The Journal of Nutrition
jn.nutrition.org

J. Nutr. December 1, 2002
vol. 132 no. 12 3772–3781

Functional Foods: Benefits, Concerns and Challenges—A Position Paper from the American Council on Science and Health[1]

Clare M. Hasler[2]

[+] Author Affiliations

[2]To whom correspondence should be addressed. E-mail: c-hasler@uiuc.edu.

Abstract

Functional foods can be considered to be those whole, fortified, enriched or enhanced foods that provide health benefits beyond the provision of essential nutrients (e.g., vitamins and minerals), when they are consumed at efficacious levels as part of a varied diet on a regular basis. Linking the consumption of functional foods or food ingredients with health claims should be based on sound scientific evidence, with the "gold standard" being replicated, randomized, placebo-controlled, intervention trials in human subjects. However, not all foods on the market today that are claimed to be functional foods are supported by enough solid data to merit such claims. This review categorizes a variety of functional foods according to the type of evidence supporting their functionality, the strength of that evidence and the recommended intakes. Functional foods represent one of the most intensively investigated and widely promoted areas in the food and nutrition sciences today. However, it must be emphasized that these foods and ingredients are not magic bullets or panaceas for poor health habits. Diet is only one aspect of a comprehensive approach to good health.

functional foods health claims dietary supplements phytochemicals bioactive

That foods might provide therapeutic benefits is clearly not a new concept. The tenet, "Let food be thy medicine and medicine be thy food" was embraced ~2500 years ago by Hippocrates, the father of medicine. However, this "food as medicine" philosophy fell into relative obscurity in the 19th century with the advent of modern drug therapy. In the 1900s, the important role of diet in disease prevention and health promotion came to the forefront once again.

During the first 50 years of the 20th century, scientific focus was on the identification of essential elements, particularly vitamins, and their role in the prevention of various dietary deficiency diseases. This emphasis on nutrient deficiencies or "undernutrition" shifted dramatically, however, during the 1970s when diseases linked to excess and "overnutrition" became a major public health concern. Thus began a flurry of public health guidelines, including the Senate Select (McGovern) Committee's *Dietary Goals for the United States* (1977), the *Dietary Guidelines for Americans (1980, 1985, 1990, 1996, 2000*— a joint publication of the USDA and the Department of Health and Human Services), the *Surgeon General's Report on Nutrition and Health* (1988), the National Research Council's *Diet and Health* (1989) and *Healthy People 2000* and *2010* from the U.S. Public Health Service. All of these reports are aimed at public policy and education emphasizing the importance of consuming a diet that is low in saturated fat, and high in vegetables, fruits, whole grains and legumes to reduce the risk of chronic diseases such as heart disease, cancer, osteoporosis, diabetes and stroke.

Scientists also began to identify physiologically active components in foods from both plants and animals (known as phytochemicals and zoochemicals, respectively) that potentially could reduce risk for a variety of chronic diseases. These events, coupled with an aging, health-conscious population, changes in food regulations, numerous technological advances and a marketplace ripe for the introduction of health-promoting products, coalesced in the 1990s to create the trend we now know as "functional foods." This report includes a discussion of how functional foods are currently defined, the strength of the evidence both required

and thus far provided for many of these products, safety considerations in using some of these products, factors driving the functional foods phenomenon, and finally, what the future may hold for this new food category.

What are functional foods?

All foods are functional to some extent because all foods provide taste, aroma and nutritive value. However, foods are now being examined intensively for added physiologic benefits, which may reduce chronic disease risk or otherwise optimize health. It is these research efforts that have led to the global interest in the growing food category now recognized as "functional foods." Functional foods have no universally accepted definition. The concept was first developed in Japan in the 1980s when, faced with escalating health care costs, the Ministry of Health and Welfare initiated a regulatory system to approve certain foods with documented health benefits in hopes of improving the health of the nation's aging population (1). These foods, which are eligible to bear a special seal, are now recognized as Foods for Specified Health Use (FOSHU).[3] As of July 2002, nearly 300 food products had been granted FOSHU status in Japan.

In the United States, functional foods have no such regulatory identity. However, several organizations have proposed definitions for this new food category. In 1994, the National Academy of Sciences' Food and Nutrition Board defined functional foods as "any modified food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains" (2). The International Life Sciences Institute defines them as "foods that, by virtue of the presence of physiologically-active components, provide a health benefit beyond basic nutrition" (3). In a 1999 position paper, the American Dietetic Association defined functional foods as foods that are "whole, fortified, enriched, or enhanced," but more importantly, states that such foods must be consumed as "… part of a varied diet on a regular basis, at effective levels " for consumers to reap their potential health benefits (4).

Another term often used interchangeably with functional foods, although it is less favored by consumers, is "nutraceuticals," a term coined in 1991 by the Foundation for Innovation in Medicine to refer to nearly any bioactive component that delivers a health benefit. In a 1999 policy paper, Zeisel (5) astutely distinguished whole foods from the isolated components derived from them in his following definition of nutraceuticals: "those diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a nonfood matrix, and used to enhance health in dosages that exceed those that could be obtained from normal food."

Several factors are responsible for the fact that this is one of the most active areas of research in the nutrition sciences today: *1*) an emphasis in nutritional and medical research on associations between diet and dietary constituents and health benefits, *2*) a favorable regulatory environment, *3*) the consumer self-care phenomenon, and *4*) rapid growth in the market for health and wellness products.

Criteria for sound science

According to the Department of Health and Human Services, diet plays a role in 5 of 10 of the leading causes of death, including coronary heart disease (CHD), certain types of cancer, stroke, diabetes (noninsulin dependent or type 2) and atherosclerosis. The dietary pattern that has been linked with these major causes of death in the United States and other developed countries is characterized as relatively high in total and saturated fat, cholesterol, sodium and refined sugars and relatively low in unsaturated fat, grains, legumes, fruits and vegetables. An accumulating body of research now suggests that consumption of certain foods or their associated physiologically active components may be linked to disease risk reduction (6). The great majority of these components derive from plants; however, there are several classes of physiologically active functional food ingredients of animal or microbial origin.

Claims linking the consumption of functional foods or food ingredients with health outcomes require sound scientific evidence and significant scientific agreement. The Food and Drug Administration (FDA) outlined the criteria for "significant scientific agreement" in a guidance document released on December 22, 1999 (7). As summarized in the schematic shown in Figure 1, there is a clear discrepancy between "emerging evidence" (characterized by in vitro or animal studies, uncontrolled human studies, and inconsistent epidemiological evidence) and "significant scientific agreement." To reach such agreement requires the support of

a body of consistent, relevant evidence from well-designed clinical, epidemiologic and laboratory studies, and expert opinions from a body of independent scientists. Claims about the health benefits of functional foods should be based on sound scientific evidence, but too often only so-called "emerging evidence" is the basis for marketing some functional foods or their components. Table 1 categorizes a variety of functional foods according to the type of evidence supporting their functionality, the strength of that evidence and the recommended intake levels.

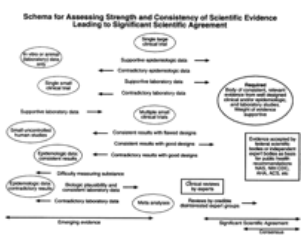

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FIGURE 1

The FDA's schematic of significant scientific agreement released in December 22, 1999 guidance document (7). This scheme differentiates "emerging evidence" on the left (e.g., animal and in vitro studies, uncontrolled human studies) from data on the right which represents "consensus" and includes evidence accepted by federal scientific bodies responsible for public health recommendations. Thus, the strength of the evidence for a diet disease relationship strengthens as one moves from left to right on the schematic.

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TABLE 1

Strength of evidence for functional foods currently on the U.S. market[1, 2]

Functional foods of animal origin

Probably the most intensively investigated class of physiologically-active components derived from animal products are the (n-3) fatty acids, predominantly found in fatty fish such as salmon, tuna, mackerel, sardines and herring (8). The two primary (n-3) fatty acids are eicosapentaenoic acid (EPA; 20:5) and docosahexaenoic acid (DHA; 22:6). DHA is an essential component of the phospholipids of cellular membranes, especially in the brain and retina of the eye, and is necessary for their proper functioning. DHA is particularly important for the development of these two organs in infants (9), and just recently, the FDA cleared the use of DHA and arachidonic acid for use in formula for full-term infants (10). Hundreds of clinical studies have been conducted investigating the physiologic effects of (n-3) fatty acids in such chronic conditions as cancer, rheumatoid arthritis, psoriasis, Crohn's disease, cognitive dysfunction and cardiovascular disease (11), with the best-documented health benefit being their role in heart health. A recent meta-analysis of 11 randomized control trials suggests that intake of (n-3) fatty acids reduces overall mortality, mortality due to myocardial infarction and sudden death in patients with CHD (12).

The 2000 American Heart Association Dietary Guidelines recommend two servings of fatty fish per week for a healthy heart (13), and the FDA authorized a qualified health claim on dietary supplements linking the consumption of EPA and DHA (n-3) fatty acids to a reduction of coronary heart disease risk (14). The qualified claim states: *"Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease. FDA evaluated the evidence and determined that, although there is scientific evidence supporting the claim, the evidence is not conclusive."* A "qualified" claim was authorized because of certain safety concerns regarding the consumption of high levels of (n-3) fatty acids, including: *1*) increased bleeding times; *2*) increased risk for hemorrhagic stroke; *3*) the formation of biologically active oxidation products from the oxidation of (n-3) fatty acids; *4*) increased levels of LDL cholesterol; and *5*) reduced glycemic control among people with diabetes. The FDA concluded that use of (n-3) fatty acid supplements is safe, provided daily intakes of EPA and DHA from supplements do not exceed 2 g/d (14).

Another class of biologically active animal-derived components that has received increasing attention in recent years is probiotics. Defined as *"viable microorganisms that are beneficial to human health"* (15), the health benefits of probiotics have been considered since the turn of the century when the Nobel prize-winning microbiologist Metchnikoff first postulated that lactic acid bacteria contributed to the longevity of Bulgarian peasants (16). It is thought that a wide variety of live microorganisms can contribute to human health, although the evidence is mainly from animal studies. In addition to numerous strains of *Lactobacillus acidophilus*, other strains of lactobacillus are being incorporated into functional food products now on the market including *L. johnsonii* La1, *L. reuteri, L. GG*, and *L. casei Shirota*. A recent Scientific Status Summary on probiotics from the Institute of Food Technologists summarized the scientific support for the therapeutic and/or preventive use of these functional ingredients for various health concerns including cancer, intestinal tract function, immune function, allergy, stomach health, urogenital health, cholesterol lowering and hypertension (17). The review emphasizes that the future success of probiotics will require strong support from medical and nutrition scientists and that studies documenting these effects in humans are limited.

More recently, research efforts have focused on prebiotics, i.e., nondigestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of beneficial bacteria in the colon, thus improving host health (18). Prebiotics include short-chain carbohydrates such as fructooligosaccharides and inulin, which enter the colon and serve as substrates for the endogenous colonic bacteria. Newer still is the concept of "synbiotics," which are mixtures of probiotics and prebiotics that beneficially affect the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, and thus improving host welfare (18).

Another nonplant ingredient that has been the focus of increased research efforts in recent years is conjugated linoleic acid (CLA). This component, which was first identified as a potent antimutagenic agent in fried ground beef by Pariza and co-workers (19), is a mixture of structurally similar forms of linoleic acid (*cis*-9, trans-11 octadecadienoic acid). CLA is present in almost all foods, but occurs in particularly large quantities in dairy products and foods derived from ruminant animals (20). For example, uncooked beef contains 2.9–4.3 mg CLA/g fat, whereas lamb, chicken, pork and salmon contain 5.6, 0.9, 0.6, and 0.3 mg CLA/g fat, respectively, and dairy products contain 3.1–6.1 mg CLA/g fat (21). The inhibition of mammary carcinogenesis in animals is the most extensively documented physiologic effect of CLA (22), and there is also emerging evidence that CLA may decrease body fat and increase muscle mass both in rodent models (23) and in humans (24), although not all human studies have been positive in this regard. There is also preliminary evidence that CLA may increase bone density in animal models (25).

Functional foods of plant origin

Numerous plant foods or physiologically active ingredients derived from plants have been investigated for their role in disease prevention and health. However, only a small number of these have had substantive clinical documentation of their health benefits. An even smaller number have surpassed the rigorous standard of "significant scientific agreement" required by the FDA for authorization of a health claim, which will be discussed in further detail below. Those plant foods currently eligible to bear an FDA-approved health claim include oat soluble (β-glucan) fiber (26), soluble fiber from psyllium seed husk (27), soy protein (28) and sterol- and stanol-ester-fortified margarine (29).

Some plant-based foods or food constituents currently do not have approved health claims, but have growing clinical research supporting their potential health benefits, and thus would be described as having moderately strong evidence. These include cranberries, garlic, nuts, grapes and chocolate and are discussed briefly below.

Cranberries have been recognized since the 1920s for their efficacy in treating urinary tract infections. A landmark clinical trial (30) confirmed this therapeutic effect in a well-controlled study involving 153 elderly women. More recent research has confirmed that condensed tannins (proanthocyanidins) in cranberry are the biologically active component and prevent *E. coli* from adhering to the

epithelial cells lining the urinary tract (31). New preliminary research suggests that the antiadhesion properties of the cranberry may also provide other health benefits, including in the oral cavity (32).

Garlic (*Allium sativum*) has been used for thousands of years for a wide variety of medicinal purposes; its effects are likely attributable to the presence of numerous physiologically active organosulfur components (e.g., allicin, allylic sulfides) (33). Garlic has been shown to have a modest blood pressure–lowering effect in clinical studies (34), while a growing body of epidemiologic data suggests an inverse relationship between garlic consumption and certain types of cancer (35), particularly of the stomach (36). The latter may be due in part to garlic's ability to inhibit the activity of *Helicobacter pylori* (the bacterium that causes ulcers). The best-documented clinical effect of garlic, however, concerns its ability to reduce blood cholesterol. A meta-analysis of 13 placebo-controlled double blind trials (37) indicated that garlic component(s) (10 mg steam distilled oil or 600–900 mg standardized garlic powder) significantly reduced total cholesterol compared with placebo by 4–6%. However, the Agency for Healthcare Research & Quality (38), which examined randomized, controlled trials at least 1 mo in duration, concluded that, although clinical trials show several promising, modest, short-term effects of garlic supplementation on lipid and antithrombotic factors, "effects on clinical outcomes are not established …" This is likely due to lack of consistency among studies in type of preparation used and overall study design.

Although foods high in fat have traditionally not been regarded as "heart-healthy" (except for fatty fish), evidence is accumulating on the cardiovascular benefits of a variety of nuts, when they are part of a diet that is low in saturated fat and cholesterol (39). Clinical trials, which have specifically examined the effect of almonds on blood lipids, have found that these tree nuts significantly reduced total cholesterol by 4–12% and LDL cholesterol by 6–15% (40,41). More recently, a Life Sciences Research Office review of six clinical intervention trials with walnuts consistently demonstrated decreases in total and LDL cholesterol that should lower the risk of CHD (42).

In the late 1970s researchers noted that residents in certain areas of France, who were avid drinkers of red wine, had less heart disease than other Western populations even though they consumed more fat in their diet. This observation triggered numerous investigations into this so-called "French Paradox" (43) and subsequent research confirmed the presence of high concentrations of antioxidant polyphenolics in red grape skins. It must be noted however, that moderate consumption of any alcoholic beverage, e.g., beer, wine or distilled spirits, has been shown in a number of studies to reduce the risk of heart disease in selected populations (44).

For those wishing to abstain from alcohol, recent clinical trials demonstrate that grape juice may also exert beneficial effects similar to those of red wine because both are rich in phenolic antioxidant compounds. Consumption of grape juice has been shown to reduce platelet aggregation (45).

Another food that is a source of polyphenolics and is just beginning to be investigated for its potential benefits to heart health (46) is chocolate. Chocolate contains flavonoids (procyanidins), which may reduce oxidative stress on LDL cholesterol. In a recent clinical trial involving 23 subjects consuming a diet supplemented with chocolate and cocoa powder providing ~466 mg procyanidins/d, time to oxidation of LDL cholesterol was increased by 8% compared with subjects consuming a normal American diet (47).

Epidemiologic data are accumulating on the health benefits of several additional functional foods or food components of plant origin, including tea (catechins), lycopene from tomatoes, particularly cooked and/or processed tomato products, and the carotenoids lutein and zeaxanthin from green leafy vegetables.

The effect of green or black tea consumption on cancer risk (48) has been the focus of numerous studies. Studies in animals consistently show that consumption of green tea reduces the risk of various types of cancers. Only a few studies have thus far assessed the effects of black tea. Green tea is particularly abundant in specific polyphenolic components known as catechins (49). The major catechins in green tea are (−)-epicatechin, (−)-epicatechin-3-gallate, (−)-epigallocatechin and (−)-epigallocatechin-3-gallate (EGCG) (50). One cup (240 mL) of brewed green tea contains up to 200 mg EGCG, the major polyphenolic constituent of green tea.

Although ~100 epidemiological studies have examined the effect of tea consumption on cancer risk, the data are conflicting (51). A recent study (52) involving 26,311 residents from three municipalities in northern Japan found no association of green tea consumption with the risk of gastric cancer. Phase I clinical trials are currently ongoing at the MD Anderson Cancer Center (Houston, TX) in collaboration with the Memorial Sloan-Kettering Cancer Center in New York on the safety and efficacy of consuming the equivalent of >10 cups of green tea by 30 cancer patients with advanced solid tumors.

Tomatoes and tomato products are also being investigated for their role in cancer chemoprevention and are unique because they are the most significant dietary source of lycopene, a non-provitamin A carotenoid that is also a potent antioxidant (53). A comprehensive review of 72 epidemiologic studies (54) found an inverse association between tomato intake or plasma lycopene concentration and the risk of cancer at a defined anatomical site in 57 of the 72 studies reviewed (79%); in 35 of these studies, the inverse associations were statistically significant. No study indicated higher risk with increasing tomato consumption or lycopene blood levels. Further, the risk reduction for about half of all studies reviewed was 40% (i.e., a relative risk estimate of 0.6). Cancers of the prostate, lung and stomach showed the strongest inverse associations, whereas data were suggestive for cancers of the pancreas, colon and rectum, esophagus, oral cavity, breast and cervix.

Most ongoing clinical trials involving lycopene and cancer prevention are focused on prostate cancer, in large part because a 1995 study (55) involving > 47,000 participants from the Health Professionals Follow-Up Study (HPFS) followed from 1986 to 1992 found that >10 servings/wk of tomato sauce, tomatoes, tomato juice or pizza could reduce risk of prostate cancer by 35%; advanced prostate cancer (i.e., more aggressive tumors) was reduced by 53%. More importantly, of the 46 fruits and vegetables evaluated, tomato products were the only foods that were associated with reduced risk of prostate cancer. Additional follow-up data from the HPFS through 1998 further supported the earlier observation that lycopene reduces prostate cancer risk and, more specifically, found that that intake of tomato sauce (2+ servings/wk) was associated with a 23% reduction in prostate cancer risk (56). The protective effect of tomato products may result from lycopene's ability to selectively accumulate in the prostate gland, perhaps serving an antioxidant function in that organ (57). This hypothesis was strengthened by a recent study that found that men with localized prostate adenocarcinoma had significantly reduced prostate DNA oxidative damage after consumption of tomato-sauce based meals containing 30 mg lycopene for 3 wk (58).

Another carotenoid that has received recent attention for its role in disease risk reduction is lutein, the main pigment in the macula of the eye (an area of the retina responsible for the sharpest vision). More specifically, research is focusing on the role of lutein in eye health due to its ability to neutralize free radicals that can damage the eye and by preventing photooxidation. Thus, individuals who have a diet high in lutein may be less likely to develop age-related macular degeneration (AMD) (59,60) or cataracts (61,62), the two most common causes of vision loss in adults. Because of the increasing evidence for lutein's role in eye health, supplements that contain this carotenoid are now appearing on the market. There is some concern, however, that lutein in supplement form may not provide the same benefit as the lutein found naturally in foods (63). In March 2000, the National Eye Institute of the NIH released a statement on lutein and its role in eye disease prevention (64): *"Claims made about an association between lutein and eye health should be approached with caution. The possible benefits of lutein on the eye remain uncertain."* The statement indicates that there is little direct scientific evidence at this time to support a claim that taking supplements containing lutein can decrease the risk of developing AMD or cataract. Nevertheless, the possibility that lutein may reduce the risk of oxidant-related diseases of the eye clearly warrants further research. Good sources of lutein include green leafy vegetables such as spinach (7.4 mg/100 g) and cooked cabbage (14.4 mg/100 g).

Although not yet supported by clinical or epidemiologic data, evidence from in vitro and in vivo (animal) studies supports the cancer-preventive benefits of flaxseed lignans (65), citrus fruit limonoids (66) and various cruciferous vegetable phytochemicals, including isothiocyanates and indoles (67). With respect to the latter, broccoli sprouts are currently being marketed both as a dietary supplement, highlighting the potential cancer-preventive action of one purported physiologically active component, sulforaphane, and as a food containing high

levels of sulforaphane. In vitro and in vivo, this component has been shown to be a potent inducer of Phase II detoxifying enzymes in the liver. Such enzymes speed the inactivation of toxic substances and thus accelerate their elimination from the body (68). The marketing of conventional foods as dietary supplements has engendered controversy, however, as will be discussed below.

Safety considerations

Although there is evidence that certain functional foods or food ingredients can play a role in disease prevention and health promotion, safety considerations should be paramount. Safety concerns have recently been raised, particularly with regard to the seemingly indiscriminate addition of botanicals to foods. A plethora of "functional" bars, beverages, cereals and soups are being enhanced with botanicals, some of which may pose a risk to certain consumers. The safety issues related to herbs are complex and the issue of herb–drug interaction has received increasing attention. One example is St John's wort, a popular herb utilized for treating mild depression. Hypericum extract from St. John's wort significantly increases the metabolic activity of liver cytochrome P_{450}. This enzyme inactivates several drugs, and thus would be expected to decrease their levels and activities in the body. Consuming St. John's wort has been shown to cause concomitant decreases in plasma concentrations of theophylline, cyclosporine, warfarin and ethinylestradiol/desogestrel (oral contraceptives) (69). Such data prompted the FDA to issue a Public Health Advisory about St. John's wort in February of 2000, as have Canadian authorities. In the United States, some consumer groups have lobbied the FDA to halt the sale of 75 functional foods enhanced with St. John's wort as well as the following additional herbs: guarana, gotu kola, ginseng, ginkgo biloba, echinacea, kava kava and spirulina. Also in 2000, the General Accounting Office (GAO) released a report that raised concerns about the safety of certain functional foods (70). The GAO report stated that the FDA "has not developed regulations or provided guidance to companies on the type of safety-related information that should be included on their labels for functional foods and dietary supplements. The absence of such safety information poses a significant safety risk to some consumers." In June of 2001, the FDA issued warning letters to the food industry concerning the use of "novel ingredients" such as St. John's wort in conventional food (71). The GAO has made the following recommendations regarding the safety of functional foods:

- Develop and promulgate regulations or other guidance for industry on the evidence needed to document the safety of new dietary ingredients in dietary supplements
- Develop and promulgate regulations or other guidance for industry on the safety-related information required on labels for dietary supplements and functional foods
- Develop an enhanced system to record and analyze reports of health problems associated with functional foods and dietary supplements

A favorable regulatory environment

Three important changes that affected the dissemination of information to consumers about the relationship between diet and health in food regulations occurred in 1990, 1994 and 1997. The first of these is the Nutrition Labeling and Education Act of 1990 (NLEA). The NLEA allows statements on food labels that characterize the relationship of any food or food component to a disease or health-related condition. Such "health claims" must be preapproved by the FDA before their use. Under the NLEA, the FDA was mandated by Congress to review 10 diet–disease relationships, eight of which were eventually approved as health claims (see Table 2).

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TABLE 2

Diet–disease relationships mandated for review by FDA under the NLEA and currently approved as health claims[1]

The NLEA also enables the authorization of new health claims after submission of a petition to the FDA. Because of the complexity and expense involved in the

petition process, however, as of July 2002, only five additional health claims have been approved under NLEA in response to food industry petitions (Table 3).

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TABLE 3

Health claims approved by the Food and Drug Administration following petitions submitted by the food industry

To expedite the health claims approval process and thus hasten the availability of health messages to consumers, Congress enacted the FDA Modernization Act (FDAMA) in 1997. This legislation streamlines the FDA preapproval process by enabling the use of so-called "authoritative statements" on food labels as health claims. Such statements must be published by certain U.S. government bodies responsible for the protection of public health such as the NIH, the Centers for Disease Control and Prevention or the National Academy of Sciences.

Food manufacturers intending to use authoritative statements as health claims must notify the FDA at least 120 d before marketing a product bearing the claim; it is then the responsibility of the FDA to prohibit or modify the claim within that time frame. If the FDA fails to respond, the claim may be used as submitted. To date, two health claims have been authorized under FDAMA (Table 4).

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TABLE 4

Health claims authorized by the FDA under the Food and Drug Administration Modernization Act of 1997

The third and probably most important (and controversial) change in food regulations was the passage of the Dietary Supplement Health and Education Act of 1994 (DSHEA). This act regulates dietary supplements as foods, not as food additives, defining them as "vitamins, minerals, herbs or other botanicals, amino acids, or other dietary substances for use by man to supplement the diet by increasing the total dietary intake, including concentrates, metabolites, constituents, extracts, or any combination of the above." In contrast to health claims, which require preapproval by the FDA after "significant scientific agreement" about a diet-disease relationship after a review of the "publicly available evidence," dietary supplements are allowed to bear so-called "structure/function" claims without FDA preapproval, thereby putting the burden of proof for safety and efficacy on the FDA. Such claims are those that: *1*) describe the role of a nutrient or dietary ingredient intended to affect the structure or function in humans; *2*) characterize the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function; *3*) describe the general well-being from consumption of a nutrient or dietary ingredient; or *4*) claim a benefit related to a classical nutrient deficiency disease and the prevalence of such disease in the United States. Manufacturers using structure/function claims on product labels must simply notify the FDA within 30 d of marketing the product that displays the claim. The following disclaimer must accompany the claim: *"This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease."* The FDA has received several thousand dietary supplements structure/function claim notifications since the passage of DSHEA. Examples of structure/function claims include "helps support a healthy immune system" for dietary supplements containing echinacea, and "maintains cholesterol levels that are already in the normal range" for a combination product containing fish oil, flaxseed oil and garlic. Structure/function claims may also appear on conventional foods without displaying the disclaimer that must appear on dietary supplements. When they are used on conventional foods, the claims must include an indication of how the nutrient in question affects the structure or function of the body.

Thus, since the early 1990s, because of Congressional action, which some feel have imposed serious limitations on the FDA, the national trend has been toward a loosening of requirements for scientific substantiation of health-related messages on many foods and food-related items.

Rapid growth in the market for health and wellness products

Because of the opportunity to make statements on food labels related to the health benefits of functional foods, it is not surprising that major companies are interested in developing such foods for the health and wellness market.

A recent survey of 38 Chief Research Officers of major food companies conducted by the Institute of Food Technologists ranked research efforts into the development of foods considered to be healthful well ahead of research efforts directed toward food safety, or toward the development of either organic or reduced fat foods (72). Similarly, Food Processing Magazine's 2001 Top 100 R&D Survey (73) identified functional foods/nutraceuticals as one of the leading food categories in which to devote R&D efforts for the next five years. This is not surprising, given the fact that during the 1990s, the health foods industry (encompassing functional foods, fortified foods, supplements, organic foods and dietary supplements) had sales increases of ~10–20%/y. Although the size of the functional foods market is difficult to quantify because much of the data includes other types of health-related products, according to a recent survey, the U.S. functional foods market is currently estimated at ~$18.5 billion (74). The market for foods positioned for their health benefits will continue to be strong for the next several decades given the consumer interest in self-care, aging demographics and increasing healthcare costs.

The consumer self-care phenomenon

Numerous surveys conducted over the last decade have indicated that increasing numbers of consumers are taking greater responsibility for their own health and well-being, and that they are increasingly turning to their diet to enable them to do so. The tendency for consumers to view the "kitchen cabinet as the medicine cabinet" was initially identified as a leading trend in the food industry in 1994 (75). This "self-care" phenomenon remains a leading consumer trend today (76).

The 10th annual consumer trend report from the Food Marketing Institute and Prevention Magazine found that that 76% of consumers strongly or mostly agree that eating healthfully is a better way to manage illness than medication (77).

The aging demographics of the 21st century will continue to fuel this self-care phenomenon. Those over the age of 50 y will increase by 48% compared with 16% for the 13- to 24-y-old age group over the next decade. Of greater importance, however, is the growth in the number of individuals >65 y old. By 2035, ~70 million people will be in this age bracket (78). With a continued increase in the overall age of the population, chronic diseases of aging such as heart disease, cancer, osteoporosis, Alzheimer's disease and age-related macular degeneration, among others, are inevitable, imposing an enormous stress on the cost of health care. The total yearly costs of treating chronic illnesses in the U.S. have been estimated at $659 billion. Preventative healthcare strategies, including nutritional approaches, could save as much as $60 billion in annual healthcare costs. Consumer interest in self-care and dissatisfaction with the current healthcare system will continue to be a leading factor motivating consumer food purchasing decisions.

The future of functional foods

Extensive research is currently directed toward increasing our understanding of "functional foods." Academic, government and private research institutes around the globe are devoting substantial efforts to identifying how functional foods and food ingredients might help prevent chronic disease or optimize health, thereby reducing healthcare costs and improving the quality of life for many consumers. An emerging discipline that will have a profound effect on future functional foods research and development efforts is *nutrigenomics*, which investigates the interaction between diet and development of diseases based on an individual's genetic profile (79). Interest in nutrigenomics was greatly augmented by the recent announcement that a rough draft of the complete sequence of the human genome had become available. In February 2001, the complete sequence of the human genome was announced by Ventor and colleagues (80). This technological breakthrough could eventually make it feasible to tailor a diet for an individual's specific genetic profile. Nutrigenomics will have a profound effect on future disease prevention efforts including the future of the functional foods industry.

Another technology that will greatly influence the future of functional foods is biotechnology (81). Recent examples of biotechnology-derived crops which have

tremendous potential to improve the health of millions worldwide include golden rice and iron-enriched rice (82). These grains are genetically engineered to provide enhanced levels of iron and β-carotene which could, in turn, help prevent iron deficiency anemia and vitamin A deficiency-related blindness worldwide. In the future, other foods enhanced with other nutritive or nonnutritive substances may even help to prevent chronic diseases such as heart disease, osteoporosis or cancer (83). The acceptance of biotechnology by consumers (currently a major issue in Europe) will be important if the potential of this powerful methodology is to be realized.

Conclusion

Although many functional foods may hold promise for public health, there are concerns that the promotion of functional foods and structure/function claims may not rest on sufficiently strong scientific evidence. Confusion also exists about claims applied to foods and those applied to dietary supplements. With the addition to foods of ingredients usually found only in dietary supplements, such confusion has increased. Although claims about the potential health benefits from functional foods or food ingredients must be communicated effectively to consumers, the differences between health claims and structure-function claims must also be more widely addressed to allow consumers to understand the differences in the scientific bases of such claims.

Any health benefits attributed to functional foods should be based on sound and accurate scientific criteria, including rigorous studies of safety and efficacy. Interactions with other dietary components and potential adverse interactions with pharmaceutical agents must be clearly imparted. Consumers must realize that functional foods are not a "magic bullet" or a panacea for poor health habits. There are not good and bad "foods," only good and bad dietary patterns. Thus, they should be wary of many of the promoted or implied benefits of these foods, and must realize that there is no consistent regulation or enforcement of existing regulations in the functional foods area. Diet is only one aspect of a comprehensive lifestyle approach to good health, which should include regular exercise, tobacco avoidance, stress reduction, maintenance of healthy body weight and other positive health practices. Only when all of these issues are addressed can functional foods become part of an effective strategy to maximize health and reduce disease risk.

Footnotes

[1] Funded by a grant from the American Council on Science and Health.

[3] Abbreviations used: AMD, age-related macular degeneration; CHD, coronary heart disease; CLA, conjugated linoleic acid; DHA, docosahexaenoic acid; DSHEA, Dietary Supplement Health and Education Act; EGCG, (−)-epigallocatechin-3-gallate; EPA, eicosapentaenoic acid; FDAMA, Food and Drug Administration Modernization Act; FOSHU, Foods for Specified Health Use; GAO, General Accounting Office; HPFS, Health Professionals Follow-Up Study; NLEA, Nutrition Labeling and Education Act.

Manuscript received: August 26, 2002.
Revision accepted: September 10, 2002.

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