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Review

Development of functional agricultural products and use of a new health claim system in Japan

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ABSTRACT

Background: In Japan, there is a need for development of functional foods that contribute to the maintenance and improvement of health in the elderly.
Scope and approach: In April, 2015, Consumer affairs Agency launched a new food labeling system known as "**Food with Function Claims (FFC)**." Under this system, industry and agricultural producers independently evaluate scientific evidence on agricultural and marine health foods and describe the functional properties that warrant health claims to promote informed use by consumers. To clarify the effects of functional foods on human health, the National Agriculture and Food Research Organization (NARO) implemented the "Research Project on Development of Agricultural Products and Foods with Health-Promoting Benefits."
Key findings and conclusions: As of May 26, 2017, 931 functional foods were classified as FFC. We demonstrated that Satsuma mandarins are rich in **β-cryptoxanthin** and reduce the risk of osteoporosis in postmenopausal women. The Japanese tea cultivar Benifuuki is rich in ***O*-methylated catechins**, which are present at low levels in common green tea, and has anti-allergic effects. Satsuma mandarins and Benifuuki green tea were subsequently released as FFC in 2015. We elucidated the health-promoting effects of **functional agricultural products** to produce healthy boxed lunches and established a database of functional agricultural products. There is a need for additional FFC, including processed foods, that contain only raw materials from agriculture, forestry, and fisheries.

1. Introduction

Prior to April 2015, the Japanese Cosumer Affairs Agency (CAA) regulated "foods for special dietary uses (FOSDU)" and "foods with health claims (FHCs)" (http://www.caa.go.jp/en/pdf/syokuhin338.pdf) as "foods for specified health uses (FOSHU)" and "foods with nutrient function claims (FNFC)" (Fig. 1). Herein, we address the Japanese health claim labeling system and the development of functional agricultural products.

2. Regulation of health claims and new foods using the health claim labeling system in Japan

The CAA permitted FOSDU labeling of foods that contribute to health maintenance and/or recovery from disease under the following four categories: (1) medical uses for diseases (low-sodium foods, low-calorie foods, low-protein foods, no/low-protein and high-calorie foods, high-protein foods, allergen-free foods, lactose-free foods, sodium-reduced meals, meals for diabetes, meals for liver disease, and meals for adults with obesity); (2) formulas for pregnant and lactating women; (3) infant formulas; and (4) foods for elderly individuals with chewing or swallowing difficulties.

The CAA grants permission for FOSDU labeling according to 1. Standard approval processes (2, 3, and 4) and 2. Individual approval processes (1), in which foods are reviewed without established standards.

FOSHU are scientifically recognized for their health maintenance and health-promoting effects and may bear claims, such as "slows cholesterol absorption." The government evaluates these claims, as well as product safety, and the Secretary-General of the CAA approves the labeling of food products that satisfy all requirements. Each FOSHU is approved only after detailed review of scientific evidence.

Conditions necessary for FOSHU recognition are:

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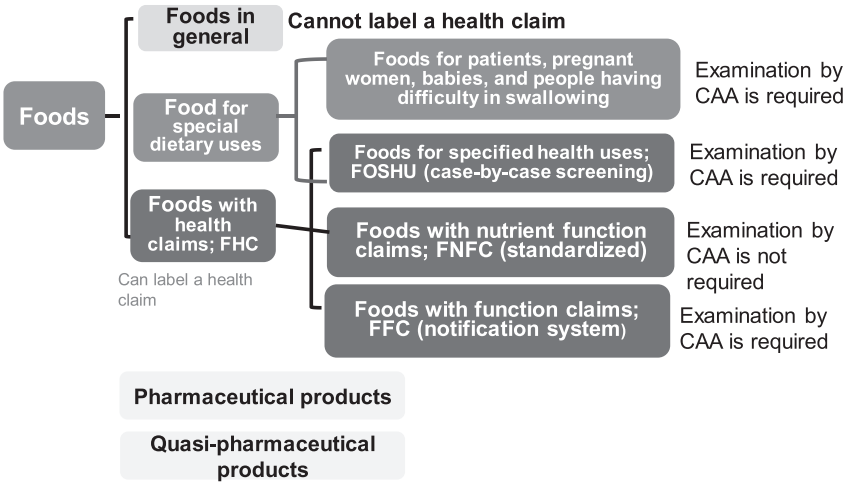

Fig. 1. Classification of orally ingested products in Japan.

1. Improvements in dietary habits, health maintenance, and enhancement can be expected by those who consume the product.
2. Available scientific evidence to support the product's health claims.
3. Established clinical and nutritional information and/or functional ingredients.
4. The product and/or functional ingredient are safe for human consumption.
5. The functional ingredients are defined in terms of:
   a) Physical, chemical, and biological characteristics
   b) Methods of qualitative and quantitative analytical determination
6. No significant changes in nutrient constituents of the food
7. The food is intended to be consumed daily and not on rare occasions.
8. The product or its functional ingredient is not considered as pharmaceutical.

Categories of FOSHU include (1) Standardized FOSHU: 1. No detailed review process for food products meeting established standards and specifications, 2. Must be accompanied by sufficient accumulation of scientific evidence, and 3. Fast-track approval for products with previously approved safety; (2) Reduction of disease risk FOSHU: 1. Detailed review process requiring scientific evidence, and 2. Products with clinically and nutritionally established ingredients that reduce the risk of certain diseases (i.e., calcium for osteoporosis and folic acid for neural tube defects); and (3) Qualified FOSHU: 1. Detailed review process requiring scientific evidence, 2. Products with ingredients with demonstrated health effects that do not reach established standards for FOSHU approval, and 3. Labeled as "Qualified Food for Specified Health Uses." Hence, FOSHUs can be sold with a seal of FOSHU approval.

The examples of approved "foods with specified uses" products are as follows (1099 items as of July 29, 2017):

1. Specified health uses: Foods that modify gastrointestinal conditions;

principle ingredients (ingredients exhibiting health functions): oligosaccharides, lactose, bifidobacteria, lactic acid bacteria, dietary fiber (ingestible dextrin, polydextrose, guar gum, and psyllium seed coat)

2. Foods that act on blood cholesterol levels: Chitosan, soybean protein, degraded sodium alginate
3. Foods that act on blood glucose levels: indigestible dextrin, wheat albumin, guava tea polyphenol, and L-arabinose
4. Foods that act on blood pressure: lactotripeptide, casein dodecapeptide, tochu leaf glycoside (geniposidic acid), and sardine peptide
5. Foods that promote dental hygiene: palatinose, maltitol, and erythritol
6. Foods that act on cholesterol plus gastrointestinal conditions: degraded sodium alginate and dietary fiber from psyllium seed husk
7. Foods that affect mineral absorption: calcium citrated malate, casein phosphopeptide, heme iron, and fructooligosaccharide
8. Foods that promote osteogenesis: soybean isoflavone and milk basic protein
9. Foods that relate to triacylglycerol: Middle chain fatty acids, green tea catechin, oolong tea polyphenol, and cholorogenic acid
10. Foods that may reduce the risk of specific diseases: osteoprosis; principle ingredient: calcium
11. Foods that prevent neural tube defects (spondyloschisis): Folic acid

FNFC can supplement daily nutritional intake. Because these foods contain known concentrations of nutrients with scientifically substantiated functions, their claims can be applied according to standards without submitting a notification to the government. Hence, FNFC labeling indicates specific nutrient activities so that consumers can supplement their diets in accordance with the criteria specified by the CAA. Accordingly, FNFC refers to all foods that are labeled with nutritional claims specified by the CAA, which include nutrient and calorie contents, recommended daily consumption, consumption methods, notes for consumption, recommendations for a well-balanced diet, and language indicating that the food has not been subjected to case-by-case reviews by the CAA. Standards and specifications for nutritional labeling are established for 13 vitamins (niacin, pantothenic acid, biotin, vitamin A, vitamin B_1, vitamin B_2, vitamin B_6, vitamin B_{12}, vitamin C, vitamin D, vitamin E, folic acid and vitamin K), n-3 polyunsaturated fatty acids and six minerals (zinc, calcium, iron, copper, magnesium and potassium), as shown in Table 1. These foods may

Table 1
Standardized function claims for FNFCs.

Nutritional ingredient	Specified range of nutritional ingredient in the advised daily intake allowance	Nutritional claim	Warning indication
Niacin	3.9–60 mg	Helps to maintain healthy skin and mucosa	Excess intake of these products will not cure disease or promote health. Please comply with the advised daily intake.
Pantothenic acid	1.44–30 mg		
Biotin	15–500 μg		
Vitamin A	231–600 μg (450–2000 IU)	Helps to maintain vision in the dark and healthy skin and mucosa	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake. Women within the third month of pregnancy or women considering pregnancy should be careful of over consumption.
Vitamin B1	0.36–25 mg	Helps to produce energy from carbohydrates and to maintain healthy skin and mucosa	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake.
Vitamin B2	0.42–12 mg	Helps to maintain skin and mucosa healthy	
Vitamin B6	0.39–10 mg	Helps to produce energy from protein and to maintain healthy skin and mucosa	
Vitamin B12	0.72–60 μg	Assists in red blood cell formation	
Vitamin C	30–1000 mg	Helps to maintain healthy skin and mucosa and has an antioxidant effect	
Vitamin D	1.65–5.0 μg (60–200 IU)	Promotes intestinal calcium absorption and assists in bone growth	
Vitamin E	1.89–150 mg	Helps to protect against fatty acid oxidation and maintains cellular health	
Folic acid	72–200 μg	Facilitates red blood cell formation and contributes to normal fetal growth	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake. This product facilitates normal fetal development, but increased intake of this product will not result in better fetal development.
Vitamin K	45–150 μg	Helps to maintain normal blood coagulation ability	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake. Persons taking blood-coagulation inhibitor should avoid use of this product.
n-3 polyunsaturated fatty acid	0.6–2.0 g	Helps to maintain healthy skin	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake.
Zinc	2.64–15 mg	Necessary for maintenance of normal taste and helps to maintain healthy skin and mucous membranes. It is involved in the metabolism of protein and nucleic acids and is helpful in maintaining health	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake. Excessive zinc intake might inhibit copper absorption. Please comply with the advised daily intake. Infants and young children should avoid use of this product.
Calcium	204–600 mg	Necessary for the development of bone and teeth.	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake.
Iron	2.04–10 mg	Necessary in red blood cell formation	
Copper	0.27–6 mg	Facilitates red blood cell and bone formation and proper functioning of various enzymes	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake. Infants and young children should avoid use of this product.
Magnesium	96–300 mg	Necessary for development of bone and teeth, maintains proper blood circulation, and helps proper functioning of various energy producing enzymes	Excess intake of this product will not cure disease or promote health. Increased intake might cause diarrhea. Please comply with the advised daily intake. Infants and young children should avoid use of this product.
Potassium	840-2800 mg	Necessary for maintenance of normal blood pressure	Excess intake of this product will not cure disease or promote health. Please comply with the advised daily intake. Person reduced in renal function should avoid use of this product.

be freely manufactured and distributed without permission from, or notification to, the national government, provided they meet established standards and specifications.

Standards and specifications

- Nutritional ingredient quality, within the recommended daily allowance, must be within a specified range.
- Nutritional claims must be displayed with warning indications.

In June 2013, the Japanese Prime Minister Abe published new economic policies and growth strategies, commonly referred to as "Abenomics." These policies require review of the novel labeling system for health foods from the viewpoint of convenience for consumers and manufacturers. As described above, before this system was in place, nutritional claims on food labels were only allowed for government-approved FOSHUs and FNFCs that complied with government-designated specifications and standards. Although these systems remain in place, an additional category for new types of FHCs, known as "foods with function claims" (FFC) (http://www.caa.go.jp/foods/pdf/151224_2.pdf), was introduced in April 2015 (Fig. 1) to make more products available with clearly labeled nutritional or health benefits, and to enable consumers to make more informed choices. Hence, these food products can be labeled with the food function and its specified health effects. To ensure safety, food products are labeled with nutritional claims based on scientific evidence, and labeling is the responsibility of the

Table 2
Foods with function claims (931 items; A1–A310, B1–B620, C1–C9 by May 26, 2017).

Health claims	Functional ingredients	Scientific evidence[a]	Fresh foods	Processed foods	Supplement
Helps to reduce visceral fat and high BMI	Lactoferrin, chitoglucan, isoflavone from Ludzu flower, Licorice glabridin, acetic acid, *Lactobacillus gasseri* sp., EGCG, procyanidin, CP1563, BB536, procyanidin	RCT: 12, SR: 89	0	63	38
Slows elevation of postprandial serum triglyceride levels by inhibiting dietary fat absorption	Indigestible dextrin, β-glucan, wheat albumin, salacinol, 5-aminolevulinic acid, chitosan, gymnemic acid, mulberry leaf, procyanidinB1	RCT: 3, SR: 139	0	120	22
Decreases serum triglyceride and LDL cholesterol levels	Monoglycosyl hesperidin, EPA/DHA, indigestible dextrin, procyanidinB1, lycopene, polydextrose, chitosan, Terminalia bellirica polyphenol, α-linoleic acid, gallate type catechin, indigestible dextrin	RCT: 5, SR: 91	0	68	28
Helps to maintain normal blood pressure in individuals with hypertension	Lactotripeptide, valyl-leucine, γ-glutamyl-S-allylcysteine, cacao flavanol, α-linoleic acid, GABA, wakame seaweed peptide, acetate, piperine, lycopene	RCT: 5, SR: 75	0	59	21
Improves bowel movements by increasing intestinal flora	*Bifidobacterium longum*, *Bifidobacterium bifidum* (BifiX), indigestible dextrin, genkwanin glycoside, gasseri sp., Bacillus. coagulans lilac-01, psyllium dietary fiber	RCT: 2, SR: 73	0	57	18
Helps to moisturize skin	Sodium hyaluronate, rice glucosylceramide, N-acetylglucosamine, astaxanthin, proteoglycan	RCT: 0, SR: 79	0	44	35
Supports eye function	Lutein, astaxanthin, cyanidin-3-glucoside, bilberry anthocyanin, crocetin	RCT: 1, SR: 73	0	6	68
Decreases stress and promotes healthy sleep	Theanine, glycine, L-serine, sake yeast GSP6, crocetin, GABA, cyclo-(Leu-Pro), cyclo-(Phe-Pro), cyclo-(Tyr-Pro), ornithine, isoquercitrin	RCT: 2, SR: 31	0	8	25
Suppresses oxidation of blood lipids; skin moisturization	Astaxanthin	RCT: 0, SR: 2	0	0	2
Joint function	Collagen peptide, glucosamine hydrochloride, unmodified type II collagen, S-adenosylmethionine, proteoglycan, sodium hyaluronate	RCT: 5, SR: 55	0	2	58
Reduces fatigue and stress	Theanine, GABA, Imidazole peptide, reduced form coenzyme Q10, litchi polyphenol, sesamin, histidine, BCAA, citrate, lactoferrin	RCT; 2, SR: 62	0	29	36
Alleviates ocular and nasal irritation	*O*-methylated catechin, *Bidens pilosa* caffeic acid	RCT: 1, SR: 9	0	7	3
Maintains bone health by facilitating bone metabolism	β-cryptoxanthin, isoflavone	RCT: 1, SR: 31	8	13	11
Improves memory	Gingko leaf flavonoid glycoside, gingko leaf terpene lactone, DHA, EPA	RCT: 0, SR: 46	0	11	35
Maintains peripheral temperature	Monoglycosylhesperidin,6-gingerol	RCT: 0, SR: 15	0	13	2
Maintains healthy liver function	Curcumin	RCT: 1, SR: 0	0	0	1
Helps to maintain muscle tone during aging	Leucine, 3-hydroxy-3-methylbutyrate	RCT: 0, SR: 8	0	4	4
Helps to maintain walking ability in the elderly	Black ginger 5,7-dimethoxyflavone	RCT: 0, SR: 2	0	0	2

[a] RCT; randomized clinical trial, SR; systematic review.

food business operator (including food importers, food manufacturers, food producers, and food retailers).

The CAA launched a new food labeling system for FFC in April 2015. Under this system, companies and agricultural producers can independently evaluate and describe scientific evidence of health food benefits and functional properties to promote informed consumption. This labeling system differs from FOSHU and FNFC criteria, and FFCs are foods that are described to the Secretary-General of the CAA as products whose labels bear nutritional claims based on scientific evidence, as assessed by food business operators. Hence, it is advisable to carefully check product label warnings and the information disclosed on the website of the CAA before purchasing and consuming FFCs. As of May 26, 2017, 931 FFCs were notified and received (Table 2). Companies and agricultural producers have high expectations for this labeling system and anticipate continued development of foods with labeled nutritional and health-related claims.

Characteristics of the FFC system are as follows:

1. FFCs are for people who are not suffering from disease (excluding minors, pregnant women and those planning for pregnancy, and lactating women).
2. All food products including fresh produce are subject to oversight.
3. Prior to market entry, food business operators are required to submit food safety and effectiveness information and demonstrate to the Secretary-General of the CAA that a system is in place to collect information concerning adverse health effects.
4. Unlike FOSHU, the government does not evaluate the safety or effectiveness of the submitted product.
5. The submitted information is disclosed on the website of the CAA.

Requirements of this labeling system are as follows:

1) The distributor is responsible for providing scientific evidence of food safety (prior notification system).
2) The functional ingredient has been identified using a validated method.
3) The mechanisms of action have been characterized using *in vitro* and *in vivo* testing, and in human clinical trials.
4) Scientific evidence has been acquired from human clinical trials or research reviews of functional ingredients.
5) Nutritional components contribute to maintenance and/or improvement of health.
6) Sufficient history of consumption and safety in Japan.
7) Notice is given to the CAA within 60 days of sale and is displayed on the packaging.
8) The adequate daily intake is an appropriate volume to eat.

In December, 2016, the CAA announced the results of committee investigation on nutritional information. The committee suggested that carbohydrates and saccharides, which were removed from the original functional food labeling guidelines, should be recognized as functional ingredients. However, the new functional ingredients do not include carbohydrates and saccharides, such as glucose, fructose, galactose, sucrose, lactose, maltose, starch, and glycogen, as the source of nutrients. Moreover, the committee suggested that plant-derived “extracts and secretions” (abbreviated as “extract”) should be recognized as functional ingredients, and the “extract” should be included as a specific functional ingredient which would clearly show as part of the functionality clearly. The “extract” that would label the functionality is required to be the equivalent of the “extract” that scientific evidence provided. In addition, the CAA decided that all methods for qualitative and quantitative analyses should be disclosed on the CAA website.

3. Study of health-promoting effects of agricultural products in the National Agriculture and Food Research Organization (NARO)

The Ministry of Agriculture, Forestry and Fisheries in Japan has investigated functional foods since 1989 and continues to fund functional food research. NARO assesses agricultural products that contribute to health maintenance and improvement in the elderly. To clarify the effects of functional agricultural products on human health, NARO implemented the “Research Project on Development of Agricultural Products and Foods with Health-Promoting Benefits” (study duration, 2012–2015; total budget, 2 billion yen; number of projects, 18 studies). NARO developed agricultural products expected to improve health in human clinical trials, and established production and distribution technologies in collaboration with a prefectural agricultural experimental station, a university, and private companies. In addition, NARO aims to build a database of functional agricultural products and a functional food delivery system that treats personal health conditions, to establish a nutrition care station, and to produce a functional boxed lunch (O-Bento) that contributes to the maintenance and improvement of personal health. As the results of this project, NARO contributed assessments of the health benefits of β-glucan rich barley (Aoe et al., 2017), β-conglycinin rich soybean (Nishimura et al., 2016a), rutin rich tartary buckwheat (Nishimura et al., 2016b), quercetin rich onion, β-cryptoxanthin rich satsuma mandarins (Nakamura, Sugiura, Ogawa, Ikoma, & Yano, 2016; Sugiura, Nakamura, Ogawa, Ikoma, & Yano, 2015a, 2015b), procyanidin rich apple (Shoji et al., 2017) and green tea, which is rich in *O*-methylated catechin (epigallocatechin-3-*O*-(3-*O*-methyl) gallate (EGCG3″Me)) (Imbe et al., 2016), and various other catechins (Momose, Maeda-Yamamoto, Nabetani, 2016).

Intake of high-β-glucan barley (cultivar; Kirarimochi, 2 g of β-glucan per day intake) led to significant and safe reductions in visceral fat area (VFA), body weight, BMI, and waist circumference in subjects with visceral fat obesity with VFA $\geq$ 100 cm^2 compared with the placebo group (cultivar; bgl, 0 g per day intake). Barley high in β-glucan may help prevent visceral fat obesity (Aoe et al., 2017).

Serum triglyceride (TG) levels significantly decreased in the enriched-β-conglycinin soybean (cultivar; Nanahomare) intake subject group (5.5 g of β-conglycinin per day) compared with the placebo group (low-β-conglycinin soybean) (cultivar; Nagomimaru) group (0.5 g of β-conglycinin per day) at weeks 4 and 12. In addition, for subjects whose baseline TG levels were $\geq$100 mg/dL, the levels significantly improved in the enriched-β-conglycinin soybean group at weeks 4 and 12. These results suggest that the ingestion of enriched-β-conglycinin soybean improves serum TG levels (Nishimura et al., 2016a).

Thiobarbituric acid reactive substances (TBARS) levels, body weight, and body mass index in the rutin-rich Tartary buckwheat (cultivar; Mantenkirari, 320 mg of rutin per day) intake group were significantly lower than those in the placebo group at week 8. Body fat percentage in the Mantenkirari group at week 4 was significantly lower than that in the placebo group. Thus, it was suggested that rutin-rich Tartary buckwheat intake might be effective for body weight due to its antioxidant properties (Nishimura et al., 2016b).

The 12-week consecutive administration of apple polyphenol (AP; 600 mg per day) significantly reduced the increase in glucose at 30-min post-75g OGTT ($OGTT_{30\text{-min glucose}}$) value, compared to the placebo regimen in high-normal blood glucose and borderline human subjects. It was suggested that chronic AP administration significantly improved impaired glucose tolerance (Shoji et al., 2017).

Serum LDL cholesterol levels in subjects who took *O*-methylated catechin (epigallocatechin-3-*O*-(3-*O*-methyl) gallate (EGCG3″Me)) rich green tea (cultivar; Benifuuki) were significantly lower than those who received barley infusion (not containing catechins) without green tea. Furthermore, the lectin-like oxidized low-density lipoprotein receptor-1 containing apolipoprotein B (LAB) levels in “Benifuuki” drinkers were significantly lower than those in the barley infusion group and the “Benifuuki” baseline LAB level. In subjects whose green tea intake was not regular, “Benifuuki” significantly reduced serum LDL cholesterol levels and the LAB levels compared to those observed after barley infusion consumption (Imbe et al., 2016).

In previous studies by NARO, Satsuma mandarin oranges were found to have high levels of β-cryptoxanthin, potentially reducing the risk of osteoporosis in postmenopausal women (Sugiura, Nakamura, Ogawa, Ikoma, & Yano, 2012) (Fig. 2). In addition, NARO developed the Japanese tea cultivar Benifuuki that is rich in

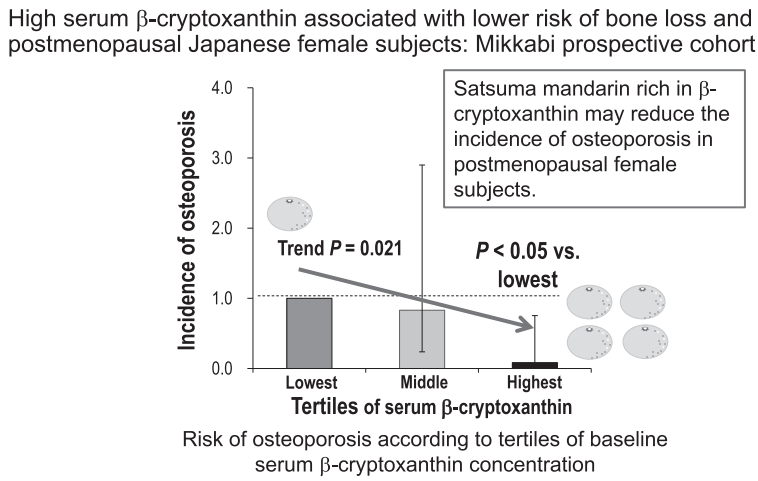

Fig. 2. Risk of osteoporosis according to tertiles of baseline serum β-cryptoxanthin concentrations in the Mikkabi prospective cohort study.

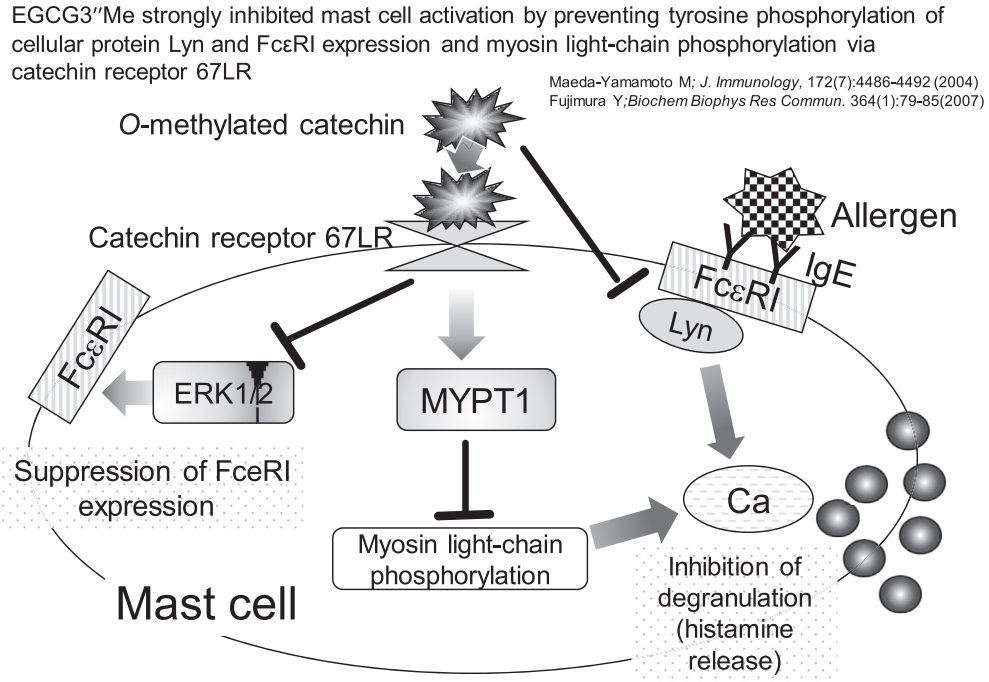

Fig. 3. Illustration of inhibitory pathways mediated by *O*-methylated catechin.

O-methylated catechin, which is present at low levels in common green tea and has anti-allergic effects (Maeda-Yamamoto, Ema, Tokuda, Monobe, & Tachibana, 2012; Sano, Suzuki, Miyase, Yoshino, & Maeda-Yamamoto, 1999). *O*-methylated catechins relieve allergies by inhibiting the release of histamines from mast cells and basophils (Fujimura et al., 2002, 2007; Maeda-Yamamoto et al., 2004). Specifically, *O*-methylated catechin inhibits mast cell activation by preventing tyrosine phosphorylation (Lyn, Syk, and Btk) in cellular proteins (Maeda-Yamamoto et al., 2004), leading to decreased FcεRI expression (Fujimura et al., 2007) and phosphorylation of myosin light chains (Fujimura et al., 2002). These data suggest that mast cell degranulation, histamine and leukotriene release, and interleukin secretion after FcεRI cross-linking are inhibited by *O*-methylated catechin (Fig. 3). In a randomized placebo controlled clinical trial, symptoms such as rhinitis and itchy eyes were reduced in subjects with symptoms of cedar pollinosis who drank Benifuuki containing 1.5%–2.5% *O*-methylated catechins (dry weight). This was equivalent to a daily total *O*-methylated catechin intake of >34 mg (Masuda, Maeda-Yamamoto, & Usui, 2014). Furthermore, subjects who started to ingest Benifuuki 1.5 months before pollen dispersal showed reduced frequencies of nose-blowing, tearing, and sore throats compared with those who started drinking Benifuuki after pollen dispersal (Maeda-Yamamoto et al., 2009). As previously mentioned, the efficacy and safety of Benifuuki green tea in subjects with mild perennial allergic rhinitis were evaluated in a double blind, randomized

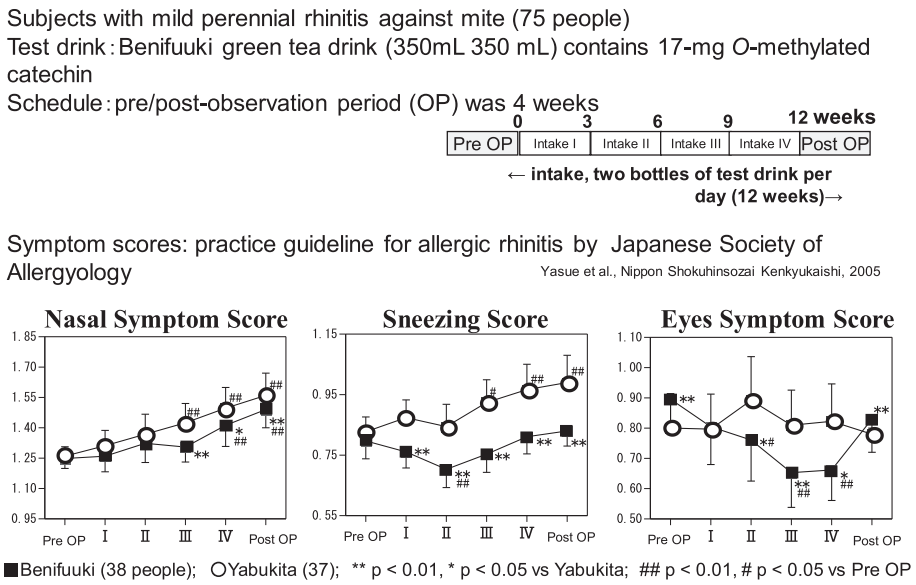

Fig. 4. RCT of the effects of regular green tea consumption on allergic perennial rhinitis.

Table 3
Agricultural products with FFC classification or possible FFC.

Agricultural products (cultivar or cultivation method)	Notified or possible function claims
Satsuma mandarin (Unshu) (fresh food) (A79)	This food contains β-cryptoxanthin, which reportedly maintains bone health; 3 mg/day (Sugiura et al., 2012)
Green tea (Benifuuki) (A67)	This food contains O-methylated catechin, which reportedly alleviates eye or nose discomforts following exposure to house dust or cedar pollens; 34 mg/day (Yasue et al., 2005b)
Soybean sprout (fresh food) (A80, A206)	This food contains isoflavone, which reportedly maintains bone health; 56 mg/day (Taku et al., 2010)
Barley (A49)	This food contains β-glucan, which reportedly decreases serum LDL cholesterol levels and improves bowel movement; 3 g/day (Behall, Scholfield, & Hallfrisch, 2004; Li, Kaneko, Qin, Wang, & Wang, 2003)
Rice (spouted brown rice) (A114)	This food contains γ(gamma)-aminobutyric acid (GABA), which reportedly maintains blood pressure at normal levels in people with relative hypertension; 10 mg/day (Nishimura et al., 2015)
Spinach from cold climate cultivars (Watanabe & Ayugase, 2015)	This food contains lutein, which reportedly increases ocular pigment contents and facilitates health maintenance of eyes (Schalch et al., 2007)
Soybean (Nanahomare)	This food contains β-conglycinin, which reportedly helps to maintain serum triglyceride levels and reduces free fatty acid levels (Nishimura et al., 2016a)
Apple (Rubysweet)	This food contains procyanidin, which reportedly helps to maintain normal postprandial blood glucose levels (Shoji et al., 2017)
Onion (Quergold)	This food contains quercetin, which reportedly helps to maintain normal cognitive function.

parallel-group study. In this study, seventy-five subjects with mild perennial allergic rhinitis that met predetermined criteria were assigned to either Benifuuki (containing 34 mg of EGCG3″Me) or Yabukita (not containing EGCG3″Me) green tea consumption groups. Subjects consumed 700 mL of tea and recorded nasal and ocular symptoms every day for 12 weeks, and visited the hospital every six weeks for consultation and blood collection. In subsequent data analyses, the scores for nasal and ocular symptoms in the Benifuuki group were lower than those of the Yabukita group, and significant differences in nasal and ocular scores were observed at weeks 7–12 and 4–12, respectively (Yasue et al., 2005a, 2005b). These data indicate that Benifuuki green tea significantly inhibits symptoms of allergic rhinitis. Moreover, no adverse effects were observed in physiological, hematological, or biochemical parameters, with normal immune responses of peripheral blood leukocytes and no subjective symptoms throughout the experiment. An additional study of nine healthy subjects without any allergic symptoms, subjects were given 700 mL of Benifuuki green tea daily for 12 weeks (Fig. 4) and no adverse effects were noted throughout the study.

Because of these results, NARO initiated research collaborations with private companies to develop Satsuma mandarin oranges and Benifuuki green tea as functional agricultural products, and “Mikkabi mikan” (notification number; A79), “Ashitanokarada” (A105), “Benifuuki green teabag” (A67), and “Memehanacha” (A69) were released as FFCs last year (Table 3). Memehanacha is a green tea that contains about 34 mg of *O*-methylated catechin in two bottles (700 mL). It is classified as an FFC because it alleviates the eye and nose discomfort caused by exposure to house dust and cedar pollens. Ashitanokarada is a fruit drink made from Japanese mandarin oranges that facilitates efficient processing of by-products. Due to technology for retention of large quantities of β-cryptoxanthin (3 mg), essential for the maintenance of bone metabolism, each pack contains the caloric equivalent of one piece of fruit and the β-

cryptoxanthin contents from three pieces of fruit.

Agricultural products for which FFC classification is anticipated, following clinical studies or systematic reviews (http://www.naro.affrc.go.jp/project/f_foodpro/2016/063236.html), are listed in Table 3.

NARO also investigated the abdominal visceral fat (AVF)-lowering effects of a functional boxed lunch (O-bento) to develop foods with combinations of functional agricultural products that prevent metabolic syndrome. Subsequently, we performed a randomized placebo-controlled trial of 159 healthy adults with BMIs of 25–30 and over 100 cm^2 AVF areas (AVF-A). Test foods were 50% barley rice and brown rice, Benifuuki green tea, and side dishes of functional agricultural products such as lycopene-rich tomato and quercetin-rich onion. Placebo controls consumed foods that did not contain functional agricultural products. Three test groups were administered only one test food each, and one test group was given all 3 test foods (rice, tea, and side dishes). All subjects consumed study foods at lunchtimes on all weekdays for twelve weeks, and the primary endpoint was AVF-A. Secondary endpoints included HbA1c and 1,5-anhydroglucitol (AG) levels. In this study, the intervention reduced AVF-A significantly and subgroup analyses of AVF-A among subjects with a median baseline AVF-A of less than 127 cm^2 showed a mean reduction of 7.9 cm^2. Moreover, among women in the rice group, AVF-A was significantly decreased by 14.9 cm^2 ($p = 0.012$). Similarly, Benifuuki tea consumption led to significantly lower serum levels of 1,5-AG and no side effects were observed, suggesting that the changes in eating habits during daily intake of functional boxed lunches can reduce AVF (Maeda-Yamamoto et al., 2017).

4. Technical problems for developing functional agricultural products

As with fresh products such as vegetables and fruit, functional ingredient contents vary greatly between cultivars, production centers (farms), cultivation times, and cultivation methods, and may deteriorate during the retail period. Accordingly, the Ministry of Agriculture, Forestry and Fisheries summarized the corresponding countermeasure as “Technical Measures for Functional Labeling” and released it online August 24, 2015 (http://www.s.affrc.go.jp/docs/kinousei_pro/reference.htm). This document describes data collection methods before FFC notification; setting methods for functional ingredient standards before notification; monitoring of functional ingredient contents after notification; and labeling nutritional claims on fresh and processed foods such as green tea, barley, rice, dried mushrooms, and freshly squeezed juice. These claims assert that the products only contain raw materials from agriculture, forestry, and fishery. Accordingly, companies and agricultural producers may add package statements such as “We manage cultivation and shipment closely so that functional ingredient contents are present within a definite range. However, actual functional ingredient contents may be lower than the lower labeled limit value due to cultivation conditions of raw fresh food.” Future developments of technologies for non-destructive determination of all functional ingredient concentrations are essential.

Finally, in clinical trials of fresh food effects, the selection and production of placebo controls is difficult because the placebo food needs to have a similar appearance to the functional food, yet be completely free of the functional ingredient. Thus, future protocols for clinical food trials require careful adaptation.

Because of information available on the CAA website, consumers can acquire more accurate information and make product choices with increased precision. Consequently, demands have increased for consumer freedom and free choice. Enhancing consumer nutritional literacy will likely facilitate the beneficial use of agricultural products as FFCs.

For public health promotion, we need to increase the availability of fresh food items containing raw materials from a variety of sources.

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