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BCHD Bioactive Compounds in Health and Disease

Functional Food Science and Bioactive Compounds

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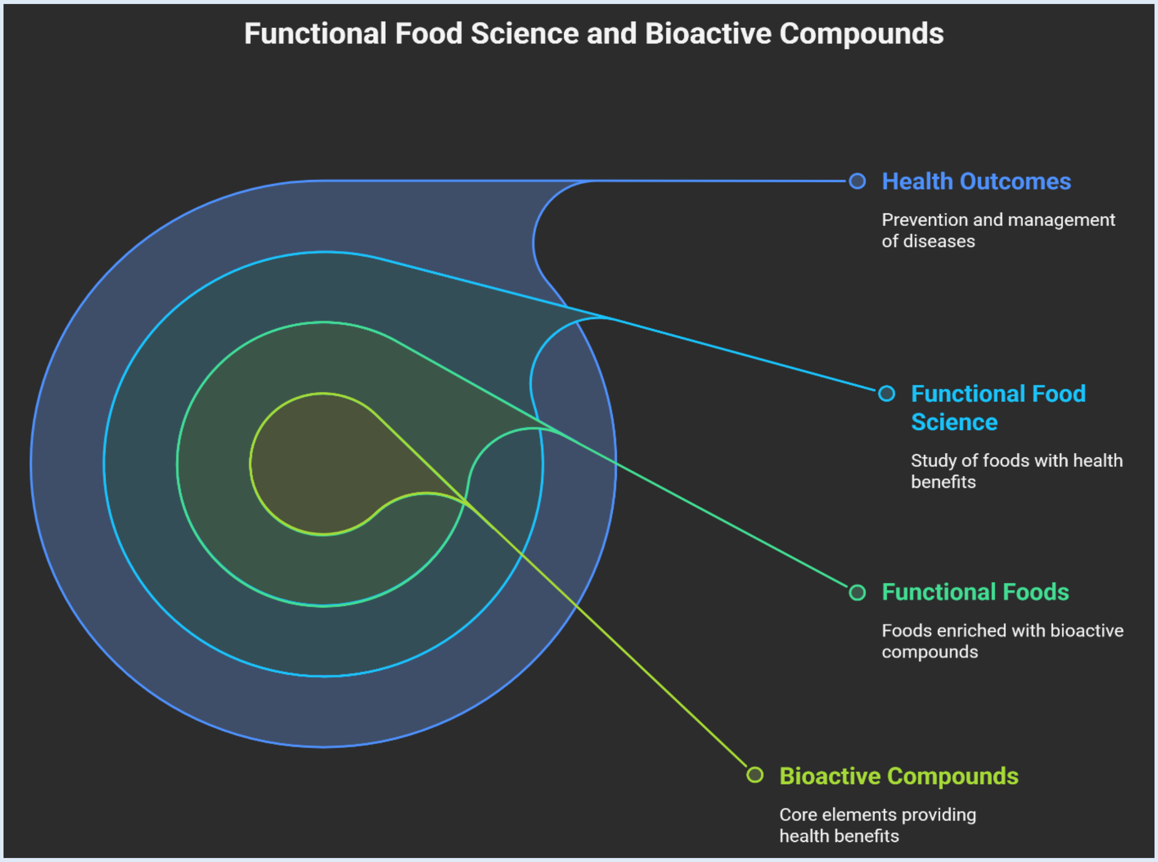
ABSTRACT

Bioactive compounds (BCs) are key components in the development of functional foods (FFs) that offer health benefits beyond basic nutrition. Compounds such as polyphenols, carotenoids, flavonoids, fatty acids, fiber, and probiotics contribute to metabolic regulation, immune support, and a reduced risk of chronic diseases, including cardiovascular conditions, diabetes, and certain types of cancer. This review examines the classification, mechanisms of action, and safety considerations of BCs, drawing on recent research and the framework of the Functional Food Center (FFC). It also highlights the impact of environmental factors on BC composition and explores technologies, such as encapsulation, to improve bioavailability.

Functional food science (FFS) emerges as an interdisciplinary field linking food technology, biomedical research, and nutrition policy. The review highlights the importance of standardized terminology, regulatory clarity, and scientifically validated interventions in advancing FF development and combating non-communicable diseases globally.

Novelty: This review offers a structured and integrative framework on FF that unites scientific, technological, and regulatory perspectives on BC. It highlights the value of FFS as a discipline that proposes updated, evidence-based definitions for FF and BC. The focus on dosage, delivery mechanisms, and long-term efficacy provides a framework for future FF evaluations designed for targeted health outcomes.

Keywords: bioactive compounds, pharmaceutical bioactive compounds, functional food science, functional foods, Functional Food Center



Graphical Abstract: Food, pharmaceutical bioactive compounds, and functional food science

INTRODUCTION

BC plays a crucial role in formulating and understanding FF. These compounds, which encompass a wide array of phytochemicals, provide various health benefits beyond basic nutrition through their potential role in preventing and managing chronic diseases [1-3]. FFs are recognized for their capability to mitigate chronic diseases, improve metabolic health, and enhance overall well-being through their bioactive constituents [3-5].

BC plays a pivotal role in FFS, which is defined as the specialized branch of food science focusing on foods that provide health benefits beyond basic nutrition. These BCs include antioxidants, polyphenols, and dietary fibers, which are all integral to the efficacy of FF in managing and preventing chronic diseases [1,6].

The definition of BC is crucial to understanding their role in FF. According to the FFC, BC are "constituents of foods" that offer beneficial health properties. These food constituents include phenolics, carotenoids, fatty acids, fibers, prebiotics, and probiotics [7-8]. Many of these compounds are found in natural products, such as fruits, vegetables, and whole grains, which contribute to the food's health benefits, ranging from improved digestion to enhanced metabolic health [9].

Incorporating BC into FF requires an adequate understanding of their dosage and interaction within the food matrix. Research indicates that the optimal dosage of each item may enhance the health benefits while ensuring the safety of continuous consumption [7,10]. Advancements in this technology, particularly in encapsulation and controlled release, support the effective delivery of BC to achieve desired health outcomes [10]. Recent studies highlight the importance of BC in preventing and managing various health conditions, including cardiovascular diseases and metabolic disorders. Bioactive constituents such as resveratrol and omega-3 fatty acids improve insulin sensitivity and reduce the risk of diseases associated with obesity and diabetes [11]. Moreover, emerging evidence suggests that BC possesses cancer-preventive capabilities, targeting molecular pathways involved in cancer progression [2].

As FFS evolves, the emphasis on establishing a clear and comprehensive definition of FF and their bioactive contents will enhance communication among researchers, practitioners, and consumers. This clarity may facilitate regulatory processes and consumer acceptance of FF as legitimate health-promoting products [8,12].

This review aims to examine the current landscape and development of FFS, offering key definitions and historical context surrounding functional foods, food bioactive compounds, and pharmaceutical bioactive compounds. Additionally, it will highlight significant limitations within existing literature. By synthesizing recent findings, this review seeks to present the field in an accessible manner while laying a foundation for the advancement of future research and understanding.

Research Strategy: Literature searches were conducted on online publishing platforms and databases, including Web of Science and the Functional Food Center / Food Science Publisher's journals, to determine the relationship between the proliferation of bioactive compounds and the field of functional food science. Recent research articles published in the last four years were prioritized, and caution was taken to critically analyze and identify challenges, gaps in research, and other issues facing the field of functional food science.

Key search terms included "functional foods", "bioactive compounds", functional food science", and "functional food center".

Food bioactive compounds: Food BCs have gained significant interest due to their potential health benefits. Specifically, food BCs encompass various metabolites such as polyphenols, carotenoids, dietary fibers, and bioactive peptides that may have anti-inflammatory, antioxidant, and anticancer effects [1,13,14].

The classification of a BC is broad and encompasses a wide range of chemical structures with diverse biological activities. Polyphenols and carotenoids are among the most extensively researched categories, as they play vital roles in reducing oxidative stress and inflammation [13-15]. Evidence suggests that diets rich in these BC are associated with a lower risk of chronic diseases such as cardiovascular disease, cancer, and diabetes [16-18]. This association was identified through epidemiological research, which demonstrated a correlation between high intake of fruits, vegetables, and whole grains—foods rich in BC—and improved health outcomes [7,18]. Foods BCs are often categorized based on their origins. These items may be derived from plants, animals, or microorganisms. Flavonoids, for example, are found in fruits and vegetables and have potent antioxidant and anti-inflammatory activities. Bioactive peptides derived from protein sources can enhance immune function and metabolic health [1, 11, 16]. Additionally, the extraction and bioavailability of these compounds are critical factors that affect their efficacy. Namely, techniques such as nanoencapsulation enhance the stability and absorption of BC in the body, thus maximizing their potential health benefits [19,20].

Overall, the definition and implications of food BC illustrate their significance in a FF context, where they serve not only as nutrients but as powerful agents with therapeutic properties. The recognition of these compounds underscores the shift toward a preventive approach in healthcare, emphasizing the importance of dietary choices [1,7].

Definition of functional foods (FF): The Functional Food Center 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" [6-8]. FF are natural or processed foods that provide health benefits extending beyond basic nutrition due to BC. This definition is crucial for both scientific purposes and regulatory and marketing strategies in various contexts worldwide. A well-established articulation from the FFC describes FF as those that contain biologically active compounds, which provide clinically proven health benefits targeting chronic diseases and overall well-being when consumed at adequate levels [8, 21, 22].

The term "functional foods" first emerged in Japan during the 1980s and has spread globally, with definitions varying among countries. For instance, in the EU, FF are recognized when they demonstrably improve one or more bodily functions, thus enhancing health or reducing disease risk and aligning with the principles of bioactive compound efficacy [10,24]. However, despite recognizing the health benefits these foods may provide, regulatory frameworks remain inconsistent. There is no universal definition that impacts the categorization and formal regulation of these products [22,24-25].

FF are increasingly associated with preventive health strategies, particularly regarding how specific foods can mitigate disease risks or symptoms. The relevance of FF is highlighted by studies on diabetes prevention, where regular consumption of FF containing bioactive ingredients, such as antioxidants and anti-inflammatory agents, is known to play a role in managing health risks associated with the condition [26]. In essence, while all foods may serve some functional role from a nutritional perspective, FF are distinguished by their scientifically validated effects on health when included in a regular and diverse diet [27].

Furthermore, the role of BC in defining FF cannot be overstated. These compounds are central to the health-promoting properties attributed to FF. Their efficacy is often assessed through specific biomarkers to substantiate health claims, a practice supported by scientific bodies and regulatory agencies. These assessments provide rigorous standards of evidence, such as replicated randomized controlled trials [1,28]. As the FF sector evolves, aligning scientific understanding with consumer expectations and regulatory requirements is key to advancing the field and promoting public health [2,29].

FFs occupy an important niche in dietary health, characterized by their bioactive components and associated health benefits. Although there is no universal definition, these items are recognized for their implications in the fields of nutrition science, health policy, and consumer education.

Functional food science as a new branch of science: FFS has emerged as a distinctive and vital branch of inquiry within the broader fields of food science and nutrition, specifically focusing on food products that confer health benefits beyond basic nutrition. This branch of science is relevant due to growing public interest in health promotion and disease prevention. FFs are generally defined as those that contain biologically active compounds that can provide clinically documented health benefits when consumed in adequate, non-toxic amounts, thereby aiming to reduce the risk of chronic diseases and manage related health issues [6,30]. The historical context of FFS suggests that their benefits can be traced back to evolving consumer expectations regarding the role of food in health. The FFC has significantly contributed to this evolution by refining the definition of FF to emphasize not only their nutritional components, but also their bioactive properties that engage biological mechanisms in the body [1,8,12]. As such, FFS diverges from traditional food studies, which often concentrate on taste, preservation, and packaging. Therefore, FFS centers on the potential of food to act as a preventive or therapeutic agent against chronic conditions [6,31].

Research indicates that FF encompasses a vast array of products, including those enriched with probiotics, prebiotics, and other BC aimed at addressing specific health concerns like metabolic syndrome, vitamin D deficiency, and cardiovascular health [32-34]. Nutraceuticals, often incorporated into functional foods, face various regulatory challenges that differ by region, impacting their marketability and consumer confidence [35-36]. This regulatory landscape and increasing consumer demand for health-promoting foods have fortified FFS's place in public health discussions [12,37].

Additionally, future developments in FFS depend on the need for rigorous, evidence-based research to substantiate health claims associated with FF. This includes understanding how BC interacts within complex biological systems and establishing the dosage required to elicit specific health outcomes while ensuring consumer safety [2,7]. As FFS continues to mature, it is positioned at the nexus of public health, nutrition, and food technology, thus requiring multidisciplinary collaborations to explore and validate its expansive potential in combating chronic diseases and promoting wellness.

In summary, FFS is a transformative domain focused on bridging the gap between food and health. It fosters a deeper understanding of food's roles, not merely as sustenance but as a pivotal element in enhancing quality of life through disease prevention and health promotion.

Pharmaceutical Bioactive Compounds (PBC): PBC are molecules that exhibit biological activity and are used in pharmacotherapy. These compounds play a pivotal role in developing therapeutic agents that address various health conditions. They can be of synthetic or natural origin, with diverse mechanisms of action in various biological systems, influencing processes such as inflammation, infection, and cellular proliferation [38-39].

BCs can be categorized based on their specific biological activities. For instance, cephalosporin-oxazolidinone conjugates have demonstrated promising antimycobacterial activity, making them potential therapeutic agents against tuberculosis [38]. Additionally, α-aminophosphonates possess significant antioxidant properties, linked to their potential in mitigating oxidative stress-related diseases [40]. This highlights a broad spectrum of biological activities, ranging from antimicrobial to anticancer effects.

Furthermore, the structural diversity of BCs contributes significantly to their efficacy. For example, pyrazolo3,4-bpyrazines exhibit anticancer and anti-inflammatory properties, making them versatile candidates for various therapeutic applications [39]. Similarly, novel derivatives such as pyrazolo4,3-gpteridines have shown substantial anti-inflammatory and antibacterial activities, reaffirming the importance of heterocyclic structures in drug development [41]. The intimate relationship between the chemical structure of these compounds and their pharmacological effects highlights the importance of medicinal chemistry in developing effective therapeutic agents.

Recent studies have emphasized the ongoing exploration of compounds derived from both terrestrial and marine sources. Marine organisms, such as sponges, have yielded abundant bioactive natural products with unique structural features and varied therapeutic potential [42-43]. The continued study of these compounds expands the therapeutic arsenal for conditions such as cancer and bacterial infections, demonstrating their importance in modern medicine [44-45].

PBCs are essential to medicinal science, influencing various therapeutic outcomes. Their development is integrally linked to advances in synthetic techniques and a deeper understanding of their biological mechanisms, thereby paving the way for innovative treatments in health care.

Food Bioactive Compounds vs. Pharmaceutical Bioactive Compounds: While both "food bioactive compounds" and "pharmaceutical bioactive compounds" refer to substances that have a biological effect on living organisms, their context, typical uses, regulation, and mechanisms of action differ significantly.

Food bioactive compounds are non-nutrient compounds found naturally in small quantities in various foods (fruits, vegetables, whole grains, legumes, nuts, etc.), as well as in novel sources like medicinal mushrooms, plants, and agri-food byproducts. They are not essential for basic human nutritional needs but are associated with beneficial health effects, often contributing to disease prevention [46, 47]. Several kinds of food-derived bioactive compounds can be found in nature, such as polyphenols, carotenoids, phytosterols, and specific fatty acids (e.g., omega-3s) [46, 48].

Pharmaceutical bioactive compounds are substances, either naturally occurring (often isolated and concentrated from plants, animals, or microorganisms) or synthetically produced, that are intended to have a specific pharmacological action for the diagnosis, cure, mitigation, treatment, or prevention of disease [49]. They are typically developed and administered as drugs and encompass a wide array of compounds, from plant-derived molecules with antimicrobial or anticancer properties to synthetically designed drugs targeting specific pathways [49-50].

Food bioactive compounds are primarily consumed as part of a regular diet to promote general health, prevent disease, and maintain well-being. Recent research highlights their potential in developing functional foods and nutraceuticals that offer health benefits beyond essential nutrition, often by modulating physiological processes through dietary intake [46, 51]. In contrast, pharmaceutical bioactive compounds are used therapeutically to treat specific diseases or conditions. They are typically administered at precise dosages to achieve a targeted biological response, often after extensive preclinical and clinical trials [49, 52].

Food bioactive compounds exhibit a wide range of mild and complex mechanisms, including antioxidant, anti-inflammatory, immunomodulatory, and gut microbiota-modulating effects. Their actions are generally subtle and may involve modulating multiple pathways rather than targeting a single specific receptor [47, 38, 51]. For instance, specific food bioactives have shown promise in reducing inflammation and oxidative stress, as well as modulating lipid metabolism [51]. On the other hand, pharmaceutical bioactive compounds are designed to have precise and potent mechanisms of action. They often interact with defined biological targets (e.g., receptors, enzymes, ion channels) to elicit a precise physiological response. Recent advancements highlight the exploration of precise molecular actions, such as the impact of plant-derived compounds on cancer pathways or the induction of apoptosis [50, 52].

In terms of dosage and efficiency, food bioactive compounds occur in relatively small, variable amounts in foods. Their efficacy is often observed over prolonged periods as part of a healthy diet, contributing to cumulative health benefits. Research is exploring quantified intake recommendations for non-essential bioactive compounds to achieve specific metabolic and health-related effects; however, this remains challenging due to the complex interactions [48, 53]. However, pharmaceutical bioactive compounds are administered in carefully controlled, precise dosages to achieve a desired therapeutic effect. Their efficacy and safety are rigorously tested through extensive research and clinical trials, as evidenced by the increasing number of new drug approvals focusing on specific diseases [49, 52].

When examined in terms of their pharmacokinetic properties, the absorption, distribution, metabolism, and excretion (ADME) of food bioactive compounds can be highly variable and influenced by factors such as the food matrix, processing methods, gut microbiota, and individual genetic variations. Many food bioactives have low bioavailability and undergo extensive metabolism, an area of active research aimed at improving their efficacy through novel delivery systems, such as nanotechnology [46, 54]. On the other hand, pharmacokinetics are thoroughly studied to optimize dosage, formulation, and administration routes, ensuring adequate absorption, distribution to target tissues, appropriate metabolism, and safe excretion. In vitro pharmacokinetic techniques are crucial for characterizing the ADME properties of various bioactive compounds, including those from medicinal plants, to ensure their safe and effective therapeutic use [52, 55].

Food bioactive compounds are regulated as food components or dietary supplements. The regulatory frameworks are less stringent than for pharmaceuticals, focusing primarily on safety and preventing misleading health claims [53]. Recent discussions highlight the need for clearer regulatory frameworks and safety assessments for bioactive food components to ensure consumer protection and proper labeling [56]. Meanwhile, pharmaceutical bioactive compounds are subject to rigorous regulatory approval processes by agencies like the FDA or EMA. This involves extensive preclinical and clinical trials to demonstrate safety, efficacy, and quality before a drug can be marketed [49, 52]. The development of novel drugs from natural sources underscores the stringent regulatory pathways required for therapeutic claims [57].

Table 1. Summarizes the differences between food bioactive compounds and pharmaceutical bioactive compounds.

Aspect	**Food Bioactive Compounds**	**Pharmaceutical Bioactive Compounds**
Definition	Non-nutrient compounds naturally present in foods and novel sources with health-promoting properties	Naturally derived or synthetically produced compounds with specific pharmacological actions
Sources	Fruits, vegetables, whole grains, legumes, nuts, medicinal plants, mushrooms, agri-food byproducts	Plants, animals, microorganisms, or fully synthetic origins
Examples	Polyphenols, carotenoids, phytosterols, omega-3 fatty acids	Antimicrobial agents, anticancer drugs, synthetic receptor agonists, or enzyme inhibitors
Primary Use	Health promotion, disease prevention, and general well-being	Diagnosis, treatment, cure, or prevention of a specific disease
Mechanism	Modulate multiple physiological pathways (e.g., antioxidants, anti-inflammatory, and gut microbiota-modulating) with subtle and complex effects.	Act on specific biological targets (e.g., receptors, enzymes) for potent, targeted responses
Dosage and Efficacy	Naturally, it occurs in small, variable amounts; long-term cumulative effects; efficacy is influenced by diet and lifestyle.	Precisely dosed; efficacy confirmed through clinical trials; short- to long-term therapeutic effects.
Pharmacokinetics (ADME)	Variable absorption and metabolism; influenced by food matrix, genetics, gut microbiota; often low bioavailability	Thoroughly studied for optimized formulation, absorption, distribution, metabolism, and safe excretion.
Regulatory Framework	Regulated as foods or dietary supplements, with less stringent oversight; safety and labeling emphasized	Regulated as drugs (e.g., FDA, EMA); require extensive preclinical and clinical trials for approval.
Development and Innovation	Focus on functional foods and nutraceuticals; delivery systems (e.g., nanoformulations) under investigation.	The drug discovery pipeline encompasses both plant-derived and synthetic compounds with well-defined molecular targets.
Overall Purpose	Promote general health and reduce disease risk through diet	Treat or prevent specific diseases with high precision and validated clinical outcomes

In summary, while both categories involve substances that influence biological processes, food bioactive compounds are consumed as part of a general healthy diet for broader, long-term health benefits and disease prevention, with ongoing research into their functional properties. In contrast, pharmaceutical bioactive compounds are specifically developed and rigorously regulated as medicines to treat or prevent diseases, with targeted, potent actions and well-defined pharmacokinetic profiles.

Challenges and Limitations in Functional Food Science Research: The translation of in vitro or preclinical results concerning bioactive compounds into substantiated human health benefits remains a challenge. Most polyphenols and carotenoids exhibit poor oral bioavailability due to limited water solubility, instability within food matrices, and extensive metabolic transformation during digestion and first-pass metabolism [58-60]. Encapsulation techniques, such as nanocarriers and nanoemulsions, have shown potential to enhance bioaccessibility by protecting compounds and facilitating controlled release; however, they introduce additional complexities in terms of safety assessment, regulatory clearance, and long-term efficacy evaluation when incorporated into functional food products [58,61-62].

High inter-individual variability in response to bioactive compounds represents another significant challenge. Variability in gut microbiota composition, genetic polymorphisms affecting metabolism, and differences in dietary patterns result in markedly different bioavailability and health benefits across individuals, complicating efforts to establish generalized intake recommendations or valid health claims [63-65]. Clinical trials often rely on surrogate biomarkers rather than definitive health outcomes, and inconsistent dosing protocols, heterogeneous methodologies, and insufficient sample sizes further limit the strength of the evidence base [59, 64, 66]. This variability, coupled with the high cost and logistical complexity of long-term, adequately powered randomized controlled trials, continues to impede regulatory acceptance, consumer confidence, and the commercial advancement of functional foods supported by rigorous science.

Scientific Innovation: This review represents a novel synthesis of emerging research at the intersection of FFS and BC development, offering a comparative analysis of food-derived and pharmaceutical bioactive compounds within a unified framework. By systematically evaluating the definitions, sources, mechanisms of action, and regulatory landscapes of these compounds, the article underscores the need for a cohesive scientific and regulatory approach that bridges nutrition science and pharmacology. Furthermore, the review highlights recent technological advancements, such as nanoencapsulation and controlled-release delivery systems, that enhance the bioavailability and efficacy of BCs. In addressing current limitations in FFS, ranging from variable bioaccessibility and individual response to inconsistent clinical validation, this work not only identifies key knowledge gaps but also provides a critical foundation for future interdisciplinary research and innovation. Ultimately, the review advances the conceptual understanding of FFS as a transformative scientific domain with significant implications for the prevention of chronic diseases and public health policy.

Practical Implications: The findings support a more strategic formulation of FF to improve public health through nutrition. By identifying optimal soil sources, delivery systems, and effective dosages of key BC, this review guides food technologists, clinicians, and health policymakers in developing preventive dietary strategies. The insights also inform consumer education and encourage regulatory clarity, which may facilitate the integration of scientifically validated FF into dietary guidelines and health care practices.

In summary, BC are the cornerstone of FFS, offering scientifically validated health benefits beyond basic nutrition. Understanding the mechanisms, optimal dosages, and delivery systems of these compounds is essential for developing effective dietary strategies to prevent and manage chronic diseases as the field matures. FFS bridges the gap between food and medicine, promoting a proactive and preventative approach to public health. Continued interdisciplinary research, regulatory clarity, and public education will be critical in advancing this promising field and translating its findings into practical health solutions.

Abbreviations: FFC: Functional Food Center; BC: bioactive compounds; PBC: pharmaceutical bioactive compounds; FFS: functional food science; FF: functional foods

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REFERENCES:

1. Martirosyan D., Miller E. Bioactive compounds: the key to functional foods. *Bioactive Compounds in Health and Disease* 2018;1(3): 36. DOI: https://doi.org/10.31989/bchd.v1i3.539
2. Monika J., Singh R., Pella D., Fatima G., Nagrenda Y., Pavol Z., et al. Effects of bioactive compounds in foods on metabolic diseases. *Preprints* 2023. DOI: https://doi.org/10.20944/preprints202305.1474.v1
3. Mondal S, Soumya N, Mini S, Sivan S. Bioactive compounds in functional food and their role as therapeutics. Bioact Comp Health Dis. 2021;4(3):24. DOI: https://doi.org/10.31989/bchd.v4i3.786.
4. Jiang L, Gong X, Ji M, Wang C, Wang J, Li M. Bioactive compounds from plant-based functional foods: a promising choice for the prevention and management of hyperuricemia. *Foods.* 2020;9(8):973. DOI: https://doi.org/10.3390/foods9080973.
5. Hu P, Li D, Wang K, Wang H, Wang Z, Li Z, et al. New phenolic compounds from Vitex negundo var. heterophylla and their antioxidant and NO inhibitory activities. *J Funct Foods.* 2015; 19:174-81. DOI: https://doi.org/10.1016/j.jff.2015.09.016.
6. Martirosyan D, Liufu J. FFC's advancement of the establishment of functional food science. *Functional Foods Health Disease*. 2020;10(8). DOI: https://doi.org/10.31989/ffhd.v10i8.729.
7. Martirosyan D, Sanchez S. Establishment of dosage of bioactive compounds in functional food products. *Funct Food Sci.* 2022;2(3):79. DOI: https://doi.org/10.31989/ffs.v2i3.915.
8. Gur J, Mawuntu M, Martirosyan D. FFC's advancement of functional food definition. *Funct Foods Health Dis*. 2018;8(7):385. DOI: https://doi.org/10.31989/ffhd.v8i7.531.
9. Rashidinejad A. The road ahead for functional foods: promising opportunities amidst industry challenges. *Future Postharvest Food*. 2024;1(2):266-73. DOI: https://doi.org/10.1002/fpf2.12022.
10. Granato D, Barba F, Kovačević D, Lorenzo J, Cruz A, Putnik P. Functional foods: product development, technological trends, efficacy testing, and safety. *Annu Rev Food Sci Technol*. 2020; 11:93-118. DOI: https://doi.org/10.1146/annurev-food-032519-051708.
11. Larona M. Effects of food bioactive compounds on human health and disease prevention in Botswana. *Int J Food Sci.* 2024;7(2):11-21. DOI: https://doi.org/10.47604/ijf.2594.
12. Martirosyan D, Singh J. A new definition of functional food by FFC: what makes a new definition unique? *Functional Foods Health Dis*. 2015;5(6):209. DOI: https://doi.org/10.31989/ffhd.v5i6.183.
13. Carnauba R, Sarti F, Hassimotto N, Lajolo F. Bioactive compounds intake of the Brazilian population according to geographic region. *Plants*. 2023;12(13):2414. DOI: https://doi.org/10.3390/plants12132414.
14. Câmara J, Albuquerque B, Aguiar J, Corrêa R, Gonçalves J, Granato D, et al. Food bioactive compounds and emerging techniques for their extraction: polyphenols as a case study. *Foods*. 2020;10(1):37. DOI: https://doi.org/10.3390/foods10010037.
15. Acevedo-Fani A, Dave A, Singh H. Nature-assembled structures for delivery of bioactive compounds and their potential in functional foods. *Front Chem.* 2020; 8:564021. DOI: https://doi.org/10.3389/fchem.2020.564021.

16. Evans L, Romanick S, Ferguson B. Natural product inhibitors of acetyl-lysine erasers in the prevention and treatment of heart failure. *Funct Foods Health Dis*. 2017;7(8):577. DOI: https://doi.org/10.31989/ffhd.v7i8.376.
17. Sorrenti V, Burò I, Consoli V, Vanella L. Recent advances in health benefits of bioactive compounds from food wastes and by-products: biochemical aspects. *Int J Mol Sci.* 2023;24(3):2019. DOI: https://doi.org/10.3390/ijms24032019.
18. Pendyala B, Patras A. In silico screening of cyanobacterial and food bioactive compounds to predict potential inhibitors of COVID-19 main protease (Mpro), papain-like protease (PLpro), and RNA-dependent RNA polymerase (RdRp). [Preprint]. 2022. DOI: https://doi.org/10.26434/chemrxiv-2022-jsb0h-v3.
19. Simões L, Madalena D, Pinheiro A, Teixeira J, Vicente A, Ramos Ó. Micro- and nano bio-based delivery systems for food applications: in vitro behavior. *Adv Colloid Interface Sci*. 2017; 243:23-45. DOI: https://doi.org/10.1016/j.cis.2017.02.010.
20. Gökmen V, Mogol B, Lumaga R, Fogliano V, Kaplun Z, Shimoni E. Development of functional bread containing nanoencapsulated omega-3 fatty acids. *J Food Eng*. 2011;105(4):585-91. DOI: https://doi.org/10.1016/j.jfoodeng.2011.03.021.
21. Chen S, Martirosyan D. Marketing strategies for functional food products. *Funct Foods Health Dis*. 2021;11(8):335. DOI: https://doi.org/10.31989/ffhd.v0i0.817.
22. Martirosyan D, Stratton S. Advancing functional food regulation. *Bioact Comp Health Dis*. 2023;6(7):166. DOI: https://doi.org/10.31989/bchd.v6i7.1178.
23. Agarwal P, Rutter E, Martirosyan D. Analysis of contemporary epidemiological study research design formats on addressing functional food efficacy. *Funct Food Sci.* 2021;1(12):97. DOI: https://doi.org/10.31989/ffs.v1i12.882.
24. Ye Q, Nicolas G, Selomulya C. Microencapsulation of active ingredients in functional foods: from research stage to commercial food products. *Trends Food Sci Technol*. 2018; 78:167-79. DOI: https://doi.org/10.1016/j.tifs.2018.05.025.
25. Gafare C, Serafini M, Lorenzoni G, Gregori D. Integration of functional and traditional food in emerging markets: regulatory and substantive aspects of yerba mate and quinoa. *Open Agric J*. 2016;10(1):75-80. DOI: https://doi.org/10.2174/1874331501610010075.
26. Alkhatib A, Tsang C, Tiss A, Bahorun T, Arefanian H, Baraké R, et al. Functional foods and lifestyle approaches for diabetes prevention and management. *Nutrients.* 2017;9(12):1310. DOI: https://doi.org/10.3390/nu9121310.
27. Hasler C, Brown A. Position of the American Dietetic Association: functional foods. *J Am Diet Assoc*. 2009;109(4):735-46. DOI: https://doi.org/10.1016/j.jada.2009.02.023.
28. Hasler C. Functional foods: benefits, concerns and challenges—a position paper from the American Council on Science and Health. *J Nutr.* 2002;132(12):3772-81. DOI: https://doi.org/10.1093/jn/132.12.3772.
29. Sadohara R, Martirosyan D. Functional food center's vision on functional food definition and science in comparison to FDA's health claim authorization and Japan's foods for specified health uses. *Funct Foods Health Dis*. 2020;10(11):465. DOI: https://doi.org/10.31989/ffhd.v10i11.753.
30. Williams K, Oo T, Martirosyan D. Exploring the effectiveness of Lactobacillus probiotics in weight management: a literature review. *Funct Food Sci*. 2023;3(5):45. DOI: https://doi.org/10.31989/ffs.v3i5.1115.
31. Grubor B, Калењук Б, Radivojša M, Ćirić M. Functional food: supply and demand in a modern society. Zbornik Radova Departmana Za Geografiju Turizam I Hotelijerstvo. 2020;(49-2):195-207. DOI: https://doi.org/10.5937/zbdght2002195g.
32. Trachtenberg T, Martirosyan D. Addressing vitamin D deficiency through nutritional strategies. *Bioact Comp Health Dis*. 2024;7(6):289-301. DOI: https://doi.org/10.31989/bchd.v7i6.1364.
33. Khan M, Anjum F, Sohaib M, Sameen A. Tackling metabolic syndrome by functional foods. *Rev Endocr Metab Disord.* 2013;14(3):287-97. DOI: https://doi.org/10.1007/s11154-013-9270-8.
34. Jurek J. Health benefits of functional foods. *J Biomed Res Environ Sci.* 2022;3(12):1307-16. DOI: https://doi.org/10.37871/jbres1598.
35. Augustin M, Sanguansri L. Challenges and solutions to incorporation of nutraceuticals in foods. *Annu Rev Food Sci Technol.* 2015; 6:463-77. DOI: https://doi.org/10.1146/annurev-food-022814-015507.
36. Santini A, Cammarata S, Capone G, Ianaro A, Tenore GC, Pani L, et al. Nutraceuticals: opening the debate for a regulatory framework. *Br J Clin Pharmacol*. 2018;84(4):659-72. DOI: https://doi.org/10.1111/bcp.13496

37. Birch C, Bonwick G. Ensuring the future of functional foods. *Int J Food Sci Technol*. 2018;54(5):1467-85. DOI: https://doi.org/10.1111/ijfs.14060

38. Yan S, Miller M, Wencewicz T, Möllmann U. Syntheses and biological evaluation of new cephalosporin-oxazolidinone conjugates. *Medchemcomm*. 2010;1(2)

39. El-Kashef H, El-Emary T, Verhaeghe P, Vanelle P, Samy M. Anticancer and anti-inflammatory activities of some new pyrazolo[3,4-b] pyrazines. *Molecules*. 2018;23(10):2657. DOI: https://doi.org/10.3390/molecules23102657.

40. Rao A, Pasupuleti V, Rao V, Mohan C, Raju C, Reddy C. Microwave-assisted one-pot synthesis of novel α-aminophosphonates and their biological activity. *Bull Korean Chem Soc*. 2010;31(7):1863-8. DOI: https://doi.org/10.5012/bkcs.2010.31.7.1863.

41. Abdel-Mohsen S, El-Emary T, El-Kashef H. Synthesis, anti-inflammatory and antibacterial activities of novel pyrazolo[4,3-g] pteridines. *Chem Pharm Bull* (Tokyo). 2016;64(5):476-82. DOI: https://doi.org/10.1248/cpb.c16-00044.

42. Dobretsov S, Dahms H, Qian P. Antilarval and antimicrobial activity of waterborne metabolites of the sponge Callyspongia (Euplacella) pulvinata: evidence of allelopathy. *Mar Ecol Prog Ser*. 2004; 271:133-46. DOI: https://doi.org/10.3354/meps271133.

43. Alparslan L, Şekeroğlu N, Kijjoa A. The potential of marine resources in cosmetics. *Curr Perspect Med Aromat Plants* (Cupmap). 2018;1(2):53-66. DOI: https://doi.org/10.38093/cupmap.488904.

44. Azam M. Biological activities of 2-mercaptobenzothiazole derivatives: a review. *Sci Pharm*. 2012;80(4):789-823. DOI: https://doi.org/10.3797/scipharm.1204-27.

45. Cano N, Ballari M, López A, Santiago A. New synthesis and biological evaluation of benzothiazole derivates as antifungal agents. *J Agric Food Chem*. 2015;63(14):3681-6. DOI: https://doi.org/10.1021/acs.jafc.5b00150.

46. Jian H, Wei L, Xin P. Bioactive compounds in foods: new and novel sources, characterization, strategies, and applications. *Foods*. 2024;14(9):1617. DOI: https://doi.org/10.3390/foods14091617.

47. Morales D. Insights on the Health Benefits and Functional Potential of Food Bioactive Compounds. *Foods.* 2025;14(11):1984. DOI: https://doi.org/10.3390/foods14111984.

48. Zeng F, Chen Z, Pan Y, Zhang Y, He Y, Li W, et al. Recent advances in health benefits of bioactive compounds from food wastes and by-products: *Biochemical aspects. Int J Mol Sci.* 2023;24(3):2019. DOI: https://doi.org/10.3390/ijms24032019.

49. Kinch MS, Kraft Z, Schwartz T. 2023 in review: FDA approvals of new medicines. *Clin Transl Sci.* 2024;17(3): e13768. DOI: https://doi.org/10.1111/cts.13768.

50. Abedi E, Saeidi S, Khayyamian S, Hosseini SM, Salimi M. Unlocking the potential of bioactive compounds in pancreatic cancer therapy: A promising frontier. Biomed Pharmacother. 2024; 178:117188. DOI: https://doi.org/10.1016/j.biopha.2024.117188.

51. Liu Q, Guo R, Ding W, Wang X. Functional foods and bioactive compounds: A comprehensive review on their role in mitigating drug-induced liver injury. *Front Nutr*. 2024; 11:1499697. DOI: https://doi.org/10.3389/fnut.2024.1499697.

52. Zhang Q, Li Z, Wang C. The latest advances with natural products in drug discovery and opportunities for the future: a 2025 update. *Expert Opin Drug Discov*. 2025 May 20. DOI: https://doi.org/10.1080/17460441.2025.2507382.

53. Alves-Silva I, Cabral L. Dietary bioactive compounds and human health: The role of bioavailability. *Nutrients.* 2025;17(1):48. DOI: https://doi.org/10.3390/nu17010048.

54. Zaki NM, Rashed EA, Rabea KM. Nanotechnology for enhancing bioavailability of food bioactive compounds: Current status and future perspectives. *Curr Drug Discov Technol*. 2022;19(1): e20220302-e20220302. DOI: https://doi.org/10.2174/1570163819666220302143714.

55. Senevirathne M, Egodage D, Gnanapragasam A, Rajapaksha R. The in vitro pharmacokinetics of medicinal plants: A review. *J Pharm Pharmacogn Res*. 2025;13(2):331-345. DOI: https://doi.org/10.56499/jppres24.1837_13.2.331.

56. Pounis G, Sanlier N, Visioli F. The Regulation of Functional Foods, Bioactive Compounds, and Health Claims: An Overview. *Int J Mol Sci.* 2021;22(22):12335. DOI: https://doi.org/10.3390/ijms222212335.

57. Newman DJ, Cragg GM. Natural Products as Sources of New Drugs over the Last 40 Years and Future Directions for Drug Discovery. *J Nat Prod.* 2023;86(4):795-812. DOI: https://doi.org/10.1021/acs.jnatprod.2c00902.

58. Chen L, Liu X, Zhang Z, Rocchetti G, Lucini L., Tanase C. Current understanding of polyphenols to enhance bioavailability for human health. *Front Nutr*. 2023; 10:1184535. DOI: https://doi.org/10.3389/fnut.2023.1184535.

59. Tomas, M., Wen, Y., Liao, W., Zhang, L., Zhao, C.,

McClements, D. J. Recent progress in promoting the bioavailability of polyphenols in plant-based foods. *Crit Rev Food Sci Nutr.* 2024 Apr 9:1–27.
DOI: https://doi.org/10.1080/10408398.2024.2336051.

60. Ul Alam MA, Khatun M, Ul Alam MA. Recent trend of nanotechnology applications to improve bio-accessibility of lycopene by nanocarrier. arXiv. 2023 Jan 25.
DOI: https://doi.org/10.48550/arXiv.2301.10397.
61. Rocha DMUP, Caldas IM, de Moura NF, et al. Bioactivity and bioavailability of carotenoids applied in human health. *Int J Mol Sci.* 2024;25(14):7603.
62. Jacquier EF, van de Wouw M, Nekrasov E, Contractor N., Kassis A, Marcu D. Local and systemic effects of bioactive food ingredients: Is there a role for functional foods to prime the gut for resilience? *Foods.* 2024;13(5):739.
DOI: https://doi.org/10.3390/foods13050739.
63. Kerimi A, Kraut NU, Encarnacao JA, Williamson G. The gut microbiome drives inter- and intra-individual differences in metabolism of bioactive small molecules. *Sci Rep*. 2020; 10:19590.
DOI: https://doi.org/10.1038/s41598-020-76558-5.
64. Pinto PL, Capanoglu E, Nemli E, et al. Factors driving the inter-individual variability in the metabolism and bioavailability of polyphenols: a systematic review. *Trends Food Sci Technol.* 2024; 131:381–394.
65. Possemiers S, Vincken JP, Verstraete W, James Murrough J, Pasinetti GM. How to better consider and understand interindividual variability in polyphenol response. *Mol Nutr Food Res*. 2023;67(22): e2300156.
DOI: https://doi.org/10.1002/mnfr.202300156.
66. Bas T.G. Bioactivity and bioavailability of carotenoids applied in human health. *Int J Mol Sci.* 2024;25(14):7603.
DOI: https://doi.org/10.3390/ijms25147603.