



An evidence review project for food with function claims ~Challenges of the Japan society for vascular failure for the promotion of adequate evidences for food with function claims

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Received: 22 June 2023 / Revised: 30 September 2023 / Accepted: 2 October 2023
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Keywords Food with Function Claims · Evidence review project · The Japan Society for Vascular Failure

The “Food with Function Claims (Kinousei-hyouji-shokuhinn)” system was launched in Japan in 2015 to provide the public with a wider choice of health food products that display their functionality in an easy-to-understand manner, and to enable consumers to make informed choices about the products they are consuming. Yet, the government does not examine the safety and functionality of Food with Function Claims, but the business operator is responsible for notifying the government and labeling the product with its functionality based on scientific evidence. Consequently, the question of whether the quality of scientific evidence used in Food with Function Claims application is sufficiently assured has arisen. To address this issue and to contribute people’s health, the Japan Society for Vascular

Failure (JSVF) devised an evidence review project for Food with Function Claims associated with vascular function, which will be discussed in this comment.

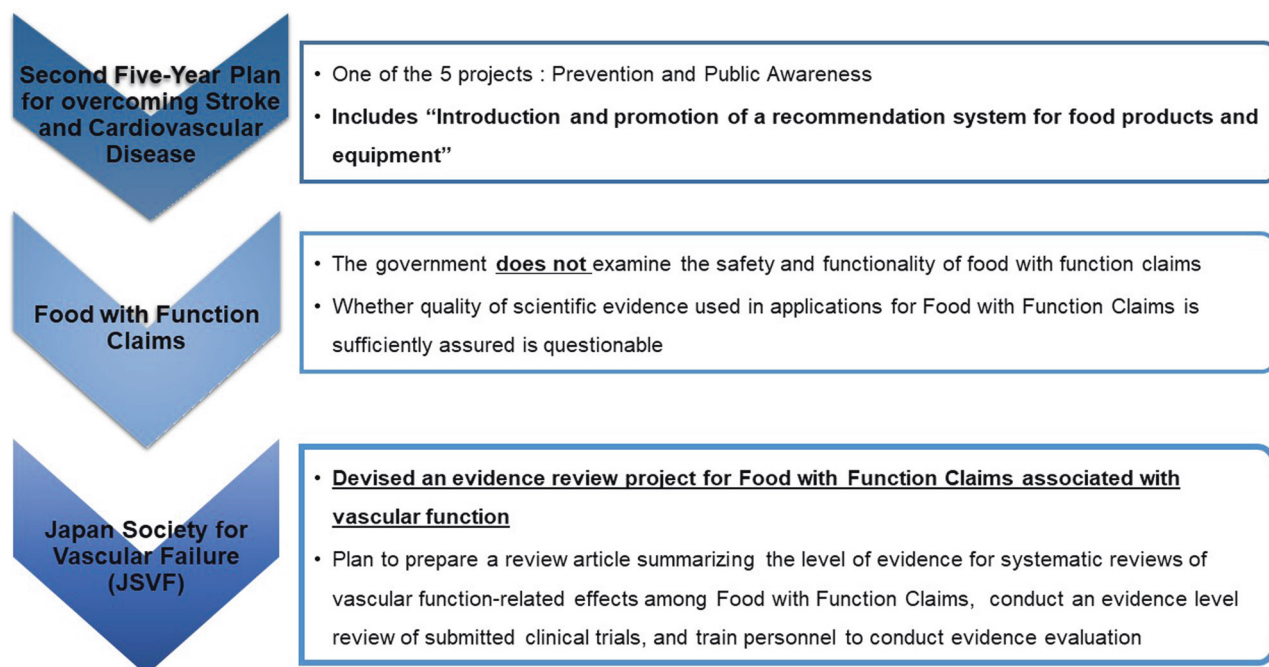
In 2021, the Japanese Circulation Society and the Japan Stroke Society have released the “Second Five-Year Plan for overcoming Stroke and Cardiovascular Disease” to elucidate the objectives and strategies for overcoming stroke and cardiovascular disease. Based on this Five-Year Plan, the two societies are advocating five projects: (1) “Human capital Development”, (2) “Enhancement of the Medical System”, (3) “Promotion of Registration Projects”, (4) “Prevention and Public Awareness”, and (5) “Strengthening Clinical and Basic Research” for the three diseases of “stroke”, “heart failure”, and “vascular

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Graphical Opinion



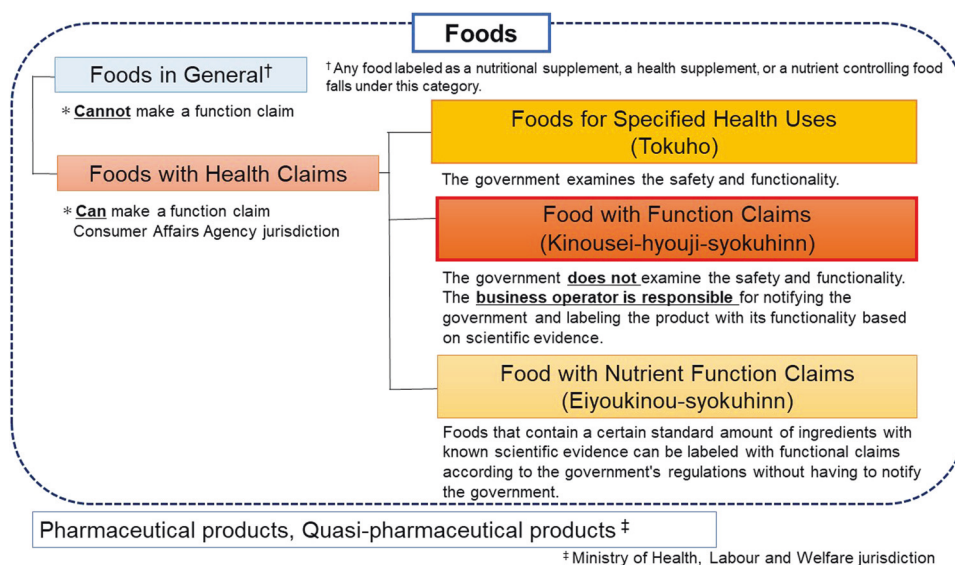
diseases”. The aspect of “Prevention and Public Awareness” includes the introduction and promotion of a recommendation system for food products and equipment [1].

The market for health foods products is expanding in tandem with the rise in health awareness in Japan. It is estimated that the size of the health food market in 2020 reached ~1.274 trillion yen and the average monthly expenditure of a household consisting of two or more individuals on health food products amounts to about 1200 yen [2]. In addition, the Comprehensive Survey of Living Conditions by the Ministry of Health, Labour, and Welfare reported that 28.3% of women and 21.7% of men consume supplement-type health foods in 2019 [3]. While health food systems may vary across countries and regions, in Japan, health foods are classified into two categories: (A) Foods in General and (B) Foods with Health Claims. Unlike pharmaceuticals and quasi-pharmaceutical products, Foods with Health Claims are not intended to be taken for the treatment or prevention of disease, but for the purpose of maintaining and improving health. Thus, the indication for Foods with Health Claims is basically for people who do not contract a disease. Foods with Health Claims are foods that are labeled with food functions in accordance with government standards for safety and efficacy and the Consumer Affairs Agency has jurisdiction over the management of Foods with Health Claims. In contrast, the Ministry of Health, Labour and Welfare has jurisdiction over the management of pharmaceuticals and quasi-pharmaceutical products. There are three types of Foods with Health Claims:

(1) Food for Specified Health Use (Tokuho), (2) Food with Function Claims (Kinousei-hyouji-shokuhinn), and (3) Food with Nutrient Function Claims (Eiyoukinou-shokuhinn). (Fig. 1).

“Foods for Specified Health Use (Tokuho)” encompass comestibles containing ingredients with health functions (e.g., to help maintain normal blood sugar, blood pressure, blood cholesterol, etc.), which have received the government’s (Consumer Affairs Agency) endorsement for labeling. The government evaluates the claimed effects and safety, and the Secretary-General of the Consumer Affairs Agency gives approval for the labelling of each food product that satisfies the requirements. Nonetheless, the time and monetary investment necessary for approval have rendered it challenging for small and medium-sized enterprises to enter the market. In contrast, the “Food with Function Claims” system was initiated in 2015 to offer the public with a wider choice of health food products that display their functionality in an easy-to-understand manner, and to enable consumers to choose products based on clearly labeled certain nutritional or health functional information. However, it should be noted that Foods with Function Claims are not subject to the government review of safety and functionality. Instead, they are labeled with function claims based on scientific evidence under the food business operator’s own responsibility. As a source of evidence for safety and functionality, they are required to submit one of the following types of evidence; (1) Clinical trial(s) with a finished product, (2) Systematic literature review(s) (SR) on

Fig. 1 Types of Health Foods Products in Japan (Foods with Health Claims)



contained functional substance(s), (3) SR(s) on a finished product. Notifications of Foods with Function Claims have increased rapidly in recent years. As of April 20, 2023, the number of notifications for Foods with Function Claims amounted to 6767 [4]. Of note is that the majority of these notifications use SR on contained functional substance(s) as the evidences of functionality, and that number amounts about 95% of total notifications. However, various problems have been pointed out regarding the notification of Food with Function Claims based on SRs on contained functional substance. For instance, the foundation for the product's functionality does not primarily reside in the final product itself. Also, the interaction of food products is unknown since they are composed of multiple raw materials, and even for specific ingredients with functionality, there is no clear evidence of the functionality of the final product. From a safety perspective, unlike Tokuho, which is generally categorized as a food product, numerous Foods with Function Claims are available in tablet or capsule form, raising concerns of potential confusion with pharmaceutical products or the risk of overdose. Furthermore, since both SRs and clinical trials were carried out under the responsibility of the notifier (food business operator), concerns arose regarding the assurance of quality of notified evidences. Considering these challenges, the Consumer Affairs Agency undertook a verification project of SRs submitted as scientific evidence of functionality in the subsequent year following the implementation of the Food with Function Claims System. The quality of SRs was verified based on the PRISMA checklist [5], and the results showed that 22 out of 45 items were inadequate in more than 40% of the SRs. Based on these results, points for improvement in SRs of notified Food with Functions were indicated, and it was hoped that the quality of SRs

would be improved in the future [6]. However, a study that re-evaluated the quality of SRs submitted prior to and after the verification project by the Consumer Affairs Agency, utilizing PRISA [5], demonstrated a significant increase in inadequacies for 13 out of 45 PRISMA items following the verification [7]. Also, the verification conducted using AMSTAR revealed that the quality of SRs after the verification project was superior to those submitted post-verification [8]. These indicated an overall decline in the quality of SRs. Moreover, the verification of clinical trials using final products submitted as scientific evidence of functionality is being undertaken by both the Consumer Affairs Agency and researchers [9, 10]. However, it has been also pointed out that numerous studies lack sufficient description according to CONSORT guidelines [11], lack transparency, and exhibit a mixture of studies with a high risk of bias. Consequently, it becomes challenging to assert that the overall quality of the research is adequately high. The prevalence of such inadequately described studies based on CONSORT, alongside the inclusion of studies lacking transparency or with a high risk of bias, has raised significant concerns. In fact, as of September 17, 2023, the Consumer Affairs Agency investigated 88 Food with Function Claims with questionable scientific evidence and 86 of them had withdrawn their notification or indicated an intention to withdraw [12]. Given these circumstances, there is a strong apprehension regarding the growing number of Food with Function Claims that have not adequately demonstrated scientific evidence.

The JSVF serves as an academic organization that specifically focuses on vascular failure, which stands as a primary causative factor for both stroke and cardiovascular disease. As part of introduction of a recommendation system for food products and equipment, as well as promotion

projects of the “Second Five-Year Plan for overcoming Stroke and Cardiovascular Disease”, the JSVF has devised an evidence review project for Food with Function Claims associated with vascular function. This project takes into account the aforementioned concerns regarding the evidence quality of Food with Function Claims. Specifically, we plan to prepare a review article summarizing the level of evidence for SRs of vascular function-related effects (blood pressure, blood glucose, lipids, vascular function, obesity, etc.) among Food with Function Claims, conduct an evidence level review of submitted clinical trials, and train personnel to conduct evidence evaluation. While various other academic societies have conducted accreditation and review programs for health food products, none of them have elucidated their evaluation methodologies and levels of evidence. Hence, there is considerable anticipation that the evidence review program initiated by the JSVF will contribute to the widespread adoption of appropriate Food with Function Claims and ultimately enhance the availability of nutritional foods in Japan.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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