Functional foods and their utilization in Japan

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Abstract

In Japan over the past two decades, a number of food substances' potential for disease risk reduction rather than simply for health maintenance have been studied for their body-modulating functions. Some of these substances have already been applied to the industrialization of functional foods in terms of 'foods for specified health use' (FOSHU). More than 300 items of FOSHU were available as of August 2002—these include foods to improve gastrointestinal conditions, foods to enhance mineral absorption, and foods for people with a high blood glucose or cholesterol levels or hypertension. These FOSHU products are becoming popular in Japan and now form a market of several billion dollars.

Research and development of new types of functional foods are also progressing. One example is progress in the studies of antioxidative food factors. Since the age-related diseases, such as cancer, could be correlated with oxidative stresses, antioxidative food factors may be beneficial for prevention of those diseases. Another example is progress in the studies on immunomodulatory food factors. Immunomodulatory food is strongly required because the number of patients with allergies is rapidly increasing in Japan. Antioxidative and immunomodulatory food substances have been discovered in various agricultural products. The importance of evaluating absorption/modification of the food factors in the intestine is also being recognized.

Thus, the studies of functional foods in Japan are still progressing from a wide variety of viewpoints. The discovery of functional substances from agricultural products will enhance the production of more FOSHU with novel functions.

Introduction

THERE is an ancient Chinese saying that 'medicine and food are isogenic'. In the early 1980s, Japanese food scientists started to prove this saying from the scientific viewpoint under a large national project which started in 1984 and which has produced a large number of experimental results over the last two decades (Arai 1996; Arai et al. 2001). These experiments demonstrated that various food substances had modulatory effects on the body's systems. The concept of 'functional food' was thus established, which encompassed 'science-based food for disease prevention'. In 1991, the Ministry of Health and Welfare of Japan established a policy of officially approving selected functional foods in terms of 'foods for specified health use' (FOSHU). More than 300 items of FOSHU were available in Japan as of August 2002. These include foods to improve gastrointestinal conditions and foods helpful for people who are concerned about their blood glucose, cholesterol or triglyceride levels, or people with mild hypertension. Although more than 60% of the FOSHU products are foods which promote an increase in beneficial bacteria in the intestinal microflora and help to maintain a healthy intestinal environment, the number of foods with other physiological functions is rapidly increasing. In addition to the research and development of the functional foods mentioned above, new research trends are apparent in functional food science in Japan.

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Analysis of antioxidative food factors

SINCE the start of the Designer Foods Program in the United States of America 10 years ago (Caragay 1992),

a number of 'phytochemicals', or chemical components of plant foods with cancer-preventive functions, have been discovered. Japanese food scientists have also searched for phytochemicals with anti-cancer activity. Ohigashi and coworkers, using an assay system with Epstein-Barr virus, examined various plant foods for anti-tumor promotion activity. Interestingly, they found that plants from tropical countries had stronger inhibitory activity against Epstein-Barr virus activation than plants from Japan, indicating that tropical vegetables have higher anti-tumor promotion activity. About two-thirds of the edible plants obtained in Indonesia had high activity, whereas only one-quarter of those from Japan were active (Murakami et al. 1999).

Researchers have found that many of these promising substances possess antioxidative activity. Since age-related diseases such as atherosclerosis and diabetes, as well as cancer, are supposed to be correlated with oxidative stress, these antioxidative food factors may be beneficial for prevention of, not only cancer, but also many other age-related diseases. From this viewpoint, screening for new types of antioxidative food factors has been performed by many research groups. Osawa and his group have recently developed many types of antibodies which specifically recognize oxidatively damaged deoxyribonucleic acid (DNA) bases, such as 8-OH-deoxyguanosine and lipid peroxidation products (Toyokuni et al. 1997). By monitoring these oxidatively damaged products as biomarkers, they have found many different types of dietary antioxidants that could be beneficial for prevention of age-related diseases. Attempts to find good biomarkers for the screening of new food factors are also in progress.

The detailed mechanisms for the action of food factors on the modulation of physiological conditions are still not well understood. New techniques have been introduced to reveal these mechanisms. The DNA microarray technique is one example. Changes in the expression of genes by such food factors as anti-carcinogenic carotenoids have been reported (Narisawa et al. 1999). Effects of dietary polyphenols on cellular functions have also been analyzed at the molecular level, with, for example, regulation of transcription factors by these compounds, being observed.

Food factors with immunomodulatory functions

THE number of patients with allergies is rapidly increasing in Japan. According to the recent data in Japan, more than 40% of the children of 3 years old or younger have some symptom of allergy, such as asthma and atopic dermatitis. Autoimmune diseases and infectious diseases are also becoming big problems in an aged society. Food factors with immunosuppressive and immunopotentiating activity have therefore been analyzed in many dietary sources. Researchers have found that such food factors as tea catechins, flavonoids, polysaccharides and nucleotides have immunomodulatory activity, although these functions have not yet been applied to the FOSHU products. Yamazaki and his group found that oral administration of a perilla extract suppressed the production of tumor necrosis factor in mice (Ueda and Yamazaki 1997). The active compounds in perilla responsible for this immunosuppression would be useful in functional foods for people with allergies or other hyper-immune diseases. Suppression of allergic reactions by lactic bacteria (probiotics) and oligosaccharides (prebiotics) has also been studied. Shida et al. (2002) reported that oral administration of lactobacillus suppressed the production of immunoglobulin E (IgE) in a food allergy model. Oral administration of nucleotide decreased the level of IgE in mouse blood serum, particularly in the serum of young mice (Nagafuchi et al. 2000a). Use of these allergy-suppressive food factors may decrease the number of infants with allergic reactions in the future. The importance of the mucosal immunity is now being recognized and mechanisms for the action of food factors on the intestinal immune systems have been analyzed in detail (Kaminogawa et al. 1999).

In addition to the studies on immunomodulatory food factors, development of hypoallergenic food products is progressing. Hypoallergenic rice, wheat, soybean and milk products have been successfully developed by enzymatic methods (Tanabe and Watanabe 1999) and are already available in the market. Production of hypoallergenic foods using a molecular breeding techniques or genetic manipulation has also been considered.

Food factors and intestinal functions

THE bioavailability of food factors depends strongly on their behavior in the intestinal tract. Evaluation of intestinal absorption and metabolism of food factors is therefore important. Although mechanisms for the intestinal absorption/metabolism of such major nutrients as glucose, amino acids, cholesterol and vitamins have been fully investigated, those of food factors, such as flavonoids, their glycosides and oligopeptides, in the intestine are not well understood. Recent studies have demonstrated that many dietary phytochemicals can be absorbed to some extent across the intestinal epithelium, probably via the non-specific transcellular or paracellular pathway. We have found that the rate of intestinal absorption of food factors could be altered by various food substances (Shimizu 1999). Since the intestinal epithelium is a tissue that is always exposed to high concentrations of food substances, it is possible that functions of the intestinal epithelial cells are modu-

lated by food substances. Our studies have suggested that the tight junctional permeability of the intestinal epithelium is modulated by various food substances, thereby affecting the intestinal absorption of certain types of food factors (Hashimoto et al. 1994, 1997). Intestinal absorption of major nutrients such as glucose could also be affected by food substances (Kobayashi et al. 2000; Ogawa et al. 2000).

Modification of food factors also occurs in the intestinal epithelial cells. For example, curcumin, an antioxidative substance in turmeric, is converted to tetrahydrocurcumin—which has more potent antioxidative activity than curcumin—during the absorption process from the intestine. Nagafuchi et al. (2000b) have recently reported that dietary nucleotides enhance the production of IL-7 by intestinal epithelial cells, thereby modulating the growth and differentiation of intraepithelial T lymphocytes. These findings suggest that the intestinal epithelium is not a simple gate for nutrients and food factors but also plays a role as a 'converter' of food factors. Thus, the intestinal epithelium must play important roles in expressing food functions. The contribution of food factors to human health cannot be completely understood until the behavior of food factors in the intestinal epithelium is revealed.

Conclusion

A great number of papers concerning the food functionality are presented every year in the annual meetings of many Japanese scientific societies relating nutrition and food science. The number of such papers is still increasing year by year. The area they cover is also expanding. Food factors modulating endocrine, circulation, gastrointestinal, immune, and nerve systems have been studied in terms of screening, isolation, identification and application. Studies on the mechanisms of food functions are also being carried out at the ceilular and molecular levels. Since a large amount of information regarding the functional food substances is now available from these diverse studies, we are now constructing a database with the support of the Ministry of Education, Culture, Sports, Science and Technology. Standardization of evaluation systems for functional food factors, isolation and identification of food factors, and epidemiological assessment will be accomplished in the near future.

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