A comprehensive review on the role of food bioactive compounds in functional food science

Danik Martirosyan*1,2, Trevor Lampert1,3, Michelle Lee1,4

1Functional Food Center Inc, Dallas, TX, USA; 2Functional Food Institute, San Diego, CA, USA; 3National University of Natural Medicine, Portland, Oregon, USA; 4Cornell University, Ithaca, New York, USA

*Corresponding author: Danik Martirosyan, PhD, Functional Food Institute, San Diego, CA, USA

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ABSTRACT

Health promotion and reducing disease risk are the primary benefits of functional foods. However, the definition of functional foods is still unclear and undecided. This has made it difficult to produce a consensus of functional food products and consumers often must rely on companies rather than an official definition. As a result, the Functional Food Center (FFC) has previously proposed a multi-step outline of the processes needed to develop a functional food product and ways to introduce them to the market. This process of identifying a functional food involves rigorous, systematic research to determine the nutritive components of the food that promote positive health effects. An integral step that functional food science uses to identify functional foods is to determine the food bioactive compound(s) that influence beneficial health. Food bioactive compounds are the foundations to all functional foods and come from a variety of sources, like plants, mushrooms, and animals. Bioactive compounds are the basic structural blocks and the biochemical components of functional foods, which is the reason behind the therapeutic efficacy of functional foods. While more research needs to be done on food bioactive compounds, this is the first step closer to legitimizing functional foods. The purpose of this review is to support appropriate and advanced research methods for the identification and screening of food bioactive compounds to define and legitimize the health claims of functional foods. In addition, this review will also discuss the future of food bioactive compounds with our current understanding of them.

Keywords: functional foods, bioactive compounds, anti-inflammatory, health, nutrition, bioavailability, biomarkers, extraction
INTRODUCTION

As research provides evidence of a relationship between food and health, it is necessary to address this new realm of understanding to be properly regulated. Functional food science can be viewed as an interdisciplinary field that is dedicated to discovering and developing food bioactive compounds for symptom management and risk reduction for chronic and viral diseases [1]. These food bioactive compounds are studied for their positive effect on health beyond basic nutrition, as well as testing their security, potency, and quantifiable effects [2]. Functional food science has a legitimate role to play in integrative medicine, and it will only grow in relevance as the world seeks preventative options that will keep people healthy. The concept of functional foods requires systematic and a regulated categorization. The release of official definition of functional foods by FDA needs time because functional food is a new science with unknown details [3]. This leaves the consumer to rely on health claims provided by the corporation or brand for their product. The FFC’s working definition and proposed steps may serve as the protocol for functional foods to be globally recognized by governmental agencies. The FFC utilizes a focus on the complete understanding of food bioactive compounds to legitimize potential health claims of functional foods and their ability to reduce the risk of disease and promote health [4]. As a result, food bioactive compounds are the foundation of functional foods.

Food bioactive compounds are the foundation to all functional foods: Food bioactive compounds (FBCs) are nutritive and non-nutritive compounds naturally found in food and elicit a bioactive impact on the human body, ideally to promote health [5]. FBCs are present in small amounts in functional food products and their effect on human health is being continuously investigated. Epidemiological data supports that high intake of natural functional foods, such as specific fruits and vegetables,
which are rich in FBCs, is associated with decreased risk of chronic diseases, like cardiovascular diseases, cancer, metabolic syndrome, diabetes type II, and obesity [6]. Natural FBCs—such as resveratrol, epigallocatechin, curcumin, oleuropein, sulforaphane, quercetin, ellagic acid, anthocyanins, beta-glucans, and other biomolecules—have been studied as factors with possible direct or indirect effect on specific molecular pathways, associated with the pathophysiology of cardiovascular diseases, diabetes, metabolic syndrome, and cancer. However, an increase in both clinical and epidemiological studies are essential to ensure their possible effect [7,8,9]. The study on the protective and health promoting effects of FBCs have made these components particularly important for the categorization of functional foods [10]. Functional food scientists may use this information to identify, extract, locate the mechanism of action, assess bioavailability, observe clinical biomarkers, and consider all safety parameters of FBCs.

**Identifying FBCs:** Finding new physiologically active FBCs is an important element of classifying functional foods. The isolation of FBCs from plants and other sources remains difficult since they often include a mixture of several kinds of bioactive compounds or phytochemicals [11]. Many analytical, chromatographic, and molecular approaches are used to fingerprint bioactive chemicals, with an emphasis on high performance liquid chromatography/high performance thin layer chromatography (HPLC/HPTLC), Fourier-transform infrared spectroscopy (FTIR), and immunoassay techniques [12] (Fig 1). Identification of bioactive substances may be done using HPLC after chemical separation. An isocratic system is used to identify and separate bioactive chemicals. One may choose from either HPLC water (methanol) or acetonitrile (acetonitrile). High-performance thin-layer chromatography (HPLC) is a crucial method for fingerprinting bioactive chemicals in plants, fungi, and animal functional food sources [13]. A functioning detector, suitable detection parameters, and a separation assay must be properly configured before HPLC can correctly identify bioactive chemicals [14]. Since food bioactive substances have distinct properties, an analytical approach called Fourier-transform spectrum (FTIR) may be used to detect and describe them in functional foods, whether they are liquid or solid. Immunoassay methods are used for both qualitative and quantitative analysis of bioactive chemical spectrums [15]. Receptor binding analysis, enzyme analysis, and quantitative and qualitative study of bioactive chemicals are all benefits of immunoassay methods [16]. When it comes to fingerprinting extract mixtures, ELISA is both faster and more accurate than any traditional HPLC technology presently in use [17].

![Fig 1. Techniques for identifying FBCs [12-17]](image-url)
Using proper extraction processes: The research of a specific FBC may be determined after isolating the compound using the proper extraction method. An important area of focus during the extraction process is removing the FBC from the bound membrane without the substance becoming inactive. Extracting FBCs from food sources requires careful attention to several different variables. These variables include the method employed, input materials, and extraction solvent. Additionally, the correct solvent type, the ratio of solvent to chemical, the temperature, and the particle size are all critical to the extraction process. Extraction techniques vary widely depending on the FBC. The conventional extraction methods usually use organic solvents and require a large volume of solvents and a long extraction time. These conventional methods include maceration, percolation, and reflux extraction [18]. Modern or greener extraction methods offer some advantages such as lower organic solvent consumption, shorter extraction time, and higher selectivity. These greener extraction methods include supercritical fluid extraction (SFE), pressurized liquid extraction (PLE) and microwave assisted extraction (MAE) [18].

Identifying the mechanism(s) of action: Once a bioactive compound has been identified and extracted, researchers may use in vitro and in vivo studies to determine the mechanism(s) of action by which the bioactive compound imparts health benefits. FBCs perform their activities through interaction with specific biologic mechanisms and the synergistic effect of other nutrients and food matrix components could be involved in the described effect [19]. Mechanisms of action of FBCs may be multiple, especially in the food matrix [19]. This issue becomes complex because food ingredients and FBCs may interact, enhancing their desirable or undesirable effects, which is not the case for a single bioactive compound administered as an extract [19].

Accounting for this complexity, the mechanism(s) of action of the FBC needs to be adequately characterized, as a prerequisite for a given claim for its authorization. Basic knowledge on the interaction with other components of the food matrix are essential parts of a basic health claim. In this line, to accept a specific health claim, the science supporting it should contain all information on a plausible mechanism(s) of action of the given FBCs.

Assessing the bioavailability: Bioavailable molecules, whether derived from plants, mushrooms, or animals, are necessary for functional foods to work [20]. The pace and degree to which a bioactive molecule is absorbed and made accessible at the site of action are referred to as its bioavailability [21]. Functional foods and health claims based on dietary components must be bioavailable. The FBC of interest must be able to withstand food processing, be released from the food matrix after ingestion, and be bioavailable in the gastrointestinal tract before it can exert a beneficial effect on health [22]. Diverse absorption pathways may make it difficult to determine the bioavailability of FBCs. Lipophilic and hydrophilic compounds with a variety of absorption processes are among them, an example being vitamins [23]. Even within the same class of polyphenols, there is a wide range in absorption rates. Due to the wide variety of structural and dietary forms and structures of PUFAs, such as triacylglycerides and phospholipids, their bio-accessibility is problematic [23]. These bioactive dietary components have been studied extensively, but it is important to carry out further research to better understand their metabolism and interactions with one another.

Choosing an appropriate food vehicle: Choosing a bioavailable and suitable food vehicle as a carrier of the FBC is essential. In the development of functional foods,
it is often necessary to fortify everyday natural or processed food staples, snacks, or beverages with FBCs [24]. According to the Functional Food Center these are

the seven criteria for suitable food vehicles for FBCs (Table 1):

<table>
<thead>
<tr>
<th>Criteria Number</th>
<th>Description of Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The selection of a food vehicle depends on the acceptability, stability, and bioavailability of the bioactive ingredients within the food, as well as the consumption and lifestyle practices of the intended population.</td>
</tr>
<tr>
<td>2</td>
<td>The vehicle should contain the amounts of the FBCs necessary to impart desired physiological actions.</td>
</tr>
<tr>
<td>3</td>
<td>The vehicle should be such that it will target specific chronic diseases.</td>
</tr>
<tr>
<td>4</td>
<td>The FBC should be stable under conditions of packaging, storage, distribution, and usage.</td>
</tr>
<tr>
<td>5</td>
<td>The FBC should be easily available from the food vehicle.</td>
</tr>
<tr>
<td>6</td>
<td>Fortification should not impart undesirable taste, color, aroma, or texture to the food.</td>
</tr>
<tr>
<td>7</td>
<td>The cost of the fortified food should be reasonable for consumers.</td>
</tr>
</tbody>
</table>

**Utilizing biomarkers to prove efficacy:** There is a need to accurately quantify and objectively observe improvement of health status when consuming functional foods to better understand the link between functional foods and health. Nutritional studies must use a variety of biomarkers that measure overall health conditions [25]. Biomarkers are indicators in the body that may be examined or monitored for signs of illness or physiological changes [25]. To assess subcellular, cellular, tissue, and whole-body interactions with FBCs, an integrated approach incorporating ideas and data from nutritional sciences, food science, molecular biology, biochemistry, and plant science is required [26]. When it comes to boosting health and well-being, the actions of FBCs begin at the cellular level where they have a direct effect, producing or inhibiting chemical interactions. Scientists can then examine the results of these chemical interactions in unique indicators such as exposure biomarkers, effect biomarkers, and health/disease biomarkers [27].

Exposure biomarkers are identified by the chemical byproduct of a person's food exposure or dietary choices [28]. For example, an exposure biomarker for protein consumption can be seen in nitrogen levels of urine [29]. These exposure biomarkers may not only reflect one nutrient but may also be associated with dietary patterns, for example, the plasma concentration of alkylresorcinol is considered a biomarker of the intake of whole grains [30].

Effect biomarkers may be used to identify a target response of biological reactions, specifically regarding metabolism and physiological processes. For example, disturbed homocysteine metabolism is associated with cancer [31]. The metabolism of homocysteine, not the compound itself, is the effect biomarker associated with the physiological states [32,33].

Health/disease biomarkers are indicators that represent a state of health or a disease risk. Health/disease biomarkers are commonly employed in clinical practice and indicate disease severity. For example, fasting glucose levels is a health/disease biomarker linked to diabetes, whereas cholesterol and triglycerides is a health/disease biomarker linked to cardiovascular disease [34]. Biomarkers make important
health statuses quantifiable, which is essential for clearly defining the effectiveness of bioactive compounds found in functional foods.

Safety considerations when working with FBCs: Biological activity has been acknowledged with FBCs that have a positive effect, but negative effects is also a form of bioactivity [35]. This includes adverse effects such as toxicity, allergenicity, and mutagenicity, which are usually dependent on the dose and bioavailability of a given substance. An important question when defining a functional food with respect to the FBCs is whether they propose a risk from a safety perspective. The perception that since these are natural products, they do not carry real associated risks is much extended among consumers. In fact, evidence exists regarding the risk of consuming an excess number of healthy substances such as antioxidants, omega 3, and soy isoflavones [36]. The evaluation of relevant data from toxicological studies within a development process must demonstrate that a FBC does not provoke toxic effects at reasonable doses or dosages suggested for consumption. The potential toxic effects in cases where the product is consumed incorrectly, such as taking it in quantities superior to those recommended, must be predicted. Therefore, the objectives of a toxicological evaluation of FBCs developed do not substantially differ from those required by regulation for clinical drugs or even for chemical products. The safety assessment of the FBCs is a necessity for the functional food industry, derived from the acquired obligation of commercializing safe products. The specific strategy should be defined case by case; therefore, prior to any toxicological development, it is essential to study all the information regarding the FBCs that are available [37]. A general strategy may be applied in developing the safety considerations of FBCs. The objective of the general toxicity studies is the establishment of the toxicological profile of the test substance, determining the relationship between the dose administered and the response observed, identifying target organs, toxic doses, and evaluating the reversibility of the toxic effects [38]. In vivo experimental systems may be used, and the studies are classified in terms of their duration, in single-dose toxicity studies or repeated-dose toxicity studies [38]. Choosing the amount of the active ingredient and the frequency at which it is taken should involve consideration of efficacy and safety.

Sources of food bioactive compounds: The majority of FBCs can be found in plant foods (such as whole grains, fruits, vegetables, herbs, and spices), but are also well studied in medicinal mushrooms (such as *Ganoderma*, *Chaga*, *Cordyceps*, and *Shiitake*) and animal products (such as milk, fermented milk products, and cold-water fish) [39,40].

Food bioactive compounds from plant sources: Plant-based foods contain bioactive compounds that promote positive health and reduce the risk of disease [41]. These bioactive compounds are an essential component to plant-based functional foods, as well as prospective functional foods (Table 2). Phytosterols, terpenoids, alkaloids, glucosinolates, isothiocyanates, polysaccharides, polyunsaturated fatty acids, and triterpenes are just a few of these categories of plant based FBCs that will be discussed in this section (Fig 2). Phytosterols, which are generated from triterpenes in plants, play an important function in human health [42]. Multiple clinical investigations have shown that a diet high in phytosterols including campesterol, sitosterol and stigmasterol helps decrease LDL cholesterol [42]. Terpenoids are the most diverse category of plant based FBCs, with hundreds of different examples. Many terpenoids in plants and fruits are responsible for the distinctive scent of plants and fruits, such as limonene in numerous citrus fruits. [43]. The common plant sources of terpenes are tea, thyme, cannabis, Spanish sage, and citrus fruits. Terpenes have a wide range of medicinal
uses among which antiplasmodial activity is notable as its mechanism of action [44]. Triterpenes are slightly rarer in nature but constitute a large structurally diverse group of natural compounds derived from active isoprene [45]. Lupane, oleanane, and ursane seem to be the most promising anti-cancer compounds in this diverse group of triterpenoids [46]. Alkaloids include any compounds with alkali-like characteristics and/or include at least one nitrogen atom in the heterocyclic ring structure [47]. One of the most often consumed FBCs is caffeine, an alkaloid. Coffee and tea are the most common sources of caffeine. In epidemiological studies, a link between chronic caffeine consumption and a significantly lower risk of developing neurodegenerative diseases, such as Alzheimer’s disease, has been described [48]. Glucosinolates (GSLs) are described mainly in cruciferous plants (such as broccoli, cabbage, cauliflower, and brussel sprouts) and show chemopreventive and anti-inflammatory properties [49]. Isothiocyanates (ITCs) are FBCs in cruciferous vegetables with anticarcinogenic properties. Consumption of cruciferous vegetables is associated with a decreased risk of cancer, which may be explained in part by consumption of ITCs [50]. Sulforaphane is a specific ITC found in broccoli that is being studied as a potential anticancer drug. Polysaccharides may be found all throughout nature, specifically in plant cell walls [51]. A few well-known polysaccharides are starch, glycogen, and cellulose, which serve as structural backbones in plants and are very significant to human health [52]. Some studies have shown that dietary polysaccharides, as well as its derivative fructooligosaccharides (FOS), play a critical role in maintaining the healthy symbiotic relationship between humans and their gut bacteria [52]. Polyunsaturated fatty acids (PUFAs) in plants consist mainly of linoleic acid (LA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). According to epidemiological evidence, a diet deficient in PUFAs is associated with an increased risk of chronic illnesses including cancer, cardiovascular disease (CVD), and diabetes. According to this association, lipid mediators originating from PUFAs modulate the inflammatory response at the gene expression and membrane composition levels. Overconsumption of these substances, on the other hand, should be avoided since it may result in oxidative damage to cellular structures, notably blood vessel walls, which is a characteristic of the development of cardiovascular illnesses [53]. PUFAs may be found in a wide variety of plants including walnuts, seeds, and oils from sources such as sunflower, flax, soybean, and maize [54].

Table 2. Summary of the benefits of FBCs from plant sources

<table>
<thead>
<tr>
<th>Food bioactive compound</th>
<th>Benefits</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phytosterols</td>
<td>Decreases LDL cholesterol</td>
<td>[42]</td>
</tr>
<tr>
<td>Terpenoids</td>
<td>Frequently utilized in medicine for its antiplasmodial activity</td>
<td>[43]</td>
</tr>
<tr>
<td>Triterpenes</td>
<td>Shows anti-cancer effects</td>
<td>[45-46]</td>
</tr>
<tr>
<td>Alkaloids</td>
<td>Decreases risk of neurodegenerative diseases</td>
<td>[47-48]</td>
</tr>
<tr>
<td>Glucosinolates</td>
<td>Contains chemopreventive and anti-inflammatory properties</td>
<td>[49]</td>
</tr>
<tr>
<td>Isothiocyanates</td>
<td>Has anticarcinogenic properties to reduce the risk of cancer</td>
<td>[50]</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td>Maintains healthy symbiotic relationship between humans and their gut microbiota</td>
<td>[51-52]</td>
</tr>
<tr>
<td>Polyunsaturated fatty acids</td>
<td>Decreases risk of chronic illnesses (ex: cancer, diabetes)</td>
<td>[53-54]</td>
</tr>
</tbody>
</table>
**Food bioactive compounds from mushroom sources:** In recent years, research into medicinal mushrooms has progressed exponentially, but much remains to be done (Table 3). In terms of pharmacological properties, the most important are polysaccharides, the structural component of the fungal cell wall. Polysaccharides have antitumor, immunomodulatory, antioxidant, anti-inflammatory, antimicrobial, and antidiabetic activity. The mechanisms of action involve the gut microbiota, meaning the polysaccharides act as prebiotics in the digestive system [55]. Extracts of *Coriolus versicolor*, commonly known as tunzhi in China or turkey tail, have been approved in routine clinical practice, especially in integrated cancer therapy in conjunction with chemotherapy or radiotherapy [56]. The immunomodulatory properties of this mushroom are due to two protein-bound polysaccharides present in the fungal extract: the polysaccharide peptide (PSP) and the glycoprotein PSK (krestin). Another class of compounds that are very important for the bioactivity of medicinal mushrooms are terpenes. Terpenes modulate the immune system by stimulating the expression of genes coding for proteins involved in the immune response, but also have anti-inflammatory, antioxidant, and antitumor properties [57]. High terpenoid contents are found in *Ganoderma lucidum*, commonly known as reishi or lingzhi [58]. *G. lucidum* terpenes, especially the ganoderic acids (GAs), are bioactive components responsible for several biological effects, including anti-inflammatory, anti-tumorigenic, anti-HIV, and hypolipidemic activity [59, 60, 61]. To date, more than 150 terpenes have been identified from the fruiting bodies, spores, and mycelia of *G. lucidum* [62]. The therapeutic properties of fungal metabolites are well established in traditional medicine. The administration of an extract of medicinal mushrooms can be used in modern medicine to help treat patients or protect people from many diseases [63]. Chemically defined FBCs may develop medicinal mushrooms as functional foods.
Table 3. Summary of the benefits of FBCs from mushroom sources

<table>
<thead>
<tr>
<th>Food bioactive compound</th>
<th>Benefits</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polysaccharides</td>
<td>Contains antitumor, immunomodulatory, antioxidant, anti-inflammatory,</td>
<td>[55-56]</td>
</tr>
<tr>
<td></td>
<td>antimicrobial, and antidiabetic activity</td>
<td></td>
</tr>
<tr>
<td>Terpenes</td>
<td>Regulates the immune system, and has anti-inflammatory, antioxidant, and</td>
<td>[57]</td>
</tr>
<tr>
<td></td>
<td>antitumor properties</td>
<td></td>
</tr>
<tr>
<td>Ganoderic acids</td>
<td>Anti-inflammatory, anti-tumorigenic, anti-HIV, and hypolipidemic qualities</td>
<td>[59-61]</td>
</tr>
</tbody>
</table>

Food bioactive compounds from animal sources:

Animals are abundant sources of FBCs that have a range of biological roles for human health [64] (Table 4). Marine fishes are a diverse source of bioactive compounds with a wide variety of novel bioactive substances [65]. The main therapeutic potential of marine fish consumption has been ascribed with the presence of long-chain omega-3 polyunsaturated fatty acids (PUFAs) in high content. After consumption, PUFAs can be incorporated into cell membranes and reduce the amount of arachidonic acid available for the synthesis of proinflammatory eicosanoids and reduce the production of inflammatory cytokines [66]. Similarly, meat and meat products are rich in FBCs such as vitamins, minerals, peptides, and fatty acids, many of which are beneficial to human health. Meat is a well-balanced essential amino acid, especially sulfate ones, as it contains an abundance of highly biologically essential proteins. Besides major components, meat is rich in bioactive components, primarily taurine, l-carnitine, choline, alpha-lipoic acid, conjugated linoleic acid, glutathione, creatine, coenzyme Q10 and bioactive peptides [67]. Mammalian milk has various peptides that influence immune function by suppressing or stimulating certain immune responses [68]. Whey is a protein found in cow’s milk. Bioactive peptides of whey proteins modulate both specific and non-specific immune responses [69]. Egg comprises several bioactive ingredients with pro-and/or anti-inflammatory effects. The white fraction of eggs contains many bioactive proteins, including ovalbumin, ovotransferrin, ovomucin, lysozyme, and avidin [70]. These proteins have anti-bacterial and immunoprotective effects [71]. Much attention must therefore be given to develop functional food products from animal origins with physiological functions that promote human health.

Table 4. Summary of the benefits of FBCs from animal sources

<table>
<thead>
<tr>
<th>Source</th>
<th>Food bioactive compound</th>
<th>Benefits</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marine fish</td>
<td>Omega-3 polyunsaturated fatty acids</td>
<td>Reduces amount of arachidonic acid and production of inflammatory cytokines</td>
<td>[65-66]</td>
</tr>
<tr>
<td>Meat products</td>
<td>Vitamins, minerals, peptides, fatty acids</td>
<td>Beneficial to human health and provides nutrients for protein synthesis</td>
<td>[67]</td>
</tr>
<tr>
<td></td>
<td>Taurine, l-carnitine, choline, alpha-lipoic acid, conjugated</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>linoleic acid, glutathione, creatine, coenzyme Q10, bioactive</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>peptides</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mammalian milk</td>
<td>Bioactive peptides in whey</td>
<td>Regulates specific and non-specific immune responses</td>
<td>[68-69]</td>
</tr>
<tr>
<td>Eggs</td>
<td>Ovalbumin, Ovotransferrin, ovomucin, lysozyme, avidin</td>
<td>Contains anti-bacterial and immunoprotective activity</td>
<td>[70-71]</td>
</tr>
</tbody>
</table>
Focusing on food bioactive compounds to formally define functional foods: There is no consensus on a regulated definition of functional foods, and accordingly, many institutions have individual definitions. However, the Functional Food Center (FFC) is actively seeking to establish a definition using health-promoting food bioactive compounds as the backbone to functional foods [1]. The goal of a clear definition of functional foods is to create an understanding of how functional food products must be developed, evaluated, and used for general health, risk reduction of disease, and management of their symptoms [1]. The FFC defines functional foods as "natural or processed foods that contain biologically-active compounds, which, in defined, effective, non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, to promote optimal health and reduce the risk of chronic/viral diseases and manage their symptoms" [1]. As the FFC’s definition explains, bioactive compounds found in food are responsible for potential benefits of functional foods to reduce the risk of disease and promote health. As a result, food bioactive compounds are the focus of defining functional foods and require a fundamental understanding for developing functional food products [1].

While the Food and Drug Administration (FDA) does recognize the efficacy of certain food compounds having disease-related health benefits, they have not recognized functional foods as a separate category [1]. This requires the identification of the molecular and biochemical mechanisms of the medical effects of functional foods and bioactive compounds. It will be able to contribute to the shortening of the path to a comprehensive, FDA-approved definition. Linking the consumption of functional foods with health claims should be based on sound scientific evidence. The FFC proposes a multi-step process that incorporates the themes discussed in this paper to classify functional foods. The FFC protocol can serve as a guide for using food bioactive compounds to regulate functional food product health claims [1].

Challenges of experimenting with FBCs: As mentioned previously, in vitro and in vivo experimental systems may be used to analyze the toxicity studies of the dosage of FBCs [38]. This ensures that there is an accurate amount of FBCs to promote positive results. However, there are challenges in transitioning from in vitro to in vivo experiments and each have their advantages and disadvantages. While in vivo studies are more beneficial in seeing how an organism would react, it is difficult to find a model organism that could both be easily studied and have similar functions and reactions to humans [72]. On the other hand, with in vitro experiments, it is more commonly used in biological fields because samples are quicker to obtain and use, but these procedures are mostly performed on cell lines that already have abnormal function so it would not show the benefits of a healthy sample [72]. Therefore, there needs to be a smooth transition from in vitro to in vivo experiments to cover the advantages and disadvantages from both. A mini review from Marco Fiorentino and John A Kellum discusses this transition in acute kidney injury [73]. The main reason for the disconnect between in vitro and in vivo studies is that the in vitro experiments do not imitate the human condition [73]. The transition would be difficult as the results from the in vitro studies will not accurately predict what will happen in in vivo studies. Therefore, for experimenting with FBCs, it is important that we should have a successful transition from in vitro to in vivo studies to appropriately test the dosage.

Future of functional foods: Academic, government and researchers around the globe are dedicating a great amount of effort to identifying how functional foods and food ingredients might help prevent chronic disease or optimize health, thereby reducing healthcare costs and
improving the quality of life for many consumers. Only after functional food products are regulated and established can the broad public trust and can access a wide range of health benefits. Alongside the health benefits of functional foods, the potential combination of functional foods alongside other therapies and treatments may increase the efficacy of all treatments [74]. This message has resonated with consumers and driven market growth. Further growth in the functional foods market, is likely to require greater evidence of the bioavailability of active ingredients, clinical effect, and support for health claims by regulators especially in the US.

CONCLUSIONS

The process of identifying functional foods is a complex and rigorous journey. However, through the advancing understanding of the role bioactive compounds play in functional foods, society will gradually come to accept a formal definition for functional foods. The principal of all functional foods is that they contain bioactive compounds. The sources of these bioactive compounds can come from plants, mushrooms, or animals. Through several phases of identifying the food bioactive compounds, testing for bioavailability, safe and effective dosage, and identifying the relevant biomarkers, we would have a better understanding of the role that a certain bioactive compound plays in functional food. With this understanding, we can better distinguish the definition for functional food to legitimize the role they play in health promotion.

List of Abbreviations: FFC: Functional Food Center; BAC: bioactive compound; FBC: food bioactive compound

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