Functional Foods: Their role in disease prevention and health promotion

NOVEMBER 1998
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 Kritchevsky, 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 di-
Functional Foods (CONTINUED)

The health claim petition, submitted by the Quaker Oats Company (Chicago, Ill.), requested that the amount of soy protein required to qualify an individual food to bear the health claim be 6.25 g with a minimum of 12.5 mg of total isoflavones (aglycone form) per reference amount customarily consumed. On August 12, 1997, 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, sa- ponins, 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 both naturally-occurring and synthetic estrogens. Although they are weak estrogens, isoflavones may act as antiestrogens by competing with the estrogen receptor. This may explain why populations that consume significant amounts of soy (e.g., Southeast Asian) have reduced risk 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 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).

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.

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. Thus, a food bearing the health claim 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). This, 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 β-glucan per serving. In February of 1998, the soluble fiber health claim was extended to include psyllium fiber.

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 flushes 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, α-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 weak 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 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.
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 (Burger, 1998). The purported health benefits of garlic are numerous, including cancer chemopreventive, antibiotic, anti-hypertensive, 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 alilnase 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 (Doran 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 epidemiologic 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, Silag 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. Epidemiologic 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-substrate 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...
Functional Foods

CONTINUED

breast cancer. However, since I SC 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 glucosinate 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 have 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, peryllyl 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 uroepithelial 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 on the surface of Escherichia 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 (Harbouy 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 (Katyar 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., Cab-
ernet 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 (Obisenan 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, hypolipidemic 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 Maaasi tribesmen in Africa (Mann et al., 1964). The Maaasi 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., β-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 "indigestible 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 starchy, dietary fibers, other non-absorbable 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

**Pathogen Temperature Time to toxin Food**

Currently on the market in Europe. Many synbiotic products are currently on the market in Europe. 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 monounsaturated 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 over-all 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**


Functional Foods CONTINUED


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. ☛