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# Trends and current food safety regulations and policies for functional foods and beverages containing botanicals

REVIEW ARTICLE

# Trends and current food safety regulations and policies for functional foods and beverages containing botanicals

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**Abstract**

**Globally, the demand for functional foods and beverages has significantly increased due to socioeconomic changes, particularly in health consciousness to enhance their functionality. Functional ingredients derived from botanicals are widely used because of their phytochemical properties with health benefits. This study aims to (1) review the capabilities and challenges of botanical addition in functional foods, (2) review current policies and regulations for functional foods containing botanicals in the European Union (EU), Canada, Japan, the Republic of Korea, and Thailand, and (3) provide recommendations on effective food safety control measures for better consumer trust and trade facilitation. This critical review was analyzed from online publications and available guidelines, regulations, and control measures published by food industries and governments in the EU and the four selected countries. The result confirmed that potentialities of botanicals arise from numerous bioactive compounds with varieties of sources. However, the usage may potentially raise health risks through hazardous substances in different species or plant parts, contaminants from environments and uncontrolled processes. Inadequate knowledge of botanical formulation and the maximum limit for daily consumption may elevate health risks through food-drug interaction or adverse effect incidents. Current policies and regulations show that varieties of measures are implemented influencing both economic growth and consumer awareness. The novel finding is that countries that provide a comprehensive national food control system influence not only the growth of the functional food subsectors but also build trust in food safety among trade partners and consumers.**

*Keywords:* Botanicals, Functional foods, Policy, Regulations, Safety

## 1. Introduction

Recently, consumer behavior in food consumption turns towards the concept of good health and disease prevention, which leads to increased investment in research and development of functional foods which generally refer to food products in a conventional form that provide a specific function for health benefits beyond basic formulation for general consumers [1–6]. The global market reported that the total value of functional food products would be USD 228.79 billion in 2025 with a Compound Annual Growth Rate (CAGR) of about 8 percent since 2022 [7], while the market for functional beverages is the most popular and fastest-growing segment. In 2019, the market value of functional beverages in the US was estimated as USD 99 billion, or over half of the total market value of functional foods, while the market value of functional beverages in the Asia Pacific region was about USD 36 billion [8]. Functional beverages such as vitamin-infused water and ready-to-drink coffee with functional ingredients are highly demanded by high-income consumers during the COVID-19 outbreak and even in the post-COVID-19 scenario. Many functional ingredients with immune-boosting properties are vastly added to foods and beverages such as vitamin A, vitamin C, selenium, zinc, probiotics, and botanicals (e.g., curcumin, turmeric, flavonoids, catechins, etc.) [9].

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Rising consumption of functional foods and beverages containing botanicals results from changes in socioeconomic status, consumer preferences, and innovative technologies. For example, the population structure has continually changed to have longer life expectancy, influencing consumers' need for functional foods to boost or maintain vigorous life styles [1]. Health-conscious consumers prefer functional foods to prevent expensive medicines or healthcare services, especially during the COVID-19 pandemic [4,10]. In addition, natural ingredients with high nutritional values such as bioactive substances from berries, plant-based protein, fiber from seeds, and nuts are more attractive for creating healthier diets by consumers' perception [11]. Modern technologies can also support the formulation of valuable, sensory, and natural characteristics to provide specific health benefits raised from consumer demand [12].

Even though demand for functional beverages significantly increases in the global markets, most countries face challenges in controlling the safety of these products. Neither specific international standards nor national guidance is implemented on safety and efficacy requirements for functional foods and beverages containing botanicals, posing higher risk to consumer health [11]. Botanical ingredients differ from micronutrients and the process of food addition is more complicated. Overlapping application of some botanicals between foods and natural health products or medicines leads to negative effects on consumers' health [13]. In addition, different factors including parts of botanicals, types of solvents, and conditions for extraction of bioactive materials influence the safety of botanicals and their bioactive compounds as well as beneficial properties in the final products. The guideline for recommended daily intakes of botanical ingredients is not adequately published due to a lack of scientific information [14].

Without establishing a baseline for a limit of botanical addition, it may raise health risks to consumers who lack knowledge and have less awareness of those botanical ingredients, considered as natural sources. In fact, unexpected adverse effects are reported after over-consumption of botanicals in foods, herbal products, and traditional medicines [1,15]. Food safety concerns also arise from a misleading claim as an essential part of the product influencing consumers' acceptance and purchase intention for functional food products [3,8]. Apart from food safety concerns to consumers, the absence of clear government directions and specific standards for functional foods and beverages containing botanicals with reliable claims also affects business growth due to a bureaucratic procedure of authorization and strict requirements for claims [16,17].

To the best of our knowledge, a comprehensive report regarding the capability of botanical utilization, their safety concerns, policy direction, and food safety guidelines on using botanicals in functional foods and beverages has not yet been published. This study thus provides an overview of these issues with structured sections as follows: the following section explains the review methodology; the third section presents results and discussions in four sub-topics: (1) the potentiality of botanical addition in foods and beverages; (2) safety concerns of botanicals and addition in functional foods and beverages; (3) current food safety regulations regarding botanical ingredients and functional food products based on production, product, and presentation requirements with relevant supportive control measures; and (4) policy guidelines for functional beverages containing botanicals in the targeted one region and four countries; then, the last section provides conclusions and recommendations towards an effective food safety regulatory framework for functional foods containing botanicals to serve consumer health protection as well as facilitate trade in the global markets.

## 2. Materials and methods

One region and four relevant countries were selected for this review, namely, the EU, Japan, the Republic of Korea, Canada, and Thailand. Japan and the Republic of Korea are two major countries providing clear policy directions and regulations on functional foods and relevant claims to support their food business operators, while many pre- and post-market control measures are applied to maintain food safety in the market. The EU is the first region that published the clearly defined scope of botanicals and guidelines for the safety assessment of botanicals for addition to foods. In Canada, regulations on functional foods were recently enforced, and the criteria to differentiate functional food products from natural health products are available to reduce confusion in both food industries and consumers. Lastly, Thailand is one of the emerging countries producing botanical ingredients for application in food, drugs, and herbal products. While the Thai government encourages the commercialisation of health products containing botanicals, there are needs for improvement in definitions of functional foods containing botanicals, interface criteria with herbal products, and specific regulations with relevant claims.

Literature was collected from two main sources during 29 June 2022–10 April 2023. The first source

is scientific publications using two databases – Science Directs and Google Scholar. Key terms for the search include "functional food", "functional beverages", "fortified foods", "fortified drinks", "enriched food", "enriched beverages", "enriched drink", "botanicals", "plants" or "phytochemicals". The second source of literature includes reports, publications, relevant guidelines and regulations, and food control measures published by food industries and governments in the one region and the other four countries. Apart from food safety measures in a regular situation, additional guidelines or rules required during the COVID-19 crisis were also explored. To select the documents for analysis, three inclusion criteria were applied: (1) studies published in English language between 2001 and 2023; (2) the scope of functional foods/beverages are similar or the same as defined under this study; and (3) existing guideline and regulations at both national and international levels by both voluntary and compulsory approaches. After a comprehensive search, 125 articles and publications were included and assessed.

## 3. Result and discussion

### *3.1. Potentiality of botanicals in functional foods and beverages*

Similar to functional foods in general, a scope of botanicals for functional food products is not yet globally standardized. The term of botanicals which are summarized from European Food Safety Authority (EFSA) and some food business groups in the EU market is defined as *"fresh or dried plants including whole, fragmented, or cut parts of plants, fungi, lichens, and their preparations obtained from botanicals by various processes such as pressing, squeezing, extraction, fractionation, distillation, concentration, drying, and fermentation to provide chemical components, essential oils, or other extractives used for flavoring, functional health benefits, or other uses"* to control safety and efficacy aspects for safety assessment before addition [14]. This definition covers permitted ingredients derived from botanicals for addition in foods and beverages in many countries including Canada, Japan, the Republic of Korea, and Thailand [18–21]. Hence, this definition and scope of botanicals are applied in this study.

Botanicals have two main potentialities for increasing application to functional food products. First, numerous phytochemicals with health benefits induce more research and development of their functionalities [22]. Moreover, contents of bioactive compounds in botanicals can be altered by processing methods, influencing the biological properties. For instance, the yield of essential oil from the lemongrass plant (*Cymbopogon citratus*) was studied with four different extraction methods, indicating that the highest yield of essential oil was attained by hydrodistillation, while the different extraction methods provided different chemical profiles [23]. The process also helps transform the substances into active formats and improve the compound structure for high bioavailability, as well as remove some unwanted compounds such as pesticide residues, heavy metals, and filth in the final products [24–26]. Hence, it is necessary to specify the detail of processing methods to control both the quality and quantity of bioactive substances.

Second, a variety of botanical sources potentially serve for food additions. The sources of botanicals broadly range from historically edible plants to no history of use as human food. Many edible parts and their extracts are commercially added to food products to enhance health benefits from existing bioactive compounds such as a group of Allium plants (i.e., leek, garlic, and onion) which is regularly consumed as vegetables to create special flavor and aroma in foods. From scientific research, organosulfur compounds are found as a major phytochemical in these Allium vegetables which have physiological effects on antimicrobial, lipid-lowering, and hypoglycemic abilities. Then, the relationship between the functionalities of these bioactive substances and health benefits in humans was studied further, including extraction techniques [24].

Currently, inedible parts of food plants obtained from food loss/food waste offer alternative sources of functional ingredients to enhance by-product values, increase incomes for food business operators, as well as achieve sustainable production under the limitation of natural resources. From this trend, studies showed that potential by-products and wastes from various food industries can produce functional ingredients applied in food, cosmetic, and pharmaceutical sectors [27]. An example is by-products from the grain processing industry that can produce natural antioxidant compounds such as polyphenols, tocotrienols, and carotenoids by extracting rice bran by-products. Moreover, beta-glucans and soluble fibers can be extracted from grain flour waste for use as a source of dietary fiber in functional beverages [28].

### *3.2. Safety concerns on functional beverages containing botanicals*

Despite the development of health benefits in functional food products, some cultivars and parts

of plants can pose a safety concern to human health as they not only provide different phytochemical fingerprints but also deliver unknown substances or toxins from plants [14]. For instance, the group of pyrrolizidine alkaloids (PAs), which is a natural toxin produced against insect herbivores, can be differently found in over 6000 plant species. This compound can cause liver damage and possible carcinogenicity after ingestion [13]. To avoid diversities of bioactive compounds and unknown substances, identities of botanicals should be provided such as the scientific name, genus, species, synonyms, geographic source, variabilities, etc. [25].

For botanicals derived from by-products or food wastes which are not commonly consumed, hazardous contamination in botanicals may raise concerns about food safety such as pathogens developed during improper post-harvest practices and processing, pesticides, heavy metals, and organic matter contaminated from environments [29]. Furthermore, the step of extracting phytochemicals from inedible parts may also aggravate hazards in the functional ingredients. The study of Socas-Rodríguez et al. [27] revealed that the phenolic compounds extracted from grape by-products contain ochratoxin A, which migrates about 36–88% during the extraction process, leading to elevated carcinogenic risks in functional ingredients to consumers. To avoid producing hazardous substances during the extraction, regular monitoring and testing of processing factors are required, such as types of solvents, extraction time, extraction ratio, temperature, and extraction technique [14].

Overdose intake of some botanicals may negatively affect consumers' health. An example is the foods and beverages added with cannabis plant extracts in some countries including Thailand. Adverse effects on Thai consumers have been increasingly reported [30], while analytical testing of functional drinks added with cannabis identified an overdose of THC (tetrahydrocannabinol) contents [31]. Moreover, although many phytochemicals derived from botanicals present physiological effects on human health, not all of them are permitted for addition to food and beverages because of insufficient scientific evidence of their toxicity and efficacy [13,14]. The mixture of botanicals with either other micronutrients or botanicals may also create hazards or interfere with drug metabolism [32]. For example, milk-based products should not be added with flavonoids because milk has been reported to negatively influence the bioavailability of flavonoids [1]; while functional foods with high fiber content can cause drug interaction by reducing drug absorption, especially lipophilic medicines as well as reduce drug-metabolism of gut microbiota at GI track [33]. This indicates that basic knowledge of botanicals and scientific research will help design an appropriate formulation of botanicals with a specific statement to prevent side effects. Examples of health benefits and food safety concerns from botanical addition show in Table 1.

### *3.3. Current food safety regulations for functional beverages containing botanicals*

There are diverse regulations on functional foods containing botanicals. Some countries such as Japan and the Republic of Korea have already enforced specific regulations and defined the list of permitted botanical addition in foods with related health claims [18,19]. Presently in the Republic of Korea, more than 60 functional ingredients derived from plants and algae are allowed to add in functional health foods including beverages. These functional ingredients are made from various plant parts and processes to provide both nutrients and non-nutrient substances such as ginseng, plants containing chlorophyll, extracts from green tea, aloe, guava leaves, ginkgo leaves, banana leaves, marigold flowers, and saw palmetto fruits, etc. [19]. The Canadian regulation for supplemented food was lately published in 2022, to prevent potential risks from supplemented ingredients due to overconsumption in either general or sensitive groups of consumers [21]. This regulation stipulates the supplemented ingredients including vitamins, minerals, amino acids, and caffeine as in the "List of Permitted Supplemental Ingredients". Since this regulation is new, the list is still in the process by Health Canada based on scientific evidence [21].

On the contrary, the EU and Thailand do not enforce specific regulations on functional foods added with botanicals. However, some measures are currently implemented to ensure consumer health protection. For example, the guidelines on safety assessment are developed in the EU to evaluate any botanicals before addition to foods, while in Thailand, the list of permitted botanicals and extracts (or a positive list) for addition in beverages including coffee is published based on a pre-market consideration, except for beverages mixed with caffeine or energy drinks [20]. Therefore, in the subsequent sections, food safety requirements related to functional foods in the EU and the other four countries were explored in dimensions of botanical ingredients and final products based on production, products, and presentation requirements. It should be noted that energy drinks or

*Table 1. Examples of health benefits and food safety concerns from botanical additions in functional food products.*

| Botanicals (Scientific name and plant part) | Major phytochemical compounds | Health benefits | | | | | | | Food safety concern | Ref |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Antioxidant | Anti-inflammatory | Anti-microbial | Anti-diabetic/ anti-obesity | Antitumor/ anticancer | Neuroprotective | Other activities | | |
| *Aloe vera* : Inner pulp from the leaves | Aloresin A, lophenol, cycloartenol, emodin | x | x | | x | | | immunomodulatory | Hydroxyanthracene derivatives (aloe-emodin and emodin) are genotoxic and carcinogenic effects. | [34,35] |
| *Camellia sinensis* : leaves | Catechins (epi gallocatechin-3-gallate or EGCG) | x | x | | x | x | x | anti-anthrax lethal, vasculoprotective, cardioprotective | 1. High consumption of EGCG (≥800 mg/ day) may cause hep atoxicity; 2. Drug-interaction, especially with CYP3A4 substrates may reduce efficiency. 3. Overconsumption of polyphenols may inhibit food digestive enzymes causing gastrointestinal effects. | [35–38] |
| *Cinnamonum cassia*, *Cinnamonum verum*, *Cinnamonum zeylanicum* : barks | Methylhydroxychalcone polymer, proanthocyanidin, cinnamaldehyde, cinnamic acid, tannins, volatile oils | x | x | x | x | x | | | High amount of coumarin may cause hepatoxicity. | [35] |
| *Cordyceps militaris* : Mycelium and fruiting bodies | Cordycepin, adenosine | | x | x | x | x | | antiallergic, anticoagulant, immune boaster | 1. Drug-interaction, especially pentostatin may cause gastrointestinal and bone marrow toxicities. 2. Mycotoxins may contaminate during the fungal culture and storage. | [39,40] |
| *Curcuma longa* : rhizomes | Curcuminoids (curcumin, desmethoxycurcumin, bisdemethoxycurcumin), volatile oils | x | x | | x | x | | anti-apoptotic, anti-atherosclerotic, immunosuppressive | Overconsumption may cause tongue redness, gastrointestinal problem and atrial fibrillation. | [35,41–43] |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Ganoderma lucidum* : fruiting bodies | Polysaccharides (glycoproteins, glucans), peptidoglycans, triterpenoids (ganoderic acids, ganodermin, ganoderic acids), germanium, steroids, alkaloids | x | x | x | x | x | | hepatoprotective | 1) Drug-interaction, especially for anticoagulant, immunosuppressive, and chemotherapeutic drugs may reduce their efficacy. 2) Overconsumption may cause diarrhea, aplastic anemia, and hepatotoxicity. | [44,45] |
| *Garcinia cambogia* : fruits | Alkaloids, flavonoids, phenolic compounds, saponins, tannins, garcinol, isogarcin, hydroxycitric acid, mangostin, xanthoquimol | x | x | | x | x | | immunomodulatory | 1) Overconsumption my cause from mild symptoms (i.e., gastrointestinal problems, headaches, rash) to severe effects (i.e., liver damage). 2) Impact of sterol and steroid hormone production leads to affect some vulnerable consumers (i.e., pregnancy and children). | [46,47] |
| *Ginkgo biloba* L. : leaves | Flavonoid glycosides, terpenes lactones, ginkgolides A, B and C, bilobabides, ginkgolic acid | | | | | | x | | 1) Drug-interaction, especially anticoagulant drugs may cause haemorrhaging events 2) Long-term intake ($\geq$6 months) may cause nervous system effects (i.e., insomnia, dizziness). | [35–37] |
| *Medicago sativa* : leaves and stems | Flavonoids, isoflavonoids, saponins, lignin, phytosterols, coumestrol, alkaloids, chlorophyll | x | x | x | x | x | | anti-coagulant | 1. Overconsumption may cause photosensitivity and gastrointestinal effects. 2. Contamination of canavanine from seed may harm to Systemic lupus erythematosus (SLE) patients. | [48,49] |

(*continued on next page*)

*Table 1. (continued)*

| Botanicals (Scientific name and plant part) | Major phytochemical compounds | Health benefits | | | | | | | Food safety concern | Ref |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Antioxidant | Anti-inflammatory | Anti-microbial | Anti-diabetic/ anti-obesity | Antitumor/ anticancer | Neuro-protective | Other activities | | |
| *Momordica charantia* L. : fruits | Sterols, triterpenes (charantin, vicine, cucurbitane, momordicin II, Kuguaglycoside G), conjugated fatty acids like (a-eleostearic acid) | x | x | x | x | | x | anti-depressant | 1. Over anti-hyperglycemic activity in Diabetes Mellitus patients who regularly take medicines.<br>2. Contamination of vicine-like compounds in seeds may induce risk of red-blood cell breakdown. | [35,50,51] |
| *Panax ginseng* C. A. Meyer : roots | Ginsenoside Rb1/2/c/d/e/f and g1, panax adiol, protopanaxadiol | x | x | | x | | | | 1. Drug-interaction, especially warfarin may affect efficacy.<br>2. Drug-interaction, especially antidepressant drugs may cause adverse effects on central nervous system.<br>3. Formulation of ginseng with *Paullinia cupana,* may induce synergistic effects resulting in cardiovascular symptoms. | [35–37] |
| *Salvia officinalis* : leaves | Monoterpenes (α- and *b*-thujone, 1,8-cineole, camphor), diterpenes (carnosic acid, carnosol, rosmadial, manool), triterpenes (oleanolic andursolic acids), phenolic components (phenolic acids (caffeic, vanillic, ferulic, rosmarinic acids), flavonoids (luteolin, apigenin, quercetin) | x | x | x | x | x | x | antinociceptive, antimutagenic | 1. overconsumption may cause adverse effects (vomiting, tongue swallowing, and convulsion).<br>2. Contamination of harmful compounds from other plant parts, especially camphor, thujone, and terpene ketones may induce reproductive toxicity. | [52,53] |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Vaccinium myrtillus* L. : fruits | Anthocyanins, terpenoids (triterpenoids, tetraterpenes, iridoids), resveratrol, flavonols (quercetin, myricetin), flavanols (catechin, epicatechin), tannins, phenolic acids | x | x | x | x | | x | eye-protective | Interaction with antiplatelet drugs may reduce drug efficacy. [54–56] |
| *Zingiber officinale* Roscoe - root or rhizome | Gingerols (zingerone, zingeberol), shogaols, volatile oils (aryl alkanes, paradols, diterpenoids, diarylheptanoids, monoterpenoids) | x | x | x | x | x | x | | Overconsumption may accelerate gastric emptying and enhances antral contractions. [35,36] |

beverages added with caffeine derived from both natural sources and chemical synthesis are excluded from the scope of this study because these products have been solely controlled by specific regulations to limit sources and amounts of caffeine.

### *3.3.1. Food safety requirements for botanical ingredients*

In the EU, botanicals are controlled by various regulations depending on their applications such as food supplements, addition to food, food for specific groups, GMOs (genetically modified organisms), and novel foods [57]. Focusing on functional foods, botanical ingredients are controlled as other substances in *"the EC regulation on the addition of vitamins and minerals and of certain other substances to foods"* [58]. If botanicals fall in the scope of novel food, which referred to any food that had not historically been consumed by humans in the EU region before 15 May 1997, they shall be authorised by the European Commission before launching in the EU market [59]. The pre-market authorisation process requires a safety assessment of botanicals conducted by the European Food Safety Authority (EFSA). Then, the EFSA provided a guideline entitled *"Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements"* which focuses on botanicals and their preparations intended for use in food supplements; however, this guideline also recommends to apply for safety assessment of botanicals and their preparations used in any food and feed products [60].

In 2014, the EFSA issued another guideline named *"Scientific Opinion on a Qualified Presumption of Safety (QPS) approach for the safety assessment of botanicals and botanical preparations"* to extend a structured concept of the two-tier approach to safety assessment of botanicals in foods with consistent and transparent methodology [61]. Furthermore, a *"Compendium of Botanicals"* was developed and maintained by the EFSA as a database system to collect and share current information regarding botanicals, their compounds, and adverse effects on humans to fulfill the hazard identification and support scientific evidence on toxic substances in botanicals [57,62]. It was noted that all the EFSA guidelines and the compendium database are voluntary information to support the process of safety assessment, and not for legal enforcement.

Under the EFSA guidelines, the assessment criteria for botanicals are based on current information and knowledge relevant to such botanicals classified into Levels A and B. Level A botanicals are defined to bear a presumption of safety. Major criteria for the safety presumption are a history of

food use and the presence of hazardous compounds. Under the criteria for the history of food use, a long-term application as a food ingredient, spice, flavor, or food supplement at the level of intended use is assessed in comparison to its historical levels of intake. For hazardous compounds, reported adverse effects and other evidence related to such botanicals and an existing harmful substance are evaluated for the presumption of safety. In case of containing unknown compounds or consuming a significantly higher dose than the level of historical intake, supplemental data shall be submitted for additional assessment at Level B to appraise whether the botanical poses a safety concern or not [60]. Table 2 presents the summary of evidence and criteria of the two-tier approach to safety assessment provided by the EFSA. It is highlighted that not all listed data are required for the safety assessment of botanicals and the consideration is given on a case-by-case basis.

For supplemented foods in Canada, the safety and quality of botanicals are controlled by relevant regulations. For example, the botanical ingredients that are prohibited from adding any food products are issued in the *"list of contaminants and other adulterating substances in foods"* (called a negative list) under the Food and Drug Regulations [63]. In addition, some botanicals are listed in the supplemented food guide as inappropriate ingredients for addition in foods such as Arnica (*Arnica montana*), Cascara sagrada, Ephedra, Kava–kava, and Pleurisy root (*Asclepias tuberosa*) [64]. If any botanical or its bioactive substance either has no history of food use for humans in Canada, or has been genetically modified by various techniques, or proceeded to result in a major change in general nutrient, structure, physiological properties, or metabolism in the human body, that botanical is classified as novel food that requires safety evaluation before addition to foods or beverages for commercialisation. Regarding novel botanicals, food safety criteria and required information for pre-market authorisation are similar to those in the EU to ensure that the botanical is safe for Canadian consumers [65].

A botanical can add to foods if it is permitted in the positive list. To facilitate food business operators during the legalisation process, Health Canada develops a Temporary Marketing Authorization Letter (TMAL) as a process of temporary permission of supplemented ingredients including botanicals to add in foods under specific conditions (e.g., specification of ingredient, addition limit, and particular statement, etc.) by case-by-case consideration. Under this provisional permission, the food business operator is responsible for controlling the quality, safety, and condition of use as allowed until the legislation takes effect. Examples of botanical ingredients under the TMAL system are ginseng root (*Panax ginseng*), Cha de Bugre leaf (*Cordia salicifolia*) powder, grape seed extract, raspberry seed extract, green tea extract, and passionflower extract [66].

Unlike the EU and Canada, neither novel food regulations nor specific quality and safety requirements are implemented for botanicals in Japan. Borderlines between food and drugs including their ingredients are generally applied. Botanicals on the list of Japanese Pharmacopoeia developed by the Ministry of Health, Labour and Welfare (MHLW) such as Pueraria (*Pueraria mirifica*) root, Dioscorea (*Dioscorea batatas*) rhizome, and Nux Vomica (*Strychnos nux-vomica* L.) seed extract are prohibited from adding to food products [67]. Currently, Japanese functional foods and beverages containing botanicals are widely marketed, while the authorisation depends on the type of labeling and claims on the final products. Hence, the safety and quality of botanicals are considered on a case-by-case basis, with scientific information relating to beneficial functions for consumer health and the claims presented on the product label [68].

In the Republic of Korea, the quality and specification of functional ingredients including list of prohibited functional ingredients are addressed in the Health Functional Food Code 2021 [19]. The requirements cover standards for specifications of botanicals as raw materials, preparation and requirements for functional ingredients as a final product, specific testing methods for ensuring amount of active substance or marker compounds to meet the health benefits, and cautions for preparation or consumption. For instance, the standard and specification of ginseng consist of (1) the standard of manufacturing that specifies the part and scientific name as roots of *Panax ginseng* C.A. Meyer, method of preparation or processing, and marker compound in the final extracts as the sum of ginsenoside Rg1 and Rb1; (2) the specification of extracts that covers physical characteristics, amount of marker substance, and maximum limits of contaminants and pathogens in the functional ingredient; and (3) the prerequisite for the application to health functional food that includes a maximum limit for daily intake, specific health claim related to beneficial functions of active compounds, and warning statement for some vulnerable consumers. Moreover, a negative list consisting of 68 prohibited plants ingredients provided in this code [19]. In the case of any functional ingredient outside the approved list, the food business operator should submit application forms together with scientific information regarding the safety and functionality aspects for pre-

*Table 2. List of the required information and food safety criteria for safety assessment of botanicals [60,61].*

| Assessment level | Information | Criteria | Result |
|---|---|---|---|
| A | 1. Technical data<br>- Botanical identity (scientific and common names, part of use, source, growth conditions);<br>- Manufacturing procedure (processing flow, standardization criteria);<br>- Chemical compositions (major compounds/marker type, chemical structure, quantity, physiological properties);<br>- Specification (major compounds/marker concentration, maximum level of possible contaminants, analytical methods);<br>- Stability/shelf-life of botanicals;<br>- Intended use level<br>- Existing safety information by international or national agencies<br>2. Exposure data<br>- Historical use of human food as plant/specific compounds<br>- Exposure level in humans (maximum or average exposure with frequency and duration).<br>3. Toxicological data<br>- Possible food-drug/herbal−drug interaction;<br>- Existing heath-based guidance values (acceptable/tolerable daily intake; threshold of toxicological concern values);<br>- Available adverse effect reports | 1. Long history of use as human food with fortification level linked to the traditional consumption patterns<br>2. Absence of hazardous compounds (mainly genotoxic and carcinogenic substances) | 1. No safety concern (permission)<br>2. Safety concern (prohibition)<br>3. Need further data (go to Level B) |
| B | 1. Additional data<br>- Toxicokinetic and metabolism studies (investigation, *in-vitro* test)<br>- Genotoxicity testing (*in-vitro* test, and *in-vivo* test if the *in-vitro* test shows a positive result)<br>- Sub-chronic toxicity testing (a 90-day oral study in animals)<br>2. Other studies (depending on the result of genotoxicity and sub-chronic toxicity)<br>- Reproductive/developmental toxicity;<br>- Neurotoxicity, immunotoxicity;<br>- Chronic toxicity;<br>- Carcinogenicity | 1. Exposure level is under the safety guidance value<br>2. No other existing harmful substances exceeding a safety limit | 1. No safety concern (permission)<br>2. Safety concern (prohibition) |

authorisation [69]. Similar to the EU and Thailand, scientific evidence is required for safety assessment such as consumption data, bioavailability, and toxicity studies. Required information about functionality shall be based on human studies including intervention and observational studies, while animal studies, *in-vitro* studies, reviews, meta-analysis, or evidence data of traditional use can be used to supplement the human study only [70].

In Thailand, some regulations are implemented to control the safety aspects of botanicals. First, the Notification of the Ministry of Public Health issues a list of prohibited plants as food or food ingredients [71]. The list includes scientific names, common names with particular parts based on available scientific evidence, and the document of "*the ASEAN guiding principles for inclusion into or exclusion from the negative list of substances for health supplements*" [72]. Second, the novel foods regulation applies to botanicals that have not been significantly consumed as human foods. Under this regulation, quality and scientific evidence, especially toxicity studies, are required for consideration in safety assessment prior to approval [73]. For the safety criteria, the list of information and scientific data is largely the same as in the EU and Canadian regulations, while not all of the data are required. In the case of no safety concern, the scientific name, part of use, specification of botanical ingredients, types of food products allowed for addition with maximum limits of addition, and warning statement, if necessary, are listed for permission.

From observation of the requirements for botanical ingredients in the EU and the other four countries, three possible options are revealed based on food safety criteria: prohibited, novel, and permitted botanical ingredients. First, plants either specified in pharmaceutical products or containing hazardous compounds based on the scientific evidence of such botanicals or their bioactive compounds that show possible harmful or adverse effects to human health either short or long-term consumption are prohibited from adding to foods and join the list of prohibited or negative substances to stipulate the scientific name and part of plants that pose food safety concerns to consumer health. Apart from regulations on the prohibited substance list, the EFSA compendium of botanicals also provides scientific information on toxic compounds naturally present in botanicals that imply safety concerns. For instance, *Pueraria tuberosa* (Wild.) DC., which is a different species from *Pueraria candollei* Graham & Benth. var. mirifica (Airy Shaw et Suvatabhandhu) Niyomdham in the negative list in Thailand [71] and is reported to hepatotoxic effects and considered as the prohibited plant for food use. This example shows that different species of plant may pose different toxic compounds to human health, and the published database is useful for supporting the safety evaluation of botanicals.

Second, any botanical that neither falls on the negative list nor presents known toxic compounds is conducted the safety evaluation of botanicals by the history of using traditionally as human foods. Two major points considered from the historical uses are the period of consumption and the quantity of the compounds. For the period of consumption, some countries such as Japan, the Republic of Korea, and Canada do not specify how long the historical use is, but broadly suggest that the historical use should be as a part of diets for majority groups of consumers over generations. On the other hand, Thailand regulation requires the history of use as human food not less than 15 years in domestic or overseas markets [73]; while EU regulation requires that the experience of food use should be before May 1997 in EU countries [59]. Scientific publications, international guidelines, or official documents from government sectors such as Codex Advisory Specification for the Identity and Purity of Food Additives, reports from expert committees such as the scientific committee of Codex or EFSA journal can support the history of food use for safety evaluation [70,73]. The amount of intake of those materials are also considered from the history of food use by comparing the recommended intake and average daily intake of the same ingredient or substance from national consumption surveys or studies on consumer behaviors. In the Republic of Korea, the recommended intake of botanicals in foods, that is lower than three times of average daily intake or recommended daily allowance (RDA), or lower than high level of intake (or over than the 95-percentile value of consumer-only basis for such substance), or lower than a daily dose of medical plants is assumed as permitted ingredients [70]. In case the history of food use shows an interaction between botanical ingredients and drugs or food components, additional information on its mechanism is required such as altering absorption or metabolism of drugs or nutrients [70].

Finally, if a plant with no history of use as human food or the concentration of bioactive compounds is significantly higher concentration than the conventional level leading to raising a food safety concern, it requires additional safety evaluation or classified as novel food that shall go through the safety evaluation process. Moreover, any botanical substance extracted by methods rather than physical techniques or allowed organic solvents (e.g. water, alcohol, hexane, acetone, etc.) also requires additional safety evaluation [70]. The food safety

evaluation for botanicals considers bioavailability, metabolic, and genotoxic studies from available *in vitro* or *in vivo* tests. The repeated 90-days oral-based dosages' toxicity studies are essential for conducting exposure assessment and setting a safety limit for addition of botanicals in foods. In case of potential effects from the genotoxic or toxicity reports, additional studies on chronic toxicity, carcinogenicity, and reproductive and development toxicity may be required [70,73,74]. Recently, only the EU published safety evaluation reports and two cases were selected to elaborate the safety assessment process for botanical addition in foods. The first case is the safety evaluation of tetrahydrocurcuminoids from turmeric (*Curcuma longa* L.), which is a modified structure of curcuminoids by hydrogenation technique [75]. Tetrahydrocurcuminoids as a marker compound were tested for bioavailability by pharmacokinetic animal test and the result showed low bioavailability and main excretion through the urine; while some studies reported that tetrahydrocurcuminoids are naturally present from *in vivo* metabolism of curcumin and excreted via bile. Then, studies from bacterial reverse mutation tests and *in vitro* mammalian erythrocyte micronucleus tests were considered for genotoxicity and the results of all studies showed negative genotoxicity. A study of a 90-day repeated dose oral toxicity was considered for the safety of this compound and the result showed that no clinical signs, normality, and adverse effects were found in both control and treated rats. No observed adverse effect level (NOAEL) was set based on the highest dose tested of 400 mg/kg bw/day, and the safety level was established by applying an uncertainty factor of 200 to 2 mg/kg bw/day for human use. This can convert to 140 mg/day of ingredients from an average body weight of 70 kg in the EU population.

The second case was a safety evaluation of water-extracted powders derived from the dried root of *Eurycoma longifolia* [76]. This botanical is commercially added to herbal products in several countries, especially in the South-East Asia region. Major compounds are glycosaponins and eurycomanone, considered as markers, whereas more than 85 substances have been detected in the plant extracts. The bioavailability test was evaluated from *in vitro* and *in vivo* studies that present low bioavailability of eurycomanone in the extravascular fluid of rodents, however, the genotoxic study by *in vitro* chromosomal aberration test and *in vivo* comet assay showed cytotoxicity at the dose of 2500 μg/mL and potential DNA damages. Even the human studies were available, most studies focused on health benefits without safety evaluation. In conclusion, EFSA did not provide a safety limit for this extract. These examples presented that a set of scientific information is generally required for safety consideration in the EU and the other four countries, however, the safety limit from evaluation may be different based on the exposure evaluation that considers consumer behaviors (such as diet patterns, genders, body weight, etc.) and a national consumption data. The main challenge for safety evaluation for botanicals is insufficient information to conduct safety evaluation, but publication and sharing reports of the safety assessment is an alternative solution. After the safety assessment, in the case of a safe botanical for addition, permission would be provided by the competent authority to food business operators. In contrast, if the assessment shows a hazard for consumption, it is classified as a prohibited ingredient and further published in the negative list. Fig. 1 summarizes a decision tree for the three options resulting from food safety criteria for botanical ingredient addition in one region and four countries.

### *3.3.2. Safety requirements for functional foods and beverages containing botanicals*

In general, responsible authorities of each country establish food regulations in line with the international Codex standards covering both general and commodity-specific standards [77]. General regulations refer to the requirements applicable to all food categories such as those for good hygienic practices, contaminants, additives, and labeling, while commodity-specific regulations are applicable to a particular food product to provide certain identity, quality, and safety such as those for fats and oils, honey, fish sauce, and beverages, etc. In EU and the other four countries studied, both general and specific regulations apply to control the aspects of production, product, and presentation, which are elaborated in the following subsections.

*3.3.2.1. Production requirements*. EU and the other four countries recognize the importance of implementing quality assurance systems in every step of the food supply chain through regulations on production of food, including functional foods and beverages, under different regulatory systems [68]. Functional foods and beverages sold in EU markets shall be produced under the principles of the Hazard Analysis and Critical Control Point (HACCP) system, which applies to both domestic and imported functional food products. The HACCP requirements are in line with the relevant Codex standards for ensuring consumer health protection

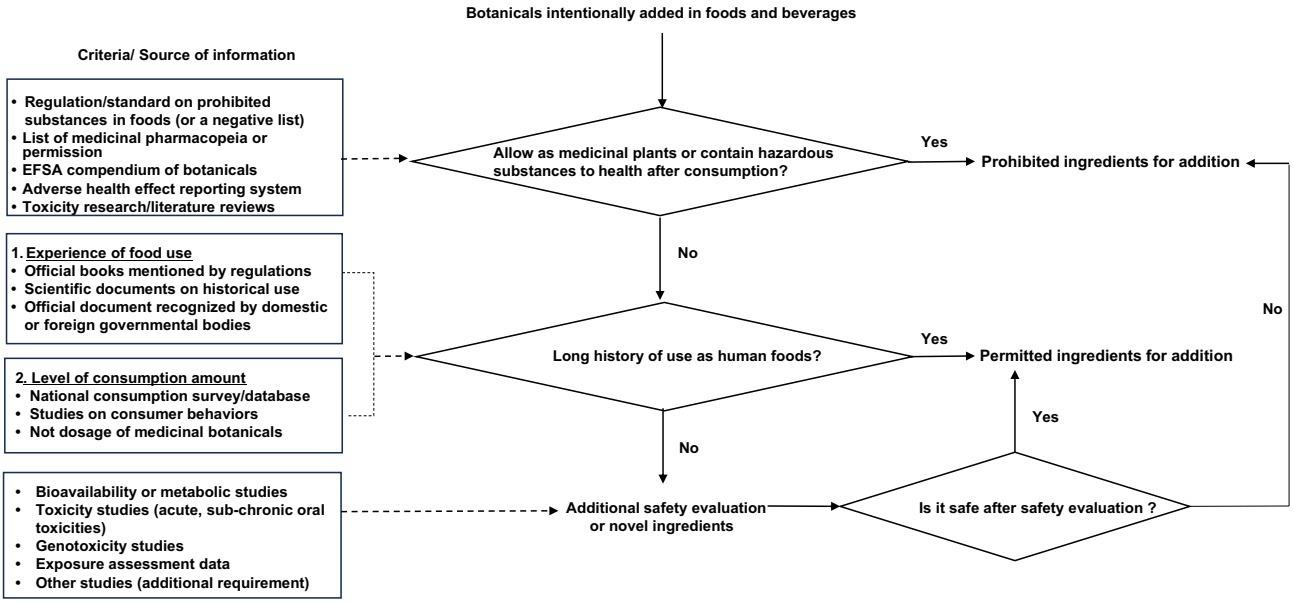


*Fig. 1. Summary of the three options resulting from the safety criteria for botanical ingredients in the EU and the other four countries.*

and fair practice in food trade [78]. Similarly, the HACCP requirements under the Food Sanitation Act are fully implemented in all food industries including the manufacturing of health foods exported to the Japan market [68].

On the other hand, quality assurance systems to produce food products in Canada, the Republic of Korea, and Thailand are based on the Good Manufacturing Practice (GMP) system, which also applies to functional foods and beverages [68,79,80]. During the COVID-19 crisis, many countries including Thailand voluntarily developed a remote auditing system for the inspection and monitoring of food factories as part of social distancing measures [81]. This procedure supports both inspectors and food industries to provide sufficient facilities and adequate evidence for auditing food establishments based on the requirements for quality assurance.

*3.3.2.2. Product requirements*. Many general requirements applicable to functional foods and beverages in the same way as for other food products. For example, regulations on contaminants in food define maximum limits of heavy metals and mycotoxins in vegetables, fruits, legumes, and cereals as ingredients for foods and beverages [63,82,83]. Another example is the maximum residue limits of pesticides that are possibly present in botanicals since cultivation. All regulations provide both lists of pesticides and types of agricultural commodities to be controlled, while the hazardous pesticides that are not allowed to be present in any food commodities are also specified in the regulations [84–88]. Moreover, other general requirements including for food packaging, food additives, and pathogens are regularly applied to functional foods and beverages containing botanicals.

Apart from the general regulations, the Republic of Korea and Thailand implement commodity-specific regulations especially on beverages to ensure both the quality and safety of the products in their markets. Under the Korean Standards for each food product [89], specifications for beverages include scope of classes and types, specific requirements for heavy metals and microbial, preservatives, and a description of testing methods. In Thailand, functional beverages are mainly regulated under the Notification of the Ministry of Public regarding beverages in sealed containers, which encompass carbonated drinks, fruit and vegetable juices, and water-based beverages in both ready-to-drink and dried forms. The additional requirements for both quality and safety parameters under this notification are microbiological limits, moisture content for dried beverages, and the maximum quantity of alcohol contained in ingredients naturally or generated through the production process [90]. Hence, the food industries must comply with both the general and product requirements for functional beverages to maintain the quality and safety of products.

*3.3.2.3. Presentation requirements*. For labeling requirements under EU regulations, the mandatory information for prepackaged foods complies with the Codex standards with supplementary requirements such as the actual alcoholic strength by volume for any beverage containing more than 1.2% of alcohol by volume, and a specific warning

statement related to botanical ingredients, as necessary. An example is beverages containing glycyrrhizin acid or its ammonium salt derived from the addition of liquorice plant (*Glycyrrhiza glabra)*. The specific statement required on the label depends on the concentration of the substances in the product. With the concentration of 10 mg/L or above, a statement *"contains liquorice"* shall be displayed either in the ingredient list or the name of the food product. With the concentration of 50 mg/L or above, the statement *"contains liquorice – people suffering from hypertension should avoid excessive consumption"* should be present after the list of ingredients or accompany the name of the food [91].

In Thailand, the labeling requirements for functional foods for direct sale to consumers comply with the Codex standards, while additional requirements are mandated such as a list of food additives, a food serial numbers for presenting the numbers of production or importation licenses, product registration, and warning statements based on the addition of specific ingredients [92]. Similarly, Japan's Food Labelling Act requires ten mandatory sets of information to appear on the label of processed foods and beverages, which mostly complies with the Codex standards, while two sets of information are additionally required, namely, (1) a list of food additives that are displayed in descending order of weight on a separate line from other ingredients, and (2) a list of certain genetically engineered ingredients that are labelled as *"GE"* [93].

Canada and the Republic of Korea mandate specific labeling in relation to the functional ingredients and finished products. Under the Canadian regulations, a food facts table is mandated for all supplemented foods to bear information including serving size, total calories, amount of fat, saturated fat, and trans-fat, a sum of saturated and trans fatty acids, cholesterol, sodium, carbohydrate, fiber, sugar, protein, potassium, calcium, iron, statement of daily value percentage, and supplemented ingredients with the declaration statement as *"supplemented with"* [94]. Likewise, the specific labeling standards for health functional food in the Republic of Korea are administered to display the following information on their labels: (1) letters of *"health functional food"* with a specified symbol or letters of *"health functional food ingredient"* for a functional ingredient; (2) the name of the product; (3) the name and address of the food industry; (4) sell-by-date and storage method; (5) net content; (6) nutrition and function information covering nutrition facts and details of functional ingredients and their contents; (7) the consumption amount and warning statement; (8) list of raw materials; and (9) a statement that the product is not a pharmaceutical product that prevents or heals diseases [95]. This literature review discovered that the specific declaration linked with functional food products helps consumers easily differentiate a product category from other health products as well as raise consciousness to acknowledge what botanical ingredient is added in the food product.

For requirements for nutrition labels and health claims with reference to the Codex guidelines, the EU, Canada, and Thailand enforce general regulations on all food products including functional foods and beverages. However, the criteria and procedures for pre-market authorisation are different [96–98]. For example, Health Canada approves a functional claim *"promote laxation"* for foods containing 7 g of fiber from coarse wheat bran for one serving size [97], while the Thai FDA permits a claim "Dietary fiber contributes to an increase in fecal bulk and stimulates the bowel movement" in food product containing 2.5–4.75 g of fiber per one serving size [99]. Moreover, functional beverages in both ready-to-drink and dried forms directly sold in the Thailand market shall display the label of Guideline Daily Amounts (GDA) as a Front-of-Package labeling to present the nutrient content of energy, sugar, fat, and sodium in the entire package. The GDA label is mandated with an aim to raise consumer awareness of good diets and support the reduction of nutritional problems resulting from food consumption [100].

In Japan, different types of claims are regulated with flexible criteria and procedures for pre-market authorization. There are three categories of health claims for functional food products. First, the Food for Specified Health Uses (FOSHU), or *"TOKUHO"* refers to foods officially entitled to a claim related to functional ingredients in relation to their physiological effects on the human body to the extent of claiming reduction of disease risks. The FOSHU requires pre-approval by the Consumer Affairs Agency (CAA) in consultation with the Consumer Commission, the Food Safety Committee, and the MHLW. In addition, a sample of the product should be analyzed by the National Institute of Health and Nutrition. The approved product shall be labelled with the TOKUHO logo [68]. The second type of health claim is for the Foods with Nutrient Function Claims (FNFC), which are related to the functions of nutritional ingredients in the human body. Recently, there are 20 main ingredients including vitamins, minerals, and omega-3 fatty acids allowed for the FNFC. To carry the FNFC, food industries are not required to submit any sample, or document for pre-authorisation, or display a specific logo. They

can add to food with nutrients in the permitted range to declare the related nutrient functions as well as specified warning statements [101]. Lastly, the Foods with Function Claims (FFC) refer to a claim related to functional ingredients other than nutrients specified in the FNFC on improvement or maintenance of good health [101]. Examples of functional substances endorsed by the FFC are probiotics, gamma-aminobutyric acid (GABA), astaxanthin, soy isoflavone, bilberry extract anthocyanin, *Ginkgo Biloba* flavonoid glycoside, and terpene latone, etc. [102]. The FFC is prohibited from claiming alcoholic beverages and foods with excess nutrient contents. Unlike the FOSHU, the FFC does not require pre-market authorisation. However, the food industries must submit specifications of products and production, as well as scientific information of the specified claim based on clinical trials with human subjects, or data from systematic reviews of human studies, to the CAA at least 60 days before the product launch in the markets [68].

Under the Health Functional Food Act of the Republic of Korea, positive claims regarding health benefits are available for food industries if they comply with the standards and specifications of permitted functional ingredients listed in the code of health functional foods approved by the MFDS (Ministry of Food and Drug Safety) [19,69]. For other functional ingredients and claims outside the approved list, the food business operator should submit application forms together with scientific information regarding the safety and functionality aspects of the functional ingredients to the MFDS for pre-authorisation [69]. The evaluation process takes less than 120 days upon receipt of the application. The period can be extended, if supplementary data are required [70]. Comparative criteria of botanical addition in functional foods and beverages between the Republic of Korea and Thailand in Table 3 present various requirements of botanical ingredients, preparation, and presentation of claim and warning information to consumers.

In the EU and the other four countries, the addition criteria for botanical ingredients are basically allowed on the basis of the safety principle as mentioned in item 3.3.1. Apart from safety evaluation, to claim health benefits, the addition of botanical ingredients is also considered from scientific information between botanical ingredients and health conditions. Currently, neither specific guideline nor standards for functionality evaluation is published in the EU and the other four countries, but a guideline for preparing scientific substantiation is generally provided depending on their regulations. In the EU, Canada, and Thailand, submission of the dossiers from clinical studies, or meta-analysis in humans is generally required for all health claims for efficacy evaluation and approval, whereas efficacy studies such as meta-analysis in animals or *in vitro* are only acceptable as supportive evidence. An example of efficacy reports is plant sterols in relation to blood cholesterol maintenance [103] by EFSA. Meta-analysis in clinical trials is major evidence to evaluate beneficial effects between food added with plant sterols (about 0.8–1.0 g/day or maximum of 2 g/day) and a significant reduction of LDL-cholesterol concentration, however, these studies did not show a direct effect of plant sterols to reduce coronary heart disease. Among of clinical studies, only one study conducted the efficacy of plant sterols by adding in fat-based foods. Then, the European Commission as the policy-maker considered the EFSA report and allowed the other functional claim for plant sterols as *"contribute the normal blood cholesterol levels"* to food added this ingredient with a daily intake of at least 0.8 g of plant sterols [104]. Plant sterol with its functional claim to *"contribute to the reduction of cholesterol absorption"* is also allowed by the Thailand regulation newly published [105] for dairy products and fat-based foods containing this ingredient (0.8 g of plant sterol/100 g) with a warning statement to not consume over than 2 g/day and not recommend to some consumer groups, however only the EU published the scientific report on efficacy evaluation.

In contrast, Japan and the Republic of Korea provide flexible requirements for scientific information based on categories of the claims. Only claims of FOSHU and disease risk reduction strictly require reliable evidence on intervention studies or meta-analysis in humans [69,102,106,107]. FFC and other functional claims can be solely considered from adequate animal and *in vitro* studies, if they can show a relationship between physiological functions and health effectiveness in relation to human metabolism [102,106]. There is a limitation to access reports of the efficacy evaluation or database system in Japan and the Republic of Korea, only the permitted list of other functional claims is available for food business operators and consumers. For instance, other functional claims for liver health protection, body fat reduction, blood glucose control, joint/bone health, and gut health are mostly popular in the Korean markets [106,107], while, health foods with FFC in relation to triglyceride level, GI tract, blood sugar level, body fat, and eye's function are mainly launched in the Japanese market [107]. The flexible procedures result in significantly increasing the functional foods in both

*Table 3. Examples of permitted botanicals for addition in functional foods addition sold in the Republic of Korea [19] and Thailand [20,92].*

| Botanicals (Scientific name and plant part) | Country | Specification of functional ingredients | | | Permitted claim statements | Warning statements |
|---|---|---|---|---|---|---|
| | | Process requirement | Active substances | Addition requirement | | |
| *Aloe vera* : Inner pulp from the leaves | Republic of Korea | n/s | Total polysaccharides | 100−420 mg of total polysaccharides/ day | May help to maintain healthy skin, maintain healthy gastrointestinal function, support immune system | n/s |
| | Thailand | Fresh or dried form | n/s | n/s | − | 1) Should not be consumed by children;<br>2) Not a medical food", "Stop to consume when unusual symptom occurs |
| *Camellia sinensis* : leaves | Republic of Korea | Water/ethanol/ water−ethanol/ ethyl acetate extraction | EGCG, catechin | ≤300 mg of EGCG/ day; 0.3−1 g of catechin/day | May help to support anti-oxidant activity, reduce bodyfat, maintain healthy blood cholesterol level | 1) Children, pregnant and lactating women should avoid to intake;<br>2) Consult a health care practitioner prior to intake if you are taking medicines or having liver disease;<br>3) It may cause side-effect such as anxiousness, insomnia or etc., due to caffeine;<br>4) Intake after meal;<br>5) Be careful for taking food containing caffeine;<br>6) Consult a health care practitioner and stop intake if you are having adverse event. |
| | Thailand | Water/water-ethanal extraction | Flavonoids, catechins, EGCG, Epicatechin | ≤1800 mg of extract/day[a] | − | n/s |

(*continued on next page*)

*Table 3. (continued)*

| Botanicals (Scientific name and plant part) | Country | Specification of functional ingredients | | | Permitted claim statements | Warning statements |
|---|---|---|---|---|---|---|
| | | Process requirement | Active substances | Addition requirement | | |
| *Cinnamonum cassia*, *Cinnamonum verum*, *Cinnamonum zeylanicum* : barks | Thailand | Water extraction | Tannins, cinnamaldehyde, polyphenols | ≤500 mg of extract/day[a] | − | n/s |
| *Cordyceps militaris* : Mycelium | Thailand | Dried or powder form | Cordycepin ≤0.3 mg/g and adenosine ≤1.7 mg/g | ≤230 mg/day[a] | − | n/s |
| *Curcuma longa* (Turmeric) : rhizomes | Thailand | Water extraction | Curcuminoid | ≤2 g of extract calculated as crude/day; ≤50 mg of Curcuminoid/day | − | n/s |
| *Garcinia cambogia* : fruits | Republic of Korea | Water/ethanol/water−ethanol extraction | Hydroxycitric acid | 0.75−2.8 g of hydroxycitric acid/day | May help to reduce body fat by inhibit carbohydrates from being synthesized into fat | 1) Children, pregnant and lactating women should avoid to intake;<br>2) Consult a health care practitioner prior to intake if you are taking medicines or having liver, heart, kidney diseases, allergy and asthma;<br>3) Consult a health care practitioner and stop intake if you are having adverse event. |
| | Thailand | Water extraction | Hydroxycitric acid, phenolic compounds | ≤3.3 g of extract calculated as crude/day; ≤1.5 g of hydroxycitric acid/day | − | n/s |

| | | | | | | |
|---|---|---|---|---|---|---|
| *Ginkgo biloba* L.<br>: leaves | Republic of Korea | Water/water−ethanol extraction | Flavonol glycoside, ginkgolic acid | 28−36 mg of flavonol glycoside/day; ≤5 mg of ginkgolic acid/kg of extract | May help to improve memory, improve blood flow and circulation | 1) Pregnant and lactating women, children, perioperative patient should be careful for intake;<br>2) People who are taking medicine (related with blood coagulation) should be careful for intake |
| | Thailand | Water/water−ethanol extraction | Ginkgo flavone glycosides, terpene lactones, bilobalide, ginkgolides | ≤120 mg of extract/day; ≤5 mg of ginkgolic acid/kg of extract | − | 1) May slow blood clotting;<br>2)Should not be consumed by children and pregnant woman |
| *Ganoderma lucidum*<br>: fruiting bodies | Republic of Korea | Water extraction | β-glucan | 24−42 mg of β-glucan/day | May help to maintain healthy blood flow | n/s |
| | Thailand | Water extraction | Triterpene, Triterpenoids, polysaccharides | ≤1.5 g of extract calculated as crude/day; ≤20 mg of triterpene/day | − | n/s |
| *Medicago sativa*<br>: leaves and stems | Republic of Korea | Pressed and dried | Chlorophyll | 8−150 mg of total chlorophyll/day | May help to maintain healthy skin, anti-oxidant activity | n/s |
| | Thailand | Water extraction | Chlorophyll, flavonoids, Flavone | ≤3.45 g of extract calculated as crude/day | − | n/s |
| *Momordica charantia* L.<br>: fruits | Thailand | Fresh or dried | n/s | n/s | − | n/s |
| *Panax ginseng* C.A. Meyer<br>: roots | Republic of Korea | Water/ethanol/water−ethanol extraction. Concentration or fermentation after extraction | Sum of ginsenoside Rg1 and Rb1 | 3−80 mg of sum of ginsenoside Rg1 and Rb1/day | May help to support immune function, relieve from fatigue, maintain bone health | The individual who are taking medicines related with diabetes and/or blood coagulation should be cautious to intake |
| | Thailand | Water/water−ethanol extraction. | Ginsenosides | ≤2 g of extract calculated as crude/day | − | n/s |

(*continued on next page*)

*Table 3. (continued)*

| Botanicals (Scientific name and plant part) | Country | Specification of functional ingredients | | | Permitted claim statements | Warning statements |
|---|---|---|---|---|---|---|
| | | Process requirement | Active substances | Addition requirement | | |
| *Vaccinium myrtillus* L. : fruits | Republic of Korea | Ethanol/water −ethanol extraction. | Anthocyanosides | 160–240 mg as bilberry extracts (50–108 mg as anthocyanosides) | May help to improve eye fatigue | |
| | Thailand | Water extraction | Anthocyanin, anthocyanidins, Proanthocyanidins | ≤166 mg of extract/ day | – | n/s |
| *Zingiber officinale* Roscoe : rhizomes | Thailand | Water extraction | Gingerols | ≤1 g of extract calculated as crude/ day | – | n/s |

**Remark:** n/s = not specified; - = prohibited and required further claim authorization.
[a] Addition in beverages (excluded energy drinks) is permitted only.

countries as the result of policy direction [69,102,106,107].

From EU and the other four countries, the three aspects of regulations based on the comprehensive overview of current food safety regulations for functional beverages containing botanicals were summarized in Table 4.

### 3.3.3. Supportive control measures

Some countries enforce specific control measures for functional food products, especially Japan and the Republic of Korea. For instance, in Japan, reporting of adverse health events is required of all food business operators who commercialize functional foods with FFC labels. This system is one of the six criteria for the permission by the FFC to collect cases from Japanese consumers and evaluate defects found in both quality and safety aspects [68]. Similarly, the functional health food act in the Republic of Korea was amended in 2014 to mandate food business operators to register in the *"tracking management of records on functional health foods"*, which is used to record information from manufacturing and importing states to the sale of functional health food products for proactive traceability in case of a health problem [108]. Moreover, a *"Health Functional Food Side Effect Reporting System"* has been established by the MFDS and managed by the National Food Safety Information Service to collect incident reports regarding side effects from consumers who possibly suffer from consuming functional health products. Consumers can immediately report the adverse effect through an online number "1577–2488" as mandated information on the label of health functional foods [109].

No specific adverse effect reporting system for functional foods in Canada and Thailand. For instance, Health Canada provides the adverse effect reporting system are currently provided for some market health products such as medicines, medical devices, natural health products, cannabis, and biological product (i.e., vaccines and fascinated blood products) [110]. Thailand also implements the post-marketing safety reporting system responsible by Health product Vigilance Center (HPVC) for human drugs, narcotics, medicinal neuro-psychotropic medicines, and vaccine that excluded functional foods [111]. Even some traceability mechanisms are provided for functional foods and beverages such as the TMAL by Health Canada or the food serial numbers recording registered premises and product information by the Thai FDA, lack of linkage with the specific adverse effect reporting system for this particular product may reduce the effectiveness of traceability from product

*Table 4. Summary of current regulations in EU the other four countries related to functional foods and beverages containing botanicals in the aspects of production, products, and presentation.*

| Requirements | | EU | Canada | Japan | Republic of Korea | Thailand |
|---|---|---|---|---|---|---|
| 1. Production | | HACCP | GMP | HACCP | GMP | GMP |
| 2. Products | 2.1 Raw materials (botanicals) | 1) Negative and strict list of substances<br>2) Novel foods | 1) Negative list of substances<br>2) Permitted substance list<br>3) Novel food | Not specified | 1) Negative list;<br>2) Positive list of substances | 1) Negative list<br>2) Positive lists (case-by-case basis)<br>3) Novel foods |
| | 2.2 Finished products (beverages) | General requirements | General requirements | General requirements | Both general requirement and regulation for beverages in sealed containers | Both general requirements and regulation for beverages |
| 3. Presentation | 3.1 Label | General label;<br>Nutritional label | General label;<br>Supplemented food format label | General label;<br>Nutritional label | General label;<br>Nutritional and Health functional food label | General label;<br>Nutritional label;<br>and GDA label |
| | 3.2 Nutrition label and claims | Nutrient claims<br>Health claims (Function health claims/Risk reduction claims/Claims referring to children's development) | Nutrient claims<br>Health claims (Function claims/Nutrient function claims/Probiotic claims/Disease risk reduction claims/Therapeutic claims) | Nutrient claims<br>Health claims (FOSHU/FNFC/FFC) | Nutrient claims;<br>Health claims (Nutrient function claims/Other function claims/Disease risk reduction claims) | Nutrient claims;<br>Health claims (Nutrient function claims/Other function claims/ Disease risk reduction claims) |

Remark: general requirements refer to food safety requirements that apply to all food products including beverages such as food additives, food pathogens, food contaminants, and food packaging, etc.

to consumer and absent supportive data for the risk-based inspection program. In EU, no specific adverse effect reporting system for functional foods, but the Rapid Alert System for Food and Feed (RASFF) legally developed in 2002 is mainly conducted for all food products including functional food as the platform of all member states to share information about health risks to human and animal, tracking the products on the EU markets, and required control measures by member states [112]. This system provides not only food safety management for incident or crisis situation but also the information source for the risk-based inspection plan.

Apart from the adverse effect reporting system, risk-based inspection and risk-based sampling plan also support effective post-market control measures with sufficient resource allocation [113]. Similar to other food products, a risk-based inspection is developed from key factors such as history of non-compliance establishment and product/ingredient characteristics, number of production or consumption, epidemiological incidents, as well as information from the adverse effect reporting system. Even though consumption demand for this product significantly increases in the global market, functional foods are regularly inspected as similar to other food products in the EU and the other four countries. This may be caused by no specific requirement for functional foods; while some preventive measures have been taken such as pre-approval or safety evaluation of botanical addition before launching to the markets [114]. In the Republic of Korea, *"the preliminary prediction import inspection system (Observation & Prediction by Endless Risk Analysis: OPERA)"* is conducted to classify risk-based food products that are imported from other countries. The categorization is based on the on-site inspection of the food premises, volume of the importation, and inspection results. The system provides a history-based inspection plan as well as designs an adequate sampling plan for imported foods including functional food products; whereas, annual reports showed the number of inspected food, livestock, and marine products were increased in 5 years (2013–2017) [115]. Although no specific report of non-compliance with functional foods, it still recommends implementing the risk-based inspection for functional foods by collecting more data from the adverse effect reporting system, recall system, and consumers' complaints regarding the effects of food/drug interaction [114].

The sampling plan provides a statistical technique to take representative samples for monitoring the safety and quality of the food products. A good sampling plan consisting of appropriate sample size and selection method should be designed based on the purposes [116]. From available information, only the Republic of Korea specifically issued the random sampling tool for functional foods. This guides food inspectors to collect appropriate samples, especially imported agricultural ingredients that pose potential risks to consumer health such as pesticide residues, contaminants, and pathogens, as well as to monitor the quality of the plant identities and bioactive compounds [19]. The guide recommends collecting 1 of 1000 boxes of agricultural products for sample collection as well as a random number table to casually select a sample from the whole population. Hence, by following this guide, a selected random number provides a direction to randomly take a sample for further testing. While the guide does not explain the methodology for sampling plan development, the MFDS elaborated that this sampling plan is designed from the data of OPERA and regularly revised to ensure the risk-based perspective. This is a beneficial study to other countries to develop and implement risk-based inspection and sampling plans based on the country situation.

### *3.4. Policy guidelines related to functional foods and beverages*

One of five elements of the national food control system is a food safety policy which plays an important role in not only increasing consumer trust but also facilitating fair trade practices [113]. For functional foods and beverages, the policy can drive the economic trend, while a good regulatory system should be continuously maintained for ensuring consumer trust in the safety and efficacy of functional food products. Practices in this positive direction by the national policy are observed in Japan and the Republic of Korea. Japan was mentioned as the first country that provided a food policy and strategy for functional foods because of the aging population crisis. Japanese consumers prefer to consume functional foods to maintain healthy conditions rather than pay medical costs [68,117]. Then, the Japanese government provided a set of regulatory systems for FOSHU and FNFC in 1991, after the 3-year preliminary period [117]. This policy facilitates Japanese industries to develop functional foods and beverages supporting the high consumer demand, resulting in forming the largest market in the Asia Pacific region [68]. Moreover, after the enforcement of the FFC in 2015, a more flexible registration process and data submission led to growing the domestic market of functional foods. From 2015 to 2018, about 1412 FFC products were launched, ranging from processed foods to fresh

agricultural commodities to encourage consumption of a variety of foods with vivid information on the health benefits [117].

In the Republic of Korea, the Health Functional Foods Act was developed and came into force on January 31, 2004, to reduce problems with medical costs and improve national consumer health. After the policy provided clear scope and regulations, it led to the economic growth for industries of functional foods and beverages about 5.5 times in 2011 and continuously increased in recent years at an average annual growth rate of 11.8% from 2016 to 2020 [115,118]. A major policy direction is to enforce reasonable regulations that facilitate product innovations and promote consumer health and trust. Key strategies are to support technical assistance for food industries, inspect non-compliant products, and educating consumers. The Korean government supports technical assistants working in each food industry from the early stage of product research and development, especially in establishing a specification of functional ingredients including valid testing methods for their production. For a novel ingredient, the government provides advisory experts to review and evaluate the safety and quality of the new ingredient for developing specific standards. Apart from technical assistance, the government routinely inspects high-consumption functional foods, especially their labels and advertisement, to maintain consumer confidence. Education programs and reports of adverse events are normally conducted and published to raise consumer awareness [118].

National policies for functional food products as in Canada, the EU, and Thailand are driven by the consumer trend. In Canada, the policy direction for functional foods has been developed since 2021. With the expanding market of functional food products resulting from consumer demand, the Canadian Government decided to establish a regulatory system for supplemented foods based on a regulatory impact analysis [94]. According to the analysis report, the cost savings after enforcing the regulation on supplemented food was estimated at USD 5.1 million annually or about a seven percent reduction rate over 10 years, which is especially due to the removal of the TMAL procedure. These benefits do not only help food business operators increase their production and competitiveness, but also enhance consumer trust in the national control system. For instance, consumers can easily differentiate supplemented foods from both conventional food products and natural health products by a specific supplemented food label, as well as the list of permitted functional ingredients, which contributes to reducing the risk of overconsumption or overexposure by sensitive consumer groups [94].

In the EU, the food safety policy primarily aims for the highest level of consumer health protection [112], as reflected by the compulsory authorisation of any botanical ingredients newly consumed in the EU region. From the instructional policy, the EFSA is responsible for food safety assessment to provide a scientific opinion to the European Commission as a risk management body [112]. This policy direction supports the transparent procedures for safety evaluation and the achievement of the government objective. However, this is a major barrier to industrial growth and innovations. The report on functional food in the EU states that the market of functional food is less developed than in Japan and the USA, while many EU consumers have a positive attitude towards functional foods, depending on personal knowledge, and believe in advertisements or claims [16]. Without a specific policy and regulation for functional foods and beverages, some consumers doubt the authenticity of these products and their benefit claims, resulting in mistrust in the government. In addition, food business operators have a problem with competition in product research and development as well as marketing of functional ingredients to other countries, affecting economic growth [16].

The policy guideline for functional food is not as clear in Thailand. Even though the list of permitted functional ingredients from nutrients and botanicals is available to support food industries, the beneficial claims are not yet permitted due to lack of scientific substantiation, especially claims related to reduction of the disease risk, which is one of the major burdens for food industries to promote health benefits [17]. Currently, the national policy related to utilization of natural plants and herbs influences the government's direction for functional foods and beverages. The national master plan for Thai herbs development No. 1 (BE 2560–2564) was developed and implemented based on the industrial assessment. The major objective of this plan is to support the sustainable development of herbal processing industries for domestic production and export with high quality and efficacy for health. These processed herbs including their extracts can be widely used in medicines, herbal products, cosmetics, spa products, and food products (i.e., food supplements and beverages) [119]. Recently, a draft national master plan for Thai herbs development No. 2 (BE 2566–2570) was developed and circulated for a public hearing process prior to endorsement by the government [120].

In addition, the national policy allowing use of cannabis plants in health products influences the market growth of functional foods and beverages in

Thailand. *Cannabis sativa* L., also known as Marijuana or Hemp, is a tropical plant of which the use was prohibited for over 60 years under the Narcotics Act BE 2522 [121]. In 2019, however, the government led by H.E. Anutin Charnvirakul as the Minister of Public Health from the policy of Bhumjaithai Party adopted the deregulation of cannabis plants (both Marijuana and Hemp varieties) for medical use and commercialisation for the grass-root economy. This led to the declassification of all parts of cannabis plants in Category 5 of the Narcotics Act, allowing cultivation for business and personal use [122]. Lately, food regulations were developed to allow use of many parts of cannabis including their extracts for food addition. This has caused a significant increase in the number of functional beverages containing cannabis components in the domestic markets such as water-based beverages added with cannabis leaves, hemp seed protein, and herbal infusions containing cannabis leaves and stems, etc. In contrast, cases of adverse health effects are increasingly reported [30]. This implies that the government should develop a comprehensive regulatory framework for functional food products including effective post-market control and rapid traceability systems leveraging blockchain technology [123].

From reviews of Japan, the Republic of Korea, and Canada which currently implement the food policy and regulations for functional foods, two principal steps should be included in the development process of a clear policy and control measures for functional foods. At the beginning step, the government as a policy-maker should consider potential factors influencing consumer health such as socioeconomic matters, consumer trends, and growth of industrial and economic issues [113]. For example, In Japan, a crisis of an aging society is a potential factor initiating the policy and regulations for functional food. the Japanese government intended to encourage consumers with functional foods to maintain good health and prevent disease rather than hospitalization which is more costly [17,124]. Apart from population pattern changes, the positive trend of the global market for functional foods is the major factor triggering the Korean Government to develop the regulatory system for functional foods which is flexible and convenient for the food business operators resulting in increasing the market share of this product in Asia, especially functional foods containing Korean ginseng [124]. In Canada, these relevant factors were taken into account for analysis of risk and benefit impacts for proving good policy and regulatory measures. The second step is the consultation with relevant stakeholders, particularly food business operators, trade partners, academic institutes, and consumers. The involvement patterns include focus group meetings, conferences, and public hearings through online and offline channels. An engagement of these stakeholders is not only to get comprehensive feedback for revision of the clear policy and practical control measures but also to provide a transparency mechanism for global trade facilitation.

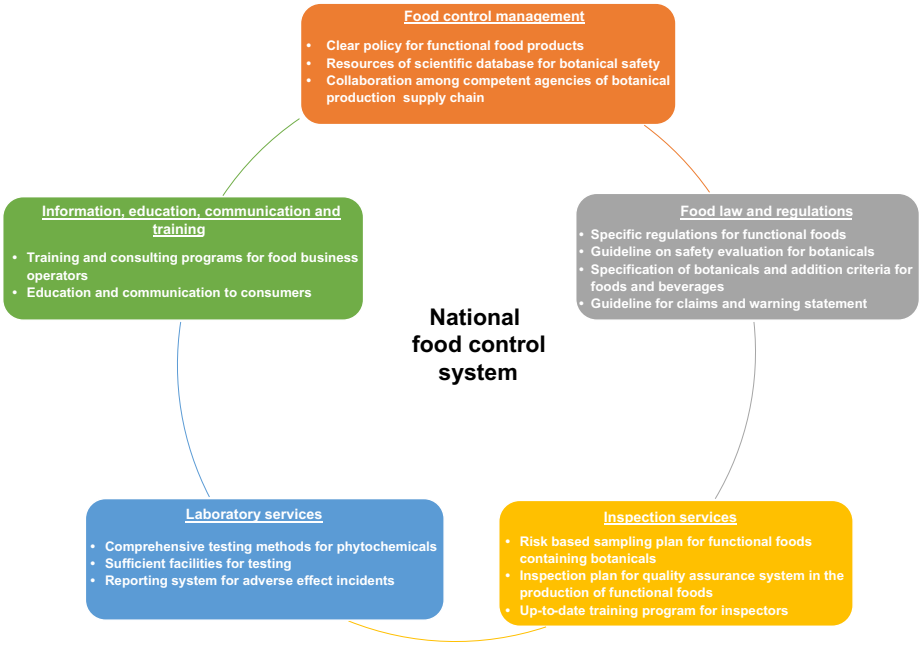


*Fig. 2. Recommendation of a national food control system for functional foods and beverages containing botanicals.*

Moreover, the key stakeholder participation in the evaluation of the food policy and regulations can support continuous improvement such as a case of changing the policy and regulatory system for FFC in Japan resulting from the consultation with Japanese food industries. After implementing the regulations of health food in 1991, the new policy and regulatory system for FFC has been enforced since 2015 leading to an increase in domestic trade of functional foods served for consumer demands [117].

## 4. Conclusion

The critical review of functional foods and beverages containing botanicals shows that this product category is highly attractive in global markets, meeting consumer preferences in terms of taste, formulation, and package designs. The rising demand for functional food products is driven by several factors such as increases in average expenditure per capita population size, and capacities of new technology, as well as changes in socioeconomic structure and policy directions. Botanicals contribute potential ingredients with beneficial effects on human health, supporting the food industries in promoting their products through health claims. Varieties of botanical sources and modern techniques create more opportunities for product research and development, resulting in boosting market growth. However, food addition with botanicals should be controlled from sources to production, and criteria for addition in foods and beverages need to be developed for mitigating health risks to consumers such as food-drug interaction, overdose consumption, and misleading health claims.

Current food safety regulations regarding this product category in the EU, Canada, Japan, the Republic of Korea, and Thailand present that various measures are in place. All observed EU region and four countries are concerned about the safety of botanical ingredients and their functionalities related to human health, and thus the history of food use and scientific substantiation are commonly applied. Nonetheless, the major differences are observed in the permission criteria, specification of botanicals, lists of permitted functional ingredients, and claims published in the regulations. The additive criterion is considered from both safety and functionality data such as specificity of functional ingredients, safety and functionality evidences based on the animal/human studies or meta-analysis publications. Hence, list of these information can be standardized with relevant international standard such as *"Codex guideline for use of nutrition and health claims (CAC/GL 23–1997)"* to ensure quality and reliability of these information. For functional food products, EU and the other four countries have enforced both general and specific requirements in the production, products, and presentation, based on international guidelines and standards, to ensure that the products bear correct information and are fit for consumption. Furthermore, post-market control measures assist governments with proactive risk management.

The review also shows that an implementation of the national food control system can support consumer health protection and fair practices in food trade. The strong commitment and clear policy direction from the government influence the development of a specific regulatory system for functional foods, contributing to economic growth and building consumer trust in food safety. Appropriate regulations on functional foods can diminish administrative costs for the government as well as minimize misunderstanding among consumers. Flexible and clear procedures for pre-authorisation and lists of permitted functional ingredients with related claims can also support food business operators, especially of small and medium sized enterprises, to compete with larger companies. Besides, the establishment of a system for reporting adverse effects and any problem along the supply chain can enhance effective control. Then, collected adverse effect reports, annual result of monitoring plan, tracking information of functional foods, and pre-market registration database can be considered together with capacity of the laboratories and existing resources for development of risk-based sampling plan. For botanical addition, developing a clear guideline on safety evaluation as well as the establishment of a database for collecting information and scientific data related to botanicals from governments, academic institutes, and food industries is essential for fulfilling the gap of data insufficiency. Recommendations for comprehensive elements of the national food control system for functional foods and beverages containing botanicals are summarised in Fig. 2.

Several factors influent the elements and management of the national food control system of each country such as institutional infrastructure and economic and social status. Hence, an analysis of the current situation of consumer perception of and attitude towards functional foods containing botanicals, an in-depth study on opportunities and challenges of food industries, and an assessment of the governance capacities with current national food control systems are needed to develop an effective food control system for functional food products.

## Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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