

FUNCTIONAL FOODS IN ASIA

Current Status and Issues



ASEAN * Australasia & Pacific

INTERNATIONAL LIFE SCIENCES INSTITUTE
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MONOGRAPH SERIES

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CONTENTS

| | | |
|-----|---|----|
| 1. | INTRODUCTION | 5 |
| 2. | GLOBAL STATUS OF FUNCTIONAL FOODS | 7 |
| 2.1 | Definition and Regulatory Status | 7 |
| 2.2 | Consumer Perceptions of Functional Foods in the United States | 10 |
| 3. | FUNCTIONAL CLAIMS AND SCIENTIFIC SUBSTANTIATION | 12 |
| 3.1 | Codex's Draft Recommendations | 12 |
| 3.2 | Europe | 15 |
| 3.3 | The United States | 18 |
| 4. | STATUS OF FUNCTIONAL FOODS IN ASIA | 22 |
| 4.1 | Definition and Regulatory Status | 22 |
| 4.2 | The Market for Functional Foods | 25 |
| 4.3 | Consumer Perceptions of Functional Foods in Japan and China | 26 |
| 4.4 | Systems for Regulatory Vetting and Approval | 28 |
| 4.5 | Functional Foods in Traditional Asian Culture | 30 |
| 4.6 | Asian Position on Functional Foods | 30 |
| | ANNEX – Functional Foods in Traditional Asian Culture | 33 |
| 1. | Mushrooms | 33 |
| 2. | Tea | 35 |
| 3. | Hawthorn Fruit and Its Extracts | 38 |
| 4. | Chinese Wolfberry (Fructus lycii) | 40 |
| | REFERENCES | 42 |
| | AUTHOR AND CONTRIBUTORS | 47 |

1. INTRODUCTION

Foods are traditionally recognized as providing essential nutrients for nourishing the human body. With the increase in diet-related chronic diseases, even in developing countries, there has been increased interest in the relationship between diet and diseases. In recent years, a great deal of attention has been given to components other than nutrients that are found in foods. Much interest has been generated on the potential health significance of these components. Foods containing such components have been termed “functional foods”.

The term “functional foods” may have gained prominence only in recent years, but in Asia, foods with functional properties have been regarded as an integral part of some cultures for centuries. Among the Japanese and Chinese, for instance, it is believed that foods and medicine are of equal importance in preventing and treating diseases; that foods and medicine originate from the same source, are based on the same basic theories and have the same uses (Weng and Chen, 1996; Arai, 2002). It is also believed that the functionality of functional foods are found in whole foods rather than in their individual components. Japan may be the first country to have officially defined functional foods although the term itself is not used in its regulatory system. Instead, a system called “foods for specified health use”, or FOSHU, was introduced in 1991 under the Nutrition Improvement Law, which made it possible to make limited health claims on specific food items.

Subsequently, there has been a marked increase in research and development activities on functional foods, regulatory discussions as well as the trade and marketing of functional foods. There has been much scientific debate and discussions through numerous seminars and conferences. In 1995, ILSI Southeast Asia Region (ILSI SEAR) organized the First International Symposium on East-West Perspectives on Functional Foods in Singapore (Clydesdale and Chan, 1996). This also spurred a series of ILSI-sponsored meetings, research and publications in Europe, USA, Australia, Japan, China and Singapore. ILSI Europe organized a major international symposium in 2001 to deliberate on various aspects, including the European, Asian, Latin American and United States perspectives of functional foods (Verschuren, 2002).

To date, there is as yet no unanimously accepted global definition of functional foods, although several definitions have been proposed. A generally accepted understanding is that functional foods are foods that, by virtue of physiologically active food components, provide health benefits beyond basic nutrition. However, the term “functional foods” is currently not used in any of the relevant regulations.

Recognizing the need for a more coordinated approach to the global development of functional foods, the Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Regional Coordinating Committee for Asia first commenced discussions on the inclusion of functional foods in the Codex Alimentarius system (Codex) during its 13th session in Kuala Lumpur in September 2002. The Coordinating Committee recommended that FAO and WHO organize an expert consultation to discuss various aspects of functional foods. A regional consultation in Asia on the subject, to be facilitated by the FAO, is scheduled for late 2004.

In recognition of the continued interest in functional foods in Asia, ILSI SEAR continues to play an active role in stimulating and coordinating research and development of functional foods in the region. Such activities include coordinating the development of a position paper on functional foods, published as this monograph, which serves to summarize the global status on functional foods, especially with regards to the situation in Asia.

This monograph begins with an introduction to the global regulatory status of functional foods, followed by a summary of recent activities in scientific substantiation of functional and health claims among various countries and international organizations. A summary of the Asian position on functional foods is set out next, and topics discussed include the results of an extensive survey of the status of functional foods conducted in 11 countries and regions in Asia, the regulatory systems implemented in certain Asian countries, the market for functional foods and consumer perceptions of functional foods in some of these countries. This monograph also sets out the consensus on various aspects of functional foods that were agreed upon by participants in the 1st Asia Region Workshop on Functional Foods held on October 22 – 23, 2003 in Kuala Lumpur, Malaysia. The Annex to this monograph provides summaries of the functional properties of certain functional foods which have been used in Asian culture for centuries, and the studies conducted on their physiological and functional properties.

2. GLOBAL STATUS OF FUNCTIONAL FOODS

2.1 Definition and Regulatory Status

2.1.1 *ILSI's Survey on Attributes of Functional Foods*

In 2003, the International Life Sciences Institute (ILSI) conducted a survey among all its branches and entities to obtain a general sense of the attributes associated with the concept of functional foods across the globe. Responses were received from the following ILSI branches: Southeast Asia Region, Europe, Japan, North Andean, Mexico, Brazil, Korea and North America.

There was general agreement that functional foods contain nutrients and/or non-nutrients that confer physiological or health benefits over and above basic nutritional properties. It was also generally agreed that these functional benefits should be scientifically proven and that these foods should have been proven to be safe over long-term usage.

There was, however, no general agreement on whether the term “functional foods” should pertain only to conventional foods. ILSI SEAR and ILSI Brazil felt that it should be, whereas ILSI Mexico, ILSI Korea and ILSI North America were of the opinion that it should not be. Similarly, on whether the term can be used for food components (as against whole foods), ILSI SEAR and ILSI Brazil felt that it should not. It was felt that the food components would be the nutrients and/or non-nutrients conferring the functional properties and would best be referred to as “functional food components”. There was another suggestion from ILSI North Andean that they should be called “functional ingredients”. ILSI Japan, ILSI Mexico, ILSI Korea and ILSI North America, however, felt that the term can also be used for food components.

Except for ILSI North America, there was general agreement amongst all respondents that the term “functional foods” cannot be used for dietary supplements. ILSI SEAR felt that if a food component is extracted from food and presented in pharmaceutical dosage form, it is a “nutraceutical” and may be regulated as a drug. There was also general agreement that fortified foods can also be termed as “functional foods”, provided that the fortification is to augment a constituent normally present in the food to confer a property beyond its natural nutritional attribute.

A discussion of the relevant regulatory systems in Europe, North America and Latin America is set out in the following paragraphs. Please refer to Chapter 4 of this monograph for a discussion on the regulatory systems in relation to functional foods in Asia.

2.1.2 *Regulatory Status in Europe*

European scientists and experts in nutrition and related sciences have been actively working on the

concept of functional foods over the last decade. Coordinated by ILSI Europe, the European Commission Concerted Action on Functional Food Science in Europe (FUFOSE) reached a consensus on "Scientific Concepts of Functional Foods in Europe" in 1999 (Ashwell, 2002). The three main steps taken to achieve the consensus were:

- * A critical assessment of the science base required to provide evidence of the specific nutrients and food components which positively affect target functions (biological responses) in the body.
- * An examination of the available science from a function-driven rather than a product-driven perspective.
- * An elaboration of a consensus on targeted modification of food and food constituents and on options for the applications.

Since functional foods is a concept rather than a well-defined group of food products, the FUFOSE Consensus Document proposed a working definition, the main points of which included:

- * Food nature of functional food: it is not a pill, a capsule, or any form of dietary supplement.
- * Demonstration of the effects to the satisfaction of the scientific community.
- * Beneficial effects on body functions, beyond adequate nutritional effects, that are relevant to improved state of health and well-being and/or reduction of risk (not prevention) of disease.
- * Consumption as part of a normal food consumption pattern.

It is also emphasized that a functional food may not necessarily induce a health benefit in all members of the population.

From a practical point of view, a functional food can therefore be:

- * A natural food in which one of the components has been naturally enhanced through special growing conditions.
- * A food to which a component has been added to provide benefits (e.g. the addition of selected probiotic bacteria with proven health benefit characteristics to improve gut health).
- * A food from which a component has been removed so that the food has less adverse health effects (e.g. the reduction of saturated fatty acids (SFA)).
- * A food in which the nature of one or more components has been chemically modified to improve health (e.g. the hydrolysed protein in infant formulas to reduce the likelihood of allergenicity).
- * A food in which the bioavailability of one or more components has been increased to provide greater absorption of a beneficial component.
- * Any combination of the preceding possibilities.

2.1.3 Regulatory Status in North America

There is continued widespread interest in functional foods in North America among scientists, legislators and consumers. The United States' Federal Food, Drug, and Cosmetic Act (FFDCA) does not provide a statutory definition of functional foods. Thus, the Food and Drug Administration (FDA) has no authority to establish a formal regulatory system for such foods. The primary determinant of the regulatory status of these foods is thus their intended use. The distinction

between a food and a drug has been blurred because of recent scientific findings suggesting that the former may have some medicinal properties (Milner, 2002).

In Canada, the recognition of the health effects of various food components has sparked legislative interest in functional foods. Foods containing the beneficial ingredients, whether naturally occurring or as a result of the addition of an isolated component, are termed “functional foods”. The proposed Health Canada definition of a functional food is as follows: “similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions”.

The term “functional foods” has arisen from a general belief in the health benefits of certain foods. Although, as mentioned above, it has no legal meaning, it signifies a proactive appreciation that some foods may confer health benefits (Milner, 2000). While the term “functional foods” has been defined in several ways, ILSI North America defines it as: “Foods, that by virtue of physiologically active food components, provide health benefits beyond basic nutrition” (Milner 2002).

A large amount of literature has accumulated, indicating that numerous foods may be associated with health promotion and disease prevention. The diversity of these foods suggests that a variety of bioactive components may be involved. It has been estimated that about 25,000 different chemical compounds occur in fruits, vegetables and other plants eaten by man. Some of those compounds that have received much attention and which show potential to influence a variety of cellular processes that would be expected to influence health include carotenoids, dithiolthiones, flavonoids, glucosinolates, isothiocyanates, allyl sulfhydryls and fermentable fibres (Milner, 2002).

2.1.4 Regulatory Status in Latin America

In Latin America and the Caribbean, regulations concerning functional foods, functional supplements and functional and health claims differ from country to country. There is no official or legal definition of functional foods, or specific regulations for functional foods/ingredients. In general, basic nutrient content/functional claims are allowed and subject to some norms, but only a few countries allow or have norms for such health claims. Nonetheless, health authorities have allowed product claims on a case-by-case basis in several countries (Lajolo, 2002).

Brazil is the only country to have well-defined regulations for functional and health claims for either nutrient or non-nutrient components and also for the demonstration of safety efficacy. In almost all Latin American countries, functional or health claims associated with non-nutrient compounds or non-essential nutrients are neither prohibited nor regulated. As a consequence, except for Brazil, there is also a lack of criteria for scientific substantiation of claims. In popular markets and supermarkets all over Latin America, hundreds of foods and drugs with curative allegations are sold.

In Brazil, despite the absence of a legal definition, the norms in relation to functional foods were based on the idea of a food (not being a drug) that is part of a normal diet and that can produce benefits beyond basic nutrition. Legislation requires demonstration of the safety and efficacy of novel foods and foods/ingredients that have a claim on the label. All of these products should be

registered and approved by health authorities.

Latin American consumers are, in general, unfamiliar with functional foods, although there is an increasing number of health-conscious consumers in the more urbanized areas who are aware of the importance of diet for health and well-being. In the last two years, a number of new foods that may be considered as functional foods due to functional or health properties acknowledged by health authorities, have appeared on the market in some countries. These include a wide variety of foods such as spreads and milk containing phytosterols; milk containing long chain polyunsaturated fatty acids; milk and products with added oligofructose; margarine and yoghurt with fibre; cookies engineered to have low glycemic index; milk fermented with selected *Lactobacillus* and *Bifidobacterium* strains; products containing soybean proteins and isoflavones, low-cholesterol eggs; and energy and isotonic drinks containing caffeine and other herbal extracts. A number of products in pharmaceutical forms are also included, eg fibre-containing products, anti-oxidants and oils containing freeze-dried vegetable/fruit extracts.

2.1.5 *Codex Alimentarius*

The topic of functional foods was first formally discussed during the 47th Session of the Executive Committee of the Codex Alimentarius Commission in 2001 when the Asian region proposed to commence work in the area of novel foods (other than from biotechnology), functional foods, and foods that were also considered to be at the food/drug interface.

In response to the above, the delegation from Malaysia introduced a discussion paper on the subject during the 13th Session of the FAO/WHO Regional Coordinating Committee For Asia Meeting held in Kuala Lumpur, Malaysia in September 2002 (FAO/WHO, 2003a). The first part of the paper considered the need to define the scope and concept of functional foods, to establish a classification system and criteria, conditions for making health claims, and the evaluation of the safety of functional foods including methods of analysis. The second part of the document referred to the need for a clear definition of novel foods (other than from biotechnology), guidance including product information, safety assessment etc. In order to provide guidance on these issues, the Malaysian delegation recommended the convening of a Joint FAO/WHO Expert Consultation on functional foods and novel foods to examine the need for an international standard to provide better regulatory control of these foods, with the objective of benefiting the global industry and the consumers.

There was general support for the recommendations and the Coordinating Committee proposed that FAO and WHO hold an Expert Consultation on functional foods with the inclusion of Asian experts. The Committee noted that there was an urgent need to initiate work on functional foods in the near future.

2.2 Consumer Perceptions of Functional Foods in the United States

The International Food Information Council (IFIC) has been researching the awareness of and

perceptions about functional foods for several years (IFIC, 1999). IFIC conducted a series of focus groups with consumers in June 1996 and with physicians and dietitians in 1997. Participants in both sets of focus groups strongly believed people have a great deal of control over their health, and nutrition and diet are key factors in asserting that control. Consumer participants were willing to learn more about functional foods and wanted to incorporate these foods in their diet. Physician and dietitian participants also accepted the concept of functional foods. However, they lagged behind consumers in their willingness to act on that knowledge – specifically to recommend that their patients eat more of these foods based solely on their functional benefits. They agreed, however, that there is a need for more scientific substantiation of the health benefit claims of functional foods.

In 1998, a survey commissioned by IFIC was conducted through telephone interviews with a sample of 1,000 randomly selected consumers nationwide. It was found that a staggering 95% of consumers believed that certain foods provide health-promoting or disease-fighting benefits beyond basic nutrition. Further, 91% of consumers are interested in learning more about functional foods.

IFIC's 1999 qualitative research reveals how different consumer segments respond to potential benefits of functional foods. A series of focus groups among two different segments of the population provided insight into the differences in how niche consumers assimilate and act on nutrition and health information. The goals of the focus groups were to understand the importance of scientific substantiation behind food purchases and to determine the most influential information sources for niche consumers. It was found that even the unmotivated consumers would be open to consuming functional food components if added to foods they already eat and like. Information plays a strong role in shaping consumers' attitudes and behaviors. Scientific or medical testimony that supports long-held beliefs about foods will most effectively motivate consumers to purchase and consume functional foods.

It has been estimated that about 60% of adults residing in the United States are believed to select foods for health purposes, regardless of their age or gender. While younger individuals may select foods for mental and physical performance, older individuals appear to be selecting foods for their potential merits in reducing disease risk or improving the quality of life (Milner, 2002).

Regardless of the claims that are allowed, consumers are eager to learn more substantiated information about food, food components and health. To assist in clarifying the issue, ILSI North America's Technical Committee on Food Components for Health Promotion developed, in 1997, a Road Map as a strategy to "Improve the Health of the Public through Consumer Acceptance of Safe Food Products that Provide Significant Health Benefits". A number of approaches were identified to accomplish this goal, including: the creation of a comprehensive science base, the promotion of public trust, the development of consumer-preferred functional foods, the optimization of a regulatory framework and the creation of market place incentives to develop functional foods.

3. FUNCTIONAL CLAIMS AND SCIENTIFIC SUBSTANTIATION

As mentioned earlier, the generally accepted understanding is that functional foods are foods that, by virtue of physiologically active food components, provide health benefits beyond basic nutrition. Such benefits should of course be made known to consumers. Several regulatory agencies have permitted claims to be made on foods. Under the Codex system, three general categories of nutrition and health claims are being discussed, namely nutrient function, enhanced function and disease risk reduction claims. In terms of the marketing of functional foods, manufacturers would most likely want to communicate the enhanced function and disease risk reduction claims of their products to consumers. Such claims should be scientifically valid and not misleading.

The following paragraphs summarize recent activities on scientific substantiation of functional health claims in the United States, Europe and among international organizations. A discussion on similar activities in Asia is set out in Chapter 4 of this monograph.

3.1 Codex's Draft Recommendations

3.1.1 *Guidelines on Health Claims*

The current Codex General Guidelines on Claims developed after several years of review were recently revised (FAO/WHO, 2001). The document contains prescribed guidelines for nutrition labeling and claims. Health claims are not included in the document. Indeed, the guidelines prohibit claims as to the suitability of a food for use in the prevention, alleviation, treatment or cure of a disease, disorder, or particular physiological condition unless otherwise provided for.

Several years ago, the Codex Committee for Food Labeling (CCFL) began deliberations on the issue of health claims. In June 2003, a draft document on health claims was presented to the Commission for adoption. It was, however, returned to the CCFL for further discussions at the Committee level.

The recommendations contained in the draft are intended for use by governments to facilitate the evaluation of health claims used by the industry. These recommendations could also be used as reference by the industry to prepare the evidentiary dossier required to support the claims. Only the nature and the quality of the scientific evidence alleged to support these claims are taken into consideration. The guidelines are not intended for the evaluation of the safety and the quality of the products, for which other provisions are relevant. Nevertheless, definite requirements on safety and quality matters must be met.

According to the draft definitions currently being considered by CCFL (FAO/WHO, 2003b), a health claim refers to any representation that states, suggests, or implies that a relationship exists between

a food or a constituent of that food and health. Health claims include the following:

Nutrient Function Claims - a nutrition claim that describes the physiological role of the nutrient in the growth, development and normal functions of the body.

Example: "Nutrient A (naming a physiological role of nutrient A in the body in the maintenance of health and promotion of normal growth and development). Food X is a source of/high in nutrient A."

Other Function Claims - These claims were previously termed Enhanced Function Claims in the Codex draft. These claims concern specific beneficial effects of the consumption of foods and their constituents in the context of the total diet on normal functions or biological activities of the body. Such claims relate to a positive contribution to health or to the improvement of a function or to modifying or preserving health.

Examples: "Substance A (naming the effect of substance A on improving or modifying a physiological function or biological activity associated with health). Food Y contains x grams of substance A."

Reduction of disease risk claims - Claims relating the consumption of a food or food constituent, in the context of the total diet, to the reduced risk of developing a disease or health-related condition.

Risk reduction means significantly altering a major risk factor(s) for a disease or health-related condition. Diseases have multiple risk factors and altering one of these risk factors may or may not have a beneficial effect. The presentation of risk reduction claims must ensure, for example, by use of appropriate language and reference to other risk factors, that consumers do not interpret them as prevention claims.

Examples: "A healthful diet low in nutrient or substance A may reduce the risk of disease B. Food Z is low in nutrient or substance A."

"A healthful diet rich in nutrient or substance A may reduce the risk of disease B. Food Z is high in nutrient or substance A."

It should be noted that nutrition claims (i.e. nutrient content claims, comparative claims and nutrient function claims) are now grouped together with other function claims and disease risk reduction claims as "health claims". Several delegations to the CCFL meeting have objected to this re-grouping.

3.1.2 *Draft Recommendations on the Scientific Basis of Health Claims*

The above captioned draft recommendations was discussed by the Codex Committee on Nutrition and Foods for Special Dietary Uses in its 25th session in Germany in 2003 at Step 3 of the Procedure. Several main points of the document are highlighted below.

General requirements

A high level of quality of the scientific justification for the claimed effects is obligatory for using any

health claim. It seems evident that the level of scientific justification must be sufficient to support the claimed effect but that the substantiation requirements may differ depending on whether the health claim is for disease risk reduction or enhanced function.

The scientific evidence includes studies results, either already published in scientific literature, or conducted by the applicant in order to substantiate the alleged claim. In both cases, the studies used shall be consistent with generally accepted scientific procedures and principles.

Nature of the scientific evidence on the claimed effect

Any claim linking the consumption of the food, the substance or the ingredient and the enhancement of a function, the maintenance or the improvement of a state related to health or the reduction of a disease risk shall be supported by scientific evidence along one or several of the following approaches:

- * experimental in vitro and/or in vivo studies; and
- * epidemiological or clinical studies on humans; clinical interventional studies should comply with the requirements established by ethical committees and should substantiate the change in a relevant indicator.

A relevant indicator is a well-defined biological, physiological, clinical or epidemiological indicator which is modulated by the ingestion of the food or the food ingredient and for which there exists a general agreement among the qualified international scientific community on the relation between the modulation of this indicator and the state of health of the population in which it is measured. The biochemical and physiological mechanisms explaining the beneficial effect on health are either elucidated or explicable with a sufficient degree of certainty in the current state of knowledge. The magnitude of the variation of this indicator, determined under the effect of ingestion of the product or ingredient, must present (in addition to the statistical significance) a biological, physiological, clinical or epidemiological significance recognized by the scientific community.

Generally, the evidence shall be provided by studies on humans, and, if a sub-population is specifically targeted, on this group (including the higher consumers of the product). When the claim relates to the enhancement of a function, studies on humans may be limited if animal experimental models or in vitro are relevant or sufficiently close to human metabolism. Experiments on animals or in vitro studies shall often be required to precisely explain the mechanisms involved.

In addition, the trials shall be conducted on a large enough population over a sufficient period of time with appropriate dosage in the context of the usual diet of the target population.

The amount of the substance or the ingredient added to the food shall be determined according to the following criteria:

- * Toxicological evaluation: the added amount shall not expose the consumer to health risks.
- * Consumption surveys documenting adverse effects: cumulative intake risks in a situation where the same substance is present in several foods. Simulations to assess the potential risks of excessive consumption may be conducted by the appropriate methods.
- * The amount necessary to produce the alleged effect.

Statistical analysis of the data must be conducted with methods accepted for such studies by the scientific community, such as controlled studies, reference groups, statistical analysis.

Relevance of the evidence at population level

It shall be required to check that the benefit documented by experimental studies is still present at the level of the target population (general population or sub-group), preferably by simulations based on consumption data.

Evaluation of the scientific proofs used to justify a claim

The evidentiary dossier required to support the claims must be evaluated scientifically by a group of qualified experts.

The evaluation of scientific evidence shall be consistent with the principles of risk analysis. Specifically, such evaluation shall take all the available scientific data into account and conform with current norms of scientific methodology.

Periodic re-evaluation

Health claims shall be re-evaluated periodically. With this aim in view, the following shall be carried out:

- * Fundamental studies or clinical studies shall be conducted to increase knowledge on the health benefits of the food, the substance or the ingredient.
- * Monitoring of consumption of products bearing health claims in order to evaluate the real levels of consumption and ensure that the pattern of consumption, as documented, is appropriate to provide the expected benefit, specifically for the population group targeted by the claims.
- * Investigation of the expected effects and, if appropriate, the adverse effects which may appear after long-term consumption of the products.

Other considerations

Nutritional safety should be taken into account during the evaluation of health claims. The evaluation should also address any risks arising from behavioral changes in consumers, triggered by consumption of the product. The population, or the sub-population targeted by the product, shall be identified. The selection of the target population shall be consistent with the effects alleged by the claim. Where appropriate, various issues can be considered: for instance, consumption by populations outside the target group, excessive consumption, shifts in nutritional balance due to increased consumption of some foods and the replacement of others, short-term adverse effects, allergies and the introduction of new risky behaviors.

In both cases, expected or foreseeable adverse effects on vulnerable population groups (including infants, young children and pregnant women) shall be considered.

3.2 Europe

In the 1990s, ILSI Europe developed a functional food project that was submitted as a European Commission (EC) Concerted Action. This Concerted Action, known as Functional Food Science in

Europe (FUFOSE) was started in 1995. Over a period of 3 years, around 100 European experts in nutrition and medicine critically assessed the status of functional foods. They reviewed scientific literature on foods and food components and their capacity to modulate body functions.

Substantiation of a health claim should be based on a systematic review of the evidence relevant to the claim. The scientific evidence required to substantiate a health claim is likely to be drawn from three general types of studies, ranked according to the preferred hierarchy of their value in substantiating a health claim (Ashwell, 2002; Richardson et al, 2003):

- * Experimental human trials (sometimes referred to as clinical or intervention studies)
 - Randomized controlled intervention studies; and
 - Less-controlled types of intervention studies.
- * Observational human studies (sometimes referred to as epidemiological studies):
 - Case-control studies
 - Cohort (longitudinal) studies
 - Cross-sectional studies
 - Cohort studies
 - Time-series studies
 - Ecological or cross-population studies
 - Descriptive epidemiology
 - Case reports
 - Case-control studies
- * Animal studies and in vitro studies

In general, claims should be substantiated using studies from the top of the hierarchy. However, care should be taken in using this hierarchy of evidence, because validity depends not only on the type of study but also on how well it was designed, carried out and analyzed.

Markers can be biochemical (e.g., a change in an enzyme) or physiological (e.g. a change in the function of a body organ) in nature. They may be based on an objective assessment of body functions, such as physiological and physical performance or a subjective assessment of quality of life. In many cases, a consistent response of a convergent battery of markers may provide more definitive evidence of functional and health benefits, because it evaluates different aspects of the same function, and thus better targets the function and its modulation.

The main types of markers include:

- * Markers of exposure: those which evaluate biological accessibility such as digestibility, fermentability, absorption and /or tissue distribution.
- * Markers of target functions and biological responses: such as changes in body fluids or tissues, levels of a metabolite, a protein or an enzyme, or markers that relate to a change in a given function such as muscular strength, maximal oxygen consumption, cognition or gut transit.
- * Markers of intermediate endpoints of an improved state of health and well-being and/or reduction of a disease risk: such as the measurement of a biological process that relates directly to the endpoint (eg measurement of haemoglobin levels for anemia or measurement of vessel wall thickness for cardiovascular disease).

Evidence from human studies, based on markers relating to biological response or on intermediate endpoint markers of disease, could provide a sound scientific basis for messages and claims about functional food products. Two types of claims are proposed that relate directly to these two categories of markers: Enhanced function claims (type A) and reduced risk of disease claims (type B). A new European Union (EU) Concerted Action is underway with, and building upon, the principles defined within FULOSE.

The project, Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM) aims to (Asp and Contor, 2003):

- * Produce a generic tool with principles for assessing the scientific support for health-related claims for foods and food components which are edible or potable.
- * Select common criteria for how markers should be identified, validated and used in well-designed studies to explore the links between diet and health.
- * Evaluate critically the existing schemes which assess the scientific substantiation of claims.

The expected applications are as follows (Asp and Contor, 2003):

- * PASSCLAIM will offer a practical scientific framework to prepare scientific dossiers supporting health claims. This framework will ensure that all claims have a firm scientific basis. The European food manufacturing industry, including small and medium enterprises, will benefit from the competitive edge that the scientific framework will provide.
- * PASSCLAIM will enable the compilation of guidelines to prepare submissions for claims on foods. This will expedite and improve the efficiency of the regulatory review processes.
- * Consumers will benefit from an improved approach to the scientific support for claims on foods. This integrated strategy will generate greater consumer confidence in the scientific basis related to claims on foods and will better address the concerns of consumers.

In order to meet the project objectives, a European network was set up involving academic experts in different aspects of the physiological functions relating to health claims, representatives of public interest groups, regulatory experts and the food industry. The focus was on diet-related cardiovascular disease; bone health and osteoporosis; physical performance and fitness; body weight regulation, insulin sensitivity and diabetes risk; diet-related cancer; and mental state and performance. A draft set of interim criteria (set out in the paragraph below) that can be used as a basis for the scientific substantiation of health claims have been developed and reviewed in two Plenary Meetings involving around 100 scientists.

Revised interim criteria for the scientific substantiation of health claims on foods and food components (Cummings et al, 2003):

1. Foods and food components for which claims are made should comply with existing legislation.
2. Health claims should be scientifically substantiated by taking into account the totality of evidence. A scientifically substantiated mechanism is valuable but not essential.
3. When a claim is made, it should be specified who may benefit from the effect, e.g. the entire population, a subgroup or an at-risk group.
4. Claims should be based primarily on human intervention studies that show demonstrable effects consistent with the claim. They should have a scientifically valid design compatible with the purpose of the study, including the following:

- * Study groups that are representative of the target group.
 - * Controls both for the intervention itself, and for the subject groups.
 - * An appropriate duration to demonstrate the intended effect.
 - * Characterization of the target groups' background diets, which should be controlled where necessary.
 - * The amount of the food or food components being evaluated should be consistent with its intended use and the expected consumption pattern.
 - * Ideally an exposure–response relationship should be determined to identify optimum effective intake.
 - * Dietary compliance should be monitored.
 - * The statistical power to test the hypothesis.
5. If the claimed enhancement of function or reduction of risk cannot be measured, studies should use markers of effects that have been scientifically validated.
 6. Markers should be validated methodologically to include their precision and accuracy; specificity and sensitivity; and reproducibility and repeatability. Markers should also be validated biologically so that they reflect closely the process leading to the claimed health benefit and respond quickly in line with changing events.
 7. Within a study, the marker should change in a biologically relevant way and be statistically significant for the target group consistent with the claims to be supported.

3.3 The United States

From the early 1980s, food companies began using health claims as a marketing strategy. One of the first health claims was that made by a cereal company which advised consumers of the National Cancer Institute's statement that a healthy lifestyle and "eating the right foods may reduce your risk of some kinds of cancer". A FDA survey indicated that high-fiber cereal sales increased by 37% as a result of this claim. In 1987, in response to new scientific data on the relationship between diet and disease, the FDA proposed changes to its policy in order to permit health messages on labels. However, it soon withdrew the proposed changes due to widespread "misuse" of health claims by manufacturers.

In 1990, the FDA came up with a narrow definition of the term "health claims" and clarified the criteria that must be met to make such claims. The US Congress adopted the Nutrition Labeling and Education Act in that same year to regulate health claims on foods. The legislation required the FDA to evaluate 10 diet and disease relationships:

- * Calcium and Osteoporosis
- * Sodium and Hypertension
- * Lipids and Coronary Heart Disease
- * Lipids and Cancer
- * Dietary Fiber and Coronary Heart Disease
- * Dietary Fiber and Cancer
- * Folic Acid and Neural Tube Defect
- * Anti-oxidant Vitamins and Cancer

- * Zinc and Immunity
- * Omega-3 Fatty Acid and Coronary Heart Disease

Four types of claims were allowed, namely:

1. Health Claims
2. Qualified Health Claims
3. Structure Function Claims
4. Nutrient Content Claims

3.3.1. Health Claims

Health claims describe a relationship between a food, food component, or dietary supplement ingredient, and reducing risk of a disease or health-related condition. The claims may be directed at the general public or designated subgroups (e.g. women). The FDA oversees health claims through three main legislations:

- * 1990 Nutrition Labeling and Education Act (NLEA)
- * 1997 Food and Drug Administration Modernization Act (FDAMA)
- * 2003 FDA Consumer Health Information for Better Nutrition Initiative

The FDA provides guidance to the industry (eg through its website: www.fda.gov) on evaluating the scientific data required to substantiate the claims made. There should be significant scientific agreement on the review of health claims for conventional foods and dietary supplements. Significant scientific agreement means that the validity of the relationship is not likely to be reversed by new and evolving science, although the exact nature of the relationship may need to be refined. The totality of the publicly available evidence should support the substance/disease relationship that is the subject of the claim. There should also be significant scientific agreement among qualified experts that the relationship is valid.

The types of studies required for scientific substantiation are listed below in decreasing order of usefulness to support the claim:

- * Intervention Study (randomized clinical trials)
- * Observational Study
- * Cohort (longitudinal) Studies
- * Case-Control Studies
- * Cross-Sectional Studies
- * Uncontrolled Case Series or Cohort Studies
- * Time-Series Studies
- * Ecological or Cross-Population Studies
- * Descriptive Epidemiology
- * Case Reports

It may not always be possible to conduct intervention studies for all the health claims submitted for approval. For the omega-3 fatty acid and coronary heart disease (CHD) claim, 86% of them were substantiated by intervention or experimental studies. Similarly, for the dietary fibre and CHD claim, all the 38 studies carried out were intervention studies. On the other hand, all the studies for

the substantiation of the fat and cancer relationship were observational type studies.

The studies submitted are reviewed by a group of government scientists, including those from the FDA, National Institutes of Health (NIH), National Academy of Sciences (NAS), Food and Nutrition Board (FNB), Surgeon General's office, etc. Special interest groups have largely been kept away from reviewing health claims due to potential bias.

The health claims authorized by the FDA are as follows:

1. Calcium and Osteoporosis
2. Sodium and Hypertension
3. Dietary Fat and Cancer
4. Dietary SFA and Cholesterol and Coronary Heart Disease
5. Fiber-containing Grain Products, Fruits and Vegetables and Cancer
6. Fruits, Vegetables and Grain Products that Contain Fiber, Particularly Soluble Fiber, and Risk of Coronary Heart Disease
7. Fruits and Vegetables and Cancer
8. Folic Acid and Neural Tube Defects
9. Dietary Sugar Alcohol and Dental Caries
10. Soluble Fiber and Certain Foods and Risk of Coronary Heart Disease
11. Soy Protein and Risk of Coronary Heart Disease
12. Plant Sterol/Stanol Esters and Risk of Coronary Heart Disease

An example of a health claim is: "25 grams of soy protein a day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease".

Under the Food and Drug Administration Modernization Act (FDAMA), health claims in the form of an authoritative statement may be published by NAS, NIH, Centre for Disease Control (CDC), Surgeon General, Food and Nutrition Service, etc. after notification to the FDA. Examples of such health claims are: (a) Whole Grain Foods and Risk of Heart Disease and Certain Cancers; (b) Potassium and the Risk of High Blood Pressure and Stroke.

3.3.2 Qualified Health Claims

These claims describe a relationship between a food, food component, or dietary supplement ingredient, and reducing risk of a disease or health-related condition. A qualifying statement or a disclaimer must be included. The current proposal includes a "grade" for the scientific support (see table below):

| Scientific ranking | FDA category | Appropriate qualifying language |
|--------------------|--------------|--|
| Second level | B | "though there is scientific evidence supporting the claim, the evidence is not conclusive" |
| Third level | C | "some scientific evidence suggests However, FDA has determined that this evidence is limited and not conclusive" |
| Fourth level | D | "very limited and preliminary scientific research suggests FDA concludes that there is little scientific evidence supporting this claim" |

From *Guidance for Industry and FDA: Interim Evidence-based Ranking System for Scientific Data*. www.FDA.gov

An example of a qualified health claim is: "Selenium may reduce the risk of certain cancers. Some evidence suggests that consumption of selenium may reduce the risk of certain forms of cancer. However, FDA has determined that this evidence is limited and not conclusive".

3.3.3. Structure Function Claims

Structure function claims are statements that describe the role of a nutrient or dietary ingredient intended to affect normal structure or function in humans.

Examples of these claims are: (a) Calcium builds strong bones; (b) Helps maintain cholesterol levels that are already within normal range. The Codex Guidelines on Claims have similar claims and they are termed nutrient function claims (FAO/WHO, 2001).

3.3.4 Nutrient Content Claims

The claims characterize levels of nutrients (eg fat, cholesterol, sodium, calories, etc), namely: free, low, high, reduced. These are similar to the nutrient content claims as permitted under the Codex Guidelines on Claims (FAO/WHO, 2001).

4. STATUS OF FUNCTIONAL FOODS IN ASIA

4.1 Definition and Regulatory Status

4.1.1 *ILSI SEAR's Survey on Functional Foods*

In 2002, a survey on functional foods was conducted by ILSI SEAR among 11 Asian countries and regions (China, Indonesia, Japan, Malaysia, Myanmar, the Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam). Under this survey, the term "functional foods" is defined as: "foods that possess physiological or health benefits beyond basic nutritional functions". A questionnaire was circulated to regulatory agencies in all the Southeast Asian and selected Asian countries and regions. In addition, publications and seminar papers by various Asian scientists and authorities on the topic were obtained to provide additional information (Tee, 2003).

Findings of the survey showed that there was no consensus among the respondents on the definition or usage of the term "functional foods". Only Japan, China and Taiwan have regulatory systems that regulate foods falling wholly or partially within the scope of the survey's definition of functional foods. In South Korea and the Philippines, the term "functional foods" was used to include dietary supplements in pharmaceutical dosage forms.

In the remaining countries (Indonesia, Malaysia, Myanmar, Singapore, Thailand and Vietnam), the findings showed that there were no regulations on functional foods. Although these Asian countries recognize functional foods as an important area that requires further development and regulation, none have enacted specific regulations for such foods. In some countries, there are existing regulations pertaining only to dietary supplements in pharmaceutical dosage forms.

4.1.2 *Functional Foods and Health-promoting Foods*

The two main functions of food have conventionally been recognized as providing nutrients (primary function) and sensory functions such as tastes, flavors etc (secondary function). A third or tertiary function of food was thought to be those pertaining to regulating physical conditions such as functions of bio-regulation, disease prevention, recovery from disease, regulation of biorhythm and control of aging. Foods possessing these third functions were defined as functional foods. Intensive research was carried out and it was shown that many food ingredients have this third function. As a result, a system called "foods for specified health use" or FOSHU, was introduced in 1991 under the Nutrition Improvement Law. Japan may have been the first country in the world to have defined the concept of "functional foods" although the term itself is not used as it was already used in the definition of "drug" in the Pharmaceutical Affairs Law. FOSHU was one of the five categories of "Foods for Special Dietary Uses" created under this law and was defined as "foods in the case of which specified effects contributing to maintain health can be expected based on the available data concerning the relationship between the foods/food's contents and health, as well as foods with permitted labeling which indicates the consumer can expect certain health effects upon intake of these particular foods". The other 4 categories were

medical foods for the ill, milk powder for pregnant or lactating women, formulated milk powder for infants and foods for the aged with difficulty in masticating or swallowing.

In China, the term “functional foods” is also not used. Instead, the term “health foods” is used and is defined as “food that has special health functions, suitable for consumption by special groups of people and has the function of regulating human body functions, but is not used for therapeutic purposes”. The regulation for the Control of Health Food was issued by China’s Ministry of Health in November 1996.

The Health Food Control Act was enacted by Taiwan in 1999. Under this legislation, the term “health food” is used and is taken to mean foods with specific nutrient or specific health care effects as specially labeled or advertised, but do not refer to foods aimed at treating or remedying human diseases.

4.1.3 Functional Foods and Dietary Supplements in Pharmaceutical Dosage Forms

In some Asian countries, the term “functional foods” was used to include dietary supplements in pharmaceutical dosage forms. In South Korea, the Health Functional Food (HFF) Act was enacted in August 2002. HFF refers to “processed and manufactured goods in the form of tablet, powder, granule, liquid and pills that help enhance and preserve health of human body using nutritional or functional ingredients”. This legislation is similar to the Dietary Supplement and Health Education Act of the United States. Although the term “functional foods” is used in the HFF, it is not within the definition used in ILSI SEAR’s survey.

The FOSHU system in Japan was re-organized in line with the introduction of a new system of “Foods with Health Claims” in April 2001. This new system comprised foods categorized within the existing FoSHU system and a new category of foods with nutrient function claims. It was also proposed that the restriction of food forms under the FOSHU system be removed so that products in tablet and capsule forms can be included in the new system.

The Bureau of Food and Drugs in the Philippines has defined functional foods as “any finished, labeled, processed product that contains herbs/plant materials, marine/animal sources, amino acids, vitamins and minerals, and other substances, single or combined, which is not intended or marketed as a conventional food. It may come in different forms such as liquid, powder, granules, tablet for specific health use that is backed by scientific and relevant studies but is not intended to treat or cure any disease/condition”.

According to the Indonesian National Agency for Drug and Food Control (NADFC), there are currently no regulations on functional foods in the country, although the NADFC is in the process of formulating relevant regulations. It is anticipated that the proposed regulation may likely define functional foods as: “natural and processed foods which contain one or more ingredients which, based on empirical or scientific evidence, qualify for having physiological functions beneficial to health”.

There are also no specific regulations on functional foods in Myanmar. However, a system similar to the FOSHU system in Japan was reported to be in place. Products have to be subjected to review by an approval system prior to being permitted to go on sale. No details of the system are available. However,

it is doubtful if the system does indeed regulate functional foods as defined in ILSI SEAR's survey.

4.1.4 Specific Regulations for Dietary Supplements

In Malaysia, Singapore, Thailand and Vietnam, there are no specific regulations pertaining to functional foods or health-promoting foods, and there are no indications that such regulations will soon be introduced in these countries. These countries, however, have regulations pertaining to dietary supplements.

In Malaysia, the term "functional foods" is not used in the regulatory system and there is no official definition of the term. Food products are regulated under the Malaysian Food Regulations 1985. A new regulation on nutrition labeling and claims for foods was gazetted on March 31, 2003.

There are separate regulations in Malaysia for dietary supplements which come under the purview of the Drug Control Authority (DCA), with the National Pharmaceutical Control Bureau serving as its secretariat. Dietary supplements have been defined as "products intended to supplement the diet, taken orally in forms such as pills, capsules, tablets, liquids or powders and not represented as conventional foods". Each of these products must be registered with the DCA. The review process prior to registration includes safety evaluation, manufacturing process and checks on the permitted claims. Advertisements for dietary supplements are also required to be approved by the Medicines Advertisement Board.

In recent years, there has been an increase in the number of food products that contain extracts of various botanical or animal components. In many cases, these products are not clearly marketed as "foods" or "drugs". It has been difficult to determine which authority, either the Food Quality Control Division or the DCA, should regulate the marketing and sale of such food-drug interface products. To solve this problem, a Committee for the Classification of Food-Drug Interface Products was formed in 2000.

In Singapore, there is currently no legal or official definition of the term "functional foods". In general, food and supplements of a food nature, such as royal jelly, bee pollen, botanical (fruit, cereal or plant-based) beverages, protein and carbohydrate-based powdered beverages, come under the purview of the Agri-Food and Veterinary Authority. The import and sale of these products in Singapore are governed by the Sale of Food Act and the Food Regulations. Importers of these products are required to ensure that the food products they intend to import comply with the requirements of the Food Regulations, including labeling requirements. On the other hand, dietary supplements such as vitamins, minerals, amino acids, essential fatty acids, phospholipids and preparations for medicinal or pharmaceutical purposes come under the purview of the Centre of Pharmaceutical Administration of the Health Sciences Authority.

Dietary supplements are defined in Thailand as "products which are directly consumed other than normal staple food and are often in the form of tablets, capsules, powder, liquid or other forms and are intended for general persons in good health". The Food and Drugs Administration Thailand regulates these products under the regulations for Foods for Special Dietary Uses.

4.2 The Market for Functional Foods

As Japan, China and Taiwan were found to have implemented regulatory systems which regulate foods falling wholly or partially within the scope of “functional foods” as defined in the survey conducted by ILSI SEAR, findings pertaining to the market for functional foods in these countries are extracted and set out below.

4.2.1 *The FOSHU System in Japan*

Under Japan’s FOSHU system of Japan, only products in conventional food forms were approved prior to April 2001. At that date, a total of 252 items were approved. Claims for seven categories of products were allowed, namely foods:

- a. which promote an increase in the intestinal microflora and helps to maintain a healthy intestinal environment;
- b. which benefit people with a high cholesterol level;
- c. for mineral (calcium or iron) supplementation, with high absorbability;
- d. of low cariogenicity;
- e. beneficial for people with mild hypertension;
- f. beneficial for people who are concerned with high blood glucose; and
- g. beneficial for people who are concerned about their blood triglyceride level.

Functional components must be identified on the label and include:

- * oligosaccharides, lactobacillus, fibre
- * soy protein, chitosan
- * glycoside from eucommia leaves
- * calcium citrate malate (CCM), casein phospho-peptide (CCP)
- * palatinose, maltitol, green tea polyphenols
- * indigestible dextrin
- * diacylglycerol

Subsequent to April 2001, however, the FOSHU system was amended to include products in pharmaceutical dosage forms.

With this change, there were also changes to the permitted claims for FoSHU products. Reduction of disease risk claims were not permitted. Further, claims should not include diagnosis, treatment or prevention of diseases as stated in the Pharmaceutical Affairs Law and shall be limited to the following:

- a. Maintenance and improvement of indices of physical conditions which can be easily evaluated (indices evaluated by healthy persons and those evaluated during medical checkups), eg “helps you maintain normal blood sugar levels”, or “promotes decomposition of body fat”.
- b. Maintenance of good physical condition and/or organ function or its improvement eg “regulates bowel movement”, or “improves absorption of calcium”.
- c. Improvement of subjective and temporary, but not persistent or chronic, changes in physical condition, eg “helpful for those who feel physically fatigued”.

As at September 30, 2002, a total of 309 FOSHU products have been approved. A major proportion (57%) of these foods are products that contain oligosaccharides, lactobacillus, bifidobacterium and dietary fibre and are supposed to help maintain good gastro-intestinal condition. Another 16% of the products contain protein, peptides, dietary fibre and diacylglycerol, plant sterol or stanol esters and are said to be "good for those who have high serum cholesterol and triglyceride".

The total health foods market in Japan for 2001 was estimated to be US\$112 billion. FOSHU products accounted for 29%, 4% comprised foods for special dietary uses, and 7% comprised foods with nutrient function claims. A mixture "other health foods" accounted for the bulk, 60%, of the market. The estimated share of functional foods in the Japanese health foods market in 2001 was therefore US\$32.8 billion.

4.2.2 Health-promoting Foods in China

As at March 2002, a total of 3,357 products have been approved by China's Ministry of Health. However, it was estimated that only 30% of these products are currently in the market. A large proportion (about 45%) of these products were in conventional food forms or powdered beverage whilst another 46% were in the form of capsules or pills. Hence, only about half of the products may fall within the scope of functional foods as defined in ILSI SEAR's survey.

Slightly over a third of these products claimed to regulate the body's immune system. Another 18% claimed to be anti-fatigue and another similar percentage claimed to regulate hyperlipidemia. The 10 most common health functions or claims in China are as follows:

- * Regulate immune system
- * Anti-fatigue
- * Regulate hyperlipidemia
- * Delay aging
- * Improve hypoxia tolerance
- * Inhibit tumor development
- * Improve gastro-intestinal function
- * Regulate blood glucose
- * Improve memory
- * Improve sleep process

Health-promoting foods in China are not permitted to make the following claims:

- * Prevention or treatment of disease.
- * Recovery of youthful vigour, prolongation of life, anti-cancer or cancer-curing.
- * Secret traditional prescription, nourishing food, food for improvement of health and beauty, and food used in imperial palace.

4.3 Consumer Perceptions of Functional Foods in Japan and China

4.3.1 Japan

Three surveys are summarised below to highlight the consumer recognition or perception of FoSHU products in Japan. The findings suggest that recognition of FOSHU products by the Japanese public is still relatively low.

A survey of the public recognition or perception of FoSHU was conducted in April 1999 in the Tokyo metro area by Dentsu Inc (n=630) (Japan Health Food & Nutrition Food Association, 2000). An average of 25.1% of the survey's target population were aware of FoSHU products. Among this target population, 34.4 % were females in their 20's, while 29.6% were females in their 30's and 40's. It was also reported that 44.4 % of the respondents who indicated health consciousness in their lifestyle was aware of FOSHU products.

A third of the respondents (33.5%) recognized FOSHU products through product labels, while another 24.7% learnt of FOSHU products through advertisements in newspapers. Another 19% and 15.2% were exposed to these products through advertisements in TVCFs and magazines respectively.

In December 2001, a survey (n=501 households) of the public perception/recognition of FOSHU products carried out in the Tokyo metro area by Healthy Japan Council (2001), found that a higher proportion (38%) of respondents who were housewives recognized the FOSHU mark, whilst less than a quarter (21.5%) of the male respondents could identify the logo. Amongst the housewives, half of them did not recognize the FOSHU mark whilst another 43.1% had just been exposed to the mark. Only a small proportion (6.8%) had been aware of the logo for a long time.

The majority (69.5%) of the respondents recognized FOSHU products through the labels while a much smaller proportion (6.3%) were exposed to FoSHU products through advertisements in newspapers. Only 11.2% of the male subjects reported that they had consumed FOSHU products, whilst more than double that percentage (27.6%) of the female respondents had consumed FOSHU products.

The third survey was conducted in 2003 by the Agricultural Promotion Foundation Japan on the consumption of fermented milk products amongst 1,000 households. It was found that less than a quarter of the respondents (22.8%) purchased fermented milk products because they were FOSHU products. A high proportion (81.4%) of the respondents reported purchasing fermented milk products due to the belief that such products are good for health. About half (53.2%) of the households replied that they consumed such products because they were delicious. A small proportion reported consuming fermented milk products due to their low calorie-count and low sugar content, whilst 18.7% purchased the products due to favorable prices. The survey also revealed that a much higher proportion (22.7%) of the respondents who recognized the FOSHU mark were in their 60's whilst only 6.7% of the respondents were in their 20's.

4.3.2 China

Generally, interest among the Chinese for health-promoting foods was low based on the findings of a recent survey conducted to assess the public interest in health-promoting foods in China (Anon, 2001). It was found that only 6% of respondents were very interested in health-promoting foods, 15% replied that they were interested, 58% said they were not interested while 21% claimed

they were not very interested in health foods. This survey also showed that prior to purchasing health-promoting foods, 73% of respondents would first try out these foods, while 56% would consult experts and another 38% would consult family members and friends.

With regards to the reasons for not purchasing health-promoting foods, it was found in a survey conducted across 8 provinces of China that 40% of the respondents replied that high cost was the main reason, while another 45% said that they did not have enough symptoms to warrant the purchase of such foods. The remaining 15% of the respondents replied that they simply did not believe in the proclaimed functions of health-promoting foods.

The same survey also revealed that most consumers (71%) decided on particular brands of health-promoting foods prior to shopping, and only 3% of consumers claimed that they were not particular about the brand of health-promoting foods they purchased.

4.4 Systems for Regulatory Vetting and Approval

Based on the survey of functional foods conducted in 2002 by ILSI SEAR (Tee, 2003), it was found that only Japan, China and Taiwan have pre-marketing approval systems for categories of food products which are similar to “functional foods” as defined in the survey. In the other countries where functional foods generally refer to dietary supplements, the appropriate pre-marketing approval system would be that which covers products in pharmaceutical dosage forms.

4.4.1 FOSHU System of Japan

Under the FOSHU system of Japan, each application has to be vetted on a case-by-case basis by a pre-marketing approval system set up by the Ministry of Health, Labour and Welfare (MHLW). The criteria stipulated by the MHLW are:

- a. The food should be expected to contribute to the improvement of one’s diet and the maintenance/enhancement of health;
- b. The health benefits of the food or its constituents should have a clear medical nutritional basis;
- c. Based on medical and nutritional knowledge, appropriate amounts of daily intake should be defined for the food or its constituents;
- d. Judged from experience, the food or its constituents should be safe for consumption;
- e. The constituents of the food should be well-defined in terms of physico-chemical properties and qualitative/quantitative analytic determination;
- f. There should be no significant loss of nutritive constituents of this food in comparison with the same ones normally present in similar types of foods;
- g. The food should be of a form normally consumed in daily dietary patterns, rather than consumed only occasionally;
- h. The product may be in the form of a whole food, or in the form of pills or powder; and
- i. The food and its constituents should not be those exclusively used as a medicine.

Within the MHLW, the Foods for Special Dietary Use Assessment Investigation Committee investigates

each product submitted for approval. The contents of the sample products are analyzed at the National Institute of Health and Nutrition. Approved products may carry a prescribed logo of the system and an approved statement indicating the specified health benefit.

Considering the re-organization of the health claim system in Japan, new applications for FOSHU should be received by the Planning Section, Food and Health Department, Medical Bureau of the Ministry of Health, Labour and Welfare and examined by the Council on Pharmaceutical Affairs and Food Hygiene. Products in conventional food forms already approved should be examined and approved by a sectional committee on newly developed foods to be established under the Sectional Committee on Food Hygiene of the Council.

4.4.2 Health-promoting Foods in China

In China, food products which claim health functions shall be reviewed and approved by the Ministry of Health. The following requirements must be met:

- a. It must be demonstrated by necessary animal and/or human functional tests that the product has definite and stable health functions.
- b. All the raw materials and the products must meet the hygienic requirements of food production. They must not cause any acute, subacute or chronic harmful effects to the human body.
- c. There shall be scientific substantiation supporting the formulation, and the amount of ingredients used. Functional ingredients shall be identified. If the functional ingredients could not be identified under the present condition, it is necessary to show the names of the main raw materials related to the health functions.
- d. Information shown on the label, instructions for use or advertisements shall not claim that the products have therapeutic effects.

The approved products shall be issued with a Health Food Certificate and a code number. Such food products are then permitted to use the special symbol for health foods stipulated by the Ministry of Health. The functional components contained therein and the health function that the product possesses should be clearly indicated on the label.

4.4.3 Health-promoting Foods in Taiwan

In Taiwan, foods shall not be labeled or advertised as a health food unless it is registered as such in accordance with the Health Food Control Act, 1999. A manufacturer or importer of a health food must submit an application supported by information such as its ingredients, specification and methods of analysis, other relevant data and documentation as well as labels and samples of the product. Products which meet the following requirements may be given a product registration permit by the central competent authority:

- a. Contain chemical entity with definite health care effect, the reasonable intake of which is supported by scientific evidences. If current technology cannot identify chemical entities with valid health care effects in health food, the ingredients with the relevant health care effects shall be enumerated or supporting literature provided to the central competent authority for re-evaluation and identification; and
- b. Duly supported by scientific assessment and test of health effects or by academic principles that

they are harmless and carry definite, stable health care effects. The method by which health effects are assessed and the method by which toxicological assessments are made shall be established by the central competent authority.

There are specific requirements for the labeling and advertising of health foods. Besides the usual particulars of the product, the approved health effects, the intake amounts, important messages in connection with the consumption of the health food and other necessary warnings shall be clearly stated. No health food label or advertisement shall misrepresent or exaggerate any health claims or contain information beyond the approved scope. The products shall also not claim any therapeutic effects.

The effects of health claims shall be described in any of the following ways:

- a. Prevention or alleviation of illness relating to deficiency of nutrients in the human body if intake of the product can make up said nutrients;
- b. Impact on human physiological structure and functions by the specified nutrients or specific ingredients contained in the product;
- c. Scientific evidence to support the claim that the health food can maintain or affect human physiological structure and functions; and/or
- d. General advantages of taking the product.

4.5 Functional Foods in Traditional Asian Culture

In Asia, “functional foods” have been regarded as an integral part of traditional culture for centuries although the term is not formally used. The Japanese and Chinese, for instance, believe that foods and medicine are of equal importance in preventing and treating disease, that they come from the same source, are based on the same basic theories and have the same uses (Weng and Chen, 1996; Arai, 2002).

Some examples of functional foods include mushrooms, tea, the hawthorn fruit and its extracts, and the Chinese wolfberry. Summaries of the functional properties of these foods and the studies on their biological and physiological properties are set out in the Annex to this monograph. There is increasing scientific evidence to support the functional role of these foods to human health. Clearly, more research is still needed, but these foods have certainly demonstrated potential beneficial functional effects.

4.6 Asian Position on Functional Foods

Section 4.1 of this monograph clearly shows that there are differing views among Asian countries on the subject of functional foods. The state of development of functional foods, as well as the direction of such development, varies between the countries. Such divergence, if allowed to persist, would not be conducive to the development of functional foods in the region.

Recognizing that some degree of harmonization and common understanding on functional foods would help promote their development, ILSI SEAR organized the 1st Asia Region Workshop on Functional

Foods held on October 22-23, 2003 in Kuala Lumpur, Malaysia. Most of the participants in the workshop were representatives of regulatory agencies, research organizations and the academia from 10 countries in Asia. Several representatives from the food industry also participated in the workshop. A wide range of topics pertaining to functional foods were deliberated, including future developments, safety and scientific evaluation, the essential attributes or characteristics and regulatory and marketing aspects.

At the conclusion of the two-day workshop, there was general agreement on the following conclusions and recommendations:

- * There is a lot of potential for the development of functional foods in Asia. A large number of food products and biologically active ingredients are unique to the region and have much potential in promoting the well-being of the population. There should thus be greater efforts in all activities related to the development of functional foods in the region, including research and development, regulatory development as well as consumer communication.
- * There should be a harmonized approach to the future development of functional foods. This may include reaching a common understanding, setting of guidelines, promotion and regulations of functional foods. This would be beneficial to the advancement of the industry and would bring about greater consumer confidence in these products.
- * As a basic step towards this common understanding, the following are proposed to be the essential attributes or characteristics of functional foods:
 - Functional foods should:
 - (i) be in conventional food forms and possess sensory characteristics including appearance, colour, texture, consistencies and flavours;
 - (ii) contain nutrients and/or other substances that confer a physiological benefit over and above basic nutritional properties. These substances should not be used at levels for medicinal or therapeutic purposes;
 - (iii) possess functional benefits that can be scientifically proven;
 - (iv) possess functional benefits that can be derived by consuming normal amounts of the foods;
 - (v) contain “functional” nutrients and/or other substances that may be naturally present or be added to the food; and
 - (vi) have been proven to be safe over long term usage for the intended target population based on existing science.
 - A food may not be considered to be a functional food if it:
 - (i) claims to treat diseases; or
 - (ii) contains components that may be harmful to human health.
 - The term “functional food”:
 - (i) should not be used for food components in isolation. The food components would be the nutrients and/or other substance conferring the functional properties and would be best referred to as “functional components”. If these functional components are extracted from the food and presented in pharmaceutical dosage forms, they may be called “nutraceuticals”;
 - (ii) should not be used for dietary supplements; and
 - (iii) may be used for fortified foods, if the fortification or words of similar meaning is to augment a constituent normally present in a food or to add a constituent not normally

present in the food in order to confer a property beyond its natural nutritional attribute.

- Functional foods would generally be regulated by food regulatory agencies.
- * Greater attention should be given to scientific substantiation of the beneficial effects of functional foods. More research needs to be carried out on appropriate methodologies for scientific substantiation of claims. Harmonization of protocols or methodologies would facilitate advancement in this area.
- * Substantiation of functional food claims should be different from drug testing. The level of scientific evidence required for substantiation of functional foods should be less stringent than that required for drugs. Studies should be done on the whole food rather than extracted ingredients whenever possible because the benefits of functional components may not be optimal when isolated and would require to be consumed as a whole to have the desired beneficial effects.
- * Experiences from other regions of the world, including experiences in the development of scientific substantiation of claims in Europe and United States of America, would be useful to the Asian region. Nevertheless, the understanding and usage of functional foods in this region should be taken into consideration when dealing with the subject.
- * Countries should preferably establish a pre-marketing approval system which reviews all products submitted for approval to ensure safety, quality and efficacy of the products. This would also ensure that the products meet all regulatory requirements.
- * For post-marketing surveillance, attention should also be given to regular inspection and monitoring of the safety of use, sale, marketing and advertising of functional foods by the relevant authorities. Information on safety of use should also be submitted to the regulatory agencies if there is any report of adverse effects.
- * There should be greater interaction among countries and regions in Asia to bring about greater advancement in the development of functional foods. Enhanced networking in all aspects of functional foods development would be beneficial, including research and development, regulatory development as well as consumer communication.
- * A harmonized pre-marketing approval system would facilitate the marketing and trade of functional foods in Asia. Regular interactions amongst regulatory agencies in the region is necessary to realize this objective.
- * Effective communications and ethical advertising to consumers are essential to maintain credibility of functional foods. Relevant authorities as well as manufacturers of functional foods should bear this in mind and work towards achieving these practices.

ANNEX

FUNCTIONAL FOODS IN TRADITIONAL ASIAN CULTURE

1 Mushrooms

1.1 *Edible Mushrooms as a Functional Food*

Since ancient times, mushrooms have been consumed by humans not only as a part of the normal diet but also as a delicacy due to their taste and aroma. In addition, the nutritional, tonic, and medicinal properties of mushrooms have been recognized for a long time. Certain ancient religious scriptures such as the Vedas have mentioned their medicinal importance; Romans considered mushrooms to be the Foods of the Gods and the Chinese declared them to be the Elixir of Life (Johl et al., 1995).

There are probably tens of thousands of wild mushrooms distributed worldwide. However, it is estimated that only less than 10% of these species are edible and roughly an equal proportion of them is considered to be poisonous. Today, as a result of advancements in innovative cultivation techniques, huge quantities of various cultivated mushrooms are produced and sold throughout the year. The two most popular cultivated mushrooms in the world are the button mushroom (*Agaricus bisporus*) and shiitake (*Lentinus edodes*) (Miles and Chang, 1997).

Mushrooms are usually high in protein (19–35%, including all the essential amino acids) and low in fat. Mushrooms also contain relatively large amounts of carbohydrate and fiber, ranging from 51% to 88% and from 4% to 20% (dry weight), respectively, for the major cultivated species. In addition, mushrooms contain significant amounts of vitamins, namely thiamin, riboflavin, ascorbic acid, and vitamin D₂, as well as minerals (Miles and Chang, 1997; Breene, 1990). Of particular importance is the vitamin D content. Mushrooms are the only non-animal-based food containing vitamin D, and hence they are the only natural vitamin D source for vegetarians. The amount of vitamin D in wild mushrooms vary considerably. On the other hand, reasonably high contents have been found in cultivated shiitake (22–110 mg/100 g dry matter) (Takamura et al., 1991).

In addition to their nutritional value, some mushrooms in Asia have been considered to have medicinal properties such as anti-tumor, anti-viral and hypolipidemic effects (Miles and Chang, 1997; Johl et al., 1995; Breen, 1990).

1.2 *Anti-tumor/Anti-cancer Activity*

The medicinal property for which mushrooms have been most extensively investigated is their anti-tumor activity. Most of this research has been conducted in Japan. Whole mushrooms of several

species and/or extracts from them have been reported to have an anti-tumor effect. Among these species are *A. bisporus*, *Auricularia auricula*, *Collybia confluens*, *Coriolus versicolor*, *Flammulina velutipes*, *Ganoderma applanatum*, *G. lucidum*, *L. edodes*, *Pholiota nameko*, *Pleurotus ostreatus*, *Schizophyllum commune*, *Tremella fuciformis*, *Tricholoma matsutake*, and *Volvariella volvacea* (Miles and Chang, 1997; Johl et al., 1995; Breen, 1990).

Ikekawa et al. (1969) found that intraperitoneal injection of aqueous extracts of six of seven edible mushrooms species tested greatly inhibited the growth of tumors (by 72-92% versus controls) arising from sarcoma-180 cells implanted in Swiss albino mice. Based on chemical analysis the active anti-tumor agent in shiitake was suggested to be a polysaccharide. It was later called lentinan and its chemical structure was characterized as beta-1,3 glucan, having branching of the 1,6 bonds (Miles and Chang, 1997). In addition, lentinan was proven to exhibit prominent anti-tumor activity not only in allogeneic hosts, such as sarcoma, but also in syngeneic and autochthonous hosts with no noticeable side effects. Furthermore, it can prevent chemical and viral carcinogenesis and cancer metastases. Its effect results from the activation of the host's immune system (Chihara, 1992; 1993).

Until the 1980s, most evidence of the anti-tumor activity of mushrooms was from studies in which the preparations were administered by injection into test animals. Lentinan and many other polysaccharides extracted from shiitake and other mushrooms were shown to be ineffective when administered orally. Some of the most recent studies on anti-carcinogenicity have involved oral administration of powdered, dried mushroom fruiting bodies into mice, and promising results have been obtained (Nanba and Kuroda, 1988; Nanba et al., 1987; Mori et al., 1987).

The anti-tumor studies conducted with mushrooms thus far are promising and do show a potential for providing therapeutic control of cancer. Further epidemiologic and biological research is needed to clarify the role of mushrooms as preventive and curative agents.

1.3 Anti-viral Activity

For hundred of years, shiitake mushrooms have been used to cure the common cold. Recent scientific evidence supports this belief. Cochran et al. (1967) examined extracts of various parts of many different plants and fungi for activity against the influenza virus in vitro and in mice. Of the mushrooms tested, shiitake showed an activity (expressed as the percentage decrease in lung lesion score compared with the control) of 46%, which was of the same magnitude as that of amantadine hydrochloride, a common drug used against influenza (40%). A watery extract from shiitake was also reported to prevent the multiplication of the polio virus (Johl et al., 1995).

According to Chihara (1992), lentinan enhanced host resistance against infections with bacteria as well as with fungi, parasites, and viruses, including the agents of AIDS. Lentinan reduced the toxicity of AZT (a drug commonly used for treating HIV carriers and AIDS patients). Prevention of the onset of AIDS symptoms through potentiation of host defense is now being actively investigated both experimentally and clinically (Chirara, 1993).

In addition to lentinan, other substances from shiitake and other mushrooms have also been shown to have anti-viral activity. The mechanism of their effect is in most cases via induction of

interferon (Miles and Chang, 1997; Breene, 1990; Mizuno, 1995).

Asian populations regularly consumed mushrooms for, among many other purposes, the prevention and cure of colds. However, whether there are benefits to one's general feeling of well-being is a highly subjective matter. Moreover, the anti-viral studies have been performed using various extracts rather than whole mushrooms and there is currently no convincing scientific evidence that consuming mushrooms as a part of the diet could prevent or cure influenza or other viral diseases.

1.4 Hypolipidemic Activity

Initial research on the cholesterol-lowering effects of mushrooms was performed in Japan by Kaneda and co-workers. Kaneda and Tokuda (1966) demonstrated that when rats were fed a diet supplemented with 5% (dry weight) of shiitake fruiting bodies for 10 weeks, the plasma cholesterol levels of the animals decreased significantly. The active hypocholesterolemic substance in shiitake was isolated and identified as an adenosine derivative (Tokita et al., 1972). It was called lentinacin and also lentysine. The name in current use, however, is eritadenine. Eritadenine works by lowering levels of all lipoprotein types, i.e., high-density as well as low-density lipoproteins (Breene, 1990).

In addition to animal tests, the effectiveness of shiitake in lowering blood serum cholesterol was also tested on human subjects. Suzuki and Oshima (1976) found that a daily intake of 90g of fresh shiitake, 9g of dried shiitake, and 9g of UV-irradiated dried shiitake for 7 days lowered the mean serum cholesterol levels in young women by 12%, 7%, and 6% respectively. All three diets decreased serum cholesterol levels of older persons (more than 60 years of age) by 9% over 7 days. However, the authors did not provide information on the composition of the whole diets of their subjects.

The relationship between high levels of cholesterol in the blood and cardiovascular diseases is well known. Hence, the cholesterol-lowering effect of eritadenine and shiitake is interesting, especially as it has been found to have such effect in both tests and human studies. Furthermore, no enrichment of the active fraction or component is required, and consuming shiitake mushrooms as part of the normal diet appears to achieve the cholesterol-lowering effect.

1.5 Conclusions

It is clear that mushrooms contain some interesting compounds that have been shown in clinical studies to be effective in treating several common diseases. Mushrooms have been considered as a functional food in Asia for many centuries. According to studies conducted thus far, mushrooms may strengthen the immune system of both healthy and sick individuals. Furthermore, cholesterol-lowering effects of some mushrooms have been reported in both animal and human studies. More research is needed to be able to fully exploit the functional properties of mushrooms.

2 Tea

2.1 History of Tea as a Beverage

Tea is one of the most widely consumed beverages throughout the world, second only to water. Green tea and black tea are produced from the plant *Camellia sinensis*. It is one of the safest beverages since it is made with boiling water and has been popular for over 4000 years. Its health promoting properties were recognized since it was frequently used as fluid supply for patients suffering from infectious diseases.

The history of tea as a beverage is traced by the Chinese to about 2700 BC at the time of Emperor Shen Nung. The first recorded mention of tea, however, is in an old Chinese wordbook, Erh Ya, dating from about 350 BC. From China, the tradition of tea drinking came to Japan during the 6th century. It was then consumed by the privileged society, and in the middle of the 17th century the English played a major role in merchandising and popularizing tea.

Tea is consumed by hundreds of millions of people and became popular only about 700 years ago. Later, tea was introduced into what is now known as Indonesia and from there through the Dutch colonials into Holland. It was also cultivated in India and thence imported to England, where it became popular. Tea has been considered as a functional beverage for many centuries in China and Japan. By tradition, people in Asia prefer green tea or black tea. Interestingly in Asia, tea, especially green tea, has always been regarded as having medicinal properties. Now tea has entered the health arena among Asians as having a convincing functional property.

2.2 *Tea as a Functional Food*

Recent detailed research has explored the health-promoting actions of tea through epidemiological and marker studies. Experimental research in laboratory animals has demonstrated that tea inhibits carcinogenesis, associated with tobacco carcinogens or salt, at a number of organ sites; of special interest are organs such as lung, stomach and esophagus. Other investigations noted inhibition in organs related to nutritional carcinogenesis, such as the colon or mammary gland.

Numerous studies have demonstrated that aqueous extract or the major polyphenols of green tea possess anti-mutagenic, anti-diabetic, anti-oxidant, anti-bacterial, anti-inflammatory, anti-tumor, hypocholesterolemic, and above all, cancer-preventive activities in a variety of experimental animal models system. Effect on oral diseases such as dental caries, periodontal disease, and tooth loss have also been reported.

In recent years, it is believed that tea polyphenols are the main active components in tea that possess potential benefits to human health. In general, there exists a broad scientific view that many of the putative health benefits of tea polyphenols may arise from their anti-oxidant activity and their capacity to protect critical macromolecules such as chromosomal DNA, structural proteins and enzymes, low-density lipoproteins (LDL), and membrane lipids from damage arising from exposure to active species of oxygen. Active forms of oxygen are produced routinely by metabolic activity and from exposure to external prooxidant influences. However, apart from being anti-oxidants, polyphenols may also be involved in other physiologic processes due to their complex chemical structure. It has been suggested that polyphenols may impact favorably on the risks of cancer and cardiovascular disease, immune function, vasodilation, inflammation, bacterial and viral infection, prostanoid metabolism, enzyme activation, especially with respect to cellular activation and detoxification mechanisms, receptor binding, cell-cell communication, cell proliferation, and in a

hormonal role as phytoestrogens.

2.3 *Tea Polyphenols and Their Potential Functions*

More than 8,000 phenolic compounds are known to occur widely in plants. As a chemical group, polyphenols range from simple phenolic molecules to polymeric structures with molecular weights in excess of 30,000 Da. Interest in polyphenols as anti-oxidants is centered on a group referred to as the flavonoids, which are widely distributed in plants and share a common molecular structure based on diphenylpropane. Of the dozen or more classes of flavonoids, the most abundant are the flavones (e.g., chrysin, apigenin); flavonols (e.g., kaempferol, quercetin, myricetin) and their glycosides, which occur in fruit, vegetables, tea, and wine; and the flavanols or cyanidins, which occur as free monomeric catechins and catechin gallates in tea. Catechins also occur in polymeric form as theaflavins and thearubigins in black tea. The main polyphenols in tea are the flavonoids and they are made up of four catechins, namely gallocatechins epicatechin (EC), epicatechin gallate (ECG), epigallocatechin (EGC), and epigallocatechin gallate (EGCG), which together comprise 30–50% of the solids in a green tea infusion but which decline to 10% after so-called “fermentation” to black tea, with a concomitant rise in the polymeric theaflavins (3–6%) and thearubigins (10–30%). Flavonols and flavonol glycosides are also present at levels around 5% (Hollman et al., 1997). Evaluation of the anti-oxidant potential of tea flavonoids based on redox potentials and in vitro assays of anti-oxidant potential indicate that all the tea flavanols and flavonols are good anti-oxidants and in some cases are up to five times more effective than vitamin C or vitamin E. Similar levels of anti-oxidant activity are reported for the theaflavins, and the fact that the overall anti-oxidant capacity of infusions of black tea are similar to green tea suggests that thearubigins are equally effective as anti-oxidants as the catechin monomers (Dreosti, 1996; Balentine et al., 1997).

At present, the bioavailability of these catechin condensation products has not been established. However, it was found in one study that total polyphenol levels in the blood of human volunteers rose equally after consumption of green or black tea, and urine and fecal polyphenol levels in both cases were less than 10%, which suggests that thearubigins or their degradation products are significantly absorbed from the small and large bowel (Wiseman et al., 1997). Studies on the bioavailability of polyphenols are limited, but observed physiologic responses in humans and animals to consumption of flavonoids suggest significant uptake from the intestine, although few pharmacokinetic data are available. Generally, absorption and metabolism of polyphenols is influenced by their solubility and chemical structure. Most monomeric and small oligomeric flavonoids are soluble in water and to some extent in lipids. Large polymeric flavonoids are less soluble. Also important are the degree of glycosylation and conjugation with other polyphenols. On this basis, tea catechins and catechin gallates, which are not glycosylated and are readily water soluble, should be directly absorbed from the small intestine. Quantification of the efficiency of absorption of flavonoids is complicated by bacterial degradation in the terminal ileum and colon, and by metabolism of absorbed flavonoids. Nevertheless, studies on the uptake of tea catechins in rodents and human volunteers indicate that absorption of the monomers and their degradation products is rapid and peak levels in plasma are reached between 1.5 and 2.5 h, with varying uptakes for the individual compounds.

With respect to health, studies in vitro and with animals have repeatedly linked tea extracts and the

flavonoids to reduced risks of cardiovascular disease and cancer (Tijburg et al., 1997). In relation to cardiovascular disease, tea has been proposed by some workers to lower blood cholesterol levels and blood pressure, to protect low-density lipoproteins against oxidation *in vitro*, and to reduce platelet aggregation in model systems (Dreosti, 1997). A specific protective role for tea flavonoids as antioxidants has focused on the finding that the catechins strongly inhibit copper-induced and cell-mediated oxidation of low-density lipoproteins *in vitro*, but evidence that this effect occurs *in vivo* is equivocal. Nevertheless, several epidemiologic studies have demonstrated lower rates of cardiovascular disease and coronary heart disease mortality in tea drinkers (Dreosti, 1997). With respect to cancer, protection has been demonstrated repeatedly by studies *in vitro* and with animals.

Based on these findings a number of putative mechanisms have been proposed, which include reduced carcinogen formation and activation, increased carcinogen detoxification, reduced carcinogen/DNA binding, protection against oxidative damage to DNA and key control macromolecules, reduced promoter binding, improved cell-cell communication, diminished angiogenesis and tumor growth, increased apoptosis, and reduced metastasis (Wiseman et al., 1997; Blot et al., 1996; Yang et al., 1998). However, human epidemiologic studies have failed to provide a consistent dose-related pattern although some investigations have raised the possibility of somewhat lowered risks of digestive tract cancers among tea drinkers (Serafini et al., 1996).

In vivo animal studies have shown that specific pathogen-free rats infected with *Streptococcus* mutants and then fed a carcinogenic diet containing green tea polyphenols have significantly lower caries scores. Supplementing drinking water of rats with 0.1% green tea polyphenols along with a carcinogenic diet also significantly reduced total fissure caries lesions. Drinking tea (without added sugar) has been associated with lower caries levels in humans (Wu and Wei, 2002). In recent years, the general population has demonstrated increased awareness and interest in "functional foods" and researchers have explored not only desirable food habits but also beverages that may contribute to over-all health and disease prevention. With the added dental health implication, tea may be considered a "functional food for oral health" by controlling through prevention the most prevalent infectious disease of mankind, namely caries.

In summary, persuasive evidence is accumulating that suggests that tea may contribute significantly to human health, due in part to its anti-oxidant activity. Clearly more research is needed on the possible health benefits of tea but there can be little doubt that the bioactive components are now being viewed increasingly as having significant potential beneficial functional attributes.

3 Hawthorn Fruit and Its Extracts

The hawthorn fruit has a long history of use as a medicinal plant in Chinese culture. The Hawthorn fruit is a bright red berry of the *Crataegus* species. It is not only used as a medicinal herb, but also used as a major ingredient for several popular snack foods. According to the theory of Traditional Chinese Medicine and clinical experience, the hawthorn fruit possesses numerous general functions, such as improvement of loss of appetite and digestion, antibiosis activity, hemostatic activity, diuretic activity, anti-allergic activity, liver-protective function, anti-oncotic activity, and so on. Many recent

investigations have demonstrated that the consumption of hawthorn fruit and its extracts may be associated with other long-term health benefits. The main functional components of the hawthorn fruit include flavonoids and the major functions of hawthorn and its extracts are summarized in the following paragraphs.

3.1 *Hypolipidemic Activity*

Chen et al. (1995) studied a hawthorn drink and its effect on lowering blood lipid levels in human subjects. The results showed that hawthorn decreased serum total cholesterol (TC), LDL cholesterol (LDL-C) and triglyceride (TG) in hyperlipidemic subjects. In another study, He (1990) observed the effect of a mixture of Hawthorn and Motherwort (*Leonurus heterophyllus*) on the prevention of atherosclerosis. The results showed that blood cholesterol, triglyceride and blood viscosity were statistically lower than that in the controls and confirmed the effect of the mixture on the prevention of atherosclerosis.

3.2 *Hypotensive Effect*

The hypotensive effect of hawthorn extract was investigated in a randomized double-blind pilot study by Walker et al. (2002). Compared with the placebo group, a promising reduction in the resting diastolic blood pressure was found in subjects who were assigned to the hawthorn extract group. Another two similar, controlled, randomized studies on camphor-crataegus berry combination were carried out in a balanced crossover design in 24 patients each with orthostatic dysregulation and demonstrated the same results (Belz et al., 2002).

3.3 *Other Benefits on Cardiovascular System*

Hawthorn extract has been used to treat the early stage of congestive heart failure (Weihmayr and Emst, 1995) and angina pectoris (von Eiff, 1994). In addition, hawthorn fruit significantly inhibited thromboxane A₂ biosynthesis and platelet adhesion, thus reducing the formation of atheroma and thrombosis (Vibers et al., 1994).

3.4 *Anti-oxidant Activity*

Hawthorn fruit is an excellent source of anti-oxidants. Studies identified seven anti-oxidants, namely, hyperoside, isoquercitrin, epicatechin, chlorogenic acid, quercetin, rutin and protocatechuic acid in hawthorn fruit. These compounds prevented the peroxy free radical-induced oxidation of (α-tocopherol in human LDL. They also protected human LDL from Cu²⁺-mediated oxidation. An in vivo study observed that supplementation of 2% hawthorn fruit powder significantly elevated serum (α-tocopherol by 18-20% in rats (Zhang et al., 2001).

3.5 *Anti-viral Activity*

A study evaluated the anti-viral activity of some fractions of hawthorn fruit and a series of flavonoids and proanthocyanidins obtained from hawthorn fruit. The results showed that O-glycosidic flavonoids

and oligomeric proanthocyanidins exhibited significant inhibitory activity against herpes simplex virus type 1 (HSV-1) (Shahat et al., 2002).

3.6 *Anti-cancer Activity*

An in vitro study showed the inhibitory effects of hawthorn extracts on cancer cells. 4-8 ug/ml hawthorn extract significantly decreased the survival rate of the cancer cells, and the colony forming rate was significantly inhibited by 8-10 mg/ml hawthorn extract (Liu et al., 1994).

4 Chinese Wolfberry (*Fructus lycii*)

The Chinese wolfberry (*Fructus lycii*), the fruit of *Lycium barbarum L.*, is a well-known traditional tonic and commonly used as a medicinal food in Traditional Chinese Medicine (TCM). Reportedly, it has been used for health improvement and treatment for certain diseases since the Ming Dynasty. In TCM, the wolfberry is used to "improve eye sight" and "regulate Qi and nurture blood". It is also widely used as a cooking aid in preparing several types of Chinese dishes, such as wolfberry chicken soup. In addition to important nutrients such as carotene, thiamine, riboflavin, ascorbic acid, folic acid, calcium, iron and essential amino acids, the Chinese wolfberry contains a number of biologically active components, among which lycium barbarum polysaccharide (LBP) is considered to be a major active component (Duan et al., 2003). As a functional herb approved for use in Chinese health foods, the Chinese wolfberry has been shown to have important biological effects in a number of recent studies.

4.1 *Anti-aging*

The anti-aging effects of *Fructus lycii* is well documented in ancient medicine literature and modern research reports. The main mechanisms involved in the anti-aging process of wolfberry is antioxidant and free radical scavenging. Using Cu (2+)-induced oxidation model, LBP isolated from *Fructus lycii* was shown to inhibit LDL peroxidation (Huang et al., 2001). Additionally, total flavonoids from *Fructus lycii* was also found to inhibit lipid peroxidation induced by Fe²⁺ cysteine and H₂O₂ in liver mitochondria and red blood cells (Huang et al., 1999; Ren et al., 1996). In a mouse study, the Chinese wolfberry increased the activities of superoxide dismutase (SOD), catalase(CAT) and total anti-oxidative capacity, suggesting that this plant might have a protective effect on damage caused by free radical (Li et al., 2002). Furthermore, the total flavonoids of *Lycium barbarum L.* could directly scavenge O₂⁻ and OH in xanthine/xanthine oxidase system, with average scavenging rate of 25% and 46%, respectively (Huang et al., 2000).

4.2 *Lowering Blood Lipids*

Recent results from animal studies and clinical trials suggested that *Fructus lycii* could modulate the levels of blood lipids. In a rat study, *Fructus lycii* liquor was given to hyperlipemia rats by gavage for 10 days. The treated animals had total cholesterol (TC), triglyceride (TG) and LDL levels reduction in blood and liver in a dose-dependent manner (Wang et al., 1997). A clinical trial showed that, after

being treated with *Fructus lycii* liquor for 3 months, patients who were in a state of excessive of yang had lower serum TC, TG and LDL-cholesterol (Wang et al., 1996). A *Fructus lycii*-containing multiherbal preparation was also shown to decrease significantly TC and TG in 130 hyperlipemia subjects (Guan and Zhao, 1996).

4.3 *Anti-carcinogenesis*

Recently, LBP is considered as one of the natural components in Chinese herbal medicines that can be used as an anti-tumor agent (Tang et al., 2003). Some studies suggested that *Fructus lycii* components could be served as a potential protective agent against tumors and an adjuvant in the therapy of cancers. An in vitro study found that LBP could inhibit the growth of human leukemia cells and induce the apoptosis of HL-60 cells (Gan et al., 2001). In C57 BL mice model transplanted by Lewis lung cancer, when LBP alone was administered, the inhibition to growth of Lewis lung cancer was not obvious. However, the significant radiosensitizing effects were obtained by combination of LBP and radiation (Lu and Cheng, 1992). When 75 advanced cancer patients were treated with LAK/IL-2 combined with LBP, the response rate was 40.9%, which was higher than that obtained from patients treated only with LAK/IL-2 (16.1%). And LAK/IL-2 plus LBP treatment could lead to more marked increase in NK and LAK cell activity than LAK/IL-2 without LBP (Cao et al., 1994). These results suggested that LBP can be used as an adjuvant in the radiation therapy and biotherapy of cancer.

4.4 *Immuno-modulating Activity*

It was found that Chinese wolfberry extracts could increase thymus and spleen weights and pure LBP had demonstrated a remarkable effect on immunological enhancement in mice (Luo et al., 2003). LBP could increase the expression of interleukin-2 and tumor necrosis factor- α in human peripheral blood mononuclear cells at both mRNA and protein levels, which are two important cytokines in anti-tumor immunity (Gan et al., 2003). In immunosuppressive mice, Chinese wolfberry extracts could modulate the disturbed status of and enhance the expression of IL-2R in T cells and induce the production of γ -interferon in cortisone-treated mice (Yu et al., 1994; Wang et al., 1999).

4.5 *Other Biological Activities*

Some researchers found that LBP could increase the activity of LDH and decrease the increase of blood urea nitrogen after strenuous exercise, suggesting a stamina effect (Luo et al., 2000). LBP could protect isolated islet cells from damage induced by alloxan (Xu et al., 2002) and decrease vasoconstriction to phenylephrine in hypertension rat models (Jia et al., 2001), which may be beneficial to diabetes and hypertension. LBP could also raise serum levels of zeaxanthin in rhesus monkeys (Leung et al., 2001) and iron, zinc, hemoglobin in pregnant women when treated with LBP plus mixed nutrients (Ling et al., 1997).

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