

Review

Bioactive Compounds in Functional Meals: Bioavailability Challenges, Food Technology Approaches, and Health Perspectives—A Narrative Review

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Abstract

Functional meals are emerging, encompassing complete meal systems designed to deliver physiological benefits through food synergy, interactions with the food matrix, and optimized release of bioactive compounds. This narrative review examines the role of bioactive compounds in functional meals, with particular emphasis on bioavailability, food matrix effects, technological approaches, and health implications. Bioactive compounds can contribute to cardiometabolic, anti-inflammatory, gastrointestinal, and neuroprotective effects. However, their biological efficacy depends not only on their concentration in foods but also on their release from the food matrix, stability during processing and digestion, intestinal absorption, microbiota-mediated transformation, and post-absorptive metabolism. Therefore, functional meals represent complex systems in which food structure, culinary preparation, processing intensity, co-ingested nutrients, and host-related factors determine the final physiological response. Emerging technologies, including microencapsulation and nanoencapsulation, offer promising strategies to improve the stability, bioaccessibility, targeted release, and sensory acceptability of bioactives. Future research should prioritize well-designed human studies, standardized methodologies, clinically relevant outcomes, personalized nutritional approaches, and sustainable food system integration to support the development of effective, evidence-based functional meal strategies.

Keywords: functional meals; bioactive compounds; bioavailability; food technologies



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1. Introduction

The global burden of non-communicable diseases (NCDs), including obesity, type 2 diabetes mellitus, cardiovascular diseases, metabolic syndrome, and certain cancers, has intensified interest in the relationship between diet and human health. According to the World Health Organization, unhealthy dietary patterns are among the leading modifiable risk factors contributing to morbidity and mortality worldwide [1]. Simultaneously, rapid urbanization, globalization of food systems, and lifestyle transitions have accelerated

the so-called “nutrition transition”, characterized by increased consumption of energy-dense, highly processed foods and reduced intake of nutrient-rich traditional diets [2]. In this context, nutrition science has progressively shifted from a reductionist perspective focused on isolated nutrients toward a more holistic understanding of dietary patterns, food matrices, and physiological responses to meals.

This paradigm shift has contributed to the emergence of functional foods and, more recently, functional meals. Functional foods are generally defined as foods that provide physiological benefits beyond basic nutrition, potentially reducing disease risk or promoting optimal health. Traditionally, research in this field has focused on single food products enriched with bioactive compounds such as probiotics, polyphenols, dietary fibers, omega-3 fatty acids, phytosterols, peptides, vitamins, and antioxidants [3]. However, contemporary approaches increasingly recognize that health effects are not solely determined by isolated ingredients but also by the interactions between nutrients, food structure, processing, digestion, and meal composition.

Consequently, the concept of functional meals has emerged as a broader and more integrative framework. Functional meals can be understood as complete meal systems intentionally designed to deliver health-promoting effects through optimized combinations of nutrients, bioactive compounds, food matrices, and technological processes [4]. Unlike conventional functional foods, which often emphasize ingredient fortification, functional meals incorporate meal architecture, culinary design, satiety, metabolic regulation, sensory quality, and personalized nutrition strategies. Rodgers [4,5] argued that functional meals represent an intermediate category between traditional foods and nutraceutical interventions, integrating food science, gastronomy, biotechnology, and health promotion into complete meal systems. More recent perspectives also link functional meals to precision nutrition, microbiome modulation, and digitally assisted dietary personalization [6].

An important scientific advancement underpinning this transition is the recognition of the food matrix effect. Increasing evidence demonstrates that the health impact of bioactive compounds depends not only on their concentration in foods but also on their bioavailability, bioaccessibility, stability, and interactions within complex food matrices [7]. The food matrix influences digestion kinetics, nutrient release, absorption, microbial metabolism, and physiological responses. Thus, foods and meals cannot be adequately evaluated exclusively through nutrient composition or front-of-pack nutrient profiling systems. As highlighted by recent research, the structural organization of food components significantly affects metabolic outcomes and disease risk [8]. This perspective has challenged traditional reductionist approaches in nutrition and strengthened interest in meal-based nutritional strategies.

Bioavailability has therefore become a central issue in the development of functional meals. Many bioactive compounds, including polyphenols, carotenoids, curcumin, anthocyanins, phytosterols, and bioactive peptides, exhibit poor solubility, instability during processing and digestion, limited intestinal absorption, or extensive metabolic transformation [9,10]. As a result, technological innovations aimed at improving stability, delivery, and absorption have become essential. Emerging food technologies, including nanoencapsulation, microencapsulation, emulsification systems, liposomes, edible films, fermentation technologies, non-thermal processing, high-pressure processing, pulsed electric fields, and molecular gastronomy approaches, have demonstrated substantial potential to enhance the efficacy of bioactive compounds in functional foods and meals [11].

At the same time, advances in food engineering and hospitality science have broadened the functional meal concept beyond industrial fortification, with the need of food service systems and minimally processed meal production as strategic platforms for delivering health-promoting diets [5,12].

Despite rapid scientific and technological progress, several research gaps remain. First, much of the literature continues to focus on isolated bioactive compounds rather than complete meal systems and dietary matrices. Second, many studies assessing functionality rely on in vitro models or preclinical data, while robust human clinical evidence remains limited. Third, there is still no universally accepted framework integrating bioavailability, food technology, matrix effects, and health outcomes within the concept of functional meals. Finally, emerging areas such as microbiome-mediated bioactivity, personalized functional meals, and sustainable meal engineering remain fragmented across disciplines.

For this narrative review, a targeted literature search was conducted in PubMed/MEDLINE, Scopus, Web of Science and ScienceDirect. Search terms included combinations of “functional meal”, “functional food”, “bioactive compounds”, “bioavailability”, “bioaccessibility”, “food matrix”, “meal composition”, “encapsulation”, “microencapsulation”, “nanoencapsulation”, “non-thermal processing”, “gut microbiota” and “health outcomes”. Peer-reviewed articles, reviews, meta-analyses and relevant human, in vitro and food-technology studies were considered when related to the bioactive compounds, matrix interactions, technological strategies or health implications of functional meals. Priority was given to the recent literature, while seminal older studies were included when conceptually relevant. As this is a narrative review, no formal systematic screening, risk-of-bias assessment or meta-analysis was performed.

To address these research gaps, the aim of this narrative review is to critically examine the current evidence on functional meals through an integrated, systems-based perspective. Specifically, this review synthesizes the evidence on (i) the bioavailability and bioaccessibility of bioactive compounds; (ii) the influence of the food matrix and meal composition; (iii) the role of emerging food technologies in enhancing the stability and efficacy of bioactive compounds; (iv) the potential health implications of functional meal in the prevention and management of chronic diseases; and (v) the development of a conceptual framework integrating these interconnected components within the functional meal concept. Additionally, this review discusses future perspectives involving precision nutrition, personalized meal design, and technologically advanced food systems.

2. Concepts and Terminology

2.1. Functional Foods vs. Functional Meals

The term functional foods, which was first used in Japan in 1984, refers to dietary items capable of producing physiological benefits and contributing to the prevention or management of chronic diseases beyond their basic nutritional value [13–16]. Functional foods can be natural foods without modifications of any type or foods that were modified to add, remove, or modify a component, its bioavailability, or a combination of the previously described [17]. These foods have a dual role: they provide essential nutrients and play an important role in health promotion or reducing the risk of developing certain diseases. The use of this term restricted to particular foods was first questioned because most foods contain naturally present components that are beneficial to health [18,19]. The concept of functional foods has evolved to consider a specific amount, its safety (non-toxicity), and results from clinical trials and studies with specific biomarkers that prove its health claims [14,20,21]. The added value of functional foods is conferred by their bioactive components, substances naturally present or added to foods that exhibit antioxidant, anti-inflammatory, metabolic, or microbiome-regulating effects [13,14,22]. A defining characteristic is that they must be (conventional foods) consumed as part of a normal diet, distinguishing them from nutraceuticals or supplements typically presented in medicinal forms, such as capsules or pills [15,22].

Functional foods fall into three main categories: conventional foods, modified foods, and food ingredients [23]. Natural foods include whole foods that naturally contain beneficial bioactive components (e.g., tomatoes containing lycopene and blueberries containing anthocyanins). Modified foods are enriched foods, fortified foods, or foods enhanced with extra nutrients or health-promoting substances (for example Omega-3 enriched Eggs and margarines fortified with plant sterols). Food Ingredients include specific isolated bioactive components added to other consumable products (e.g., prebiotics, probiotics, and soluble fibers such as beta-glucan) [18,23].

While functional foods (or ingredients) often refer to an isolated component (such as fiber or polyphenols) or a specific food (such as blueberries or olive oil) with beneficial properties, a functional meal encompasses the complex system in which nutrients and non-nutrient components interact with each other. The food matrix defines how the bioactive compound is released and absorbed by the body (bioaccessibility and bioavailability). This distinction is crucial because an isolated compound extracted into a pill or capsule will have a different activity than that present in isolated foods. These foods also present different activities when incorporated into a complete meal, where the interactions between proteins, fats, and carbohydrates can increase or decrease their metabolic effects [14].

The concept of a “functional meal” is often approached as a “meal-based strategy” or “dietary patterns” that targets a specific physiological goal [24]. A functional meal can be defined as a complete eating occasion (meal) intentionally designed to deliver a combination of nutrients and bioactive compounds that work synergistically within the food matrix to promote specific health outcomes. Five key characteristics can be attributed to a functional meal:

- (1) combination of multiple functional foods or bioactive-rich ingredients;
- (2) consideration of matrix interactions (protein–fiber–lipid–phenolic interactions) to enhance bioavailability and physiological effects;
- (3) design with a specific health target (e.g., glycemic control, lipid lowering, menopausal symptom relief);
- (4) consumption as whole meals, not isolated ingredients; and
- (5) demonstration of measurable outcomes in clinical or metabolic markers [24–27].

A meal-based approach emphasizes the health impact of whole meals rather than isolated nutrients, showing that combining bioactive components such as isoflavones, omega-3 fatty acids, fiber, and calcium within a single eating occasion can enhance overall physiological benefits through nutrient synergy [25]. Evidence demonstrates that nutrients consumed together influence each other’s absorption, metabolic rate, and postprandial effects, producing outcomes that single-nutrient strategies cannot capture. For example, mixed meals combining white rice with beans or chickpeas significantly attenuate glycemic responses compared with rice alone, illustrating how the meal matrix modulates digestion and post-prandial glucose control [24]. Similarly, dietary patterns such as the Portfolio Diet, which integrates plant sterols, viscous fibers, soy protein, and nuts, achieve LDL-cholesterol reductions of approximately 30%, comparable to first-line statin therapy [27]. Collectively, these findings reinforce the notion that nutritional functionality emerges from the dietary matrix—the interactions among foods, nutrients, and structures within a meal—rather than from individual foods in isolation. Furthermore, functional foods can produce heterogeneous physiological effects across individuals because their bioactive constituents interact with biological systems that vary markedly among individuals. Differences in genetic architecture, including variants that influence metabolic regulation and xenobiotic metabolism, alter the absorption, transformation, and downstream activities of these compounds. In addition, epigenetic configurations shaped by prior nutritional and environmental exposure modulate the responsiveness of metabolic pathways to functional food components.

Interindividual variations in gut microbiome composition further contribute to this heterogeneity by determining the production of microbial metabolites that mediate many of the biological effects attributed to functional foods. Collectively, these genomic, epigenomic, and microbial determinants, along with lifestyle and environmental factors, support the substantial variability observed in functional food efficacy across individuals [28].

Unlike dietary patterns, which primarily describe habitual food consumption, the concept of functional meals proposed in this review focuses on the intentional design of individual meals to achieve specific physiological outcomes. This approach integrates not only the selection of bioactive ingredients but also food matrix optimization, meal composition, processing technologies, bioavailability, gastrointestinal digestion, gut microbiota interactions, and host-related factors into a single systems-based framework. Therefore, functional meals are presented as intentionally designed nutritional systems that integrate nutritional, technological, and biological determinants to achieve targeted physiological responses, rather than simply combinations of healthy foods.

2.2. Bioactive Compounds

Bioactive compounds are naturally occurring, non-essential chemical constituents of foods and other biological sources that exert measurable physiological effects that extend beyond basic nutritional requirements. Although not required for survival in the same way as essential nutrients, these molecules, which are abundant in fruits, vegetables, whole grains, nuts, herbs, and plant-derived oils, play important roles in modulating metabolic and cellular processes that influence human health [22]. Often referred to as phytonutrients or phytochemicals when derived from plants, bioactive compounds contribute to the organism's defense against environmental stressors and, when consumed, offer protective effects relevant to the prevention and mitigation of chronic noncommunicable diseases, such as cancer and cardiovascular disorders. Their capacity to regulate biological pathways, reduce oxidative stress, and their capacity to modulate inflammatory pathways highlights their increasing relevance in nutrition and public health research [29–32]. Functional foods deliver a wide range of bioactive compounds—including probiotics, prebiotics, polyphenols, carotenoids, omega-3 PUFAs, bioactive peptides, and functional fibers among others—that act on metabolism through complementary mechanisms [13,29,30,33]. Although food-derived bioactive compounds are widely categorized into distinct structural or functional groups based on their clinical mechanisms and human health outcomes, the precise taxonomic frameworks used in the literature reflect a lack of structural consensus depending on whether the authors prioritize chemical structure, biosynthetic pathways, or physiological targets [22].

2.2.1. Polyphenols

Polyphenols are a vast and structurally diverse class of natural compounds that are broadly categorized into flavonoids (such as quercetin and catechins) and non-flavonoids, which include phenolic acids (e.g., caffeic acid), stilbenes (e.g., resveratrol), and lignans. Abundant in fruits, vegetables, berries, grapes, tea, coffee, and whole grains, these molecules exert physiological effects through several complementary mechanisms that promote metabolic balance and cellular longevity [22,29]. Their strong antioxidant activity enables them to neutralize reactive oxygen and nitrogen species (ROS and RNS, respectively), thereby reducing oxidative stress-induced cellular damage. At the molecular level, polyphenols modulate inflammatory signaling by inhibiting IKK activation and preventing NF- κ B nuclear translocation, which suppresses the expression of pro-inflammatory cytokines, such as TNF- α and IL-6 [19,34]. They also contribute to metabolic regulation by inhibiting digestive enzymes, including α -amylase, α -glucosidase, and pancreatic li-

pase. Some polyphenols can attenuate DPP-IV activity, supporting incretin preservation in type 2 diabetes [29,35]. Certain flavonoids also display antimicrobial properties by targeting bacterial ATP synthase, disrupting membrane integrity, and inducing osmotic stress [34,36]. However, their *in vivo* efficacy is strongly constrained by bioavailability, as absorption is limited by interactions within the food matrix and the need for enzymatic or microbiota-mediated hydrolysis to generate absorbable aglycones [23,29].

Polyphenols are among the most extensively studied bioactive compounds, but the strength of evidence differs substantially according to the outcome considered. While *in vitro* and observational evidence is abundant, human intervention studies remain heterogeneous in terms of compound source, dose, food matrix, intervention duration and biomarkers assessed [29,30,35,37–40]. In functional meals, polyphenols may interact with other meal components in ways that either enhance or reduce their bioaccessibility. For example, dietary fat may improve the bioavailability of selected compounds such as quercetin, whereas interactions with proteins and dietary fiber can modify polyphenol release during digestion [38,41–43]. Major unresolved questions include the identification of clinically effective doses, the contribution of gut microbiota-derived metabolites, and whether short-term changes in oxidative, inflammatory or metabolic biomarkers translate into clinically meaningful long-term outcomes [37,38,40].

2.2.2. Carotenoids

Carotenoids are a major class of lipophilic tetraterpene pigments responsible for the characteristic coloration of many fruits, vegetables, leafy greens, and certain animal-derived foods, such as egg yolks. Structurally, they are grouped into two principal subclasses: hydrocarbon carotenes (e.g., β -carotene and lycopene) and oxygenated xanthophylls (e.g., lutein and zeaxanthin) [44]. Their extensive conjugated double-bond systems possess high singlet oxygen-scavenging efficiency, enabling carotenoids to mitigate oxidative stress and indirectly protect cellular components, including DNA, from oxidative damage [28,44]. In addition to their capacity to neutralize free radicals, carotenoids influence redox homeostasis by modulating cytoprotective pathways, notably through the activation of the Nrf2/Keap1 signaling axis [19,44]. Several carotenoids also function as provitamin A precursors, supporting essential physiological processes such as vision, immunity, and cellular differentiation. Their biological roles are highly tissue-specific; for example, the xanthophylls lutein and zeaxanthin selectively accumulate in the retina, where they act as natural filters of high-energy light and contribute to photoprotection [29,44]. However, the *in vivo* efficacy of carotenoids is constrained by their bioavailability. Efficient absorption requires the disruption of plant chromoplasts, facilitated by food processing, such as cooking, and subsequent incorporation into mixed micelles within the gastrointestinal tract, a process strictly dependent on the presence of dietary lipids [23,29].

Evidence regarding carotenoids is relatively strong for bioavailability outcomes, particularly changes in circulating carotenoid concentrations, but less consistent for direct clinical endpoints. Their incorporation into functional meals is highly dependent on matrix disruption, thermal processing, dietary lipid content and micellar incorporation [44–47]. Synergistic meal effects may occur when carotenoid-rich foods are consumed with lipid sources that facilitate micelle formation, whereas insufficient dietary fat or poorly disrupted plant matrices may limit absorption [45–47]. Although dose-related increases in circulating carotenoid concentrations have been reported, clinically meaningful thresholds for disease prevention remain uncertain and are likely influenced by baseline nutritional status, food source, processing method and interindividual variability [44,45,47].

2.2.3. Phytosterols

Phytosterols are a class of plant-derived sterols widely present in foods such as nuts, seeds, cereals, and vegetable oils [23]. Due to their structural similarity to cholesterol, their principal therapeutic action is the reduction in circulating low-density lipoprotein (LDL) cholesterol [23,29]. This effect arises from their ability to compete with dietary and biliary cholesterol for incorporation into mixed micelles and transport via the Niemann–Pick C1-Like 1 (NPC1L1) transporter at the enterocyte membrane. By limiting cholesterol uptake, phytosterols effectively reduce the amount of cholesterol entering the systemic circulation, thereby contributing to a decrease in cardiovascular risk [23]. However, their pronounced lipophilicity restricts absorption, meaning that *in vivo* efficacy can be enhanced through advanced dispersible formulations or co-administration with emulsifiers that improve micellar solubilization.

Compared with many other bioactive compounds, phytosterols have one of the strongest human evidence bases, particularly regarding LDL-cholesterol reduction. Meta-analyses of randomized controlled trials support a dose–response relationship between phytosterol intake and LDL-cholesterol lowering, with increasing effects reported up to intakes of approximately 3 g/day [48–51]. However, most evidence derives from enriched foods or supplements rather than complete functional meals. Within meals, phytosterol efficacy depends on the lipid matrix and their competition with cholesterol for incorporation into mixed micelles, which should be considered when designing functional meal systems aimed at lipid lowering [48,49].

2.2.4. Glucosinolates (GSLs) and Organosulfur Compounds (OSCs)

Glucosinolates (GSLs) and Organosulfur Compounds (OSCs) are two major classes of sulfur-containing phytochemicals characteristic of Brassica and Allium vegetables. GSLs are stable thioglucoside precursors that, upon cellular disruption, are hydrolyzed by myrosinase to yield bioactive metabolites such as isothiocyanates, nitriles, and indoles [31,52]. These metabolites, particularly isothiocyanates such as sulforaphane, exert potent cytoprotective effects by activating the Nrf2 pathway, thereby inducing phase II detoxification enzymes involved in xenobiotic clearance and redox homeostasis. In parallel, organosulfur compounds (OSCs) from Allium species, including allicin and related allyl-sulfur derivatives, undergo enzymatic conversion to reactive intermediates that function as indirect antioxidants and modulators of inflammatory signaling. Mechanistically, OSCs suppress NF- κ B activation, reducing downstream mediators such as nitric oxide and prostaglandin E₂ through transcriptional inhibition of iNOS and COX-2, while simultaneously enhancing endogenous antioxidant defenses via Nrf2-dependent gene expression [32]. The biological activity of both GSL-derived metabolites and OSCs is strongly influenced by their bioavailability, which depends on enzymatic hydrolysis, food matrix interactions, and interindividual variability in gut microbiota capable of contributing thioglucosidase activity. Together, these mechanisms position GSLs and OSCs as key contributors to the health-promoting properties of Brassica and Allium vegetables [52].

For glucosinolates and organosulfur compounds, epidemiological evidence supports their biological relevance, but human intervention studies remain comparatively limited and heterogeneous [31,52–54]. Their activity within meals is strongly affected by food preparation, particularly chopping, cooking and the preservation or inactivation of myrosinase. Synergistic effects may occur when Brassica vegetables are consumed in meal contexts that preserve enzymatic conversion to isothiocyanates, whereas excessive thermal processing may reduce the formation of bioactive metabolites. Key unresolved questions include the role of gut microbiota in compensating for myrosinase loss, the identification of

effective intake levels, and the translation of biomarker changes into clinically meaningful outcomes [52–54].

2.2.5. Bioactive Peptides

Bioactive peptides are short, specific amino acid sequences encrypted within parent proteins and released through enzymatic hydrolysis. Commonly derived from dairy products, meat, and marine organisms, these peptides exert diverse physiological effects once liberated [23]. They modulate metabolic function by influencing blood pressure, primarily through competitive inhibition of angiotensin-converting enzyme (ACE), and by contributing to the regulation of glucose homeostasis [33,55]. Many also display marked immunomodulatory activity; certain peptide fragments act as endogenous antimicrobial agents that support host defense and modulate inflammatory signaling [55]. Despite their therapeutic potential, their *in vivo* efficacy is often limited by poor bioavailability, as they are highly vulnerable to gastrointestinal protease degradation. Consequently, preserving peptide integrity during intestinal transit remains a major barrier to achieving effective systemic delivery [29].

The evidence for bioactive peptides is strongest for selected outcomes such as blood pressure regulation, particularly for specific food-derived peptides with angiotensin-converting enzyme inhibitory activity. Nevertheless, evidence for broader metabolic, antioxidant or immunomodulatory effects remains less consistent and is often based on *in vitro* digestion models, animal studies, purified peptides or fortified foods rather than whole functional meals. In meal systems, peptide bioactivity may be influenced by fermentation, food matrix composition and interactions with other macronutrients, while gastrointestinal degradation remains a key limitation. Important unresolved issues include peptide stability during digestion, sequence-specific bioactivity, effective dose ranges, and confirmation of clinically relevant effects in well-designed human meal-based trials [55–58].

2.2.6. Prebiotics and Probiotics

Gastrointestinal ecosystem homeostasis is highly regulated by a synergistic interplay among prebiotic fibers, probiotics, and postbiotic metabolites, which collectively modulate the gut microbiota composition to enhance digestion, immune function, and systemic health. Prebiotics are nondigestible carbohydrates, such as inulin and fructooligosaccharides (FOS), naturally present in whole grains, garlic, onions, and bananas, that resist degradation in the upper gastrointestinal tract and reach the colon intact. Within the large intestine, they act as selective metabolic substrates that preferentially stimulate beneficial commensal taxa, particularly *Bifidobacterium* and *Lactobacillus*, while limiting the competitive expansion of opportunistic pathogens. Beyond shaping microbial ecology, inulin-type fructans strengthen host defenses by lowering systemic zonulin concentrations, thereby reducing pathological intestinal permeability and reinforcing tight junction integrity [19,59]. This ecological network is complemented by probiotics, frequently characterized as live biotherapeutics, which support microbial homeostasis, although their therapeutic reliability is often constrained by high sensitivity to gastric acidity. Mechanistically, these live microbes operate through both “addition” mechanisms—such as the secretion of short-chain fatty acids (SCFAs), bacteriocins, and antimicrobial organic acids—and “subtraction” mechanisms, in which certain strains metabolize exogenous harmful substances, including toxins, carcinogens, and heavy metals. Furthermore, they provide competitive exclusion by physically occupying mucosal adhesion sites along the intestinal wall to block pathogen colonization. Ultimately, many of the physiological benefits of this axis are replicated or mediated by postbiotics, which encompass cell-free, inanimate microbial components and specific chemical byproducts, such as butyrate. Generated

through bacterial fermentation of dietary fibers or delivered as stable, non-viable formulations, these metabolites directly modulate the indigenous microbiota, enhance barrier function, and exhibit robust antioxidant and anti-inflammatory properties. Because they confer these therapeutic benefits without requiring live cell viability, postbiotics avoid the stability limitations of traditional probiotics while acting as potent signaling molecules that regulate systemic host metabolism, immunological pathways, and bidirectional brain–gut axis communication [59].

Among microbiota-targeted bioactives, prebiotics and probiotics have a substantial evidence base, but their effects are highly strain-specific, substrate-specific and context-dependent. Human trials support benefits for selected gastrointestinal, immune and metabolic outcomes; however, results cannot be generalized across all probiotic strains or prebiotic fibers. Within functional meals, synergistic effects may arise from synbiotic combinations, in which prebiotic substrates support probiotic survival and activity, whereas processing, storage conditions, acidity, oxygen exposure and matrix composition may reduce viability or efficacy. Major unresolved questions include personalization according to baseline microbiota composition, the durability of microbiome changes, and the establishment of clinically meaningful dose–response relationships [59–64].

2.2.7. Omega-3

Omega-3 fatty acids constitute a critical class of polyunsaturated fatty acids (PUFAs) essential for maintaining cellular homeostasis. This family includes eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), predominantly obtained from marine sources such as salmon and mackerel, as well as α -linolenic acid (ALA) derived from plant-based oils such as flaxseed and chia [23,65]. Structurally, these molecules, particularly DHA, are readily incorporated into membrane phospholipids, especially within highly specialized tissues such as the brain and retina. By integrating into the lipid bilayer, they modulate membrane fluidity, influence lipid raft organization, and preserve the structural environment required for efficient signal transduction and neuronal function [19,23]. Omega-3 PUFAs also regulate inflammatory pathways through two complementary mechanisms: they competitively inhibit the enzymatic conversion of arachidonic acid into pro-inflammatory eicosanoids and serve as substrates for the biosynthesis of specialized pro-resolving mediators (SPMs), including resolvins, protectins, and maresins, which actively promote the resolution of inflammation [23]. Their *in vivo* efficacy is strongly shaped by pharmacokinetic factors, as systemic bioavailability varies with the lipid content of co-ingested meals and the chemical form administered, with natural triglycerides exhibiting higher absorption efficiency than synthetic ethyl esters [65].

Omega-3 fatty acids are supported by a comparatively strong body of human evidence, particularly for triglyceride lowering and selected anti-inflammatory outcomes. However, clinical effects vary according to dose, chemical form, baseline cardiometabolic risk, background diet and the lipid composition of the meal. Synergistic effects may occur in Mediterranean-style meals combining omega-3 fatty acids with polyphenols, fiber and unsaturated fats, whereas the overall fatty acid profile of the diet may modulate downstream inflammatory pathways. Dose–response relationships are better established for triglyceride reduction than for broader cardiometabolic, neuroprotective or inflammatory endpoints [65,66].

2.2.8. Alkaloids and Terpenoids

Alkaloids and terpenoids are fundamental classes of secondary plant metabolites widely distributed across herbs, spices, and medicinal plants, exerting diverse pharmacological activities, including antimicrobial, analgesic, anti-inflammatory, and neuroprotective

effects [34,67]. In the context of infectious diseases, both groups contribute to the control of multidrug-resistant pathogens through distinct biochemical mechanisms. Alkaloids, which are nitrogen-containing compounds, exert bioactivity by forming specific hydrogen bonding and π -stacking interactions with cellular proteins, enzymes, and nucleic acids. Their main actions include blocking microbial efflux pumps to restore antibiotic effectiveness, insertion between DNA strands to disrupt replication and repair, and blocking cell division by preventing microtubule assembly or Z-ring formation. In contrast, terpenoids are lipophilic isoprenoid-derived molecules whose structural features confer broad-spectrum antimicrobial and antimalarial properties. They act primarily by compromising microbial membrane integrity, interfering with quorum-sensing pathways, and impairing cellular energy metabolism by inhibiting ATP-associated enzymes. Additionally, specialized sesquiterpenoids, such as artemisinin, exploit a unique endoperoxide bridge to generate cytotoxic carbon-centered radicals that selectively alkylate essential parasite proteins [34].

Compared with other bioactive classes, the evidence supporting alkaloids and terpenoids in functional meal contexts remains less developed. Many reported effects are derived from *in vitro*, preclinical or pharmacological studies, whereas human meal-based intervention trials are scarce. Their bioactivity may be influenced by processing, matrix interactions and potential interactions with other phytochemicals. Although some compounds may contribute to antimicrobial, anti-inflammatory or neuroprotective effects, unresolved questions remain regarding safety, effective dietary doses, bioavailability in complex meals and the clinical relevance of mechanistic findings. Therefore, their role in functional meal design should currently be interpreted with caution [34,67].

Although bioactive compounds constitute the core functional components of functional meals, their health effects cannot be interpreted independently. Rather, they are influenced by multiple interacting factors, including the food matrix, meal composition, food technologies, gastrointestinal digestion, gut microbiota, and host-related characteristics. Therefore, functional meals should be regarded as complex biological systems in which these components interact dynamically to determine bioavailability and ultimately physiological responses (Figure 1).

As illustrated in Figure 1, functional meals should not be considered as a simple combination of functional ingredients but as integrated systems in which technological, nutritional and biological factors continuously interact. Bioactive compounds are released from a complex food matrix during digestion, their bioavailability is further modulated by the gut microbiota and host characteristics, and these processes ultimately determine the magnitude of physiological responses and health outcomes. This systems-based perspective provides the conceptual foundation for the following sections, which discuss each component in greater detail.

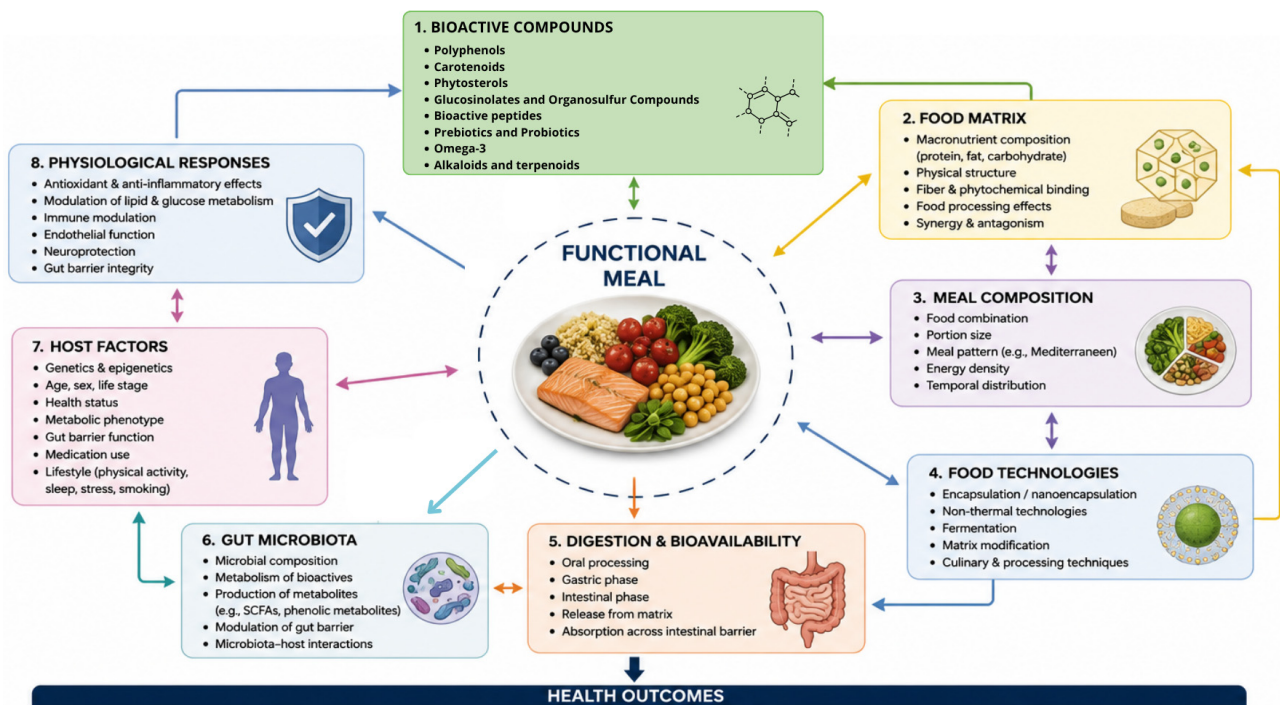


Figure 1. Conceptual framework illustrating the interactions among bioactive compounds, food matrix, meal composition, food technologies, digestion, gut microbiota and host-related factors that collectively determine the bioavailability and health effects of functional meals.

3. Bioavailability of Bioactives in Functional Meals

Bioavailability is defined as the fraction of an ingested bioactive compound that is released from the food matrix, is not affected by gastrointestinal conditions, is absorbed, metabolized, reaches the systemic circulation or target tissues, and becomes available to exert biological effects. In functional meals, in addition to the chemical concentration of the bioactive compound in the food, bioavailability is determined by its bioaccessibility, molecular form, interactions with the matrix, co-ingested nutrients, food processing, digestive transformations, microbiota-mediated metabolism, and interindividual physiological variability. The beneficial effect of bioactives on health depends not only on their nominal content, but also on their release, stability, absorption, and post-absorptive metabolism [13,68].

Bioactive compounds are generally not consumed as isolated molecules, but rather as part of complex food matrices containing proteins, lipids, carbohydrates, dietary fiber, minerals, and other phytochemicals. As illustrated in Figure 1, the food matrix represents one of the central determinants of bioactive compound bioavailability because it influences their release, stability, interactions with other meal components and gastrointestinal accessibility.

The food matrix includes the physical and chemical organization of food components, such as cell structures, particle size, viscosity, degree of emulsification, protein networks, starch granules, lipid droplets, fiber matrices, and interactions between macro and micronutrients. These structural characteristics influence the accessibility of digestive enzymes, the release of bioactives from plant or animal tissues, their solubilization in gastrointestinal fluids, and their incorporation into absorbable forms [42,43,68].

In plant-based functional meals, many bioactive compounds are trapped within cell walls, vacuoles, chromoplasts, protein bodies, or fiber-rich structures. Mechanical disruption, cooking, homogenization, fermentation, and other processing steps can increase bioaccessibility by breaking down these barriers and facilitating compound release [37,45,69]. For example, dietary lipids can improve the absorption of lipophilic or poorly water-soluble

compounds by promoting their incorporation into mixed micelles, as demonstrated for quercetin [41] and carotenoids such as lycopene [45]. On the other hand, proteins and dietary fiber can interact with phenolic compounds through covalent or non-covalent associations, modifying their release during gastrointestinal digestion [42,43]. Therefore, the matrix should be considered as an important determinant of bioactive compounds and their biological potential.

Meal composition can substantially modify the bioavailability of bioactive compounds. Lipids are among the most relevant modulators, particularly for hydrophobic or poorly water-soluble compounds, such as carotenoids, curcumin, phytosterols, fat-soluble vitamins, and some polyphenols [41,45,68,70,71]. Dietary fat promotes bile secretion, mixed micelle formation, intestinal solubilization, and chylomicron-mediated transport, thus increasing the absorption of lipophilic compounds. This has been demonstrated for quercetin, whose bioavailability increases when consumed with dietary fat [41], and for lycopene, whose absorption depends on matrix disruption, lipid availability, micellar incorporation, and lipoprotein transport [45].

Proteins can also influence bioavailability, although their effects depend on the compound class and the food matrix. Protein-polyphenol interactions can occur through non-covalent associations, including hydrogen bonds and hydrophobic interactions, or through covalent bonding after the oxidation of phenolic compounds [42,43]. These interactions can reduce the release of phenolic compounds in the small intestine, but they can also protect phenolics from degradation and promote their delivery to the colon, where microbial metabolism can generate smaller and potentially bioactive metabolites [38,69]. In addition, protein digestion can release bioactive peptides with antihypertensive, antioxidant, immunomodulatory, or metabolic effects, making proteins modulators and sources of bioactivity in functional meals [56,57].

Dietary fiber exerts equally complex effects. Soluble fiber can increase viscosity, delay gastric emptying, delay glucose absorption, and modulate postprandial metabolic responses. At the same time, fibers can trap bioactive compounds or bind them in the intestinal lumen, reducing immediate absorption in the small intestine [38,43]. However, this delayed release can increase the amount of substrate that reaches the colon, where the gut microbiota can transform unabsorbed polyphenols and fibers into bioactive metabolites, including phenolic acids and short-chain fatty acids [38,69]. Therefore, fibers can reduce acute bioavailability in some contexts, while increasing microorganism-derived bioactivity in others.

Minerals can also modulate bioavailability by forming complexes with phenolics, phytochemicals, fibers, or other charged molecules. These interactions can reduce mineral absorption or modify the solubility and release of bioactive compounds [14]. Therefore, formulating functional meals requires careful consideration of nutrient-bioactive interactions, particularly when the goal is to enhance specific physiological effects, such as glycemic control, lipid reduction, antioxidant activity, or microbiota modulation.

The gut microbiota is critical for the bioavailability and bioactivity of compounds after absorption in the small intestine. Polyphenols, fibers, glucosinolates, and some peptides can be metabolized into smaller phenolic acids, valerolactones, isothiocyanates, or other derivatives with distinct biological activities. In turn, bioactive compounds can modulate the composition and function of the microbiota, creating a bidirectional diet-microbiota-health axis [37,38].

Food processing is also a decisive determinant of bioavailability. Heat treatments, fermentation, homogenization, grinding, extrusion, non-thermal technologies, and encapsulation can disrupt plant cell walls, inactivate degradative enzymes, promote isomerization, improve solubility, or protect labile compounds during digestion. On the other hand,

excessive heat, exposure to oxygen, changes in pH, or strong matrix binding can degrade bioactive compounds or reduce their intestinal release. The same technology can have opposite effects depending on the compound class, the food matrix, and the intensity of processing [32,69].

Illustrative meal-based examples help demonstrate how meal composition can modify bioactive compound bioavailability. For example, a Mediterranean-style meal containing cooked tomato, olive oil, vegetables, legumes, whole grains and herbs provides a favorable matrix for several bioactive compounds. In this context, thermal processing and mechanical disruption of tomato tissues can enhance lycopene release, while olive oil promotes micellar incorporation and intestinal absorption of carotenoids [45–47]. Similarly, the presence of dietary fat may improve the bioavailability of selected lipophilic or poorly water-soluble compounds, as shown for quercetin [41]. At the same time, dietary fiber from legumes, vegetables and whole grains may slow glucose absorption and modulate postprandial responses, while also delaying the release of some polyphenols and increasing their delivery to the colon, where microbiota-mediated metabolism may generate bioactive metabolites [37,38,43]. Therefore, in Mediterranean-type meals, lipid-mediated absorption, fiber-driven metabolic modulation and polyphenol–microbiota interactions may act together to support cardiometabolic functionality.

By contrast, a Western-style meal rich in refined carbohydrates, processed meats, saturated fats and low in fiber and phytochemical-rich plant foods may provide a less favorable matrix for functional bioactivity. Although a high-fat meal may enhance the absorption of some lipophilic compounds, the overall meal context may be characterized by lower bioactive density, reduced fiber-mediated modulation of digestion, limited microbiota-accessible substrates and greater postprandial metabolic stress. Thus, the bioavailability and physiological impact of a bioactive compound cannot be interpreted independently of the complete meal matrix. These examples illustrate why functional meals should be designed as integrated systems in which food source, processing, lipid quality, fiber content, phytochemical diversity and microbiota interactions are considered together rather than as isolated nutritional variables [37,38,68,72–74].

Table 1 summarizes the main bioavailability constraints, study contexts, technological strategies and remaining knowledge gaps reported in representative review articles published between 2021 and 2026. Overall, the evidence indicates that low solubility, poor stability, matrix binding, digestive degradation, limited intestinal absorption, and microbiota-dependent transformation are recurrent determinants across bioactive classes. However, the direction and magnitude of these effects vary according to compound chemistry, meal composition, processing intensity, and host-related factors.

Table 1. Bioavailability of bioactive compounds and technological strategies to enhance bioaccessibility and bioavailability. Summary table with review articles published between 2021 and 2026.

Bioactive Compound/Main Food Source	Form Studied	Study Model	Main Bioavailability Limitations	Technological Strategies	Key Knowledge Gaps/Conflicting Evidence	Ref.
Mixed bioactive compounds (polyphenols, carotenoids, omega-3, probiotics/prebiotics, vitamins, peptides; plant and animal food sources)	- Whole foods - Enriched/fortified foods - Extracts - Isolated compounds - Encapsulated systems - Exact form varies across the reviewed literature	- In vitro digestion/bioaccessibility models - Preclinical studies - Human evidence - Food-system studies - Not consistently separated by compound class	- Low solubility/permeability - Enzymatic and digestive degradation - Instability to heat, pH, oxygen and light - Food-matrix interactions - Interindividual variability	- Encapsulation - Nanoemulsions - Liposomes - Biopolymer carriers - Non-thermal processing - Edible coatings - Omics/ AI-assisted formulation.	- Need compound-specific human data - Limited meal-level studies - Limited standardization of bioaccessibility/bioavailability methods - Unclear translation from improved stability to clinical outcomes.	[13,68,75,76]
Polyphenols (fruits, berries, grapes, tea, coffee, cocoa, whole grains, legumes, vegetables)	- Whole foods - Extracts - Purified polyphenols - Phenolic-rich fractions - Fermented matrices - Delivery systems.	- In vitro digestion/fermentation - Cell and animal models - Human intervention studies - Human evidence is heterogeneous.	- Low water solubility and instability - Matrix binding to proteins/fibers - Limited small-intestinal absorption - Extensive phase II and microbiota metabolism - High interindividual variability	- Fermentation - Enzymatic treatment - Emulsification - Micro/nanoencapsulation - Non-thermal processing (HPP, PEF, cold plasma, supercritical CO₂) - Food-matrix optimization.	- Limited RCTs using complete meals - Unclear dose-response for clinically meaningful outcomes - Need for better identification of active metabolites - Need for responder/non-responder profiles.	[37–40]
Quercetin (onions, apples, berries, tea, capers; often studied as quercetin glycosides or formulations)	- Different quercetin formulations - Food matrices - Systematic review focused on human intervention studies using blood or urine biomarkers	Human intervention studies	- Depends on glycoside/aglycone form - Depends on physicochemical properties - Food matrix effects - Influence of dietary fat/fiber - Absorption, metabolism and excretion variability	- Lipid complexation - Glucosylation - Cyclodextrin complexes - Self-emulsifying systems - Encapsulation - Phytosomes - Co-ingestion with dietary fat	- High heterogeneity in formulations and biomarkers - Limited meal-based comparisons - Need clinically relevant endpoints beyond plasma/urinary recovery.	[70]
Anthocyanins (berries, grapes, black carrot, red/purple fruits and vegetables; acai and similar anthocyanin-rich matrices)	- Whole foods - Extracts - Purified anthocyanins - Encapsulated systems - Whole-food vs. extract comparison not consistently reported across all reviews.	- In vitro digestion/bioaccessibility models - In vivo studies - Epidemiological/human evidence - Some reviews emphasize in vitro bioaccessibility	- Low stability at intestinal pH - Sensitivity to heat, light, oxygen and enzymes - Matrix-dependent release - Microbial metabolism - Generally limited systemic bioavailability	- Microencapsulation/nanoencapsulation - Acidification - Co-pigmentation - Lyophilization - Co-ingestion with lipid/carotenoid-rich matrices - Optimization of pectin/casein interactions	- Need for standardized human bioavailability studies - Uncertainty over whole-food vs. extract superiority - Limited evidence on meal-level interactions - Limited evidence on clinically relevant outcomes	[17,77]

Table 1. Cont.

Bioactive Compound/Main Food Source	Form Studied	Study Model	Main Bioavailability Limitations	Technological Strategies	Key Knowledge Gaps/Conflicting Evidence	Ref.
Carotenoids (lycopene from tomato/tomato products; beta-carotene from carrots, leafy greens, orange fruits and vegetables)	- Whole foods - Processed foods - Extracts/supplements - Isolated carotenoids.	- Mixed evidence strongly based on in vivo/human studies - In vitro models are less emphasized for lycopene due to carotenoid instability.	- Lipophilicity - Release from chromoplasts/plant tissue - Trans-cis isomerization - Dependence on dietary fat, bile acids - Dependence on micellarization and chylomicron/lipoprotein transport - Genetic variability	- Mild thermal processing - Mechanical homogenization - Lipid addition - Oil-based/emulsion formulations - Matrix disruption to improve micellarization	- Need for clearer distinction between effects of parent compounds and metabolites - Limited standardized meal-based bioavailability studies - Need for better integration of genotype and food-matrix effects	[45–47]
Curcumin (turmeric/rhizome of <i>Curcuma longa</i> ; curcuminoid-rich extracts and formulated curcumin)	- Pure curcumin/curcuminoids - Turmeric extracts - Adjuvant formulations - Complexes - Nanoformulations - Encapsulated systems	- In vitro studies - Preclinical studies - Human clinical/formulation studies	- Very poor aqueous solubility - Chemical instability - Low gastrointestinal absorption - Rapid intestinal/hepatic metabolism - Glucuronidation/sulfation - Rapid systemic elimination - Limited tissue distribution	- Adjuvants, e.g., piperine - Phospholipid complexes - Micelles - Liposomes - Nanoparticles - Nanoemulsions - Encapsulation and other advanced formulations	- Unclear whether higher plasma curcuminoid levels translate into stronger clinical effects - Need for long-term safety studies - Need for meal-matrix studies	[71,78]
Phytosterols (vegetable oils, nuts, seeds, cereals, legumes; fortified foods)	- Free sterols/stanols - Esterified sterols/stanols - Glycosylated sterols/stanols - Enriched foods - Emulsions - Oleogels - Liposomes - Nanoparticles	- Mechanistic studies - Preclinical studies - Human cholesterol-lowering studies - Review-level model not always separated	- Very low intestinal absorption, approximately 0.5–2% - Low oil/water solubility - Micellar competition with cholesterol - NPC1L1 uptake - ABCG5/8 efflux - Genetic variability	- Emulsions - Oleogels - Liposomes - Nanoparticles - Esterification - Chemical or enzymatic modification - Food-matrix design to improve dispersibility and micellar incorporation	- Need for food-matrix-specific delivery studies - Limited evidence on outcomes beyond LDL-cholesterol - Need for better understanding of genetic variability - Need for long-term functional meal applications	[48,49]
Bioactive peptides (dairy, meat, marine proteins; plant proteins released during fermentation, e.g., cereals, legumes and fermented plant-based foods)	- Protein hydrolysates - Peptide fractions - Purified peptides - Fermented food matrices	- Simulated gastrointestinal digestion - In vitro bioactivity assays - Food-matrix studies - Preclinical evidence - Limited human evidence - Not consistently specified across all reviews	- Susceptibility to gastrointestinal proteolysis - Sequence-dependent absorption - Matrix interactions - Loss of bioactivity during processing/storage - Limited systemic delivery	- Controlled enzymatic hydrolysis - Fermentation - Fortification with hydrolysates - Protective food matrices - Encapsulation or delivery approaches to preserve peptide integrity	- Need for identification of active peptide sequences after digestion - Limited human bioavailability and dose-response data - Few complete meal-level intervention studies	[56,57]

Table 1. Cont.

Bioactive Compound/Main Food Source	Form Studied	Study Model	Main Bioavailability Limitations	Technological Strategies	Key Knowledge Gaps/Conflicting Evidence	Ref.
Probiotics and prebiotics (live bacteria in fermented dairy/non-dairy foods; inulin, FOS and other fibers from whole grains, garlic, onion, banana and plant matrices)	• Live strains • Probiotic-enriched foods • Prebiotic substrates • Synbiotic-type matrices • Exact strain/substrate varies by study	• Food storage/processing studies • Simulated gastrointestinal survival models • In vitro microbiota studies • Human evidence • Strain-level effects vary	• Loss of probiotic viability during processing/storage • Sensitivity to oxygen, acidity, water activity, gastric acid and bile • Strain specificity • Host microbiota variability • Dose uncertainty	• Microencapsulation • Protective food matrices • Optimized processing/storage • Strain selection • Prebiotic co-delivery • Synbiotic design	• Need for strain-specific and matrix-specific evidence • Limited linkage between survival and clinical outcomes • Limited data on functional meal formats • Need for long-term safety / effectiveness.	[60–62]

Note: AI-Assisted (Artificial Intelligence assisted); HPP (High Pressure Processing); PEF (Pulsed Electric Fields); Supercritical CO₂ (Supercritical carbon dioxide); RCTs (Randomized Controlled Trials); NPC1L1 (Niemann-Pick C1-Like 1); LDL (low-density lipoprotein); FOS (fructooligosaccharides).

From Food Matrix Limitations to Technological Strategies

Although meal formulation is a central strategy for improving the bioavailability of bioactive compounds, formulation alone cannot overcome all matrix-related and physico-chemical limitations. Many bioactive compounds remain limited by intrinsic properties such as poor aqueous solubility, chemical instability, sensitivity to oxygen, light, heat or pH, extensive degradation during gastrointestinal digestion, rapid metabolism, low permeability or limited site-specific release [13,38,68,71,75,78]. These constraints cannot always be solved by combining foods within a meal.

For example, lipophilic compounds such as carotenoids, curcumin, phytosterols and omega-3 fatty acids require adequate dispersion, protection from oxidation and incorporation into absorbable structures, while hydrophilic but unstable compounds such as anthocyanins may require protection against pH changes, enzymatic degradation and thermal processing [17,45,47–49,68,71,77]. Similarly, probiotics require preservation of viability during processing, storage and gastric transit, whereas bioactive peptides may require protection from proteolytic degradation before reaching their target sites [56,57,60,61]. In these cases, food technologies provide tools that go beyond conventional formulation by modifying the physical structure of the matrix, protecting sensitive compounds, improving dispersibility, controlling release kinetics and enabling targeted delivery within the gastrointestinal tract [75,79–81].

Therefore, food technologies should not be viewed as independent from meal design, but rather as complementary strategies that address bioavailability barriers that cannot be fully resolved through food pairing or culinary formulation alone. This provides the rationale for the technological approaches discussed in the following section, including microencapsulation, nanoencapsulation, non-thermal processing and smart delivery systems.

4. Food Technologies Applied to Functional Meals

Functional meals are increasingly recognized as important tools for promoting health, preventing chronic diseases, and improving overall well-being. Unlike conventional foods, functional meals are specifically formulated to provide physiological benefits beyond basic nutrition through the incorporation of bioactive compounds, probiotics, prebiotics, antioxidants, peptides, dietary fibers, and essential micronutrients [82,83]. Advances in food technology have greatly contributed to the development of these products by enabling the preservation, stabilization, and targeted delivery of functional ingredients while maintaining sensory quality, safety, and shelf stability.

The incorporation of bioactive compounds into functional meals remains challenging. As described in the conceptual model shown in Figure 1, food technologies intervene before and during digestion, modifying the food matrix and improving the stability, protection, and controlled release of bioactive compounds. Many bioactives exhibit poor water solubility, particularly lipophilic compounds, and are highly sensitive to environmental factors such as UV radiation, heat, pH variations, and gastrointestinal digestion. These characteristics can compromise compound stability, reduce biological activity, and ultimately decrease their absorption and bioavailability in humans. To overcome these limitations, encapsulation technologies have emerged as effective strategy for protecting and delivering functional ingredients. In recent years, researchers have developed a wide range of delivery systems, capable of protecting bioactives from degradation during food processing, storage, and gastrointestinal transit [79,84,85]. These technologies not only enhance the stability and bioavailability of functional compounds but also support the development of more effective and innovative functional meals.

The main technological approaches currently employed to overcome these limitations and enhance the functionality of bioactive-rich meals are summarized in Figure 2.

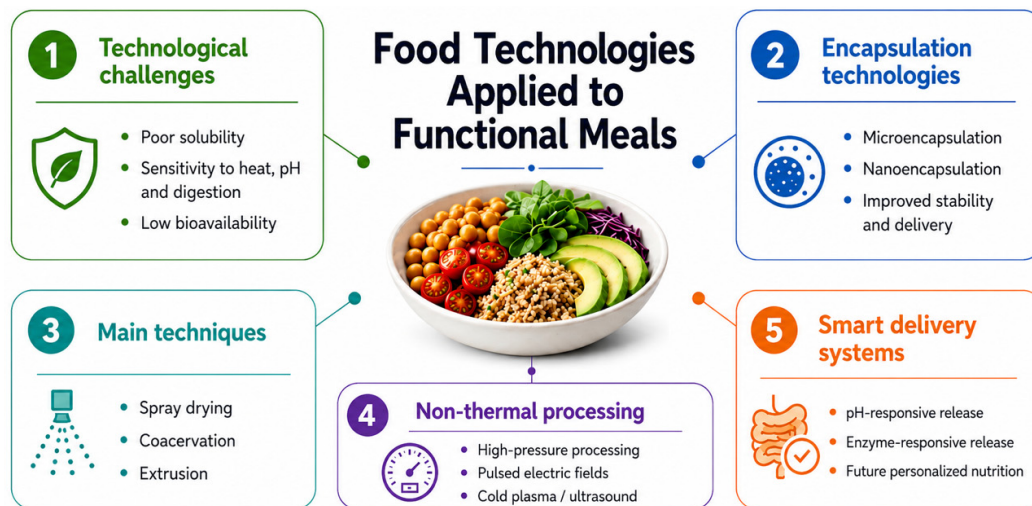


Figure 2. Overview of the main food technologies applied to functional meals.

4.1. Microencapsulation and Nanoencapsulation

Recent advances in food processing technologies have significantly transformed the development of functional foods and meals. Among these innovations, microencapsulation and nanoencapsulation have emerged as highly effective strategies for improving the stability, bioavailability, and controlled delivery of bioactive compounds. These technologies involve entrapping active ingredients within protective coating or matrix material, thereby shielding sensitive compounds from degradation caused by oxygen, light, moisture, temperature fluctuations and pH changes during processing, storage, and gastrointestinal digestion [80]. By preserving the functional, nutritional, and sensory properties of bioactive ingredients, encapsulation technologies contribute substantially to the development of stable and effective functional food products.

Encapsulation systems are widely used to protect compounds such as polyphenols, carotenoids, vitamins, omega-3 fatty acids, probiotics, essential oils, antioxidants, antimicrobials, and flavoring agents [81,86]. Beyond improving stability, these systems can enhance solubility, reduce volatility, mask undesirable flavors, and facilitate targeted delivery within the gastrointestinal tract, thereby increasing bioavailability and functional performance [87].

Microencapsulation generally produces particles ranging from 1 to 500 μm , in which bioactive compounds are entrapped within coating materials that regulate loading and release [88]. Conventional microencapsulation methods include physicochemical, chemical, and physicomachanical processes [89]. Several studies have demonstrated improved stability and bioavailability of microencapsulated carotenoids and other sensitive compounds. For example, carotenoid inclusion complexes with polysaccharides such as cyclodextrin, arabinogalactan, and glycyrrhizin showed enhanced stability and bioavailability compared with free carotenoids [90], while other studies reported improved physicochemical properties and storage stability in functional food applications [91,92].

Despite these advantages, conventional microencapsulation systems present several limitations, including low aqueous solubility, limited targeting capacity, and reduced bioavailability associated with the relatively large particle size of microcapsules [93]. Moreover, clean-label trends have restricted the use of certain wall materials containing sugars, fats, sodium, lactose, or gluten [94]. Widely used encapsulating agents such as maltodextrin may exhibit low emulsifying capacity, thereby reducing encapsulation efficiency [95].

To overcome these limitations, nanoencapsulation technologies have attracted increasing attention. Nanoencapsulation generates nanoscale delivery systems with a high surface-area-to-volume ratio, improving interaction with food matrices, solubility, absorption, and controlled-release performance [96]. Compared with conventional microcapsules,

nanosystems exhibit enhanced stability, targeting capacity, and bioavailability [97]. Their reduced particle size also facilitates deeper penetration into tissues and cells, leading to improved absorption and bioactivity [98]. Consequently, nanoencapsulation has become particularly important for delivering poorly soluble or unstable compounds to specific tissues and organs [99].

Nanoencapsulation systems are especially effective because their small particle size improves dispersion in gastrointestinal fluids and facilitates interaction with the intestinal epithelium [100]. Encapsulation also protects bioactive compounds against degradation caused by gastric acidity, oxidation, and digestive enzymes, increasing the amount of active compounds available for absorption. Certain nanoparticle systems can interact directly with intestinal epithelial cells, facilitating transcytosis and endocytosis processes that enhance transport across the intestinal barrier [101,102]. In addition, pH-sensitive nanosystems have demonstrated the ability to achieve targeted colon delivery of compounds such as curcumin and resveratrol, thereby improving therapeutic efficacy and bioavailability [103,104].

Biopolymer-based systems composed of proteins and polysaccharides such as chitosan, alginate, pectin, β -lactoglobulin, starch, maltodextrin, and inulin have also attracted considerable attention due to their biocompatibility, controlled-release properties, and ability to improve encapsulation efficiency without adversely affecting food texture or sensory quality [105,106]. Common encapsulation systems include biopolymer nanoparticles, spray-dried microcapsules, coacervates, and polysaccharide-based carriers. These delivery systems enable the controlled and sustained release of nutrients and nutraceuticals during digestion, thereby improving stability, bioaccessibility, and physiological efficacy [107–109].

The performance of encapsulation systems depends on multiple factors, including the physicochemical properties of the core material, the characteristics of the wall material, and the encapsulation technique employed. A particularly important feature of these systems is their ability to provide controlled-release mechanisms triggered by pH changes, temperature, moisture, or enzymatic activity, thereby improving both compound stability and functional efficacy [87].

Overall, microencapsulation and nanoencapsulation represent promising approaches for the development of next-generation functional foods and nutraceuticals. Their ability to protect sensitive bioactive compounds, enhance bioavailability, and provide controlled release contributes to improved food quality, product stability, and potential health benefits for consumers [80,110].

4.2. Main Encapsulation Techniques Applied to Functional Food Systems

Several encapsulation techniques have been applied to functional food systems, including spray drying, freeze drying, extrusion, coacervation, spray-freeze drying, and spray chilling. Each technique offers distinct advantages depending on the intended application, the sensitivity of the bioactive compounds, the type of food matrix, and the desired release profile [80,111]. Furthermore, advanced fabrication technologies such as electro-spraying can produce ultrafine fibers and particles capable of enhancing the dissolution and bioavailability of poorly water-soluble compounds [112].

Among encapsulation technologies, spray-based techniques remain the most widely applied at the industrial scale for protecting and stabilizing bioactive compounds. These include spray-drying, spray-freeze drying, and spray chilling, which are extensively used in food, and nutraceutical applications because of their flexibility, scalability, and relatively low production cost [113,114]. Among them, spray-drying is the most established and commercially adopted technique due to its operational simplicity, continuous processing, rapid production rates, and ease of scale-up [115]. Since the late 1950s, it has been widely

applied in the food industry for producing stable powders containing flavors, vitamins, pigments, oils, and functional ingredients [113].

Spray-drying involves converting a feed solution, suspension, or emulsion into dried particulate material through atomization into a heated drying chamber. Initially, the bioactive compounds are dispersed or emulsified in a solution containing carrier or wall materials such as maltodextrin, gum arabic, modified starch, proteins, gelatin, or other hydrocolloids [116]. The resulting feed is atomized through a nozzle or rotary wheel into fine droplets that come into contact with hot air, promoting rapid solvent evaporation and the formation of dehydrated microcapsules. During this process, the wall material forms a protective matrix around the core compounds, generating matrix-type or polynuclear microcapsules. The dried particles are subsequently collected from the bottom of the drying chamber [117].

One of the major advantages of spray-drying is the rapid evaporation of water, which enhances entrapment of bioactive compounds within the wall matrix while enhancing microbiological stability and reducing chemical degradation during storage [118,119]. Consequently, spray-drying has been widely employed for the encapsulation of flavors, vitamins, minerals, pigments, lipids, essential oils, and polyphenols to improve oxidative stability and extend shelf life [120–122]. The technology has also demonstrated considerable potential for preserving antioxidant activity and stabilizing nutraceutical compounds. For example, Ersus and Yurdagel [123] successfully spray-dried anthocyanin-rich black carrot extracts using maltodextrins as carrier agents, while Zhang et al. [124] showed that mixtures of maltodextrin and gum arabic effectively preserved grape seed procyanidins during processing and storage.

The selection of suitable wall materials is one of the most critical factors influencing encapsulation efficiency, particle morphology, oxidative stability, and retention of bioactive compounds [125]. Since most spray-drying systems employ aqueous feed, encapsulating materials must exhibit good water solubility [113,114]. Commonly used materials include low molecular weight carbohydrates, milk proteins, gelatin, and hydrocolloids such as gum arabic [116].

Maltodextrins are particularly attractive because of their high solubility, low viscosity, neutral flavor, and good film-forming properties [125], whereas gum arabic is valued for its excellent emulsifying and film-forming characteristics, especially for lipid encapsulation across a broad pH range. Other promising wall materials include chitosan, citrus fibers, and alginate-based matrices, which provide enhanced structural stability and controlled-release properties [126,127].

Chitosan has been successfully employed as a wall material for spray-drying olive leaf extracts rich in polyphenols, producing microspheres with smooth morphology and high phenolic retention. Alginate-based matrices have also attracted attention because they can be cross-linked with calcium ions, improving structural stability and enabling controlled release applications [127]. In many cases, combinations of wall materials are used to improve encapsulation efficiency and microcapsule stability. Blends of gum arabic and maltodextrin, for instance, have been widely investigated because they provide improved protection and higher retention of volatile compounds [128,129].

Despite its advantages, spray-drying also presents some limitations. High drying temperatures may promote degradation of heat-sensitive compounds such as vitamins, phenolics, and antioxidants [130]. In addition, process efficiency and final product quality are strongly influenced by operational parameters, including feed temperature, inlet and outlet air temperatures, droplet size, emulsion viscosity, feed flow rate, and wall material concentration [131]. Other technological challenges include particle agglomeration, stickiness associated with materials exhibiting low glass transition temperatures, poor

droplet size control, and product losses caused by particle deposition on drying chamber walls [113,119,132].

The structure of spray-dried microcapsules can also influence the release profile of encapsulated compounds. Core droplets located near the particle surface often results in rapid release of active ingredients, especially when highly water-soluble encapsulating agents are used [133,134]. In contrast, controlled-release systems, can be achieved using low-solubility materials such as ethyl cellulose, or cross-linked casein, enabling slower and more sustained diffusion of bioactive compounds [135].

To overcome the thermal limitations associated with conventional spray-drying, alternative spray-based technologies such as spray-freeze drying and spray chilling have been developed. Spray-freeze drying is particularly suitable for thermosensitive compounds because atomized droplets are rapidly frozen, usually in liquid nitrogen, followed by solvent removal through sublimation under lyophilization conditions [136,137]. This process minimizes thermal degradation and produces highly porous encapsulates with excellent rehydration properties. Spray chilling, also known as spray congealing is another scalable alternative that does not require high drying temperatures or organic solvents, making it particularly suitable for heat-sensitive compounds such as probiotics, enzymes, and vitamins. In this technique, alginate is frequently used as a stabilizing agent, while gelation is induced by calcium salts such as calcium chloride or calcium carbonate [138].

Another important encapsulation approach is coacervation, one of the most extensively studied techniques for protecting and controlling the release of sensitive bioactive compounds. Coacervation is based on the phase separation of one or more hydrocolloids from a solution, followed by deposition of the coacervate phase around an active ingredient suspended or emulsified in the same medium [139]. This approach is particularly suitable for encapsulating polyphenols, antioxidants, essential oils, and lipophilic compounds because it forms polymer-rich coatings that enhance stability and modulate release behavior [140].

Coacervation occurs through interactions between oppositely charged biopolymers, resulting in complexes that entrap the active compound and precipitate from solution [141]. The process may be induced by changes in pH, temperature, ionic strength, or by the addition of electrolytes and non-solvents. Depending on the number of polymers involved, coacervation may be classified as simple or complex. Simple coacervation involves a single polymer, whereas complex coacervation relies on interactions between two or more oppositely charged biopolymers such as gelatin and gum arabic or alginate and chitosan [139,142]. Complex coacervation is the most widely used form in food and nutraceutical applications because of its high encapsulation efficiency and excellent controlled-release properties [139,140].

The process generally involves three stages: formation of immiscible phases, deposition of the coacervate layer around the active material, and stabilization of the coating. Phase separation is typically induced by changes in pH, temperature, ionic strength or polymer concentration, leading to the formation of a polymer-rich phase that deposits around the core material through electrostatic, hydrogen-bonding or hydrophobic interactions. The coating is then stabilized by cooling, pH adjustment, drying or cross-linking to improve capsule integrity and control release [139,143,144].

Various wall materials have been investigated, including gelatin, alginate, chitosan, carrageenan, soy proteins, dextran, and β -lactoglobulin [139,143,145,146]. Cross-linking agents such as glutaraldehyde or enzymatic alternatives like transglutaminase can further improve mechanical stability and resistance of the microcapsules [143,145,146].

One of the main advantages of coacervation is that it operates under relatively mild processing conditions, including low temperatures and gentle stirring, thereby minimizing

thermal degradation and evaporative losses of heat-sensitive compounds [130]. In addition, the technique offers high payload capacity, excellent oxidative protection, and efficient controlled-release behavior, making it highly suitable for preserving the functionality of bioactive ingredients during storage and digestion [146]. Encapsulation efficiencies approaching 99% have been reported in some systems, highlighting the strong industrial potential of coacervation technology for sensitive nutraceutical compounds [147]. Furthermore, coacervation does not require highly sophisticated equipment and can be adapted to a wide range of raw materials and active compounds [130].

Despite these advantages, coacervation still faces limitations that restrict its large-scale industrial application. The process can be relatively expensive and operationally complex, particularly compared with spray-drying technologies, because it often requires precise control of pH, temperature, polymer ratio, ionic strength and mixing conditions, as well as additional stabilization, separation or drying steps. These requirements can increase processing time, material costs, batch-to-batch variability and scale-up complexity [142]. Concerns regarding the use of chemical cross-linking agents such as glutaraldehyde have also encouraged the development of safer enzymatic alternatives such as transglutaminase. Additional challenges include sensitivity to pH and ionic strength variations, as well as difficulties associated with large-scale standardization and long-term stability. Nevertheless, coacervation remains one of the most versatile and effective encapsulation approach for enhancing the stability, protection, and controlled release of sensitive bioactive compounds [139]. Although still less widespread industrially than spray-drying, it possesses significant potential for food and nutraceutical applications because of its high encapsulation efficiency, low thermal stress, and excellent release control properties [144].

Extrusion-based encapsulation technologies have also gained attention for the stabilization and controlled delivery of bioactive compounds, particularly in applications requiring enhanced oxidative protection and prolonged shelf life. These method includes melt injection, melt extrusion, ionic gelation extrusion, and centrifugal coextrusion, in which the active compound is incorporated into a carbohydrate or polymeric matrix [113]. Extrusion technologies are widely used for encapsulation of volatile compounds, flavors, essential oils, antioxidants, and other sensitive ingredients because they effectively reduces volatilization and improves oxidative stability [148].

In extrusion encapsulation, droplets of a polymeric aqueous solution containing the active compound are introduced into a gelling bath, where bead formation occurs through ionic cross-linking. Sodium alginate is the most commonly used encapsulating polymer, while calcium chloride is frequently employed as the gelling solution because it rapidly promotes calcium-induced gel formation [149]. The incorporation of antioxidants into the encapsulating matrix may further enhance oxidative stability and protect sensitive bioactives from degradation. Different droplet generation systems can be used during the process, including pipettes, syringes, vibrating nozzles, spraying nozzles, jet cutters, and vibrating disks. Conventional extrusion typically involves forcing a homogeneous mixture of the core material and encapsulating agents through a nozzle to produce matrix-type particles, whereas co-extrusion enables the simultaneous flow of core and shell materials, producing mononuclear microcapsules with well-defined shell structures [148–151]. In co-extrusion systems, shell thickness and particle size are mainly controlled by vibration frequency and by the flow rates of the core and encapsulating materials [148].

Alginate-based systems are particularly suitable for extrusion encapsulation because carries a negative charge over a wide pH range and readily forms hydrogels through ionic interactions with divalent cations. After encapsulation, the resulting beads can be further dried using freeze-drying or fluidized-bed drying to improve storage stability. However, freeze-drying often produces highly porous structures, which may reduce encapsulation

efficiency and weaken protection against oxidation or volatilization of the core material. Another important limitation of alginate-based extrusion systems is the relatively rapid release of encapsulated compounds in aqueous environments or during gastrointestinal digestion. This behavior is mainly attributed to the low density of alginate hydrogel networks, particularly at low alginate concentrations, resulting in porous structures and accelerated diffusion of active compounds [152]. To overcome this limitation, positively charged biopolymers such as chitosan are often combined with alginate to strengthen the gel matrix and modulate release kinetics. In addition, incorporation of dietary fibers and other polysaccharides into alginate matrices has been investigated as an effective strategy for improving encapsulation efficiency and controlled release behavior [152].

Beyond these alginate-specific limitations, extrusion technologies also present broader technological constraints. These methods generally involve higher production costs and produce relatively large particle sizes compared with spray-drying techniques, which may restrict their application in food systems requiring fine powders or transparent formulations [113]. In addition, large-scale production may be limited by relatively low throughput and difficulties in obtaining highly uniform particle sizes. Nevertheless, extrusion-based encapsulation remains a highly promising approach for improving the stability, protection, and controlled release of sensitive bioactive compounds, particularly in functional foods and nutraceutical applications where prolonged retention and targeted release are required.

Overall, spray-based encapsulation technologies represent highly versatile and economically viable approaches for stabilizing and protecting bioactive compounds in functional food systems. Among them, spray-drying remains the predominant industrial technique due to its simplicity, scalability, and ability to produce stable powders with desirable physicochemical properties. However, optimization of processing conditions and careful selection of wall materials remain essential to maximize encapsulation efficiency, preserve bioactivity, and achieve controlled release characteristics in the final product.

4.3. Non-Thermal Processing Technologies

Emerging non-thermal processing technologies have attracted considerable attention in the development of functional meals because of their ability to preserve heat-sensitive nutrients and bioactive compounds while ensuring food safety. Technologies such as high-pressure processing, pulsed electric fields, cold plasma, and ultrasound treatments effectively reduce microbial contamination with minimal impact on the nutritional and sensory properties of foods [153–155]. Unlike conventional thermal processing, these approaches better preserve vitamins, antioxidants, polyphenols, pigments, and other bioactive compounds susceptible to heat-induced degradation. In addition to improving microbial safety, non-thermal technologies help maintain the original texture, flavor, color, and overall quality of food products, thereby supporting consumer demand for minimally processed and clean-label foods [156,157].

High-pressure processing, for example, inactivates microorganisms through the application of elevated pressure without significantly affecting covalent bonds in food constituents, thereby preserving nutritional quality and fresh-like characteristics. Similarly, pulsed electric fields disrupt microbial cell membrane while minimizing thermal damage to sensitive compounds [154]. Consequently, non-thermal processing technologies contribute significantly to the production of functional meals with enhanced nutritional, sensory, and commercial value, while supporting the development of innovative minimally processed foods [155].

4.4. Smart Delivery Systems, Limitations and Future Perspectives

Encapsulation technologies have attracted considerable attention not only for protecting sensitive bioactive compounds, but also for enhancing their stability, controlled release, bioaccessibility, and bioavailability. These systems are designed to protect active compounds during processing, storage, and gastrointestinal transit, while enabling their release at the appropriate site and time [158]. By minimizing premature degradation and improving delivery efficiency, encapsulation enhances the physiological functionality and overall effectiveness of nutraceutical and functional food ingredients [159].

Initially, encapsulation systems were primarily developed for single bioactive compounds. However, many bioactives consumed in their free form exhibit poor water solubility, low chemical stability, and high susceptibility to degradation during gastrointestinal digestion and hepatic metabolism, resulting in limited bioavailability and reduced biological efficacy [39,160]. To overcome these limitations, advanced delivery systems have been designed to protect bioactive compounds from adverse environmental conditions and promote their controlled and targeted release within the gastrointestinal tract, an approach that is particularly relevant in precision nutrition.

More recently, increasing attention has been directed toward co-delivery systems capable of simultaneously encapsulating multiple bioactive compounds within a single carrier. Compared with the separate administration of individual bioactives, these systems can enhance stability, bioavailability, and synergistic interactions among bioactives, thereby improving their physiological effects [161].

One of the main advantages of smart delivery technologies is their ability to achieve controlled and targeted release of bioactive compounds. Controlled-release systems ensure that active ingredients remain protected during processing, storage, and gastrointestinal transit, while allowing release under specific physiological conditions [158]. Different release mechanisms have been developed in response to physiological stimuli such as pH changes, enzymatic activity, and temperature variations [162]. Among these, pH-responsive systems are particularly important for oral delivery applications. Polymers such as alginate and chitosan are widely used because their swelling behavior and structural stability vary according to pH conditions. For example, probiotic bacteria encapsulated in calcium alginate beads showed enhanced survival under simulated gastric conditions and were predominantly released in the small intestine, where they contributed to improving the intestinal environment [163].

Enzyme-responsive systems have also shown considerable potential in food and nutraceutical applications. In these systems, digestive enzymes degrade the encapsulating matrix, promoting the release of active compounds at specific sites within the gastrointestinal tract [164]. This mechanism protects bioactives during gastric transit and enhances their release in the lower intestinal region, thereby improving stability and absorption efficiency [165]. In addition, temperature-responsive systems and other smart delivery approaches are being increasingly explored to modulate release according to physiological conditions and maximize the biological effectiveness of encapsulated compounds [166].

Numerous studies have demonstrated that encapsulation technologies significantly improve the bioaccessibility and bioavailability of several bioactive compounds. Encapsulated lycopene, curcumin, omega-3 fatty acids, and polyphenols generally exhibit greater gastrointestinal stability and higher absorption rates than their non-encapsulated counterparts. Encapsulated omega-3 formulations, for example, have shown improved bioavailability and enhanced anti-inflammatory activity compared with conventional formulations. Moreover, encapsulation facilitates the incorporation of unstable bioactive compounds into food matrices without adversely affecting sensory quality, oxidative stability, or shelf life [45,81].

More recently, encapsulation technologies have evolved beyond conventional protection systems toward the development of smart and personalized delivery platforms. Advanced responsive systems capable of modulating release according to pH, enzymatic activity, or other physiological stimuli are increasingly being integrated into personalized nutrition strategies [103]. By tailoring capsule composition and release profiles to individual nutritional requirements, these technologies may improve nutrient absorption efficiency and therapeutic outcomes, particularly for athletes, elderly populations, and patients with chronic diseases [167].

Beyond improving the stability and bioavailability of bioactive compounds, smart delivery systems have the potential to support the development of personalized functional meals by tailoring the release and absorption of bioactives according to individual biological characteristics. Advances in precision nutrition indicate that genetic variability, metabolomic profiles, and gut microbiota composition may substantially influence individual responses to dietary bioactive compounds. For instance, colon-targeted encapsulation systems may enhance the delivery of prebiotics and polyphenols in individuals with specific microbial profiles, whereas controlled-release formulations may optimize the delivery of bioactives for individuals with impaired glucose metabolism or distinct metabolic phenotypes. However, despite these promising advances, the clinical implementation of personalized delivery systems remains limited by the lack of validated biomarkers, interindividual variability, regulatory challenges, and the scarcity of long-term human intervention studies [168,169]. Consequently, smart delivery systems may become a key enabling technology for the future development of functional meals specifically designed to maximize bioavailability while meeting individual nutritional requirements.

5. Health Benefits of Functional Meals

The increasing global burden of chronic non-communicable diseases, such as cardiovascular disease (CVD), type 2 diabetes, obesity, and neurodegenerative disorders [170], underscores the need for effective dietary interventions that extend beyond individual nutrients or specific functional foods [171]. While individual functional foods have received significant attention for their targeted health benefits, the concept of functional meals offers a more holistic approach to disease prevention and management by leveraging food synergy and complex nutrient interactions. As proposed in Figure 1, the health effects of functional meals emerge from the integrated interaction among bioactive compounds, meal composition, food matrix characteristics, food technologies, gut microbiota and host factors, rather than from isolated dietary components. This integrative perspective shifts the focus from isolated bioactive compounds to the synergistic effects of a complete dietary matrix, aligning with the understanding that overall dietary patterns, rather than individual nutrients, are the primary drivers of health outcomes [8,172].

Importantly, the health benefits attributed to functional meals should be distinguished from those attributed to isolated bioactive compounds, single functional foods or broad dietary patterns. Complete meals integrate several determinants of physiological response, including food structure, nutrient interactions, bioactive compound bioavailability, digestion kinetics, glycemic load, lipid quality, fiber content and microbiota-accessible substrates. Therefore, evidence relevant to the functional meal concept derives not only from studies of isolated compounds, but also from acute meal studies, structured meal-based interventions, repeated meal provision, medically tailored meals and dietary patterns characterized by consistent meal composition. At present, direct evidence from interventions explicitly designed as “functional meals” remains limited, and most available evidence is derived from related but not fully equivalent approaches, including food matrix studies, functional

food combinations, Mediterranean- and DASH-type dietary patterns, dietary portfolio interventions and medically tailored meal programs [24,25,27,74,173,174].

A growing body of observational and intervention studies demonstrates that dietary patterns consisting of whole foods, such as the Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets, are consistently associated with reduced all-cause mortality and lower incidence of CVD [173,175,176], type 2 diabetes [177], and obesity [178,179]. These benefits are not solely due to individual “superfoods” but to the synergistic composition of meals, in which fiber, unsaturated fats, polyphenols, micronutrients, and high-quality proteins work together through complementary pathways. For instance, the antioxidant properties of oat phenolics are enhanced by ascorbic acid [180], and the combination of tomato and broccoli shows greater anti-tumor efficacy than either vegetable alone [181]. A functional meal designed for iron repletion may include plant-based iron sources (like legumes and leafy greens) along with vitamin C-rich foods, animal-derived components, and fermented ingredients. This enhances iron bioavailability through established dietary synergisms within the meal context, where interactions between enhancers and inhibitors play a crucial role in iron absorption [182,183].

Functional meals can be designed to incorporate specific functional foods that improve cardiovascular health by leveraging multiple protective mechanisms simultaneously. Functional foods rich in fiber, polyphenols, plant sterols, and omega-3 fatty acids, can reduce low-density lipoprotein (LDL) cholesterol, improve endothelial function, decrease blood pressure, and attenuate oxidative stress and inflammation, ultimately lowering cardiovascular risk [19,184]. Cardioprotective potential has been shown for vegetable and fruit fiber, nuts and seeds, seafood, coffee, tea, dark chocolate, and whole grains, which likely act synergistically when consumed together in meals, rather than as isolated components [19,76,184]. Medically tailored meals (MTM) and other culinary medicine approaches that provide guideline-based, heart-healthy meals have been shown to improve lipid profiles, blood pressure, and heart failure outcomes. They also reduced readmissions and costs, highlighting the significance of structured meal-level interventions in CVD management [174,185–187]. Dietary patterns based on DASH principles, characterized by lower sodium intake and higher consumption of potassium-rich whole foods such as fruits, vegetables, and legumes, have been shown to be beneficial in reducing blood pressure, representing a cornerstone strategy in the prevention and management of hypertension [187]. In addition, Mediterranean-style meals that emphasize olive oil rich in monounsaturated fatty acids and polyphenols, fish with omega-3 fatty acids, and a high intake of whole grains, legumes, vegetables, and nuts, have been shown to reduce the risk of CVD through improvements in endothelial function, lipid profiles, blood pressure, inflammation, and oxidative stress [188]. Evidence from systematic reviews of randomized controlled and prospective studies has demonstrated that adherence to this dietary pattern reduces both cardiovascular events and all-cause mortality [189,190].

In the management of type 2 diabetes, functional meals should be structured in a way that promotes glucose homeostasis and improves insulin sensitivity. This can be achieved by prioritizing nutrient-dense, minimally processed plant-based foods such as whole grains, vegetables, whole fruits, legumes, seeds, and nuts, while also limiting intake of red/processed meat, sodium, added sugars, and refined grains [191]. Functional foods containing polyphenols, fibers, and other bioactive compounds can modulate key enzymes and metabolic pathways, providing multi-targeted support when incorporated into meals [192,193]. Bioactive compounds, particularly polyphenols and alkaloids found in plant-based foods, serve as natural inhibitors of carbohydrate-hydrolyzing enzymes like α -amylase and α -glucosidase. By slowing down the enzymatic breakdown of complex carbohydrates in the intestinal epithelium, these compounds effectively lower the rate

of glucose absorption into the bloodstream [192,194]. Evidence regarding the impact of Mediterranean-style meals shows that they result in more favorable postprandial lipid and glucose responses when compared to other meal patterns [72–74]. The combination of dietary fiber from legumes, vegetables, and whole grains, along with polyphenols and unsaturated fats creates a structural matrix that slows carbohydrate digestion, enhances incretin hormone secretion, such as glucose-dependent insulintropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) [195–197], and promotes satiety through mechanisms that would not occur if these nutrients were consumed separately [196]. In addition, dietary fiber-rich plants and phytochemicals (e.g., flavonoids, anthocyanins, polyphenols) may reduce oxidative stress and inflammation (TNF- α , IL-6), thereby mitigating the progression of diabetes-related complications [196]. A review of randomized controlled trials has shown that dietary patterns such as the Mediterranean and low-carbohydrate diets can significantly improve glycemic markers, including HbA1c and fasting glucose levels [198]. It should be noted that metabolic benefits appear to depend not only on dietary composition but also on meal timing and preparation practices. Strategies such as prioritizing larger meals earlier in the day or adopting smaller, more frequent meals have been associated with improved glycemic control. Additionally, home cooking practices that promote portion control and preserve nutrient quality, as well as food preparation methods like starch retrogradation (e.g., cooling or freezing carbohydrate-rich foods), can further lower the glycemic index and improve postprandial responses while still maintaining the overall nutritional value of the meal [198].

Functional meals also play a significant role in preventing and managing obesity by affecting satiety regulation, energy intake, and metabolic efficiency [199]. Meals that include functional foods rich in phenolic compounds, dietary fibers, and proteins can enhance satiety, increase energy expenditure, and provide a multi-targeted approach to the managing obesity and its metabolic comorbidities [200]. Functional foods may help in preventing obesity by inhibiting digestive enzymes such as pancreatic lipase and α -amylase, which reduces the absorption of dietary fats and carbohydrates. These foods can also increase energy expenditure by stimulating thermogenesis and promoting the browning of white adipose tissue through the activation of signaling pathways like AMPK and the upregulation of thermogenic genes such as UCP1. Furthermore, functional foods can influence the gut microbiota by acting as prebiotics or probiotics, increasing the presence of beneficial bacteria and aiding in the regulation of metabolic homeostasis [200]. Adherence to a Mediterranean meal pattern may promote the growth of short-chain fatty acids (SCFAs)-producing taxa, such as *Faecalibacterium prausnitzii* and *Akkermansia muciniphila*, while also enhancing overall microbial diversity. This shift in the microbiome helps mitigate obesity-related metabolic dysfunction by strengthening intestinal barrier integrity and reducing circulating lipopolysaccharide levels. As a result, chronic systemic inflammation may be suppressed through the downregulation of the NLRP3 inflammasome and TLR4 signaling pathways [201].

Microbiota-mediated benefits from functional meals that integrate dietary fiber, whole grains, legumes, and plant polyphenols, as well as prebiotic and probiotic components, can modulate the gut microbial composition and metabolic activity. Plant-forward functional meals can promote the selective growth of beneficial taxa and enhance the production of microbial metabolites, particularly SCFAs such as butyrate, acetate, and propionate [202]. Butyrate, in particular, serves as a primary energy source for colonocytes, reinforces intestinal barrier integrity, and exerts anti-inflammatory effects through modulation of immune and epigenetic pathways. In parallel, SCFAs contribute to lipid metabolism regulation, improve insulin sensitivity, and influence glucose homeostasis via signaling pathways involving G-protein-coupled receptors and incretin hormones [203]. Plant-derived polyphenols fur-

ther interact with the microbiota, undergoing biotransformation into bioactive metabolites that modulate oxidative stress, neuroinflammatory pathways, and may influence neuronal plasticity, cerebral blood flow, and synaptic function [202,203]. Accordingly, observational and interventional studies show that adherence to plant-rich dietary patterns, such as Mediterranean-type diets, is associated with slower cognitive decline and a reduced risk of neurodegenerative disorders [204,205]. The neuroprotective effect of bioactive compounds in the Mediterranean diet, particularly polyphenols and flavonoids, is attributed to their ability to target multiple pathways such as attenuating oxidative stress, inhibiting pro-inflammatory cytokine production, and modulating proteostatic pathways to prevent the pathological aggregation of amyloid-beta and alpha-synuclein [206]. In addition, evidence suggests that synergistic combinations of fiber, polyphenols, and omega-3 fatty acids within complex meal matrices may have stronger, network-based “food–microbiota–host” effects than isolated nutrients, reflecting the integrated and interdependent nature of dietary exposures [19,38,76]. This systems-level interaction highlights the relevance of whole-meal design in optimizing microbial functionality and metabolic signaling. It also supports the development of personalized, microbiome-targeted functional meals for the prevention and management of chronic diseases. Collectively, these interconnected mechanisms underpin the beneficial effects of plant-forward functional meals on a wide range of conditions, including obesity, type 2 diabetes, inflammatory bowel disease, cardiovascular disease, neurodegenerative disease, and neuropsychiatric disorders such as depression [19,202,203], highlighting the central role of diet–microbiota interactions in systemic health.

A key limitation of the current evidence base is that many health benefits are inferred from dietary patterns, isolated functional foods or individual bioactive compounds rather than from complete functional meals. Observational studies provide important evidence on associations between diet and disease risk, but they are vulnerable to residual confounding and cannot fully establish causality. Randomized trials provide stronger evidence, although many assess whole diets, supplements, fortified products or meal provision programs rather than standardized functional meal prototypes. Moreover, dose–response relationships are often better established for isolated compounds or specific functional ingredients than for complete meals, where multiple components interact simultaneously. Future studies should therefore distinguish more clearly between evidence from isolated bioactive compounds, functional foods, dietary patterns and complete functional meals, and should prioritize controlled human interventions using standardized whole-meal formats and clinically meaningful endpoints.

6. Challenges and Limitations

As highlighted throughout the previous sections, despite the growing scientific and technological interest in functional meals, several conceptual, methodological and regulatory challenges continue to limit their development and implementation. One of the main challenges is the absence of a universally accepted definition of a functional meal. Although functional foods are relatively well established in the literature, the concept of functional meals remains broader and less standardized, often overlapping with functional foods. This conceptual ambiguity complicates comparisons between studies, the interpretation of evidence, and the development of regulatory frameworks for meal-based functionality.

A second important limitation concerns the complexity of the food matrix. Functional meals are dynamic systems in which proteins, lipids, carbohydrates, fiber, minerals, phytochemicals, microorganisms, and processing-derived structures interact before, during, and after digestion [7,8,12]. Consequently, the biological effect of a bioactive compound observed in isolation cannot be directly extrapolated to its effect when incorporated into a complete meal.

The assessment of bioavailability also remains a critical methodological challenge. Many studies rely on *in vitro* digestion models, simulated gastrointestinal systems, cell culture experiments, or animal models. While these approaches are useful for tracking mechanisms and technological strategies, they fail to fully reproduce human digestive physiology, interindividual variability, gut microbiota metabolism, dietary intake patterns, or postprandial responses [13,37,38,68]. Furthermore, bioavailability is often assessed using heterogeneous outcomes, including bioaccessibility, plasma concentration, urinary excretion, metabolite formation, antioxidant capacity, or biomarker modulation. This methodological diversity makes it difficult to compare results between studies and to establish dose–response relationships or clinically significant thresholds.

Another limitation is the insufficient number of well-designed human intervention studies that assess complete functional meals rather than isolated functional ingredients. Much of the available evidence on bioactive compounds comes from studies that use supplements, extracts, fortified products, or isolated foods. However, functional meals require a different level of evidence, as meal composition, preparation method, matrix structure, portion size, timing of consumption, and baseline diet can influence the physiological response [4,5,12]. Randomized controlled clinical trials using realistic meal formats, clinically relevant outcomes, and adequate follow-up periods are still limited. This gap is particularly important for health-related outcomes.

Interindividual variability presents an additional challenge. The response to functional meals can vary according to age, sex, genetic history, metabolic status, gut microbiota composition, medication use, digestive function, lifestyle, and health status [6,37,38,45]. For example, two individuals consuming the same meal may produce different microbial metabolites, absorb different amounts of a bioactive compound, or exhibit distinct postprandial metabolic responses. This variability reinforces the relevance of personalized nutrition but also complicates the development of generalizable dietary recommendations and health claims. It is important that future development of functional meals integrates biomarkers, microbiota profile, metabolic phenotyping and digital tools to tailor meal composition to individual needs [6].

Technological approaches also present important limitations. Encapsulation, nano-delivery systems, fermentation, high-pressure processing, pulsed electric fields, ultrasound, cold plasma, and other emerging technologies can improve stability, bioaccessibility, and targeted delivery of bioactive compounds. However, their effectiveness depends on the type of bioactive compound, carrier material, processing conditions, food matrix, storage stability, digestion behavior, and sensory acceptability [13,68,75].

Regulatory and health claim issues represent another important barrier. In many jurisdictions, health claims are evaluated at the level of specific nutrients, ingredients, or food products rather than complete meals. Demonstrating that a whole meal produces a defined physiological benefit requires robust evidence, standardized composition, reproducible preparation methods, and validated biomarkers [3,4,12]. This is challenging because meals are inherently variable and context dependent. Clearer regulatory guidance is therefore needed to determine how functional meal claims should be substantiated, communicated, and monitored.

Finally, this narrative review itself has limitations. As a narrative rather than systematic review, it does not follow a formal systematic search, screening, and risk-of-bias assessment protocol. Therefore, although the review aims to integrate current evidence across bioavailability, food technologies, matrix effects, and health perspectives, it may be subject to selection bias.

7. Conclusions

Functional meals represent a promising evolution in the science of nutrition, moving beyond the traditional focus on isolated nutrients, individual bioactive compounds, or isolated functional foods, toward complete meal systems. This review highlights that the potential health effects of functional meals arise from the dynamic interaction between bioactive compounds, food matrices, processing methods, meal composition, gastrointestinal digestion, gut microbiota metabolism, and interindividual biological variability.

Reviewed evidence indicates that bioactive compounds, including polyphenols, carotenoids, phytosterols, glucosinolates, organosulfur compounds, omega-3 fatty acids, bioactive peptides, probiotics, prebiotics, and postbiotics, can influence multiple health-related mechanisms, such as antioxidant defense, inflammatory regulation, lipid and glucose metabolism, vascular function, intestinal barrier integrity, microbiota balance, satiety, and neuroprotection. However, their biological effectiveness in functional meals depends not only on their concentration, but also on their bioaccessibility, stability, absorption, metabolism, and interactions within the overall meal matrix. Bioavailability, therefore, represents a central determinant linking meal composition to physiological effect.

Food technologies offer important opportunities to overcome some of these limitations. Encapsulation, nanotransport systems, emulsions, fermentation, high-pressure processing, pulsed electric fields, ultrasound, cold plasma, and other emerging technologies can improve the stability, solubility, targeted release, and bioavailability of bioactive compounds. However, technological innovation must be carefully balanced with safety, regulatory requirements, consumer acceptance, accessibility, scalability, and environmental sustainability.

A central conclusion of this review is that functional meals should be understood as complex, multicomponent and context-dependent food systems. Future research should move beyond descriptive evidence and test predefined hypotheses linking meal composition, food matrix properties, technological strategies, bioavailability and physiological outcomes. Adequate randomized controlled trials should use clearly defined meal prototypes, standardized preparation methods, realistic portion sizes, nutritionally matched control meals, repeated exposure when chronic outcomes are assessed, and clinically relevant endpoints. Priority biomarkers should include postprandial glucose and insulin, lipid profile, blood pressure, inflammatory and oxidative stress markers, circulating or urinary bioactive metabolites, gut microbiota composition and short-chain fatty acids. A stepwise translational roadmap should progress from formulation and *in vitro* digestion studies to acute human trials, longer-term interventions, implementation in food service or medically tailored meal programs, and evaluation of acceptability, cost, scalability and sustainability.

Overall, functional meals provide a conceptual framework and valuable practice for developing dietary strategies that promote health, are technologically innovative, and are aligned with real-world eating contexts. The systems-based framework proposed in Figure 1 provides a conceptual basis for future research on the design, evaluation and implementation of functional meals.

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Abbreviations

The following abbreviations are used in this manuscript

ACE	Angiotensin-converting enzyme
AI	Artificial intelligence
ALA	Alpha-linolenic acid
AMPK	AMP-activated protein kinase
ATP	Adenosine triphosphate
COX-2	Cyclooxygenase-2
CVD	Cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DHA	Docosahexaenoic acid
DNA	Deoxyribonucleic acid
DPP-IV	Dipeptidyl peptidase-IV
EPA	Eicosapentaenoic acid
FOS	Fructooligosaccharides
GIP	Glucose-dependent insulintropic polypeptide
GLP-1	Glucagon-like peptide-1
GSLs	Glucosinolates
HbA1c	Glycated hemoglobin
HPP	High-pressure processing
IKK	I κ B kinase
IL-6	Interleukin-6
iNOS	Inducible nitric oxide synthase
LDL	Low-density lipoprotein
MTM	Medically tailored meals
NCDs	Non-communicable diseases
NF- κ B	Nuclear factor kappa B
NLRP3	NOD-, LRR- and pyrin domain-containing protein 3
NPC1L1	Niemann–Pick C1-Like 1
Nrf2/Keap1	Nuclear factor erythroid 2-related factor 2/Kelch-like ECH-associated protein 1
OSCs	Organosulfur compounds
PEF	Pulsed electric fields
PUFAs	Polyunsaturated fatty acids
RCTs	Randomized controlled trials
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
SCFAs	Short-chain fatty acids
SPMs	Specialized pro-resolving mediators
TLR4	Toll-like receptor 4
TNF- α	Tumor necrosis factor-alpha

UCP1 Uncoupling protein 1
UV Ultraviolet

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