

Global view on functional foods: Asian perspectives

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There is an old Chinese thought meaning that medicine and food are isogenic. In Japan, a national research project started to endorse the thought scientifically, with the birth of functional foods that are now known to function to reduce the risk of life-style related diseases. The science gave rise to a national policy in which some functional foods were legally approved in terms of Foods for Specified Health Use. China has also constructed a unique system for approving some functional foods. This paper pinpoints a recent trend of functional foods characteristic to Asia, with special reference to relevant topics in Japan.

Functional foods: Japan: Health: FOSHU

Introduction

The term 'physiologically functional food', which first appeared in *Nature* news in 1993 with the headline 'Japan explores the boundary between food and medicine' (Swinbanks & O'Brien, 1993), gave a strong international impact. Neither the terminology nor the concept of 'functional food' had existed until nine years earlier. In 1984, an *ad hoc* research group started a systematic, large-scale national project under the sponsorship of the Ministry of Education, Science and Culture (MESC) to explore the interface between food and medical sciences (Arai, 1996). It seems that the realization of this research event first in Japan reflects an underlying thought in the minds of Japanese people throughout history, which originates in the ancient Chinese saying: 'Medicine and food are isogenic'.

However, the advent of modern food science in Japan, which took place about 100 years ago, made its subsequent research proceed towards a purely nutritional rather than a medical science. Especially in the early twentieth century, the nutritive value of foods was of great academic concern. A number of scientists in the field of chemistry as well as food science made particular efforts to discover new nutrients.

More than 10 years after World War II, nutritional problems due to food shortage were almost solved in many countries and a new period characterized by high economic growth began. It prevailed in the time encompassing the 1960s, when the social climate focused on food preference and aversion. Such a trend of hedonism led to academic studies on the sensory properties of

foods. Epoch-making advances in instrumental analysis assisted the studies greatly. Japan, among many developed countries, thus contributed to two mainstays of food science: nutrition and hedonics. In accordance with this, food industries were activated to supply a great deal of nutritionally and sensorily acceptable products to the market. We enjoyed thus our rich dietary life for a long time until almost 20 years ago, when a new, antithetic situation arose.

Functional food science and policy born in Japan

In the 1980s, as the ageing society began to manifest itself in many countries of the world, prompt increases in the so-called life-style related diseases became a matter of public concern. Growing awareness was then observed of the need for eating to beat the odds. The purpose was to prevent life-style related diseases such as diabetes, arteriosclerosis, osteoporosis, allergies, cancer, and even some kinds of infectious diseases, through improved dietary practices in daily life. This gave a strong impetus to food science in Japan. In 1984, the above-mentioned MESC project entitled Systematic Analysis and Development of Food Function commenced, where the terminology and the concept of 'functional food' were first proposed. It was followed by a second project (1988–1991) entitled Analysis of Body-modulating Functions of Foods. In 1992, the last in the series of MESC 'functional foods' projects was realized, focusing on Analysis and Molecular Design of Functional Foods. A total of 60 academic professionals participated, most from medical as well as food science fields.

In this project, several interesting results were obtained. In particular, research into novel phytochemicals elucidated the occurrence of new anticarcinogens, e.g. fuosterols in seaweed and auraptenes in citrus fruits. The discovery and characterization of potent antioxidants of plant origin, e.g. curcuminoids in ginger, were also reported. Another unique example was offered by oryzacystatin, a cysteine proteinase inhibitor found in the rice, *Oryza sativa* L., which was molecularly cloned (Abe *et al.* 1987) and demonstrated to inhibit the proliferation of human herpes virus in infected animal cells (Aoki *et al.* 1995). These studies were aimed at finding factors with body-defending rather than body-modulating functions.

For body modulation, food allergies and countermeasures were studied extensively. The background was that rice-associated allergy in the form of atopic dermatitis was increasing continually in Japan, a major rice-consuming country, and countermeasures were needed urgently. In response to such a social need, an experiment was undertaken to design and produce hypoallergenic rice grains by enzymatic hydrolysis of main allergenic proteins occurring in the globulin fraction. The development of well-controlled conditions for the hydrolysis gave an immunologically and clinically satisfactory product (Watanabe *et al.* 1990) and the production process was industrialized to manufacture it. 'Fine Rice' was approved as the first Food for Specified Health Use (FOSHU) product (described below) after careful intervention tests in many medical centres. These basic and applied studies were followed by the discovery and characterization of soyabean and wheat allergens to develop hypoallergenic soyabean and flour products (Tanabe *et al.* 1996).

The orthodox way of producing functional foods is to maximize beneficially functional factors that are responsible for modulation of the immune, endocrine, nerve, circulatory or digestive system in the body. Sometimes, however, a unique approach can be adopted. Uniqueness is found in minimizing non-beneficial functional factors by enzyme technology or even genetic engineering. The importance of using this concept for the design and production of functional foods has been emphasized since 1984 when the first project began.

The Japan Ministry of Health and Welfare in 1991 initiated the world's first policy of legally permitting the commercialization of selected functional foods in terms of FOSHU, as mentioned above. The new policy is defined by new legislation and also characterized by approving the presentation of a health claim for each FOSHU product. Such legal framework is also expected to hinder the presentation of ill-defined and misleading advertisements in commercial products. Thus, since 1993, some selected food products have been approved to claim a certain degree of medical representation never before permitted for any food. The first was hypoallergenic rice grains ('Fine Rice' by commercial name) developed after extensive immunological studies in the MESC project, produced by enzyme technology and industrialized after clinical intervention tests (Watanabe *et al.* 1990). A great many FOSHU products have been approved up to now (Table 1).

Glance at Asian functional foods

Asian food processing is characterized by fermentation. This is reflected in the production of functional foods as well. Actually, FOSHU items (Table 1) include fermented milk, which originates in Caucasus and is produced industrially for particular purposes. A good example is offered by a FOSHU product in which reasonable amounts of the lacto-tripeptides Val-Pro-Pro and Ile-Pro-Pro, angiotensin-converting enzyme inhibitors, have been derived from β -casein by lactic acid bacteria. Another interesting example is provided by fermented soyabean, *natto* by Japanese name, which has long been consumed in some Asian districts as well as in Japan. Very recently, a mutant of *Bacillus natto* was developed that can produce a high quantity of menaquinone-7 (vitamin K₂) as a cofactor of γ -glutamic acid carboxylase for biosynthesis of the Ca-carrying protein, osteocalcin. The *natto* produced using this mutant is thus expected to reduce the risk of osteoporosis and was approved as a FOSHU product. Also, rice whose wild species *per se* can be found in a district near Tibet is often used as a material for fermentation. In Japan, it was found that a rice bran extract treated with a mixed *Lactobacillus-Saccharomyces* culture produces a large amount of γ -aminobutyric acid as a functional food factor for reducing the risk of neural disorders as well as hypertension, although the product remains to be approved.

In China as well, the functional food policy has made a good progress. Chinese functional foods are legally approved, with the logo, in sky blue colour, issued by the Ministry of Public Health. The functions to be considered include twenty-four items as follows (Yi *et al.* 1999):

1. immune regulation,
2. postponement of senility,
3. memory improvement,
4. promotion of growth and development,
5. anti-fatigue,
6. body weight reduction,
7. oxygen deficit tolerance,
8. radiation protection,
9. anti-mutation,
10. anti-tumour,
11. blood lipid regulation,
12. improvement of sexual potency,
13. blood glucose regulation,
14. gastrointestinal function improvement,
15. sleep improvement,
16. improvement of nutritional anaemia,
17. protection of liver from chemical damage,
18. lactation improvement,
19. improvement for beauty,
20. vision improvement,
21. promotion of lead removal,
22. removal of 'intense heat' from the throat and moistening of the throat,
23. blood pressure regulation and
24. enhancement of bone calcification.

For some categories among these, a variety of foods are considered to be approved (Table 2). These foods are also

Table 1. Data on 252 foods for specified health uses

Health claim*	Functional factor	Number of products approved†	Forms of products on the market
I	Prebiotics	61	
	Lactosucrose	22	Soft drink, yoghurt, biscuit, cookie, table sugar
	Fructo-oligosaccharides	15	Table sugar, tablet candy, pudding, soyabean curd
	Soyabean oligosaccharides	9	Soft drink, table sugar
	Xylo-oligosaccharides	5	Soft drink, vinegar, chocolate, tablet candy
	Galacto-oligosaccharides	4	Table sugar, vinegar
	Isomalto-oligosaccharides	3	Table sugar
	Raffinose	1	Powdered soup
	Lactulose	1	Soft drink
	Arabinose	1	Table sugar
	Probiotics	49	
	<i>Lactobacillus casei</i> Shirota	26	Lactic acid bacterium drink
	<i>Lactobacillus delbrueckii</i> and <i>Streptococcus salivarius</i>	6	Fermented milk
	<i>Bifidobacterium lactis</i>	4	Yoghurt
	<i>Bifidobacterium breve</i> Yakult	4	Fermented milk
	<i>Lactobacillus rhamnosus</i> GG	2	Fermented milk
	<i>Bifidobacterium longum</i>	4	Fermented milk
	<i>Lactobacillus acidophilus</i> and <i>B. longum</i>	3	Fermented milk
	Dietary fibres	58	
	Indigestible (resistant) dextrin	28	Sausage, cookie, drink, miso soup, curd
	Psyllium husks	21	Powdered drink, noodle, cereal
	Wheat bran	2	Cereal
	Galactomannan	1	Jelly
	Partially hydrolysed guar gum	3	Powdered drink, boiled rice
	Agar	2	Noodle, jelly
	Beer yeast	1	Fermented milk
	II	Soya protein and peptide	17
	Low-molecular-weight sodium alginate	7	Soft drink, soup
	Chitosan	3	Biscuit
	Sitosterol ester	1	Margarine
III	Peptides	20	
	Sardine peptides (containing VY)	9	Soft drink, soup
	Lacto-tripeptides (VPP and IPP)	5	Lactic acid bacterium drink
	Dried bonito oligopeptides (containing IKP)	2	Fermented soyabean soup
	Casein dodecapeptides (FFVAPEPEVFGK)	4	Soft drink
	Eucommia leaf glycoside (geniposidic acid)	2	Soft drink
IV	Diacylglycerol	5	Cooking oil
	Diacylglycerol and sitosterol	4	Cooking oil
V	Casein phosphopeptide	7	Soft drink, chewing gum, soyabean curd
	Calcium citrate malate	3	Soft drink
	Heme	4	Soft drink, jelly
	Menaquinone-7 producing <i>Bacillus subtilis</i>	2	Fermented soyabean (<i>natto</i>)
	Soya isoflavone	1	Tea drink
VI	Manitol, palatinose and tea polyphenols	3	Chocolate, chewing gum
	Manitol	2	Candy
	Xylitol	1	Chewing gum
VII	Wheat albumin	2	Powdered soup
	Globin digest	1	Soft drink
	Guava polyphenols	1	Soft drink

* Claim I, foods that improve gastrointestinal conditions; Claim II, foods for those with high serum cholesterol; Claim III, foods for those with high blood pressure; Claim IV, foods for those with high serum triacylglycerol; Claim V, foods related to mineral absorption and transport; Claim VI, non-cariogenic foods; Claim VII, foods for those who begin to feel concerned about their blood sugar level.

† As of 29 May 2001.

used as medicines. Thus, distinguishing between foods and traditional medicines is not an easy task. The difficulty apparently reflects the Chinese tradition that medicine and food share a common origin.

Some food factors may be studied for purely medical rather than food use. In an extensive screening study covering common vegetables and fruits in south-east Asian countries, anti-tumour promoting potential, detected

by the inhibitory rate of tumour promoter-induced Epstein-Barr virus activation, was generally higher in the plants from tropical zones than in those from Japan. Moreover, plants in the families Zingiberaceae, Rutaceae, Labiatae and Cruciferae, which are used as traditional medicines, were shown to contain potent anti-tumour promoters at high rates (Arai *et al.* 2001). For functional food scientists, Asia may thus be like a treasure house.

Table 2. Representative Chinese functional foods for body modulation in specified categories (Yi *et al.* 1999)

Immune regulation
American ginseng (<i>Panax quinquefolius</i>)
Ginseng (<i>Panax ginseng</i>)
Acanthopanax (<i>Acanthopanax senticosus</i>)
Barbary wolfberry fruit (<i>Lycium barbarum</i>)
Astragalus (<i>Astragalus membranaceus</i> , <i>A. membranaceus</i> var. <i>mongholicus</i>)
Chinese caterpillar fungus (<i>Cordyceps sinensis</i>)
Ginkgo leaf (<i>Ginkgo biloba</i>)
Walnut (<i>Juglans regia</i>)
Chinese date (<i>Ziziphus jujuba</i>)
Royal jelly
Chinese angelica (<i>Angelica sinensis</i>)
Glossy ganoderma (<i>Ganoderma applanatum</i>)
Postponement of senility
Roxburgh rose (<i>Rosa roxburghii</i>)
Green tea (<i>Camellia sinensis</i>)
Fleeceflower root (<i>Polygonum multiflorum</i>)
Black sesame (<i>Sesamum indicum</i>)
Honey
Mulberry fruit (<i>Morus alba</i>)
Barbary wolfberry fruit (<i>L. barbarum</i>)
Blood lipid regulation
Hawthorn fruit (<i>Crataegus pinnatifida</i>)
Soyabean (<i>Glycine max</i>)
Peach seed (<i>Prunus persica</i>)
Chrysanthemum flower (<i>Chrysanthemum morifolium</i>)
Super vinegar
Spine date seed (<i>Z. jujuba</i> var. <i>spinosa</i>)
Fish oil
Corn oil (<i>Zea mays</i>)
Extract of flax seed (<i>Linum usitatissimum</i>)
Safflower seed (<i>Carthamus tinctorius</i>)
Blood and urine glucose reduction
Fiveleaf gynostemma (<i>Gynostemma pentaphyllum</i>)
Hawthorn fruit (<i>C. pinnatifida</i>)
Chinese yam (<i>Dioscorea opposita</i>)
Buckweat poria (<i>Fagopyrum esculentum</i>)
Cocos poria (<i>Poria cocos</i>)
Extract of pumpkin (<i>Cucurbita moschata</i>)
Extract of pig pancreas
Powder of spirulina (<i>Spirulina princeps</i>)

International view on functional food science and policy

Meanwhile, the implementation of the Ministry of Health and Welfare's FOSHU policy as well as the initiation of functional food science in Japan had a strong impact on many countries of the world, particularly in Europe. Early in 1995, the UK Ministry of Agriculture, Fisheries and Food defined, though temporarily, functional foods as those that had components incorporated to give specific medical or physiological benefits, other than nutritional effects (Richardson, 1996).

Deeper interest was paid by the European body of the International Life Sciences Institute (ILSI Europe). ILSI Europe addressed the present status by claiming that we stand today at the threshold of a new frontier in nutritional science, and also stating that the concept of food is changing from a past emphasis on eating to get rid of hunger into a current emphasis on promising uses of foods to reduce the risk of chronic illness (Bellisle *et al.* 1998). This

new concept is of extreme importance in view of the demands of the elderly population for improved quality of their late life, increases in life expectancy and costs for health care, and technical advances in the food industry.

As recognized in the Japan MESC research project, up-to-date knowledge in the biosciences, including biochemistry and molecular biology together with sophisticated biotechnologies based on these, supports the hypothesis that foods can modulate various functions in the body and thus participate in the maintenance of a state of health that reduces the risk of life-style related diseases. Such a hypothesis exists at the origin of the concept of 'functional food' for the development of a new discipline, 'functional food science', in Europe as well as in Japan.

What may be most important at present is to evaluate the function. Since any functional food must be based on science, its evaluation should essentially depend on data from biochemistry, physiology, molecular and cell biology, and other most modern biosciences. A key approach to the development of a functional food is the identification and validation of relevant markers, including biomarkers that can predict potential benefits relating to a target function in the body. If the markers represent an event directly involved in the process, these should be considered as functional factors. On the other hand, if the markers represent correlated events, they should be considered as indicators. In detail, possible markers have been tentatively listed in relation to target functions (Diplock *et al.* 1999).

There are many options for selecting appropriate markers. A promising option may be the use of accumulated knowledge about genomics. As the human genome project has been completed (Venter *et al.* 2001), the so-called post-genomics, involving the use of genomics data, will follow, which may not be unrelated to functional food science. A number of sophisticated biotechnologies will become available, one of the most useful being DNA chip technology (Marton *et al.* 1998). It is helpful because of its high throughput potency to assess the possible effects and safety of functional food factors by total gene expression profiles.

Current genome programmes are proceeding on food organisms as well. These include rice, wheat, corn, soya-bean, and other major plant seeds for food use. A variety of post-genomics sciences, to be born shortly before and after the completion of the genomics, will lead to the development of new biosciences such as nutrigenomics. The development will support advances in proteomics, providing key information about the molecular design of functional food proteins. It will thus be possible to easily define their specific functional regions involved in the prevention of such life-style related diseases as diabetes, hypertension, hypercholesterolaemia, allergies, cancer and even infectious diseases. Among a number of trials, proteomics for the design of antiviral proteins may serve as an example. One such study involves a three-dimensional NMR analysis of solution structures of oryzacystatin, an anti-herpes protein of rice origin described above (Abe *et al.* 1987; Aoki *et al.* 1995). The analysis

provides information about the minimal effective region (Nagata *et al.* 2000), the use of which will contribute to molecular breeding of new rice cultivated with an antiviral function.

It is also noted that an *ad hoc* team headed by the present author (S.A.) has begun to make a database of functional foods under the sponsorship of the Japan MESC.

Finally, it is stressed that Asian people have always recognized the importance of sensory properties of foods. They still think that every food must be sensorily acceptable. Even functional foods cannot be ruled out. The science should include studies on the senses of taste and smell. The significance of this is emphasized since such sensations have been found to be related more or less to functions of the endocrine and exocrine systems, as well as to those of the digestive system. An interesting example can be found in red pepper, whose unique irritative component, capsaicin, has a 'hot' flavour in seasoning. This substance, shortly after entering the body per os, interacts with vanilloid receptors such as Ca channels in sensory neurons inducing a specific dynamic action, possibly with an anti-obesity result. Capsaicin can thus be regarded as a functional factor with such a bilateral effect. Sensory abnormalities and disorders are other targets of functional food science, because insights into syndromes of these kinds will supply patients with organoleptically acceptable tailor-made foods having body-modulating functions at the same time.

The design and development of functional foods should not be carried out independently of purely nutritional and sensory or cognitive properties of foods. Future advances in relevant sciences for giving rise to foods with integral attributes would distinguish functional foods from medicines. Research along this line will add a newer dimension to functional food science and will also be academically and socially understood as having great potential for the development of new food science, technology and industry in the early twenty-first century.

The reader is advised to consult recently published papers to learn more about the state-of-the-art concerning functional foods (Arai *et al.* 2001; Kwak & Jukes, 2001). The former paper is the proceedings of a symposium, A Mainstay of Functional Food Science in Japan — History, Present Status, and Future Outlook, which was organized by the Japan Branch of the International Union of Food Science and Technology in collaboration with ILSI Japan.

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