Do Functional Components in Foods Have A Role in Helping to Solve Current Health Issues?1–3

Johanna T. Dwyer*

Senior Nutrition Scientist, Office of Dietary Supplements, NIH, Bethesda, MD 20892-7517

Abstract

Functional foods and ingredients that are safe and efficacious have the potential for a positive impact on health. Current regulations in the United States governing claims about foods and dietary supplements, including functional foods and ingredients, are briefly reviewed. Research and communications challenges necessary to bring such products to the market are discussed. J. Nutr. 137: 2489S–2492S, 2007.

Introduction

Functional ingredients and foods present 2 quite different challenges to those concerned with the science of these compounds: communications and science. This contribution reflects a perspective from the United States on these issues.

Communications challenges

What functional foods and prebiotics are. There is no legal definition for functional foods at present in the United States. However, there are variable operational definitions in common use. Some define them as “foods with a purpose.” The International Food Information Council defines functional foods as dietary components that provide a health benefit beyond basic nutrition (1). Prebiotics are one example of such functional foods or ingredients. Health professionals as well as laypeople are often unclear on what they are. The latest Dietary Guidelines for Americans (2,3) fails to mention prebiotics, probiotics, or such phrases as intestinal health, nor are such phrases included in either the former USDA Food Pyramid or the new “MyPyramid” issued in 2006 (4,5). Thus, there is very little or no mention of these terms in any official dietary guidance for consumers. However, reference to all of these components is frequent on the Internet. In today’s mass media environment, it is these sources, and not health professionals, that are the main sources and gatekeepers to health information. Indeed, health professionals play only a minor role in the dissemination of health information. There are literally mountains of raw information on nutrition, unfiltered by reviewers, health professionals, or even common sense to which consumers have access over the Internet. There are no board-certified medical experts like there are board-certified physicians and health experts to assist them in interpreting it. And there are no editors or reviewers to critique the information, as there are in medical journals. The information available over the mass media ranges from good to bad.

What prebiotics do. It is often said that prebiotics are food for bacteria and that they promote intestinal health. But intestinal health is not a commonly understood phrase for either consumers or health professionals in the US, nor is the gastrointestinal tract an organ system that Americans discuss in public. Although gut health is openly discussed in other societies, its near-taboo status in the US may affect the perceptions and understanding of the American public. Therefore, functional foods, prebiotics, and intestinal health are all difficult concepts for consumers to grasp. Professionals lack knowledge about these phrases and are skeptical about whether useful concepts actually exist; there are no regulatory definitions. Consumers wonder what these terms mean, because they are not mentioned in consumer guidance materials and thus create a great deal of consumer confusion. It is not surprising that consumers may be hesitant to pay extra for functional components.

What can be said about prebiotics today? A number of different health-related statements are permissible in the US today; these have recently been summarized in several useful reviews (6–8). There are statements about ingredients and nutrient content, dietary guidance statements about the health benefits of broad categories of foods, and also structure and function statements that describe the effects of components on normal structure of function of the body. There are also “unqualified” health claims that confirm relationships between components in the diet and risk of disease or of a health condition that provide significant scientific agreement and “qualified” health claims that are used for describing developing relationships between components in the diet and disease. The important and as-yet-unanswered question is whether consumers understand what all of these various terms mean (9,10). The number of health claims continues to expand (11,12).
Science challenges

What prebiotics are. From the scientific standpoint, paradigms are shifting and often when they do, policy and practice shifts follow. Views of bioactive or functional ingredients are now included in standard nutrition texts and journals (13,14), an indication that thinking is changing. There is a paradigm shift in the association between functional components and health outcomes. The old view was that nonnutritive constituents in foods were of little health significance. Now we recognize that functional components may in fact have important health effects. Another shift regards food composition gaps in carbohydrates. The old view was that carbohydrates were relatively unimportant and that it was not necessary to measure them directly in foods. Therefore, carbohydrates were rarely analyzed directly but rather they were calculated by difference from total weight of the food, water, and other nutritive constituents. Today, increasingly in this country and somewhat more rapidly in Europe and Asia, the various carbohydrate fractions are being subjected to chemical analysis. For example, today we know a great deal about the composition of oligosaccharides in foods, as well as sugars, dietary fiber, and resistant starch. We now know more about how they are synthesized, their structure, their distribution in fruits and vegetables, and their other properties such as viscosity. More is also being learned about their physiological properties including absorption and how they are fermented in the gut. The last comprehensive review of prebiotics was published more than half a decade ago in The Journal of Nutrition. Since then, much has been learned, as the proceedings of this conference indicate.

The old paradigm was that oligosaccharides were inconsequential physiologically. Now we recognize that they may be of functional importance in foods, that there are important differences between them in such characteristics as viscosity and fermentability, and that the various oligosaccharides may have a variety of important health outcomes. The inulin-type fructans are of particular interest to this conference. However, we still do not know the most appropriate doses and mixtures of oligosaccharides to optimize effects. Even so, if there are in fact health effects, there may be lingering safety issues to be examined, and the best mixture of inulin-type fructans to maximize positive effects also needs further study. Nevertheless, there are a number of different products now on the market; these include the following: Lactulose (Ross), inulin-type fructans, inulin and oligofructose (Orafti), IsomaltoOls (Showa Sanyo), Oligomate (Yakult), Palatinose (Sudzucker), Pyrodextrin (Matsutani), Soyh OS (Calpis), XyloOS (Sutory), and Guar (Novartis).

Another paradigm shift of relevance to prebiotics is in the increased attention being paid to the gut microflora and commensals. Prior thinking was that the commensals and gut bacteria were really not of importance to health. Now we recognize that they may be of importance to health. Their significance may be due to their ability to generate short chain fatty acids and to stimulate the colonic microflora, because they have effects on glycemic index or load, or on bowel function or other disease risks. For prebiotics, the bifidobacteria and the lactobacilli are of particular importance. But there is much we do not understand from the scientific standpoint about how it might be that “good bugs” would have good effects on health, particularly gut health. The theory is that more of the so-called good bacteria (e.g., bifidobacteria and lactobacilli) produce a less toxic microfloral environment and other beneficial health effects such as better glycemic control as well as less flatus. Among the questions that need better answers are: What microbiota exist in the different regions of the gut and what are their affects on health? How are the microflora established in humans and how are they sustained? How does the microflora change over the lifetime and in illness? Is there an “ideal” population of microflora? What factors account for inter-individual differences in the microflora? What effects do prebiotics have on the metabolism of the resident microflora and the ingested microflora? Why do the flora revert after pre- or probiotics are fed?

What do prebiotics do? In the past 20 y, the view that desirable levels, types, and sources and health outcomes associated with prebiotics were inconsequential has changed. Now there is growing interest, although not yet certainty, that these constituents have important functional effects and that they are active players in the metabolic and gut functional and broader physiological realm. For example, the inulin-type fructans stimulate the growth of some colonic bifidobacteria in humans and at the same time they may inhibit others. The question that still must be answered is if this decreases risks for any or many diseases. The functionality of prebiotics needs to be better defined; is it that they alter the microflora, alter physiological functions like laxation, or that they ultimately alter risk of diseases?

What can we say today about functional components such as prebiotics? To an international audience, the American food regulatory system is complex and confusing. Not only the executive but also the legislative and judicial branches of government regularly become involved in marketing and advertising issues. The questions that may have regulatory implications are many. For example, should prebiotics be called dietary fiber? There is much to be said for defining them as dietary fiber because of their chemical and physiological characteristics. Also, consumers know what fiber is, regard it as a good thing, and connect it to the gut. But some other term, such as chemical names like oligosaccharides or inulin, might be more descriptive. Current law in the US allows for a number of health claims under the Nutrition Labeling and Health Education Act of 1995. These include claims for certain foods and/or ingredients or components and decreased risk of heart disease (such as soy protein; saturated fat and cholesterol; plant sterols/stanol esters; fruits, vegetables, and grains containing fiber, especially soluble fiber; and soluble fiber from certain foods, like oats, pyllium, and barley). Also under the Nutrition Labeling and Health Education Act, certain health claims about cancer risk reduction can be made for fruits and vegetables, fiber-containing grain products, and products low in fat. Also allowable are the claims that calcium is recognized as decreasing osteoporosis, sodium, hypertension, sugar alcohols, and dental risk and that folic acid decreases neural tube defect risks. The more recent Food and Drug Administration Modernization Act permits health claims about whole grains and decreased risks of certain cancers and heart disease; whole grains and moderate fat diets and decreased risks of coronary heart disease and certain cancers; and the relationship between potassium-containing foods and decreased risk of blood pressure and stroke. Finally, in response to rulings by the judicial system in decisions such as Pearson vs. Shalala and others, the FDA has permitted several new health claims. These include health claims about the association between tomatoes and tomato sauce and the decreased risk of prostate, ovarian, gastric, and pancreatic cancers. Health claims are allowed that discuss the relationships between intakes of calcium and decreased risk of colonic polyps and colorectal cancer, and between green tea, selenium, or antioxidant vitamins and decreased cancer risk. Health claims are also permitted regarding the association
between (n-3) fatty acids and decreased heart disease risk; folic acid, vitamins B-6, vitamin B-12, and decreased vascular disease risk; walnuts and other nuts and decreased heart disease risk; and monounsaturated fatty acids from olive oil and decreased coronary heart disease risk. Health claims are also allowed on the associations between calcium and decreased risk of hypertension; pregnancy-induced hypertension and preeclampsia; phosphatidylserine and decreased risk of cognitive dysfunction and dementia; 0.8 mg folic acid and decreased risk of neural tube birth defects; and chromium picolinate and decreased type 2 diabetes risk.

Many potential health claims are submitted to FDA each year (8,9). To evaluate them, FDA has developed an evidence-based rating system for evaluating the substance-disease relationships the health claims assert are present. Once a proposed relationship between a substance and a disease or health-related condition is identified, FDA identifies individual studies that are pertinent to that substance-disease relationship. The individual studies are classified according to the type of study design that they employ (e.g. observational vs. randomized controlled trials), because inference of cause and effect is more secure with the latter. Then each study is assigned a designation that reflects its quality. After all of the relevant studies have been reviewed, the strength of the scientific evidence in support of the substance-disease relationship is then ranked. This takes into account the quantity, consistency, and relevance to disease risk reduction of the aggregate of all the studies reviewed. Then the rank is reported. The highest level or “A” health claim is a claim that meets the standard of significant scientific agreement. The relationship is considered to be unqualified and not in need of qualifications. The other levels of claims require qualifying language to correctly portray the possible cause and effect relationship and for this reason they are called qualified health claims. The 2nd level claim is the “B” claim, which requires qualifying language such as “although there is scientific evidence supporting the claim, the evidence is not conclusive.” The 3rd level of claim is a “C” claim and it requires even more tentative qualifying language such as “some scientific evidence suggests that (claim listed here); however, FDA has determined that this evidence is limited and not conclusive.” The 4th level of qualified health claim is the “D” claim, with qualifying language that suggests only a very weak relationship between the constituent and the disease, such as the following: “Very limited and preliminary scientific research suggests (the claimed relationship).” FDA concludes that there is little scientific evidence supporting this claim.”

The Dietary Supplement and Health Education Act of 1994 addressed claims that could be used for dietary supplements. In the US, dietary supplements are regulated more like foods than like drugs. Structure-function claims can be made for dietary supplements, but claims for the prevention, treatment, or mitigation of disease are not permitted. In late 2006, the FDA promulgated a draft regulation on the definition of functional food components and it is now open for public comment (15).

In addition to the FDA, the Federal Trade Commission also regulates claims about all products, including those with functional ingredients. Truth in advertising requires that advertising be truthful and not misleading and that it be adequately substantiated. That is, competent and reliable scientific evidence must be present for all objective product claims before advertising these relationships (8).

International considerations

World trade is becoming more and more global. Regulations differ even for the same component from one country to another. In the US, the intended use of the product and the claims that are made determine whether the claims require a great deal of substantiation if a product is used as a drug and claimed to prevent, treat, or mitigate disease and thus requires a new investigatory drug application before investigations can be done on the product. If food claims are made and the product is to be used as a food, structure-function claims are allowable. At present, the U.S. law regulates dietary supplements as foods and therefore structure-function claims are allowed.

Regulations even for the same functional component therefore can differ in the US depending on the intended use and the claims that are being made about the product. Compared with Asia, functional ingredients are present in many fewer products in the US than they are in countries such as Japan. In the European Union, some functional constituents are popular. The PASSCLAIM process is now being considered as the basis for regulation. There is still much controversy about what is the best system (16).

Realizing the potential of functional components

The process of studying functional components involves studies of intake and bioavailability to estimate exposures and then additional investigations of their beneficial and possibly harmful health effects, either by directly measuring health outcomes or by relying on proven biomarkers of outcomes. All of these studies must take health status and other factors into account. The potential of functional components depends on demonstrating beneficial health effects and the absence of harm of these products at a reasonable cost. Health outcomes are the most definitive, but very few biomarkers of early outcomes are available today.

Before it is possible to demonstrate the efficacy of a prebiotic, it is necessary to determine the quality of the product. The product, whether it is composed of single components or mixtures, must be characterizable. Standards for testing prebiotics should include their identity, potency, purity, stability, and toxicity. At present in the US, the inulin-type fructans apparently have a self-affirmed generally recognized as safe status and a new dossier updating the data has just been submitted.

The efficacy of prebiotic ingredients must also be considered. Issues here include what their characteristics are, how they differ from each other in the doses needed to product various effects, and how they exert their effects. The appropriate use of these products must also be determined. Who should use them, how much should be used, and for how long should they be used?

Looking back at the progress of the field of prebiotics research over the past few years, it is gratifying to note that much has been accomplished in quality and safety issues. There is some evidence that they are effective, but human studies are difficult and it is not easy to measure effects. Well-conducted clinical trials are needed with well-characterized populations and interventions and hard endpoints instead of surrogate endpoints on all the various effects of health outcomes that are being suggested. Subgroups by age and health status may be important to investigate further. From the practical standpoint, there is interest in how beneficial effects of prebiotic feeding can be preserved without constant feeding of the prebiotics and whether prebiotic feeding avoids stimulating pathogen growth. The health outcomes must be better specified. Modification of the gut flora alone is of uncertain benefit to health; it is only if disease or risk of diseases can be lessened that the claims are likely to be regarded as scientifically important. Many conditions or processes (glycemic control, insulin secretion, lipid metabolism, and mineral absorption) as well as disease processes
(osteoporosis, constipation/laxation, irritable bowel syndrome, irritable bowel disease, colitis, colon cancer, and modulation of immune response) must be studied. Although animal models such as gnotobiotic animals colonized with human microflora may be useful as models of disease, human studies will still undoubtedly be necessary. The safety profile of prebiotics is encouraging but also needs review. Adverse effects are rarely noted other than mild gastrointestinal discomfort when large amounts of product are ingested. However, it is also true that adverse events are often not measured; the FDA is currently exploring how to better monitor adverse events in general. This supplement to the Journal of Nutrition is welcome because it provides the opportunity to review data that is currently available and to learn about present perspectives in the field.

**Bottom line: consumer acceptance**

Until now, we have not discussed consumer attitudes and desires. The International Food Information Council surveys indicate that consumers in America and other countries want to be healthy and they are beginning to hear about functional components like prebiotics, but not from traditional sources. They probably view themselves as fairly healthy but they want to be healthier, so there is a great deal of potential if such products can help to maintain or improve health.

The potential of prebiotics and other functional ingredients depends first and foremost on scientifically valid and believable health claims and other claims. Specifically, the costs must be reasonable. How is consumption going to be increased? To realize the potential of prebiotics, it will be important to focus on the effects of interventions in various target groups and to involve health professionals.

Science moves rationally by controversy that stimulates thinking and research. Scientific disagreement is common and consensus is rare. Scientists often find it difficult to craft consumer messages that include the caveats that they think are important to include as being accurate. Scientists tend to be splitters, not lumpers, and they esteem precision and details, although they often disagree about which details should be emphasized. However, it is not clear if scientists’ efforts are meaningful to consumers in conveying the level of certainty scientists believe is appropriate. Also, what scientists believe to be in consumers’ interests may not actually be in accord with consumers’ wishes, concerns, and desires for information. Therefore, it is essential in the future that scientists, communicators, and consumers engage in a dialog on these issues and collaborate more closely to ensure that truthful, straightforward, and meaningful messages about functional components can be imparted to the public and the potential of functional foods and constituents can be realized.

**Literature Cited**