boomers have made functional foods the leading trend in the U.S. food industry (Meyer, 1998). Estimates, however, of the magnitude of this market vary significantly, as there is no consensus on what constitutes a functional food. Decision Resources, Inc. (Waltham, 1998) estimates the market value of functional foods at $28.9 billion. More significant, perhaps, is the potential of functional foods to mitigate disease, promote health, and reduce health care costs.

Functional Foods From Plant Sources

Overwhelming evidence from epidemiological, in vivo, in vitro, and clinical trial data indicates that a plant-based diet can reduce the risk of chronic disease, particularly cancer. In 1992, a review of 200 epidemiological studies (Block et al., 1992) showed that cancer risk in people consuming diets high in fruits and vegetables was only one-half that in those consuming few of these foods. It is now clear that there are components in a plant-based diet other than traditional nutrients that can reduce cancer risk. Steinmetz and Potter (1991a) identified more than a dozen classes of these biologically active plant chemicals, now known as "phytochemicals."

Health professionals are gradually recognizing the role of phytochemicals in health enhancement (ADA, 1995; Howard and Kritcheveky, 1997), aided in part by the Nutrition Labeling and Education Act of 1990 (NLEA). The NLEA required nutrition labeling for most foods and allowed disease- or health-related messages on food labels.

Oats. Oat products are a widely studied dietary source of the cholesterol-lowering soluble fiber b-glucan. There is now significant scientific agreement that consumption of this particular plant food can reduce total and low density lipoprotein (LDL) cholesterol, thereby reducing the risk of coronary heart disease (CHD). For this, the Food and Drug Administration (FDA) awarded the first food-specific health claim in January 1997 (DHHS/FDA, 1997), in response to a petition submitted by the Quaker Oats Company (Chicago, Ill.).

In its health claim petition, the Quaker Oats Company summarized 37 human clinical intervention trials conducted between 1980 and 1995. The majority of these studies revealed statistically significant reductions in total and LDL-cholesterol in hypercholesterolemic subjects consuming either a typical American diet or a low fat diet. The daily amount of oat bran or oatmeal consumed in the above studies ranged from 34 g to 123 g. Quaker Oats determined that 3 g of b-glucan would be required to achieve a 5% reduction in serum cholesterol, an amount equivalent to approximately 60 g of oatmeal or 40 g of oat bran (dry weight). Thus, a food bearing the health claim must contain 13 g of oat bran or 20 g oatmeal, and provide, without fortification, at least 1.0 g of b-glucan per serving. In February of 1998, the soluble fiber health claim was extended to include psyllium fiber.

Soy. Soy has been in the spotlight during the 1990s. Not only is soy a high quality protein, as assessed by the FDA's "Protein Digestibility Corrected Amino Acid Score" method, it is now thought to play preventive and therapeutic roles in cardiovascular disease (CVD), cancer, osteoporosis, and the alleviation of menopausal symptoms.

The cholesterol-lowering effect of soy is the most well-documented physiological effect. A 1995 meta-analysis of 38 separate studies (involving 743 subjects) found that the consumption of soy protein resulted in significant reductions in total cholesterol (9.3%), LDL cholesterol (12.9%), and triglycerides (10.5%), with a small but insignificant increase (2.4%) in high density lipoprotein (HDL) cholesterol (Anderson et al., 1995). Linear regression analysis indicated that the threshold level of soy intake at which the effects on blood lipids became significant was 25 g. Regarding the specific component responsible for the cholesterol-lowering effect of soy, recent attention has focused on the isoflavones (Potter, 1998). Isoflavones, however, were not effective in lowering cholesterol in two recent studies (Hodgson et al., 1998; Nestle et al., 1997). The exact mechanism by which soy exerts its hypocholesterolemic effect has not been fully elucidated.

On May 4, 1998, Protein Technologies International (PTI, St. Louis, Mo.) petitioned the FDA for a health claim on soy protein containing products pertaining to reduced risk of CHD. Based on an effective daily level of 25 g soy protein, PTI proposed that the amount of soy protein required to qualify an individual food to bear the health claim is 6.25 g with a minimum of 12.5 mg of total isoflavones (aglycone form) per reference amount customarily consumed. On August 12, the FDA accepted PTI's petition and is in the process of formulating a proposed rule.

Several classes of anticarcinogens have been identified in soybeans, including protease inhibitors, phytosterols, saponins, phenolic acids, phytic acid, and isoflavones (Messina and Barnes, 1991). Of these, isoflavones (genistein and daidzein) are particularly noteworthy because soybeans are the only significant dietary source of these compounds. Isoflavones are heterocyclic phenols structurally similar to the estrogenic steroids. Because they are weak estrogens, isoflavones may act as antiestrogens by competing with the more potent, naturally-occurring endogenous estrogens (e.g., 17b-estradiol) for binding to the estrogen receptor. This may explain why populations that consume significant amounts of soy (e.g., Southeast Asia) have reduced risk of estrogen-dependent cancer. However, the epidemiological data on soy intake and cancer risk are inconsistent at the present time (Messina et al., 1997). To date, there are no published clinical intervention trials investigating the role of soy in reducing cancer risk.

Soy may also benefit bone health (Anderson and Garner, 1997). A recent clinical study involving 66 post-menopausal women conducted at the University of Illinois (Erdman and Potter, 1997) found that 40 g isolated soy protein (ISP) per day (containing 90 mg total isoflavones) significantly increased (approximately 2%) both bone mineral content and density in the lumbar spine after 6 months.

The theory that soy may alleviate menopausal symptoms was prompted by the observation that Asian women report significantly lower levels of hot flushes and night sweats compared to Western women. Most recently, 60 grams of ISP daily for 3 months reduced hot flashes by 45% in 104 postmenopausal women (Albertazzi et al., 1998). Although these observations are exciting, there is a significant placebo effect in these studies, and it is too premature to suggest that soy may substitute for hormone replacement therapy.

Flaxseed. Among the major seed oils, flaxseed oil contains the most (57%) of the omega-3 fatty acid, a-linolenic acid. Recent research, however, has focused more specifically on fiber-associated compounds known as lignans. The two primary mammalian lignans, enterodiol and its oxidation product, enterolactone, are formed in the intestinal tract by bacterial action on plant lignan precursors (Setchell et al., 1981). Flaxseed is the richest source of mammalian lignan precursors (Thompson et al., 1991). Because enterodiol and enterolactone are structurally similar to both naturally-occurring and synthetic estrogens, and have been shown to possess weakly estrogenic and antiestrogenic activities, they may play a role in the prevention of estrogen-dependent cancers. However, there are no epidemiological data and relatively few animal studies to support this hypothesis. In rodents, flaxseed has been shown to decrease tumors of the colon and mammary gland (Thompson, 1995) as well as of the lung (Yan et al., 1998).

Fewer studies have evaluated the effects of flaxseed feeding on risk markers for cancer in humans. Phipps et al. (1993) demonstrated that the ingestion of 10 g of flaxseed per day elicited several hormonal changes associated with reduced breast cancer risk. Adlercreutz et al. (1982) found that the urinary lignan excretion was significantly lower in postmenopausal breast cancer patients compared to controls eating a normal mixed or a lactovegetarian diet.

Consumption of flaxseed has also been shown to reduce total and LDL cholesterol (Bierenbaum et al., 1993; Cunnane et al., 1993), as well as platelet aggregation (Allman et al., 1995).

Tomatoes. Selected by *Eating Well* magazine as the 1997 Vegetable of the Year, tomatoes have received significant attention within the last three years because of interest in lycopene, the primary carotenoid found in this fruit (Gerster, 1997), and its role in cancer risk reduction (Weisburger, 1998).

In a prospective cohort study of more than 47,000 men, those who consumed tomato products 10 or more times per week had less than one-half the risk of developing advanced prostate cancer (Giovannucci et al., 1995). Interestingly, lycopene is the most abundant carotenoid in the prostate gland (Clinton et al., 1996). Other cancers whose risk have been inversely associated with serum or tissue levels of lycopene include breast, digestive tract, cervix, bladder, and skin (Clinton, 1998) and possibly lung (Li et al., 1997). Proposed mechanisms by which lycopene could influence cancer risk are related to its antioxidant function. Lycopene is the most efficient quencher of singlet oxygen in biological systems (Di Mascio et al., 1989). The antioxidant function of lycopene may also explain the recent observation in a multi-center European study that adipose tissue levels of carotenoids were inversely associated with risk for myocardial infarction (Kohlmeier et al., 1997b).

Garlic. Garlic *(Allium sativum)* is likely the herb most widely quoted in the literature for medicinal properties (Nagourney, 1998). Thus, its not surprising that garlic has ranked as the second best selling herb in the United States for the past two years (Anon., 1998). The purported health benefits of garlic are numerous, including cancer chemopreventive, antibiotic, antihypertensive, and cholesterol-lowering properties (Srivastava et al., 1995).

The characteristic flavor and pungency of garlic are due to an abundance of oil- and water-soluble, sulfur-containing elements, which are also likely responsible for the various medicinal effects ascribed to this plant. However, intact, undisturbed bulbs of garlic contain only a few medicinally active components. The intact garlic bulb contains an odorless amino acid, alliin, which is converted enzymatically by allinase into allicin when the garlic cloves are crushed (Block, 1992). This latter compound is responsible for the characteristic odor of fresh garlic. Allicin then spontaneously decomposes to form numerous sulfur-containing compounds, some of which have been investigated for their chemopreventive activity.

Garlic components have been shown to inhibit tumorigenesis in several experimental models (Reuter et al., 1996). However, additional reports have shown garlic to be ineffective. Inconclusive results are likely due to differences in the type of garlic compounds or preparations used by various investigators. Considerable variation in the quantity of organosulfur compounds available in fresh and commercially available garlic products has been demonstrated (Lawson et al., 1991).

Several epidemiologic studies show that the garlic may be effective in reducing human cancer risk (Dorant et al., 1993). A relatively large case-control investigation conducted in China showed a strong inverse relationship between stomach cancer risk and increasing allium intake (You et al., 1988). More recently, in a study of more than 40,000 postmenopausal women, garlic consumption was associated with nearly a 50% reduction in colon cancer risk (Steinmetz et al., 1994). Not all epidemiological studies, however, have shown garlic to be protective against carcinogenesis. A 1991 review of 12 case-control studies (Steinmetz and Potter, 1991b), found that eight showed a negative association, one showed no association, and three studies showed a positive association. A more recent review of 20 epidemiological studies (Ernst, 1997) suggests that allium vegetables, including onions, may confer a protective effect on cancers of the gastrointestinal tract.

Garlic has also been advocated for the prevention of CVD, possibly through antihypertensive properties. According to Silagy and Neil (1994a), however, there is still insufficient evidence to recommend it as a routine clinical therapy for the treatment of hypertensive subjects. The cardioprotective effects are more likely due to its cholesterol-lowering effect. In a meta-analysis, Warshafsky et al. (1993) summarized the results of five randomized, placebo-controlled clinical trials, involving 410 patients. They showed that an average of 900 mg garlic/day (as little as one half to one clove of garlic) could decrease total serum cholesterol levels by approximately 9%. In a second meta-analysis involving 16 trials, Silagy and Neil (1994b) reported that 800 mg garlic/day reduced total cholesterol levels by 12%. The validity of both of these reports, however, is reduced by methodological shortcomings, including the fact that dietary intake, weight, and/or exogenous garlic ingestion was not always well-controlled. In a recent multicenter, randomized, placebo-controlled trial in which dietary assessment and supervision were strictly controlled, 12 weeks of garlic treatment was ineffective in lowering cholesterol levels in subjects with hypercholesterolemia (Isaacsohn et al., 1998). It is currently unclear which component in garlic is responsible for its cholesterol-lowering effect.

Broccoli and other Cruciferous Vegetables. Epidemiological evidence has associated the frequent consumption of cruciferous vegetables with decreased cancer risk. In a recent review of 87 case-control studies, Verhoeven et al. (1996) demonstrated an inverse association between consumption of total brassica vegetables and cancer risk. The percentages of case-control studies showing an inverse association between consumption of cabbage, broccoli, cauliflower, and Brussels sprouts and cancer risk were 70, 56, 67, and 29%, respectively. Verhoeven et al. (1997) attributed the anticarcinogenic properties of cruciferous vegetables to their relatively high content of glucosinolates.

Glucosinolates are a group of glycosides stored within cell vacuoles of all cruciferous vegetables. Myrosinase, an enzyme found in plant cells, catalyzes these compounds to a variety of hydrolysis products, including isothiocyanates and indoles. Indole-3 carbinol (I3C) is currently under investigation for its cancer chemopreventive properties, particularly of the mammary gland. In addition to the induction of phase I and II detoxification reactions, I3C may reduce cancer risk by modulating estrogen metabolism. The C-16 and C-2 hydroxylations of estrogens involve competing cytochrome P-450-dependent pathways, each sharing a common estrogen substrate pool. Studies suggest that the increased formation of 2-hydroxylated (catechol) estrogen metabolites relative to 16-hydroxylated forms, may protect against cancer, as catechol estrogens can act as antiestrogens in cell culture. In contrast, 16-hydroxyestrone is estrogenic and can bind to the estrogen receptor. In humans, I3C administered at 500 mg daily (equivalent to 350-500 g cabbage/day) for 1 week significantly increased the extent of estradiol 2-hydroxylation in women (Michnovicz and Bradlow, 1991), suggesting that this compound may be a novel approach for reducing the risk of breast cancer. However, since I3C has also been shown to enhance carcinogenesis in vivo, caution has been urged before proceeding with extensive clinical trials (Dashwood, 1998), although such phase I trials are currently ongoing (Wong et al., 1998).

Although a wide variety of naturally occurring and synthetic isothiocyanates have been shown to prevent cancer in animals (Hecht, 1995), attention has been focused on a particular isothiocyanate isolated from broccoli, known as sulforaphane. Sulforaphane has been shown to be the principal inducer of a particular type of Phase II enzyme, quinone reductase. Fahey et al., (1997) recently demonstrated that 3-day-old broccoli sprouts contained 10-100 times higher levels of glucoraphanin (the glucosinolate of sulforaphane) than did corresponding mature plants. However, in view of the importance of an overall dietary pattern in cancer risk reduction, the clinical implications of a single phytochemical in isolation has been questioned (Nestle, 1998).

Citrus Fruits. Several epidemiological studies have shown that citrus fruits are protective against a variety of human cancers. Although oranges, lemons, limes, and grapefruits are a principal source of such important nutrients as vitamin C, folate, and fiber, Elegbede et al. (1993) have suggested that another component is responsible for the anticancer activity. Citrus fruits are particularly high in a class of phytochemicals known as the limonoids (Hasegawa and Miyake, 1996).

Over the last decade, evidence has been accumulating in support of the cancer preventative effect of limonene (Gould, 1997). Crowell (1997) showed this compound to be effective against a variety of both spontaneous and chemically-induced rodent tumors. Based on these observations, and because it has little or no toxicity in humans, limonene has been suggested as a good candidate for human clinical chemoprevention trial evaluation. A metabolite of limonene, perrillyl alcohol, is currently undergoing Phase I clinical trials in patients with advanced malignancies (Ripple et al., 1998).

Cranberry. Cranberry juice has been recognized as efficacious in the treatment of urinary tract infections since 1914, when Blatherwick (1914) reported that this benzoic acid-rich fruit caused acidification of the urine. Recent investigations have focused on the ability of cranberry juice to inhibit the adherence of *Escherichia coli* to uroepitheial cells (Schmidt and Sobota, 1988). This phenomenon has been attributed to two compounds: fructose and a nondialyzable polymeric compound. The latter compound, subsequently isolated from cranberry and blueberry juices (Ofek et al., 1991), was found to inhibit adhesins present on the pili of the surface of certain pathogenic *E. coli*.

Avorn et al. (1994) published the results of the first randomized, double-blind, placebo-controlled clinical trial designed to determine the effect of a commercial cranberry juice beverage on urinary tract infections. One hundred-fifty three elderly women consuming 300 mL cranberry beverage per day had significantly reduced (58%) incidence of bacteriuria with pyuria compared to the control group after six months. Based on the results of these studies, prevailing beliefs about the benefits of cranberry juice on the urinary tract appear to be justified.

Tea. Tea is second only to water as the most widely consumed beverage in the world. A great deal of attention has been directed to the polyphenolic constituents of tea, particularly green tea (Harbowy and Balentine, 1997). Polyphenols comprise up to 30% of the total dry weight of fresh tea leaves. Catechins are the predominant and most significant of all tea polyphenols (Graham, 1992). The four major green tea catechins are epigallocatechin-3-gallate, epigallocatechin, epicatechin-3-gallate, and epicatechin.

In recent years, there has been a great deal of interest in pharmacological effects of tea (AHF, 1992). By far, most research on health benefits of tea has focused on its cancer chemopreventive effects, although the epidemiological studies are inconclusive at the present time (Katiyar and Mukhtar, 1996). In a 1993 review of 100 epidemiological studies (Yang and Wang, 1993), approximately 2/3 of the studies found no relationship between tea consumption and cancer risk, while 20 found a positive relationship and only 14 studies found that tea consumption reduced cancer risk. A more recent review suggests that benefits from tea consumption are restricted to high intakes in high-risk populations (Kohlmeier et al., 1997a). This hypothesis supports the recent finding that the consumption of five or more cups of green tea per day was associated with decreased recurrence of stage I and II breast cancer in Japanese women (Nakachi et al., 1998).

In contrast to the inconclusive results from epidemiological studies, research findings in laboratory animals clearly support a cancer chemopreventive effect of tea components. In fact, Dreosti et al.(1997) stated that "no other agent tested for possible chemoprevention effects in animal models has elicited such strong activity as tea and its components at the concentrations usually consumed by humans."

There is some evidence that tea consumption may also reduce the risk of CVD. Hertog and coworkers (1993) reported that tea consumption was the major source of flavonoids in a population of elderly men in the Netherlands. Intake of five flavonoids (quercetin, kaempferol, myricetin, apigenin, and luteolin), the majority of which was derived from tea consumption, was significantly inversely associated with mortality from CHD in this population. Although several other prospective studies have demonstrated a substantial reduction in CVD risk with tea consumption, the evidence is not presently conclusive (Tijburg et al., 1997).

Wine and Grapes. There is growing evidence that wine, particularly red wine, can reduce the risk of CVD. The link between wine intake and CVD first became apparent in 1979 when St. Leger et al. (1979) found a strong negative correlation between wine intake and death from ischemic heart disease in both men and women from 18 countries. France in particular has a relatively low rate of CVD despite diets high in dairy fat (Renaud and de Lorgeril, 1992). Although this "French Paradox" can be partly explained by the ability of alcohol to increase HDL cholesterol, more recent investigations have focused on the non-alcohol components of wine, in particular, the flavonoids.

The high phenolic content of red wine, which is about 20-50 times higher than white wine, is due to the incorporation of the grape skins into the fermenting grape juice during production. Kanner et al. (1994) showed that the black seedless grapes and red wines (i.e., Cabernet Sauvignon and Petite Sirah) contain high concentrations of phenolics: 920, 1800, and 3200 mg/L, respectively, while green Thomson grapes contain only 260 mg/kg phenolics. Frankel and coworkers (1993) attributed the positive benefits of red wine to the ability of phenolic substances to prevent the oxidation of LDL, a critical event in the process of atherogenesis.

Although the benefits of wine consumption on CVD risk reduction seem promising, a recent prospective study of 128,934 adults in Northern California concluded that the benefits of alcohol consumption on coronary risk were not especially associated with red wine (Klatsky et al., 1997). Moreover, a note of caution is in order, as alcoholic beverages of all kinds have been linked to increased risk of several types of cancer, including breast cancer (Bowlin et al., 1997). Moderate wine consumption has also been associated with a decreased risk of age-related macular degeneration (Obisesan et al., 1998).

Those who desire health benefits of wine without potential risk may wish to consider alcohol-free wine, which has been shown to increase total plasma antioxidant capacity (Serafini et al., 1998). Furthermore, Day et al. (1998) showed that commercial grape juice is effective in inhibiting the oxidation of LDL isolated from human subjects. Red wine is also a significant source of *trans*-resveratrol, a phytoalexin found in grape skins (Creasy and Coffee, 1988). Resveratrol has also been shown to have estrogenic properties (Gehm et al., 1997) which may explain in part the cardiovascular benefits of wine drinking, and it has been shown to inhibit carcinogenesis in vivo (Jang et al., 1997).

Functional Foods From Animal Sources

Although the vast number of naturally occurring health-enhancing substances are of plant origin, there are a number of physiologically-active components in animal products that deserve attention for their potential role in optimal health.

Fish. Omega-3 (n-3) fatty acids are an essential class of polyunsaturated fatty acids (PUFAs) derived primarily from fish oil. It has been suggested that the Western-type diet is currently deficient in n-3 fatty acids, which is reflected in the current estimated n-6 to n-3 dietary ratio of 20:25-1, compared to the 1:1 ratio on which humans evolved (Simopoulos, 1991). This has prompted researchers to examine the role of n-3 fatty acids in a number of diseases—particularly cancer and CVD—and more recently, in early human development.

That n-3 fatty acids may play an important role in CVD was first brought to light in the 1970s when Bang and Dyerberg (1972) reported that Eskimos had low rates of this disease despite consuming a diet which was high in fat. The cardioprotective effect of fish consumption has been observed in some prospective investigations (Krumhout et al., 1985), but not in others (Ascherio et al., 1995). Negative results could be explained by the fact that although n-3 fatty acids have been shown to lower triglycerides by 25-30%, they do not lower LDL cholesterol. In fact, a recent review of 72 placebo-controlled human trials, showed that n-3 fatty acids increased LDL cholesterol (Harris, 1996).

Although eating large amounts of fish has not unequivocally been shown to reduce CVD risk in healthy men, consumption of 35 g or more of fish daily has been shown to reduce the risk of death from nonsudden myocardial infarction in the Chicago Western Electric Study (Daviglus et al., 1997), and as little as one serving of fish per week was associated with a significantly reduced risk of total cardiovascular mortality after 11 years in more than 20,000 U.S. male physicians (Albert et al., 1998).

Dairy Products. There is no doubt that dairy products are functional foods. They are one of the best sources of calcium, an essential nutrient which can prevent osteoporosis and possibly colon cancer. In view of the former, the National Academy of Sciences recently increased recommendations for this nutrient for most age groups. In addition to calcium, however, recent research has focused specifically on other components in dairy products, particularly fermented dairy products known as probiotics. Probiotics are defined as "live microbial feed supplements which beneficially affect the host animal by improving its intestinal microbial balance" (Fuller, 1994).

It is estimated that over 400 species of bacteria, separated into two broad categories, inhabit the human gastrointestinal tract. The categories are: those considered to be beneficial (e.g., *Bifidobacterium* and *Lactobacillus* and those considered detrimental (e.g., *Enterobacteriaceae* and *Clostridium* spp.). Of the beneficial microorganisms traditionally used in food fermentation, lactic acid bacteria have attracted the most attention (Sanders, 1994). Although a variety of health benefits have been attributed to probiotics, their anticarcinogenic, hypocholesterolemic and antagonistic actions against enteric pathogens and other intestinal organisms have received the most attention (Mital and Garg, 1995).

The hypocholesterolemic effect of fermented milk was discovered more than 30 years ago during studies conducted in Maasai tribesmen in Africa (Mann et al., 1964). The Maasai have low levels of serum cholesterol and clinical coronary heart disease despite a high meat diet. However, they consume daily 4 to 5 L of fermented whole milk. Although a number of human clinical studies have assessed the cholesterol-lowering effects of fermented milk products (Sanders, 1994), results are equivocal. Study outcomes have been complicated by inadequate sample sizes, failure to control nutrient intake and energy expenditure, and variations in baseline blood lipids.

More evidence supports the role of probiotics in cancer risk reduction, particularly colon cancer (Mital and Garg, 1995). This observation may be due to the fact that lactic acid cultures can alter the activity of fecal enzymes (e.g., b-glucuronidase, azoreductase, nitroreductase) that are thought to play a role in the development of colon cancer. Relatively less attention has been focused on the consumption of fermented milk products and breast cancer risk, although an inverse relationship has been observed in some studies (Talamini et al., 1984; van't Veer et al.,1989).

In addition to probiotics, there is growing interest in fermentable carbohydrates that feed the good microflora of the gut. These prebiotics, defined by Gibson and Roberfroid (1995) as "nondigestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improves host health," may include starches, dietary fibers, other nonabsorbable sugars, sugar alcohols, and oligosaccharides (Gibson et al., 1996). Of these, oligosaccharides have received the most attention, and numerous health benefits have been attributed to them (Tomomatsu, 1994). Oligosaccharides consist of short chain polysaccharides

Functional Foods
CONTINUED

composed of three and 10 simple sugars linked together. They are found naturally in many fruits and vegetables (including banana, garlic, onions, milk, honey, artichokes). The prebiotic concept has been further extended to encompass the concept of synbiotics, a mixture of pro- and prebiotics (Gibson and Roberfroid, 1995). Many synbiotic products are currently on the market in Europe.

Beef. An anticarcinogenic fatty acid known as conjugated linoleic acid (CLA) was first isolated from grilled beef in 1987 (Ha et al., 1987). CLA refers to a mixture of positional and geometric isomers of linoleic acid (18:2 n-6) in which the double bonds are conjugated instead of existing in the typical methylene interrupted configuration. Nine different isomers of CLA have been reported as occurring naturally in food. CLA is unique in that it is found in highest concentrations in fat from ruminant animals (e.g., beef, dairy, and lamb). Beef fat contains 3.1 to 8.5 mg CLA/g fat with the 9-*cis* and 11-*trans* isomers contributing 57-85% of the total CLA (Decker, 1995). Interestingly, CLA increases in foods that are cooked and/or otherwise processed. This is significant in view of the fact that many mutagens and carcinogens have been identified in cooked meats.

Over the past decade, CLA has been shown to be effective in suppressing forestomach tumors in mice, aberrant colonic crypt foci in rats, and mammary carcinogenesis in rats (Ip and Scimeca, 1997). In the mammary tumor model, CLA is an effective anticarcinogen in the range of 0.1-1% in the diet, which is higher than the estimated consumption of approximately 1 g CLA/person/day in the United States. These results are not due to displacement of linoleic acid in cells, suggesting that there may be unique mechanism(s) by which CLA modulates tumor development. Thus, there has been research designed to increase the CLA content in dairy cow milk through dietary modification (Kelly et al., 1998).

More recently, CLA has been investigated for its ability to change body composition, suggesting a role as a weight reduction agent. Mice fed CLA-supplemented diets (0.5%) exhibited 60% lower body fat and 14% increased lean body mass relative to controls (Park et al., 1997), possibly by reducing fat deposition and increasing lipolysis in adipocytes.

Safety Issues

Although "increasing the availability of healthful foods, including functional foods, in the American diet is critical to ensuring a healthier population" (ADA, 1995), safety is a critical issue. The optimal levels of the majority of the biologically active components currently under investigation have yet to be determined. In addition, a number of animal studies show that some of the same phytochemicals (e.g., allyl isothiocyanate) highlighted in this review for their cancer-preventing properties have been shown to be carcinogenic at high concentrations (Ames et al., 1990). Thus, Paracelsus' 15th century doctrine that "All substances are poisons . . . the right dose differentiates a poison from a remedy" is even more pertinent today given the proclivity for dietary supplements.

The benefits and risks to individuals and populations as a whole must be weighed carefully when considering the widespread use of physiologically-active functional foods. For example, what are the risks of recommending the increased intake of compounds (e.g., isoflavones) that may modulate estrogen metabolism? Soy phytoestrogens may represent a "double-edged sword" because of reports that genistein may actually *promote* certain types of tumors in animals (Rao et al., 1997). Knowledge of toxicity of functional food components is crucial to decrease the risk:benefit ratio.

Conclusion

Mounting evidence supports the observation that functional foods containing physiologically-active components, either from plant or animal sources, may enhance health. It should be stressed, however, that functional foods are not a magic bullet or universal panacea for poor health habits. There are no "good" or "bad" foods, but there are good or bad diets. Emphasis must be placed on overall dietary pattern—one that follows the current U.S. Dietary Guidelines, and is plant-based, high in fiber, low in animal fat, and contains 5-9 servings of fruits and vegetables per day. Moreover, diet is only one component of an overall lifestyle that can have an impact on health; other components include smoking, physical activity, and stress.

Health-conscious consumers are increasingly seeking functional foods in an effort to control their own health and well-being. The field of functional foods, however, is in its infancy. Claims about health benefits of functional foods must be based on sound scientific criteria (Clydesdale, 1997). A number of factors complicate the establishment of a strong scientific foundation, however. These factors include the complexity of the food substance, effects on the food, compensatory metabolic changes that may occur with dietary changes, and, lack of surrogate markers of disease development. Additional research is necessary to substantiate the potential health benefits of those foods for which the diet-health relationships are not sufficiently scientifically validated.

Research into functional foods will not advance public health unless the benefits of the foods are effectively communicated to the consumer. The Harvard School of Public Health (Boston, Mass.) and the International Food Information Council Foundation (Washington, D.C.) recently released a set of communication guidelines, aimed at scientists, journal editors, journalists, interest groups, and others for improving public understanding of emerging science. The guidelines are intended to help ensure that research results about nutrition, food safety, and health are communicated in a clear, balanced, and non-misleading manner (Fineberg and Rowe, 1998).

Finally, those foods whose health benefits are supported by sufficient scientific substantiation have the potential to be an increasingly important component of a healthy lifestyle and to be beneficial to the public and the food industry.

REFERENCES

ADA. 1995. Position of the American Dietetic Association: Phytochemicals and functional foods. J. Am. Diet. Assoc. 95: 493-496.

AHF.1992. Physiological and pharmacological effects of *Camellia snensis* (Tea): Implications for cardiovascular disease, cancer, and public health. American Health Foundation, Valhalla, New York, Prevent. Med. 21: 329-391 and 503-553.

Adlercreutz, H., Fotsis, T., Heikkinen, R., Dwyer, J.T., Woods, M., Goldin, B.R., and Gorbach, S.L. 1982. Excretion of the lignans enterolactone and enterodiol and of equol in omnivorous and vegetarian postmenopausal women and in women with breast cancer. Lancet ii: 1295-1299.

Albert, C.M., Hennekens, C.H., O'Donnell, C.J., Ajani, U.A., Carey, V.J., Willett, W.C., Ruskin, J.N., and Manson, J.E. 1998. Fish consumption and risk of sudden cardiac death. J. Am. Med. Assoc. 279: 23-28.

Albertazzi, P., Pansini, F., Bonaccorsi G., Zanotti, L., Forini, E., and De Aloysio, D. 1998. The effect of dietary soy supplementation on hot flushes. Obstet. Gynecol 91: 6-11.

Allman, M.A., Pena, M.M., and Pang, D. 1995. Supplementation with flaxseed oil versus sunflowerseed oil in healthy young men consuming a low fat diet: Effects on platelet composition and function. Eur. J. Clin. Nutr 49: 169-178.

Ames, B.N., Magaw, R., and Gold, L.W. 1990. Ranking possible carcinogenic hazards. Science 236: 271-280.

Anderson, J.W., Johnstone, B.M., and Cook-Newell, M.E. 1995. Meta-analysis of the effects of soy protein intake on serum lipids. New Engl. J. Med. 333: 276-282.

Anderson, J.J.B. and Garner, S.C. 1997. The effects of phytoestrogens on bone. Nutr. Res. 17: 1617-1632.

Anonymous. 1998. U.S. topselling herbs and supplements. Nutraceuticals Intl. 3 (2): 9.

Arai, S. 1996. Studies on functional foods in Japan–State of the art. Biosci. Biotech. Biochem. 60: 9-15.

Ascherio, A., Rimm, E.B., Stampfer, M.J., Giovannucci, E.L., and Willett, W.C. 1995. Dietary intake of marine n-3 fatty acids, fish intake, and the risk of coronary disease among men. New Eng. J. Med. 332: 977-982.

Avorn, J., Monane, M., Gurwitz, J.H., Glynn, R.J., Choodnovskiy, I., and Lipsitz, L.A. 1994. Reduction of bacteriuria and pyuria after ingestion of cranberry juice- A Reply. J. Am. Med. Assoc. 272: 589-590.

Bang, H.O. and Dyerberg, J. 1972. Plasma lipids and lipoproteins in Greenlandic west-coast Eskimos. Acta. Med. Scand 192: 85-94.

Bierenbaum, M.L., Reichstein, R. and Watkins, T.R. 1993. Reducing atherogenic risk in hyperlipemic humans with flax seed supplementation: A preliminary report. J. Am. Coll. Nutr. 12: 501-504.

Blatherwick, N.R. 1914. The specific role of foods in relation to the composition of the urine. Arch. Int. Med. 14: 409-450.

Block, E. 1992. The organosulfur chemistry of the genus *Allium*--Implications for the organic chemistry of sulfur. Angew. Chem. Int. Edn. Engl. 31: 1135-1178.

Block, G., Patterson, B. and Subar, A. 1992. Fruit, vegetables, and cancer prevention: A review of the epidemiological evidence. Nutr. Cancer 18: 1-29.

Bowlin, S.J., Leske, M.C., Varma, A., Nasca, P., Weinstein, A. and Caplan, L. 1997. Breast cancer risk and alcohol consumption: Results from a large case-control study. Intl. J. Epidemiol. 26: 915-923.

Clinton, S.K. 1998. Lycopene: Chemistry, biology, and implications for human health and disease. Nutr. Rev. 56: 35-51.

Clinton, S.K., Emenhiser, C., Schwartz, S.J., Bostwick, D.G., Williams, A.W., Moore, B.J. and Erdman, Jr, J.W. 1996. Cis-trans lycopene isomers, carotenoids, and retinol in the human prostate. Cancer Epidemiol. Biomarkers Prev. 5: 823-833.

Clydesdale, F.M. 1997. A proposal for the establishment of scientific criteria for health claims for functional foods. Nutr. Rev. 55 (12): 413-422.

Creasy, L.L. and Coffee, M.1988. Phytoalexin production of grape berries. J. Am. Soc. Hort. Sci. 113: 230-234.

Crowell, P.L. 1997. Monoterpenes in breast cancer chemoprevention. Breast Cancer Res. Treatment 46: 191-197.

Cunnane, S.C., Ganguli, S., Menard, C., Liede, A.C., Hamadeh, M.J., Chen, Z-Y., Wolever, T.M.S. and Jenkins, D.J.A. 1993. High-linolenic acid flaxseed (*Linum usitatissimum*): some nutritional properties in humans. Br. J. Nutr. 69: 443-453.

DHHS/FDA. 1997. Food labeling: Health claims; oats and coronary heart disease. Dept. Health and Human Services/Food and Drug Administration. Fed. Reg. 62: 3584-3601.

Dashwood, R.H. 1998. Indol-3-carbinol–Anticarcinogen or tumor promoter in Brassica vegetables. Chem.-Biol. Ineractions 110: 1-5.

Daviglus, M.L., Stamler, J., Orencia, A.J., Dyer, A.R., Liu, K., Greenland, P., Walsh, M., Morris, D., and Shekelle, R.B. 1997. Fish consumption and the 30-year risk of fatal myocardial infarction. New Eng. J. Med. 336: 1046-1053.

Day, A. P., Kemp, H.J., Bolton, C., Hartog, M., Stansbie, D. 1998. Effects of concentrated red grape juice consumption on serum antioxidant capacity and low-density lipoprotein oxidation. Ann. Nutr. Metab. 41: 353-357.

Decker, E.A. 1995. The role of phenolics, conjugated linoleic acid, carnosine, and pyrroloquinoline quinone as nonessential dietary antioxidants. Nutr. Rev. 53: 49-58.

Di Mascio, P., Kaiser, S., and Sies, H. 1989. Lycopene as the most efficient biological carotenoid singlet oxygen quencher. Arch. Biochem. Biophys. 274: 532-538.

Dorant, E., van den Brandt, P.A., Goldbohm, R.A., Hermus, R.J.J., and Sturmans, F. 1993. Garlic and its significance for the prevention of cancer in humans: A critical review. Br. J. Cancer 67: 424-429.

Dreosti, I.E., Wargovich, M.J., and Yang, C.S. 1997. Inhibition of carcinogenesis by tea: The evidence from experimental studies. Crit. Rev. Food Sci. Nutr. 37: 761-770.

Elegbede, J.A., Maltzman, T.H., Elson, C.E., and Gould, M.N. 1993. Effects of anticarcinogenic monoterpenes on phase II hepatic metabolizing enzymes. Carcinogenesis 14: 1221-1223.

Erdman, J.W., Jr., and Potter, S.M. 1997. Soy and bone health. The Soy Connection 5 (2): 1, 4.

Ernst, E. 1997. Can allium vegetables prevent cancer? Phytomed. 4: 79-83.

Fahey, J.W., Zhang, Y., and Talalay, P. 1997. Broccoli sprouts: An exceptionally rich source of inducers of enzymes that protect against chemical carcinogens. Proc. Natl. Acad. Sci. 94: 10366-10372.

Fineberg, H.V. and Rowe, S. 1998. Improving public understanding: Guidelines for communicating emerging science on nutrition, food safety and health. J. Natl. Cancer Inst. 90: 194-199.

Frankel, E.N., Kanner, J., German, J.B., Parks, E. and Kinsella, J.E. 1993. Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. The Lancet 341: 454-457.

Fuller, R. 1994. History and development of probiotics. In "Probiotics," ed. R. Fuller, pp. 1-8. Chapman & Hall, N.Y.

Gehm, B.D., McAndrews, J.M., Chien, P.-Y., and Jameson, J.L. 1997. Resveratrol, a polyphenolic compound found in grapes and wine, is an agonist for the estrogen receptor. Proc. Natl. Acad. Sci. 94: 14138-14143.

Gerster, H. 1997. The potential role of lycopene for human health. J. Am. Coll. Nutr. 16: 109-126.

Gibson, G. and Roberfroid, M.B. 1995. Dietary modulation of the human colonic mibrobiota: Introducing the concept of prebiotics. J. Nutr. 125: 1401-1412.

Gibson, G.R., Williams, A., Reading, S., and Collins, M.D. 1996. Fermentation of non-digestible oligosaccharides by human colonic bacteria. Proc. Nutr. Soc. 55: 899-912.

Giovannucci, E., Ascherio, A., Rimm, E.B., Stampfer, M.J., Colditz, G.A., and Willett, W.C. 1995. Intake of carotenoids and retinol in relation to risk of prostate cancer. J. Natl. Cancer Inst. 87: 1767-1776.

Gould, M.N. 1997. Cancer chemoprevention and therapy by monoterpenes. Environ. Health Perspec. 105: 977-979.

Graham, H.N. 1992. Green tea composition, consumption and polyphenol chemistry. Prev. Med. 21: 334-350.

Ha, Y.L., Grimm, N.K., and Pariza, M.W. 1987. Anticarcinogens from fried ground beef: Health-altered derivatives of linoleic acid. Carcinogenesis 8: 1881-1887.

Harbowy, M.E. and Balentine, D.A. 1997. Tea Chemistry. Crit. Rev. Plant Sci. 16: 415-480.

Harris, W.S. 1996. N-3 fatty acids and lipoproteins–Comparison of results from human and animal studies.

Hasegawa, S. and Miyake, M. 1996. Biochemistry and biological functions of citrus limonoids. Food Rev. Intl. 12: 413-435.

Hasler, C.M. 1998. A new look at an ancient concept. Chem. Industry Feb. 2: 84-89.

Hecht, S.S. 1995. Chemoprevention by isothiocyanates. J. Cell. Biochem. Suppl. 22: 195-209.

Hertog, M.G.L., Feskens, E.J.M., Hollman, P.C.H., Katan, M.B., and Krumhout, D. 1993. Dietary antioxidant flavonoids and risk of coronary heart disease: The Zutphen Elderly Study. The Lancet 342: 1007-1011.

Hodgson, J.M., Puddey, I.B., Beilin, L.J., Mori, T.A., and Croft, K.D. 1998. Supplementation with isoflavonoid phytoestrogens does not alter serum lipid concentrations: A randomized controlled trial in humans. J. Nutr. 128: 728-732.

Howard, B.V. and Kritchevsky, D. 1997. Phytochemicals and cardiovascular disease–A statement for healthcare professionals from the American Heart Association. Circulation 95: 2591-2593.

IOM/NAS. 1994. "Opportunities in the Nutrition and Food Sciences", ed. P.R. Thomas and R. Earl, p. 109. Institute of Medicine/National Academy of Sciences, National Academy Press, Washington, D.C.

Ip, C. and Scimeca, J.A. 1997. Conjugated linoleic acid and linoleic acid are distinctive modulators of mammary carcinogenesis. Nutr. Cancer 27: 131-135.

Isaacsohn, J.L., Moser, M., Stein, E.A., Dudley, K., Davey, J.A., Liskov, E., and Black, H.R. 1998. Garlic powder and plasma lipids and lipoproteins: A multicenter, randomized, placebo-controlled trial. Arch. Int. Med. 158:1189–1194.

Jang, M., Cai, J., Udeani, G.., Slowing, K.V., Thomas, C.F., Beecher, C.W.W., Fong, H.H.S., Farnsworth, N.R., Kinghorn, A.D., Mehta, R.G., Moon, R.C., and Pezzuto, J.M. 1997. Cancer chemopreventive activity of resveratrol, a natural product derived from grapes. Science 275: 218-220.

Kanner, J., Frankel, E., Granit, R., German, B., and Kinsella, J.E. 1994. Natural antioxidants in grapes and wines. J. Agric. Food Chem. 42: 64-69.

Katiyar, S.K. and Mukhtar, H. 1996. Tea in chemoprevention of cancer: Epidemiologic and experimental studies (review). Intl. J. Oncol. 8: 221-238.

Kelly, M. L., Berry, J.R., Dwyer, D.A., Griinari, J.M., Chounard, P.Y., Van Amburgh, M.E., and Bauman, D.E. 1998. Dietary fatty acid sources affect conjugated linoleic acid concentrations in milk from lactating dairy cows. J. Nutr. 128: 881-885.

Klatsky, A.L., Armstrong, M.A., and Friedman, G.D. 1997. Red wine, white wine, liquor, beer, and risk for coronary artery disease hospitalization. Am. J. Cardiol. 80: 416-420.

Kohlmeier, L., Weerings, K.G.C., Steck, S., and Kok, F.J. 1997. Tea and cancer prevention–An evaluation of the epidemiologic literature. Nutr. Cancer 27: 1-13.

Kohlmeier, L., Kark, J.D., Gomez-Gracia, E., Martin, B.C., Steck, S.E., Kardinaal, A.F.M., Ringstad, J., Thamm, M., Masaev, V., Riemersma, R., Martin-Moreno, J.M., Huttunen, J.K., and Kok, F.J. 1997. Lycopene and myocardial infarction risk in the EURAMIC study. Am. J. Epidemiol.146: 618-626.

Kuhn, M.E. 1998. Functional foods overdose? Food Proc. 59 (5): 21-48.

Krumhout, D., Bosschieter, E.B., and de Lezenne Coulander, C. 1985. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. New Eng. J. Med. 312: 1205-1209.

Lawson, L.D., Wang, Z-Y.J., and Hughes, B.G. 1991. Identification and HPLC quantitation of the sulfides and dialk(en)ylthiosulfinates in commercial garlic products. Planta Med. 57: 363-370.

Li, Y., Elie, M., Blaner, W.S., Brandt-Rauf, P., and Ford, J.

Functional Foods

CONTINUED

1997. Lycopene, smoking and lung cancer. Proc. Am. Assoc.. Cancer Res. 38: 113 (abstract #758).

Mann, G.V., Schaffer, R.D., Anderson, R.D., and Sandstead, H.H. 1964. Cardiovascular disease in the Maasai. J. Atheroscler. Res. 4: 289-312.

Messina, M. and Barnes, S. 1991. The role of soy products in reducing risk of cancer. J. Natl. Cancer Inst. 83: 541-546.

Messina, M., Barnes, S., and Setchell, K.D.R. 1997. Phytooestrogens and breast cancer. Lancet 350: 971-972.

Meyer, A. 1998. The 1998 top 100® R&D survey. Food Processing 58(8): 32-40.

Michnovicz, J.J. and Bradlow, H.L. 1991. Altered estrogen metabolism and excretion in humans following consumption of indole carbinol. Nutr. Cancer 16: 59-66.

Mital, B.K. and Garg, S.K. 1995. Anticarcinogenic, hypocholesterolemic, and antagonistic activities of *Lactobacillus acidophilus*. Crit. Rev. Micro. 21: 175-214.

Nakachi, K., Suemasu, K., Suga, K., Takeo, T., Imai, K., and Higashi, Y. 1998. Influence of drinking green tea on breast cancer malignancy among Japanese patients. Jap. J. Cancer Res. 89: 254-261.

Nagourney, R.A. 1998. Garlic: Medicinal food or nutritious medicine? J. Medicinal Food 1: 13-28.

Nestle, P.J., Yamashita, T., Sasahara, T., Pomeroy, S., Dart, A., Komesaroff, P., Owen, A., and Abbey, M. 1997. Soy isoflavones improve systemic arterial compliance but not plasma lipids in menopausal and perimenopausal women. Arterioscler. Thromb. Vasc. Biol. 17: 3392-3398.

Nestle, M. 1998. Broccoli sprouts in cancer prevention. Nutr. Rev. 56: 127-130.

Obisesan, T.O., Hirsch, R., Kosoko, O., Carlson, L., and Parrott, M. 1998. Moderate wine consumption is associated with decreased odds of developing age-related macular degeneration in NHANES-1. J. Amer. Geriatrics Soc. 46: 1-7.

Ofek, I., Goldhar, J., Zafriri, D., Lis, H., Adar, R., and Sharon, N. 1991. Anti-*Escherichia coli* adhesin activity of cranberry and blueberry juices. New Eng. J. Med. 324: 1599.

Park, Y., Albrigh, K.J., Liu, W., Storkson, J.M., Cook, M.E., and Pariza, M.W. 1997. Effect of conjugated linoleic acid on body composition in mice. Lipids 32: 853-858.

Phipps, W.R., Martini, M.C., Lampe, J.W., Slavin, J.L., and Kurzer, M.S. 1993. Effect of flax seed ingestion on the menstrual cycle. J. Clin. Endocrin. Metab. 77: 1215-1219.

Potter, S.M. 1998. Soy protein and cardiovascular disease: The impact of bioactive components in soy. Nutr. Rev. 56(8):231-235.

Rao, C.V., Wang, C.X., Simi, B., Lubet, R., Kellogg, G., Steele, V., and Reddy, B.S. 1997. Enhancement of experimental colon cancer by genistein. Cancer Res. 57: 3717-3722.

Reuter H.D., Koch, H.P, and Lawson, L.D. 1996. Therapeutic effects and applications of garlic and its preparations. In: Garlic. The Science and Therapeutic Application of *Allium sativum* L. and Related Species, 2nd Ed., ed., H.P. Koch and L.D. Lawson, Williams & Wilkins, Baltimore.

Renaud, W. and de Lorgeril, M. 1992. Wine, alcohol, platelets, and the French paradox for coronary heart disease. The Lancet 339: 1523-1526.

Ripple, G.H., Gould, M.N., Stewart, J.A., Tutsch, K.D., Arzoomanian, R.Z., Alberti, D., Feierabend, C., Pomplun, M., Wilding, G., and Bailey, H.H. 1998. Phase I clinical trial of peillyl alcohol administered daily. Clin. Cancer Res. 4: 1159-1164.

Sanders, M.E. 1994. Lactic acid bacteria as promoters of human health. In: "Functional Foods—Designer Foods, Pharmafoods, Nutraceuticals", ed. I. Goldberg, pp. 294-322. Chapman & Hall, N.Y.

Schmidt, D.R. and Sobota, A.E. 1988. An examination of the anti-adherence activity of cranberry juice on urinary and nonurinary bacterial isolates. Microbios. 55: 173-181.

Serafini, M., Maiani, G., and Ferro-Luzzi, A. 1998. Alcohol-free red wine enhances plasma antioxidant capacity in humans. J. Nutr. 128: 1003-1007.

Setchell, K.D.R., Lawson, A.M., Borriello, S.P., Harkness, R., Gordon, H., Morgan, D.M.L, Kirk, D.N., Adlercreutz, H., Anderson, L.C., and Axelson, M. 1981. Lignan formation in man—microbial involvement and possible roles in relation to cancer. The Lancet ii: 4-7.

Silagy, C.A. and Neil, H.A.W. 1994a. A meta-analysis of the effect of garlic on blood pressure. J. Hyper. 12: 463-468.

Silagy, C. and Neil, A. 1994b. Garlic as a lipid-lowering agent—a meta-analysis. J. Royal Coll. Physicians Lond. 28: 39-45.

Simopoulos, A.P. 1991. Omega-3 fatty acids in health and disease and in growth and development. Am. J. Clin. Nutr. 54: 438-463.

Srivastava, K.C., Bordia, A., and Verma, S.K. 1995. Garlic (*Allium sativum*) for disease prevention. S. Afr. J. Sci. 91: 68-77.

St. Leger, A.S., Cochrane, A.L., and Moore, F. 1979. Factors associated with cardiac mortality in developed countries with particular reference to the consumption of wine. The Lancet i: 1017-1020.

Steinmetz, K.A. and Potter, J.D. 1991a. Vegetables, fruit and cancer II. Mechanisms. Cancer Causes Control 2: 427-442.

Steinmetz, K.A. and Potter, J.D. 1991b. Vegetables, fruit and cancer I. Cancer Causes Control 2: 325-357.

Steinmetz, K.A., Kushi, H., Bostick, R.M., Folsom, A.R., and Potter, J.D. 1994. Vegetables, fruit, and colon cancer in the Iowa Women's Health Study. Am. J. Epidemiol. 139: 1-15.

Talamini, R., La Vecchia, C., Decarli, A., et al. 1984. Social factors, diet and breast cancer in a northern Italian population. Br. J. Cancer 49: 723-729.

Thompson, L.U., Robb, P., Serraino, M., and Cheung, F. 1991. Mammalian lignan production from various foods. Nutr. Cancer 16: 43-52.

Thompson, L.U. 1995. Flaxseed, lignans, and cancer. In: "Flaxseed in Human Nutrition," ed. S. Cunnane and L.U. Thompson, pp. 219-236. AOCS Press, Champaign, IL.

Tijburg, L.B.M. Mattern, T., Folts, J.D., Weisgerber, U.M., and Katan, M.B. 1997. Tea flavonoids and cardiovascular diseases: A review. Crit. Rev. Food Sci. Nutr. 37: 771-785.

Tomomatsu, H. 1994. Health effects of oligosaccharides. Food Technol. 48: 61-65.

van't Veer, P., Dekker, J.M., Lamers, J.W.J., Kok, F.J., Schouten E.G., Brants, H.A.M., Sturmans, F., and Hermus, R.J.J. 1989. Consumption of fermented milk products and breast cancer: A case-control study in the Netherlands. Cancer Res. 49: 4020-4023.

Verhoeven, D.T.H., Goldbohm, R.A., van Poppel, G., Verhagen, H., and van den Brandt, P.A. 1996. Epidemiological studies on brassica vegetables and cancer risk. Cancer Epidemiol. Biomarkers Prev. 5: 733-748.

Verhoeven, D.T.H., Verhagen, H., Goldbohm, R.A., van den Brandt, P.A., and van Poppel, G. 1997. A review of mechanisms underlying anticarcinogenicity by brassica vegetables. Chem. Bio. Interactions 103: 79-129.

Waltham, M.S. 1998. Roadmaps to Market: Commercializing Functional Foods and Nutraceuticals, Decision Resources, Inc., p. 5.

Warshafsky, S., Kamer R.S., and Sivak, S.L. 1993. Effect of garlic on total serum cholesterol. A meta-analysis. Ann. Int. Med. 119: 599-605.

Weisburger, J.H. (ed.). 1998. International symposium on lycopene and tomato products in disease prevention. Proc. Soc. Exp. Biol. Med. 218: 93-143.

Wong, G.Y.C., Bradlow, L., Sepkovic, D., Mehl, S., Mailman, J., and Osborne, M.P. 1998. Dose-ranging study of indole-3-carbinol for breast cancer prevention. J. Cell. Biochem. 22 (Suppl. 28-29): 111-116.

Yan, L., Yee, J.A., Li, D., McGuire, M.H., and Thompson, L.U. 1998. Dietary flaxseed supplementation and experimental metastasis of melanoma cells in mice. Cancer Lett. 124: 181-186.

Yang, C.S. and Wang, Z-Y. 1993. Tea and cancer. J. Natl. Cancer Inst. 85: 1038-1049.

You, W-C., Blot, W.J., Chang, Y-S., Ershow, A.G., Yang, Z.-T., An, Q. Henderson, B., Xu, G.-W., Fraumeni, J.F., and Wang, T.-G. 1988. Diet and high risk of stomach cancer in Shandong, China. Cancer Res. 48: 3518-3523.

INSTITUTE OF FOOD TECHNOLOGISTS

The Society for Food Science and Technology

221 N. LaSalle St., Ste. 300, Chicago, IL 60601-1291 USA

Tel. 312-782-8424 • Fax: 312-782-8348

E-mail: info@ift.org • URL: http://www.ift.org

This and other Scientific Status Summaries are published by the Institute of Food Technologists' Expert Panel on Food Safety and Nutrition in *Food Technology*. Scientific Status Summaries, which are not necessarily written by the Expert Panel, are rigorously peer-reviewed by the Expert Panel as well as by individuals outside the panel who have specific expertise in the subject. IFT's Expert Panel on Food Safety and Nutrition, which studies significant food-related issues and oversees timely production of Scientific Status Summaries, comprises academicians representing expertise in one or more areas of food science/technology and nutrition.

SCIENCE COMMUNICATIONS

By JOHN A. MILNER, PH.D.
Nutrition Department and Graduate Program in Nutrition, The Pennsylvania State Univ.

Do "Functional Foods" Offer Opportunities to Optimize Nutrition and Health?

Belief in the medicinal power of foods is not a recent event. While Hippocrates may not have started this movement, he proclaimed almost 2,500 years ago to "Let food be thy medicine and medicine be thy food." Today, while such a statement might result in severe reprimands, if not litigations, these penalties have not deterred consumers from seeking the health benefits of foods. Increasingly, scientists are being charged with the responsibility of clarifying the role that foods play in maintaining and promoting health. The Scientific Status Summary, "Functional Foods: Their Role in Disease Prevention and Health Promotion" (pp. 63–70) prepared for IFT's Expert Panel on Food Safety and Nutrition by Clare Hasler, reviews the primary plant and animal foods linked with physiological benefits.

A variety of foods and their components are emerging as factors capable of modifying growth, development, performance and disease resistance. Such discoveries may influence perceptions about what is appropriate nutrition, and necessitate a new vocabulary including terms from apigenin to zeaxanthin. In the process, a better understanding that adequate nutrition is more than energy and essential nutrients will emerge.

The term "functional food" is surfacing as a generic descriptor of the benefits from foods that go beyond those attributable to essential nutrients. Interest in the health benefits of foods is propelled by rising health care cost; legislative changes (i.e., the Nutrition Labeling and Education Act and Dietary Supplement Health and Education Act) that permit claims for foods and associated components; and by new and exciting scientific discoveries. Although not a legal term, the concept of "functional foods" is gaining consumer acceptance. Nevertheless, it is surrounded by controversy and even condemnation. Much of the concern arises from the view that while diets might justifiably be characterized as "good or bad," foods should not be so described. In fact, the concept might create a false sense of security about eating behaviors. Furthermore, while total fruit and vegetable consumption is increasingly linked to a reduction in risk of several diseases, the association is far less impressive when a specific food or component is considered. Regardless, there is little reason to believe that consumer acceptance of this concept will dwindle in the foreseeable future. Accepting this movement as an opportunity to "optimize nutrition" rather than to endorse good or bad foods or as a gimmick to foster sales will surely make it more acceptable to most scientists.

Unquestionably food components can have physiological consequences. Diverse compounds including allyl sulfurs, indoles, polyphenols and isothiocyanates have the potential to modify metabolism and ultimately influence disease risk. While phytochemicals in plants are increasingly respected for these attributes, animal products also contain positive effectors. The ability of omega-3 fatty acids in fish or conjugated linoleic acid in milk and meat products to alter several physiological processes raises questions about what intakes and proportions of animal and plant foods are needed to optimize health and well-being.

Food processing and preparation procedures also impact the physiological consequences of food. Fermented products, including dairy products, have long been recognized to alter gastrointestinal flora and even reduce circulating cholesterol. While heating tomatoes may improve lycopene availability and thus improve its antioxidant potential, results from our laboratory show that heating of unpeeled garlic reduces its anticancer potential. Clarification of the role of how processing impacts bioactive components and their interactions in foods will become increasingly important as consumers consider dietary shifts.

While it may be prudent to increase the intake of selected foods it must not be done without considering potential negative consequences. Establishing an upper safe and permissible intake for functional foods and their biologically active components will be exceedingly important for vulnerable segments of society. Such information might allow for recommendations for an amount of garlic that reduces the risk of heart disease and cancer while minimizing chances of gastrointestinal bleeding.

Any claims about the benefits of foods must be based on sound and accurate scientific information. Identification of sensitive and reliable biomarkers will be key to adequately assessing the true impact of foods and components. Universally accepted indicators of intake and the biological response will surely be needed given our global market. Finally, it is assumed that all individuals will not equally benefit, or suffer, from the enhanced intake of specific foods or components. To assess who might benefit most it, is imperative that a series of susceptibility biomarkers be employed that take into account genetics and other environmental factors.

Ingestion of functional foods represents an effective strategy to maximize health and reduce risk of diseases. However, it would be foolish to consider them as "magic bullets" that function under all circumstances. The positive message about foods, and the inclusion rather than exclusion of items from the diet, may encourage consumers to be more accepting of this "functional foods" concept. Scientific advancements and effective communication strategies will be critical to the acceptance and success of the "functional foods" movement. ●