



World Health Organization

Globalization, Diets and Noncommunicable Diseases



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Preface

Noncommunicable diseases have become a major health problem not just in developed countries but also in developing countries. Already 79% of the deaths attributed to the noncommunicable diseases occur in developing countries. The rising trends are a consequence of the demographic and dietary transition, and the globalization of economic processes. Scientific evidence shows that unhealthy diet and physical inactivity as well as tobacco use, recently highlighted in the World Health Report 2002, are major global determinants of noncommunicable diseases. Examples from several countries show that changing these determinants is possible and can have a strong effect on the trends in noncommunicable diseases.

Although national responses are crucially important, international work and global perspectives are badly needed. For this, WHO is, in response to the request from its Member States in the World Health Assembly 2002, preparing a global strategy on diet, physical activity and health. This work emphasizes integrated prevention by targeting the three main global risk factors: unhealthy diet, physical inactivity and tobacco use. In this process, WHO is looking at a number of issues related to globalization and global nutrition transition.

This publication is a collection of papers written by experts in the fields of nutrition, epidemiology, economics, and marketing. We hope that this report will make a valuable contribution to the discussion on nutrition transition, globalization and noncommunicable diseases. The views expressed in these papers are those of the authors. We are grateful to the authors for their effort.

Geneva, November 2002

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Can Functional Foods Make a Difference to Disease Prevention and Control?

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1. What Are Functional Foods?

While the link between food and health is not new, the concept of Functional Food did not gain widespread recognition until the 1980s, with the launch of the so-called world's first Functional Food; a Japanese soft drink containing dietary fibre "Fibe Mini" in 1988. Seeing the developments in Japan, the new trend of Functional Foods was promoted actively in Europe and the US during the 1990s. As food companies and policy makers struggle to enable health claims to be made for Functional Foods, the actual words and definitions used to describe these new food and health developments are extensively debated. However, in most countries currently there is no legal definition for Functional Food, but in general, a Functional Food will have at least one or more of its biological effects on humans characterized and will be intended for use on a regular basis, by the general public. Many traditional products, such as apples, soy, tomatoes and oats, are marketed with emphasis on their health-promoting properties. In the US, the focus has been on dietary fibre, vitamins and other nutritious substances. In Europe, Functional Foods often centre on lactic acid bacteria while Asia focuses on natural plant extracts.

Various definitions and terms of Functional Foods have been advanced with probably the most agreed being "Functional Foods are foods positioned in the market place for particular and identified physiological and health reasons". They may be traditional foods with newly defined significance or altogether newly formulated foods whose ingredients or formulation may be novel; and, therefore, the term "*novel food*" is used interchangeably with the term "*functional food*" in this respect. "*Nutraceuticals*" are defined as "naturally derived bioactive compounds that are found in foods, dietary supplements and herbal products, and have health promoting, disease preventing, or medicinal properties". Thus, nutraceutical products, being compounds rather than food or food ingredients, may compete with pharmaceutical products, only to be distinguished by source of active component and in what form they are ingested, recognized and/or sold as food or medicine. Although "functional food" and "nutraceuticals" are often used interchangeably, "functional food" presents items ingested as snacks, with meals, or as drinks, they are the province of food industry, while "nutraceuticals" are presented as medicinal, another province of pharmaceutical industry. However, the boundaries between these are increasingly blurred.

Food-health relationships can be categorized in various ways for the purposes of food product development (Wahlqvist, 2000), as listed in Table 1.

Table 1. Food-health relationships, which may inform the development and place of Functional Foods

Health/Condition Category	Food Characteristics
1. Disease related to environmental degradation and methods of food production	Eco-sensitive foods (e.g. produced in sustainable ways; biodegradable or edible packaging; identifiable biosecurity for animal-derived foods; nature of genetic material)
2. Food shortage and PEM (protein energy malnutrition)	Technologies which minimize post-harvest loss, increase shelf life and maintain palatability
3. Disease related to protein quality, fat quality and micronutrient status	Nutrient dense foods; fish or its plant or microbial food surrogates
4. Physical inactivity and health (especially over fatness; also loss of lean mass, particularly muscle)	Foods of low energy density and high nutrient density
5. Phytochemical deficiency disorders including menopause, macular degeneration, osteopenia	Greater emphases on plant-derived foods and their variety
6. Diseases of changing demography <ul style="list-style-type: none"> • Ageing • Rapid loss of traditional food culture and acquisition of new food cultures 	<ul style="list-style-type: none"> • Anti-ageing food, especially ones to delay body compositional change (bone, muscle and fat); loss of sensory function; decline in immune function; proneness to neoplastic disease; decline in cardio-respiratory function; and decline in cognitive function; and anti inflammatory foods • Maintenance of traditional foods in convenient, affordable and recognisable form
7. New psycho social stressors and mood change	Foods which favourably affects mood
8. Food borne illness and the microbiological safety of foods	<ul style="list-style-type: none"> • Pre- and pro-biotic foods • Immune system enhancing foods
9. Illness related to the chemical safety of foods (e.g. pesticide residues)	Regional origin and certification of foods

2. When and for Whom is a Functional Food Successful?

Thousands of products with supposed health benefits, ranging from the nutritionally beneficial to the fraudulent, are already available in the world market, and the number of products is soaring. Thus it is no longer possible for health or regulatory authorities to side-step this phenomenon. Science and technology, agriculture, food manufacture and markets are driven by the belief and actuality that food characteristics are relevant to health. For all sectors, the advent and currency of Functional Food can be seen from both individual and community or population points of view. For example, certain consumers may purchase phytoestrogen-containing food (such as soy and linseed) to reduce the impact of the menopause or the risk of prostate cancer, while the public health sector will be interested in the broader health impact and the attendant risk-benefit ratios. The long-term success of a Functional Food for health and well-being depends on perspective and the alignment of a number of interests and stakeholders. Both the health sector and food industry will be interested in costs, the one in relation to health outcomes (say, compared with the use of pharmaceuticals), the other in profitability. Technologists will be interested in product feasibility and consumer acceptance. Scientists and regulators will be concerned about the credibility of claims. Environmentalists will be interested in sustainability. And there will be other stakeholders.

2.1 Product and Market Development

Functional Foods present major challenges for much of the food industry; they appear to be a new and unfamiliar territory for product developers, for marketing and for business strategies. One of the obstacles to significant innovation in the food industry is that it is historically a low-technology business and true differentiation is very difficult to achieve. Barriers to entry are low, innovations are difficult to patent-protect, and product features are relatively easily and quickly copied by competitors. Since there are medical and public health considerations in product and market developments, it makes sense to develop Functional Foods that address the actual medical or nutritional needs of a defined population segment in a measurable way. Using concerns and worries of consumers about their health and possible future disease risk as a basis for product development and marketing of foods on a wide scale is fundamentally different from how traditional foodstuffs are normally marketed and sold.

One of the major considerations for the technical development and marketing of Functional Foods is the benefit the product will deliver, which will usually require the delivery of an outcome which is clinically measurable. Products that claim to favourably affect an intermediate point in the pathway to disease, like blood pressure or blood lipids, can be evaluated for their effectiveness by taking a recordable or blood measurement. However, for some products, such as calcium supplements for the prevention of osteoporosis and related fracture, the benefits might be short-term changes in indices of bone turnover, but, of greater interest, are the measurements of bone mineral density, in the medium term, or fracture rate in the longer term. What this means is that the costs of product development with Functional Foods must also include health outcome evaluation at some level.

2.2 Consumer Acceptance

Many consumers still have concerns as to whether they really need or want such food products, how much and for how long. While epidemiological findings indicate that dietary and other lifestyle changes should reduce the occurrence of much chronic disease, it remains to be seen whether such a cause-and-effect linkage will be in evidence in public health statistics, when long-term dietary changes are facilitated with Functional Foods. For consumers, convenient and easy access to food products that fit in with active and busy lifestyles is a consideration. Packaging provides extrinsic appearance, and it should also help meet the consumers' information demands at the point of sale. This applies to a wide range of food packages in various ways. Thus, food packaging companies are likely to be advocates for Functional Foods, and may do so without undue bias between different Functional Foods (Schannon, 2001). Consumers are not price sensitive about foods if they confer health values, for which they are often prepared to pay a premium. Thus, consumers and food industry can converge in their support for the development of Functional Foods.

Food policy could allow food producers to tell consumers, in strong and unambiguous fashion, the nature of the health benefit they may derive from consuming a particular food product. Such communication will add to the market success of Functional Food products. In this vein, health claims should enable consumers to differentiate between products that confer scientifically validated health benefits and make legally evaluated claims, against unproven and misleading ones. But the tenure of this approach may be limited as other means of providing consumers with information about foods, the regular education systems, education campaigns targeted at consumers and health professionals, nutrition informatics through communication media and internet, and broader aspects of government policy nature (Kouris-Blazos, 2002). Such health claims also provide a measure of confidence about the food-health relationships, which may not be fully justified. It however denies the value of understanding uncertainty and risk (Wahlqvist & Briggs, 1991).

While the social, food, nutrition and biomedical sciences underpin the development of Functional Foods, they allow for increasingly rational product development to fit consumers' health needs. At the same time, they also encourage the application of risk health science with due consideration of

safety, although risk can be expected to be negligible in the public health domain. The distinctions from that in the pharmaceutical domain where side effects are weighed against benefit on a regular patient-by-patient basis, with each usage (Table 2), may be poorly understood by those who enter the Functional Food area, and are unfamiliar with toxicology of drug development. Appropriate monitoring and surveillance have to be in place as a requisite of any community which is exposed to new products developed for purported physiological or health reasons.

2.3 Science and Public Health Nutrition Issues

The recognition of the relationships between food intakes and major so-called “chronic noncommunicable diseases (CNCDs), such as obesity, diabetes, cardiovascular disease, certain cancers, osteoporosis and arthritis, stimulated the development of dietary guidelines for the public. With time, there has been an emergence of a more comprehensive approach based on the knowledge of genetic predisposition, the nutritional modulation of gene expression and lifestyle factors (themselves often connected to food patterns), including physical activity, abuse of substances such as tobacco and alcohol. However, while nutritional science flourishes at present, scientific evidence of the randomized controlled trial kind may not necessarily substantiate prevailing beliefs or reasonable deduction about the health benefits of particular foods, or their nutritional components, beyond the correction of deficiencies.

Clinical nutrition trials can test biological and/or pharmacological effects of food constituents or food formulations in randomized, controlled fashion (randomized controlled trials, RCTs). However, much crucial information about foods, food patterns, food culture and health outcomes is not adducible in this way. Instead, the testing of hypotheses about desirable and measurable models of the human diet, in prospective studies of well-characterized populations, is required (Wahlqvist et al., 1999 & 2001; Benson & Hatz, 2000).

Intervention trials, especially with nutritive substances such as micronutrients and phytochemicals, have raised the prospect of major benefits for a large fraction of the population (Dalais et al, 1998; Hodgson et al, 1999; Howes et al, 2000). In order to obtain useful information on manageable sample sizes, reduction in risk factors as intermediate endpoints (such as improved blood lipid profile or blood pressure reduction) is often used in trials; in some cases high-risk groups (such as the aged) are also used. Relatively few intervention trials have studied overall health outcomes, such as fracture rates, diabetes and CVD together, or cause-specific or all-cause mortality rates as endpoints (ATBC Cancer Prevention Study Group, 1994; Cumming & Nevitt, 1997; de Lorgeril et al, 1999).

Moreover, it is easy to underestimate synergies between food consumption, as part of a general lifestyle, and other behaviours or activities. For example, reduction of blood pressure is likely to be more effective with a plant-based diet in its entirety than is one plant food alone (Beilin, 1994). Similarly, the combination of weight loss and fish consumption tends to be more impressive than either alone in lowering blood pressure (Bao et al, 1998).

One of the major limitations with Functional Food development is that a nutritive factor alone or in combination with other such factors is unlikely to provide all of the available biological advantage from a food or food pattern (Trichopoulou et al, 1995). Thus the retention of a background diet with a range of basic food commodities, against which Functional Foods may be positioned for added health advantage, is likely to be required for optimal health. When food culture is measured and its prediction of survival advantage in excess of individual foods or nutrients assessed (Trichopoulou et al, 1995), or when intact food commodities, like whole grains, are studied in conference of survival (Jacobs et al, 1999; Liu et al, 1999; Slavin et al, 1999), advantage is recognized. The extent to which background diet is replaced with Functional Foods will be a critical public health issue.

2.4 Regulatory Issues

Food and health policy experts question the relevance of Functional Foods, and the Health Claims regime thought necessary to regulate them (Heasman & Mellentin, 2001). The Codex Alimentarius Commission, the international food standards agency, defines health claims as “*any representation that states, suggests or implies that a relationship exists between a food or a nutrient or other substances contained in a food and a disease or health-related condition*”. Health claims for products and ingredients are developed to represent both efficacy and safety. The substantiation of health claims must be scientific; it requires compilation and critique of the existing literature, including clinical trials in humans, epidemiological evidence, animal studies and other evidence of biological activity. The strength of the evidence comes from the consistency of evidence across all types of quantifiable data, and it will allow greater or lesser latitude in the nature of health claims. The totality (balance and range), quality and relevance of the evidence to the claims need to be considered together. Considerations should be made to all relevant research relating to the claimed benefit, not just to that supports the effect. Where there are inconsistencies in the evidence, it is important to examine whether there is plausible explanation for those inconsistencies. Studies on biomarkers, plausible mechanisms and outcomes, and definitive health end points, can be considered, but the claim should be limited to the outcome assessed and not extrapolated further. The Consensus Document on Scientific Concepts of Functional Foods in Europe produced from the European Commission Concerted Action on Functional Food Science in Europe (FUFOSE) suggested the outline of a scheme to link claims for Functional Foods to solid scientific evidence (Diplock et al, 1999). The European Union PASSCLAIM project (Process for the Assessment of Scientific Support for Claims on Foods) is introduced in 2001 to provide industry, academics, consumer groups, and regulators with means to evaluate the scientific basis for health claims.

For European countries (the European Union), Australia and New Zealand, the first consideration with the introduction of Novel Foods is that of safety. But, although Novel Foods may be introduced for convenience, extended shelf-life, better appearance, palatability, as analogues for more expensive or less available traditional or established products, in the current climate, potential nutritional or health benefits are more likely to be the motivation behind their manufacture. Likewise, for Functional Foods, which may or may not be novel, recognition will be sought for their presumed nutritionally related health benefits. Health claims are the current strategy which regulators are using to handle this situation – the process begun as *Foods for Specific Health Uses* (FOSHU) in Japan in 1991.

There is little evidence so far that health claims are, as statements, making an impact on healthful food choices and health outcomes (ANZFA, 2000). They can however, skew food consumption in the direction of the food product so-labelled – as with the non-mandatory “Pick the Tick Program” of the National Heart Foundation of Australia (Schrapnel, 1993) and the Folate and Neural Tube Defects Claim in Australia (ANZFA, 2000); here it is arguable whether there is real food choice benefit, since not all equivalent products are identified. For example, choosing one phytosterol containing food over another, or fortified breakfast cereals for folic acid rather than liver.

A problem for consumers and health claims about Functional Foods is that the vehicle or delivery system and the background eating patterns and nutritional status may matter and not be well characterized. For health claims to provide an effective informational environment for Functional Foods is probably over-optimistic. However, a broader information framework, as part of the overall public health environment – and linked to health based non-governmental organizations (NGOs), may well prove useful (Wahlqvist, 2001; Kouris-Blazos et al, 2001). The World Wide Web is likely to be a powerful ally to the safe and effective introduction of Functional Foods, provided it itself operates with checks and balances. At present there are no agreed protocols for evaluation of the information on the internet. For the average consumer, sorting through information for credible sites can be daunting and the potential for harm from misleading and inaccurate health information

is of concern. It is suggested that a series of questions, such as whether the information contains traceable references to support the evidence, or whether the information balanced, should be asked in order to evaluate the credibility of website in question (Kouris-Blazos et al, 2001). We generally under-estimate and under-value the utility and empowerment of individuals, when some debate and appreciation of the limits of evidence prevails (Wahlqvist & Briggs, 1991). With time and increased validation of the place of a Functional Food in the general food supply, for health advantage, the information will become part of formal education, subject to revision as new evidence comes along.

Risk analysis is crucial with the rapid development and use of Functional Foods. This is because their very "raison d'être" is based on the risk that a significant proportion of the population targeted are at risk of developing the health problem and may have their health and well-being prospect enhanced. In this public health arena, rather than that of one-to-one counselling or medical care, the risk of relevant or unintended outcomes must be negligible. This is unlike pharmaceuticals, used only for sufferers, where some risk is allowable, depending on benefit. Having said this, it is noteworthy that a number of nutrient fortification programmes (as such with iron, vitamin A and even folate) have been implemented with recognized and measurable risk at the population level, because the aggregate benefit to a widely deficient community was reckoned to be sufficiently substantial.

The example of food fortification with folate, with consumption community-wide, in an effort to reduce the risk of neural tube defects (NTDs) in newborn infants, was much debated in the United States of America and Australia, when a more targeted and restricted approach using folate supplementation only for women whose offspring were at risk, could have been used. Australian research shows that while folate supplements reduce the risk of birth defects by up to 70%, they also increase the chance of having twins by 40% (Lumley et al, 2001). Is this an acceptable outcome? There is concern about long-term risks of elevated maternal folate on the fetus related to disease susceptibility later in life (Stover & Garza, 2002). Maternal folate status may influence fetal DNA methylation patterns and DNA mutation rates at the same time as embryonic and fetal survival is maximized. Critical risk analysis and ongoing monitoring and surveillance of this kind ought to be required for Functional Foods in general, but will resources and commitment allow and enable this to take place?

3. Functional Foods – Some Success Stories

The definition of Functional Foods is not limited to commercial food products, it applies to those which have been used to overcome micronutrient deficiency problems globally, often by NGOs and governmental or international agencies. Food fortification is considered to be one of the most successful examples of Functional Foods, in terms of product development and goal achievement (Asian Development Bank, 2000). It is a major and integral food-based strategy to eliminate iodine deficiency disorders (IDD), vitamin A deficiency (VAD) and iron-deficiency anemia (IDA) in developing countries with commitment from many of their leaders at the World Summit for Children in 1990.

3.1 Food Fortification and Biofortification

Over the past decade, salt iodization has contributed substantially towards the virtual elimination of IDD in several developing countries. Programmes of sugar fortification with retinol have taken place in many Central American countries. However, progress in reaching wider populations in Asia with iron and vitamin A has been more modest. While the fortification of wheat and corn flour with iron salts has been successful in many countries, the technology and capacity for fortification of flour with iron is still being developed in Fiji, India, Indonesia and the Philippines.

Overall, food fortification has provided economic benefits by reducing morbidity, improving work capacity and cognition (Popkin, 1998). While salt is used as a food vehicle for iodine, its consumption in some developed countries has fallen, as the result of public awareness of blood

pressure control. This could lead to the re-emergence of IDD in Australia (Gunton et al, 1999; Li et al, 2001), and probably in other industrially-developed communities despite a good deal of food trade and food cultural pluralism which ought to minimize the risk of IDD through the availability of iodine replete foods.

Recently, biofortification has been proposed to combat micronutrient malnutrition. “Golden Rice” is an example of biofortification through gene manipulation to improve nutritional value, vitamin A in particular, of rice. Genes from the daffodil and a bacterium were introduced to the rice line to complete the biosynthetic pathway to β -carotene, a provitamin A carotene (Ye et al, 2000). The insertion of these genes into rice to express β -carotene was necessary because parts of the pathway had been lost, although the downstream parts of the pathway were still expressed. The resultant transgenic rice line synthesizes enough β -carotene in the endosperm to meet part of the vitamin A requirements of people dependent on rice as a primary food staple in Asia, Africa and Latin America. At the same time, the re-discovery of hundreds of natural “yellow” rice cultivars which may have the missing genes has encouraged the study and propagation of rice varieties that can be used as natural food sources of provitamin A carotenoids (Graham & Rosser, 2000). An added value of such grains is likely to be their provision of a wider array of carotenoids with wider health benefits than the prevention of vitamin A deficiency (Cooper et al, 1999). As grains richer in other micronutrients, like iron and zinc, are identified in seed banks and libraries and in traditional communities, the prospects of safe and effective biofortification in the food supply increase (Bouis, 2002).

It is clear that food fortification and biofortification can provide Functional Foods, which address and mitigate major public health nutrition dilemmas. Efforts are being made to create an environment for public-private sector collaboration, amongst food regulators, the health sector, food industry, scientists and consumers, to overcome the barriers to rational use of such Functional Foods. Barriers include lack of public awareness of micronutrient deficiency, no research consensus on the need for fortified products, and the ambiguity and uncertain impact of health claims. Food-based solutions to micronutrient deficiency may be achieved through the organized production, marketing, and distribution of foods by both private and public food organizations. Sometimes public resources will need to be shifted toward public-private sector partnerships to promote the fortification and biofortification of foodstuffs. A multi-sectoral group could define feasible and affordable strategies designed for the target population, identify opportunities for the involvement of the food industry, and assist in promotional and educational efforts to reach the target population. Finally, the ultimate goal of diversification of the food supply, with less dependence on staples, for both a more comprehensive and adequate intake of nutritive substances and the maintenance of biodiversity, with its own health advantages, must be kept alive (Wahlqvist & Specht, 1998). For food fortification to be an effective means to prevent and mitigate public health problems of micronutrient deficiencies, it needs to be based on sound principles and supported by clear policies and regulations (Darnton-Hill et al, 2002).

3.2 Probiotics

An example of successful Functional Foods, at least in terms of marketing, is Probiotics, products with live microorganisms. As early as 1935, long before the concept of Functional Foods was introduced, the fermented milk drink Yakult®, was launched in Japan. This product contained a lactic acid bacterium, *Lactobacillus casei Shirota* strain, which could resist gastric juice and bile, enabling it to establish itself in the bowel. It has been claimed that the consequential shift in spectrum of intestinal microflora has health advantage (Mitsuoka, 1996). These health advantages may include resistance to pathogenic microorganisms, gut and systemic immunity, as well as colonocyte nutrition from the lumen. Probiotic products present an opportunity for dairy companies to present their products as part of a healthy diet, not by removing fat but by adding health-promoting ingredients – live microorganisms (probiotics), or substrates for them like oligosaccharides (prebiotics).

However, there is still divided opinion about the general effectiveness of lactic acid bacteria in promoting human health. This could be due to a lack of coordinated efforts between clinicians and microbiologists. Differences in strains, dose, model systems, and stringency of data interpretation have led to some of the inconsistencies in conclusions. In the meantime, although research support is lacking for many claims about live bacterial culture-induced promotion of intestinal and human health, products containing such cultures are marketed successfully worldwide. Also the place of traditional fermented foods, fruits, vegetables, grains, fish – like sauerkraut and kimchi, is relatively neglected (Leitzmann, 1994).

3.3 Phytochemical-Rich Foods: What Stage are They at Now?

In recent decades, a considerable number of epidemiological studies suggest that the high consumption of “fruit and vegetables” as a collective term, or in some studies, of specific vegetables, is associated with low morbidity and mortality from CVD and certain cancers (Kant et al, 1995; Kushi et al, 1985; World Cancer Research Fund/ American Institute for Cancer Research, 1997). Compounds found in fruit and vegetables, such as polyphenols in fruit, isoflavones in the legume soy and β -carotene in vegetables, have been considered to be the responsible active compounds (Table 3). However, several intervention studies have shown that ingestion of some of these isolated compounds, in tablet or capsule form, cannot confer similar health benefits to those observed with the intact food from which they come (MacLennan et al, 1995, Omenn et al, 1996; Stevinson et al, 2000). Studies of intact foods on health outcomes, like those with whole grains on CVD and diabetes support these findings (Jacobs et al, 1998; Salmeron et al, 1997a & 1997b). This understanding should stimulate a more food ingredient and recipe approach than the isolated phytonutrient approach to Functional Foods (Table 2). It is likely to discourage chemical fortification with phytochemicals (in the way that has happened with micronutrients) in favour of biofortification with phytonutrients – a trend that will encourage plant breeding and related horticultural research.

The dichotomy between ingredient-based phytochemical-enriched foods and the administration of isolated phytochemicals is illustrated by the field of phytoestrogens and the menopause. In the late 1980s, Wahlqvist and colleagues demonstrated that certain foodstuffs (soy flour, linseed as seeds, and red clover as sprouts) could significantly improve vaginal health (an estrogenic effect) and decrease pituitary follicle stimulating hormone (FSH) production in post-menopausal women (also estrogenic effects) – the first demonstration that foods could exhibit estrogenic effects in humans (Wilcox et al, 1990). Thereafter, there have been those who have favoured food ingredient-based studies and applications, especially bone health and breast cancer protection, to women’s health (Wahlqvist & Dalais, 1997; Murkies et al, 2000; Worsley et al, 2002), and those who have pursued a more nutraceutical (pharmaceutical) approach (Hodgson et al, 1999; Howes et al, 2000). The risk-benefit ratio in each case is quite different, with more checks and balances on intake in the food ingredient (e.g. soy-linseed bread) approaches than with over-the-counter (OTC) encapsulated phytochemicals.

Table 3. Phytochemicals and their possible roles in health (Wahlqvist et al, 1998)

Phytochemicals	Some important food sources	Possible roles in health
Carotenoids	Orange pigmented and green leafy vegetables, e.g. carrots, tomatoes, spinach	Antioxidant Antimutagen Anticarcinogen Immuno-enhancement
Flavonoids, isoflavonoids and saponins	Green and yellow leafy vegetables, e.g. parsley, celery, soy bean and soy products	Antioxidant Anticarcinogen Estrogenic Immuno-modulating
Polyphenols	Cranberries, raspberries, blackberries Rosemary, oregano, thyme	Antioxidant
Catechins	Green & black tea	Antioxidant Anticarcinogen Anticariogen Protective against cardiovascular disease
Isothicyanates and indoles	Cruciferous vegetables, e.g. broccoli, cabbage	Antimutagen
Allyl thiosulfinates	Garlic, onions, leeks	Anticarcinogen Antibacterial
Limonene	Citrus fruits, caraway seeds	Anticarcinogenic against mammary tumours
Phytoosterols	Pumpkin seeds	Reduce symptoms of prostate enlargement
Curcumin	Turmeric	Anti-inflammatory
Salicylates	Grapes, dates, cherries, oranges, apricots, gherkins, mushrooms, capsicums, zucchini	Protective against macrovascular disease
Non-digestible carbohydrates	Artichoke, chicory root, maize, garlic, oats	Stimulate growth of microbial flora

It is interesting, therefore, that attempts are still being made to develop novel (and implicitly functional) foods on the basis of isolated compounds like phytosterols (plant sterols) which represent a spectrum of molecules sometimes from unfamiliar plant products (like pine bark) into food products themselves with still limited human experience (Lichtenstein, 2002), like polyunsaturated margarine available only for about 30 years, and where we are still learning about unintended consequences – for example, their *trans*-fatty acid content and atherogenesis (Anonymous, 1995). The reduction of serum low-density lipoprotein cholesterol with phytosterols in margarine will not necessarily translate into reduced coronary events, let alone reduced all-cause mortality. Another potentially problematic development with Functional Foods is the fortification of food with nutritive substances where they are not ordinarily expected to be – like calcium in fruit juice. This is happening at a time when evidence mounts that people with traditional intakes of calcium in a dominantly plant-based diet at about 400-500 mg daily (Aspray et al, 1996; Dibba et al, 2000) are not advantaged in bone health or fracture rate by more dietary calcium – it is those who have high intakes of calcium that seem to need more. This out-of-culture, out-of-context approach to Functional Foods needs much more scrutiny. This indicates the importance of the WHO/FAO Food Based Dietary Guidelines (FBDGs) approach to food and nutrition policy, including Functional Foods.

3.4 The Functional Significance of Traditional Foods

A rather more attractive example of an emerging Functional Food, from a public health point of view, is that of the various traditional *teas*, which are based on the leaves of *Camellia sinensis* – black tea, Chinese oolong tea and Japanese green tea. Increasing evidence points to their ability to protect against macrovascular disease (Zhao & Chen, 2001; Hodgson et al, 2002) and its sequelae (Mukamal et al, 2002), certain cancers (Yang et al, 2002) and osteoporosis with fracture (Hegarty et al, 2000). These teas are the second most commonly consumed beverage, after water, worldwide. They are generally consumed hot, with the attendant microbiological safety, they have an important social (and, with it, health) role, and evidence also points to their theanine content as calming for many (Juneja et al, 1999), countering some concerns about the caffeine content, whose bioavailability is generally reduced compared with coffee. The adverse effects of tea on iron bioavailability can be managed with appropriate use away from plant sources of iron, or, together with heme iron. Here, then, is a major part of the traditional human diet for most people in Europe, the Middle East, the Far East, South Asia, and South East Asia, which can be positioned as functional.

A rather different situation has emerged with breakfast cereals. At their nutritional best, it could be argued they can provide a convenient way of having relatively intact or wholegrain cereals at a particular time of the day, namely breakfast. What is happening, for many such products, is that, at once, their nutrient density is decreased through a greater content of refined carbohydrate (usually sugar), and, this is remedied by micronutrient fortification. More than that, claims to nutritional superiority over other foods may be made when they are fortified. They are increasingly positioned to supply something like a third of the day's recommended dietary intakes of essential nutrients, with the presumption that this is all one needs for breakfast (perhaps with some added milk or fruit). In this manner, to take an example, wheat, starting out as a wholegrain, becomes a vehicle for a sweet low nutritional value food item, and acts as the vehicle for de facto micronutrient "supplementation".

This is an altogether different concept to the re-discovery of tea drinking as healthful, as low consumption is found to predispose to chronic disease – this is like recognition that, in part, "chronic disease" may be a food or beverage deficiency problem. By contrast, we do not have a "breakfast cereal deficiency problem", but many do have a "wholegrain deficiency problem". Only a few breakfast cereals have managed to maintain their principal role as providers of relatively intact grains in a mixed and varied human diet.

4 Evidence-Based Nutrition

Functional Foods are attractive to those concerned with evidence-based nutrition. Their evaluation is amenable to Randomised Controlled Trials (Trichopoulos, 2000; Wahlqvist et al, 1999 & 2001). This allows their ascendancy in evidence over traditional diets whose value only can usually be studied by observational methodology in longitudinal studies. For this reason, there is a pressing need for the scope of evidence-based nutrition to be enlarged and inclusive of "modelling science", where models of the human diet can be evaluated for health outcomes and survival. When the odds-ratios for a food or nutrient intake in relation to health outcome are large, causality is likely, and therefore the need for intervention (as with possible Functional Foods) is less. Of great importance is the need to examine the health predictive power, not only of food components or of food, but also of food patterns and whole cuisines. An integral of cuisines is likely to be more predictive of health outcomes, notably survival, than are any foods or food components. Examples are the IUNS Longitudinal studies of Food Habits in Later Life (Trichopoulou et al, 1995) and the Lyon Heart Studies (de Lorgeril et al, 1999). These broader approaches of evidence-based nutrition may actually be encouraged by molecular nutrition, which identifies genetic polymorphisms and different susceptibilities to food factors (Simopoulos, 2002; Stover & Garza, 2002). Thus, advances or otherwise in evidence-based nutrition will, to some extent, influence the quest for Functional Foods.

5. How to Manage the Future of Functional Foods

In the future, plant and animal breeding, with or without genetic modification, should be able to create nutritive factor-enhanced foods with equivalence to and superior over traditional foods from various communities. As the more detailed chemistry of food unfolds, nutritionists, industrial food technologists and regulatory authorities will face new challenges, with exciting opportunities for the use of biologically active components from animals (zoochemicals), such as heme iron from muscle or caseopeptides from milk, or components from fungi (mycochemicals). These challenges include:

- (i) Recognition of favourable health outcomes, which may be attributable to composite and/or cumulative effects of phyto-, zoo- and mycochemicals.
- (ii) Risk analysis of these food components in traditional food patterns, new cuisines, new Functional Foods – the “nutritional safety” domain of food safety.
- (iii) The cost-effectiveness of food choice, which is based on a greater food component emphasis.
- (iv) The ecological impact of shifting the food supply in new directions.

In reality, these challenges are shared by many cognate disciplines, and require the participation of those who can cross the disciplinary boundaries. They present new imperatives for training and career development, for health care systems, for economic development and for sustainable food production.

5.1 Health Outcomes

The extent to which individual food components, combinations of them, foods containing them, or whole cuisines may influence human health is much greater than we had previously thought. Functional Foods may be regarded as the third generation of health foods following the interest in dietary fibre in the 1970s, and the development of “low” and “light” foods in the 1980s. Up to now, most Functional Foods have been developed with the aim of securing beneficial effects for cardiovascular disease and bowel disorders.

The conjunction of several major new technologies will inescapably bring with them new food-health relationships – biotechnology (including genetic modification, such as biofortification), information technology (including nutrition and health informatics), and nanotechnology (machinery at the molecular level and related materials science). In addition, the social role of food, the effects of food on society, the effect behaviour has on nutritional status, and the effects of food on behaviour are likely to unravel with increasing speed. There will be profound changes in the socio-behavioural sciences, as society and culture become more international, individual behaviours are fragile and disordered amidst the changes. This is an environment which could support a Functional Food market, unless there are unforeseen consequences.

5.2 Nutritional Safety

In general, food is considered to be nutritionally safe if it delivers essential nutrients (and food components) which are expected of it, in the bioavailable form. Appealing to traditional food cultures and their health relationships, documented epidemiologically as a reference point, is invaluable in identifying potential nutritional advantage and safety considerations of Functional Foods. In particular, it takes account, to some extent, of unanticipated long-term consequence of food behaviour (Wahlqvist, 1992). It may be generations before effects are seen, given the present understanding of molecular nutrition, to say nothing of environmental-population interactions. Traditional food patterns are quickening in their intrinsic tendency to change as new information about food and health comes to hand, as food cultures intersect with migration and travel, as lifestyles change in other respects, and convenience is sought. This produces not only new risks to food microbiological safety, but also nutritional safety. At the same time, as new cuisines and Novel Foods are entering the market place, there is an increasing need for a more sophisticated

knowledge of food science in the community and amongst relevant food, health, legal and educational professionals. Competent analysts of risk and benefit and good risk communicators are also required.

5.3 Cost-Effectiveness of Choice about Food Components

One of the great dilemmas about the development of Novel and Functional Foods on the basis of the new understanding of food chemistry and health, is that the cost of food generally increases. While Functional Food science is motivated, to some extent, by its potential for public health benefits, the prevalence of diet-related disease and illness, together with other health-related problems, is skewed towards people in lower socio-economic groups. Yet the benefits of Functional Food science are generally geared to those willing and able to pay for premium-price products. This, of course, must be weighed up against benefit. As Functional Foods are rolled out into the market place, manufacturers and retailers will get economic benefits from the product more than consumers. Food industry must expect an increasingly lively debate about cost-effectiveness and safety. Efforts should be made to ensure that the community benefits from it, both in public health and economic terms.

5.4 Ecological Impact of Shifting the Food Supply in New Directions

The most pressing issue in the world food supply is sustainability. As the newer appreciation of food-health relationships grows, the pressure on certain food stocks becomes untenable – this is the case especially for fish and soy. Plant food equivalents (with shorter chain n-3 fatty acids like α -linolenic acid from linseed) may have to suffice; or genetic modification of microorganisms to produce n-3 long chain polyunsaturated fatty acids (EPA and DHA) may be required. Efforts to increase soy production by genetic modification to make it tolerant to the herbicide glyphosate, have been successful, but produced major consumer resistance (Wahlqvist, 1999a).

Food trade can increase the variety of foods available to people. Sustainability through biodiversity can be encouraged by the use of the dietary guideline of food variety (Wahlqvist & Specht, 1998). There are few new directions in food science and health, which will not have ecological implications. Well-managed, high yielding clones of food species (plant, animal and microbiological) have the potential to decrease environmental pressure and enhance human health. But ethical and philosophical issues will temper these developments.

The health, safety and sustainability hierarchies of nutritive substances, food and food culture are shown in Figure 1.

6. How to Manage the Risks from Functional Foods

It is expected that the development of new Functional Foods will always bring an element of risk with it, but in the public health domain, this risk is expected to be negligible, unlike that from pharmaceuticals, where some risks are accepted for benefit on a regular patient-by-patient basis, with each usage. This distinction seems poorly understood by entrants into the Functional Foods area, who are often unfamiliar with the toxicology of drug development. Risk analysis, management and communication are therefore required, at least at a greater level of sophistication, as environments for food production and food trade increases, new food technologies emerge, and food cultures evolve.

At a taskforce meeting in 2001 on Novel Foods in Nutrition, Health and Development held by the FAO Network of Excellence at Monash University, in collaboration with WHO, an approach with the following requirements has been recommended for the development of new Functional Foods to minimize risk (Wahlqvist, 2002).

1. Consider the health outcome in question.

2. Select a plant food or foods, which confer these characteristics, preferably with an established food cultural base.
3. Formulate a food for trial.
4. Carry out a risk evaluation.
5. Conduct a food trial using biomarkers and/or health outcomes.
6. Develop an appropriate monitoring and surveillance strategy.
7. Seek regulatory approach as Novel Food for safety.
8. Formulate a food-based educational and informational framework, (consistent with WHO/FAO Food-Based Dietary Guidelines recommendations), with or without health claims (depending on regulatory regime) (World Health Organization, 1998; Wahlqvist, 1999b).
9. In all cases, consider affordability and encourage sustainability.

With new food ingredients, bioequivalence in their formulation and application should be considered. For example, one question is whether synthetic nutritive substances confer the same physiological effects as do the ones from a natural source. A lesson was learned from the Australian Polyp Prevention Project (APPP) in which β -carotene was supplemented to prevent the recurrence of colonic polyps. But increased recurrence and, therefore, increased risk for large bowel cancer, were observed with the β -carotene capsules in comparison with placebo in the course of the trial so that this intervention had to be prematurely ceased (MacLennan et al, 1995). Similarly, the Carotene and Retinol Efficacy Lung Cancer Chemoprevention Trial (CARET) was prematurely ended due to the unexpected findings that the combination of β -carotene and retinyl palmitate had a 46% increased lung cancer mortality and a 26% increased cardiovascular mortality compared with placebo (Omenn et al, 1996). It turned out while naturally occurring β -carotene was in the isomeric mixture of *cis*- and *trans*- forms, that in the capsules was only in the *trans*-form (Gaziano et al, 1995). We still do not know whether this was biologically significant; however, whether food components from newly discovered sources are actually the same as those from conventional food sources requires evaluation. For example, before using seaweeds as a source of n-3 long chain fatty acids, it should be asked whether the carbon-configuration (*cis*-, *trans*-) of the fatty acid double bonds is the same as for fish and land plant sources, such as linseed. This is a dynamic area and the prospect of better and better analytic technologies will help us identify and differentiate one isomer from another with greater precision. Likewise, monitoring and surveillance, as the science unfolds, will be a requisite of any community exposed to novel food products introduced for purported physiological or health reasons.

7. Conclusion

New understandings of food-health relationships are defining new opportunities for the development of Functional Foods for the purposes of disease prevention and control. For the ultimate successful progress of this field of Functional Foods, there must be engagement of the community through education, and commitment of government and international agencies to appropriate regulation. Governance of the present and future dramatic global shifts in food intake, at a time when health patterns are also rapidly changing, will be a great challenge.

8. Summary

- a) The world food supply is undergoing major and rapid change. Part of this phenomenon is the increased appreciation of the health benefits of an adequate, nutritious and sustainable food supply and part the commercial opportunities provided by these considerations. International agencies and governments, the civil society and the corporate sector have an interest and responsibility to ensure that the food supply, health outcomes, and economic development progress together.
- b) Functional Foods are foods produced in the market place for particular and identified physiological and health reasons and, as such, can serve health and economic goals in a measurable way, provided that their development is science-based, culturally-relevant and risk-cost-benefit effective.

- c) The evaluation of Functional Food success or detriment needs to be comprehensive, taking into account all relevant science and technology, with consumer engagement and effective regulatory capacity, and consideration of individual and public health issues, as well as profitability.
- d) There are already success stories and problematic outcomes following the introduction of certain Functional Foods. Most of the health success has come with food-based approaches using traditional food commodities, which have been repositioned for newly understood health reasons, or have been subject to fortification or biofortification. The alleviation of micronutrient deficiencies and the increased consumption of protective foods and ingredients are examples. Some traditional food technologies, like fermentation, have found a new niche in the Functional Foods arena. Much activity can be expected in the area of phytonutrient enrichment of foodstuffs that will demand a more sophisticated approach to the nutritional safety of foods, to nutritional epidemiology, and to food toxicology in general.
- e) Risk minimization strategies for Functional Foods will depend on greater investment in food-health risk analysis and communication.

Food-health relationships provide the basis for disease prevention and control using Functional Foods.

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Figure 1 Health, safety and sustainability hierarchies of nutritive substances, food and food cultures

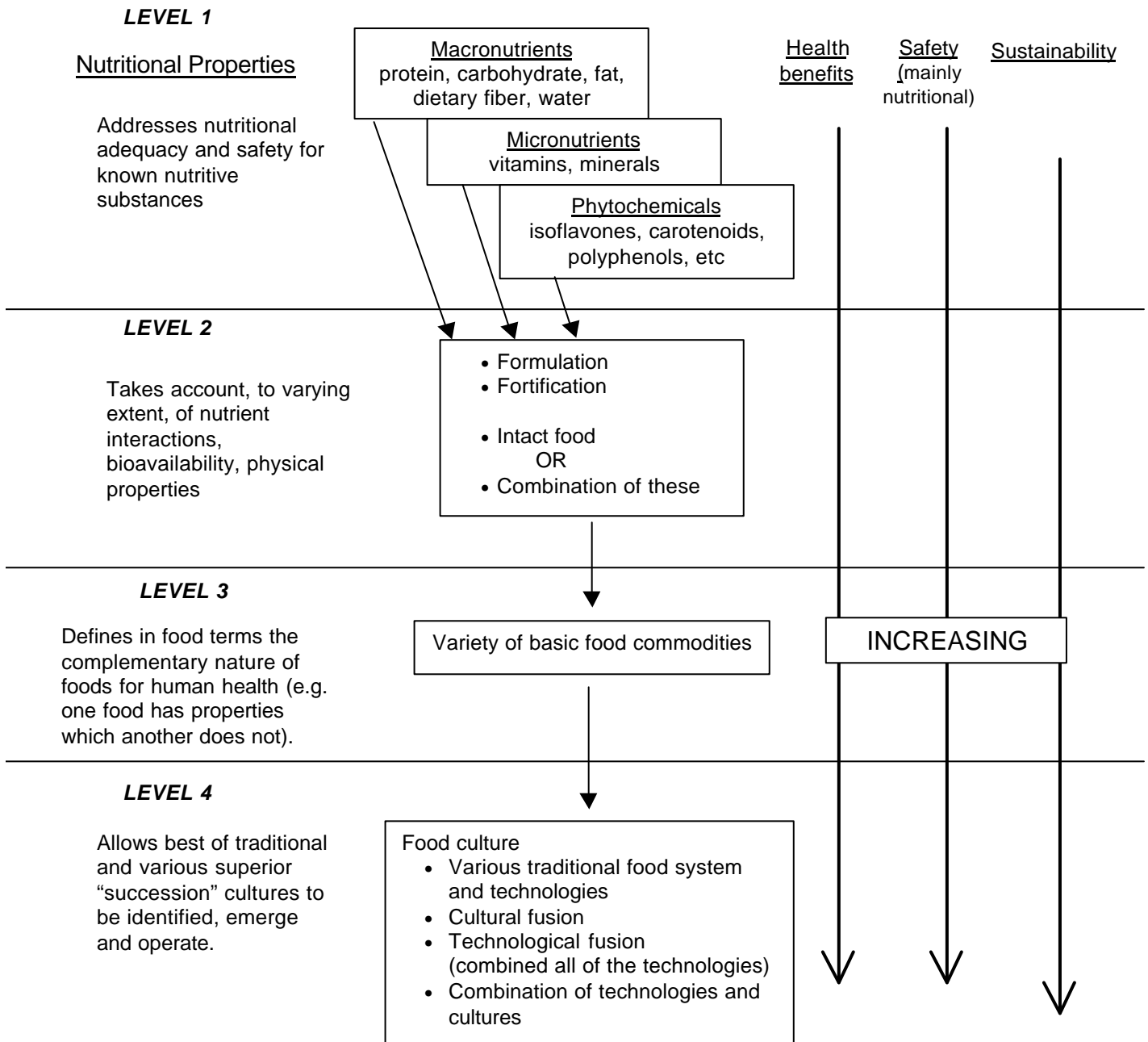


Table 2 SWOT analysis of Functional Foods

	Food		Medicinal	
	Traditional ingredients	Nutritive factor-enhanced ingredients *		Nutritive factor-enhanced recipe
STRENGTHS	<ul style="list-style-type: none"> Increasing knowledge of biological effects 	<ul style="list-style-type: none"> Consumer acceptability likely to be high Constraints of background diet still apply to a significant extent 	<ul style="list-style-type: none"> Food and culturally-based strategy 	<ul style="list-style-type: none"> High specific activity (active component per unit mass) Targets a particular health end point
WEAKNESSES	<ul style="list-style-type: none"> Discovery of chemical complexity is in the early stages Limited number of physiological effects and health outcomes of food ingredients has been identified 	<ul style="list-style-type: none"> Potential overuse 	<ul style="list-style-type: none"> Biological potential obscured by presentation 	<ul style="list-style-type: none"> Less modulation of effects by other compounds in the same chemical family Different bioavailability profile to food ingredients
OPPORTUNITIES	<ul style="list-style-type: none"> Well-established safety of traditional ingredients within established food culture 	<ul style="list-style-type: none"> Supposed enhanced biological effects 	<ul style="list-style-type: none"> Increased likelihood of use 	<ul style="list-style-type: none"> May benefit certain individuals where increased dose is needed to overcome a metabolic defect or genetic disposition (as with certain genetic polymorphisms)
THREATS	<ul style="list-style-type: none"> Distortion of the traditional ingredient mix through overemphasis of the functional ingredients 	<ul style="list-style-type: none"> Distortion of the traditional ingredient mix through overemphasis of the functional ingredients 	<ul style="list-style-type: none"> Misuse of food labelling which is not commensurate with the level of sophistication required Demand for nutrition knowledge is increased while that for food skills is diminished 	<ul style="list-style-type: none"> Unknown dose-response relationships and toxicity levels

* Includes elite cultivars (biofortified) and fortified ingredient

