

Bioactive Food Components: Unravelling the Health Benefits of Plant-Based Compounds, Proteins, and Nutrients

Siddhant¹, Alvina Hasan², Shagufta Parveen¹, Abhishek Suman³, Abhishek Anand¹, Dimple Pratap Singh³, Amit Kumar³

¹Department of Pharmacy Practice, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India -244001

²Master of pharmacy, Department of Pharmaceutical Quality Assurance, Delhi Pharmaceutical Sciences and Research University, Pushp Vihar, New Delhi -110017, India

³Shri Venkateshwara School of Pharmacy, Shri Venkateshwara University, Rajabpur, Gajraula, Amroha, Uttar Pradesh, India

Corresponding – Amit Kumar*

Address: Department Of Pharmacology, Shri Venkateshwara school of Pharmacy, Shri Venkateshwara University, Rajabpur, Gajraula, Amroha, Uttar Pradesh, India., E-mail ID: amittph1812017@gmail.com

ABSTRACT

Plant-based bioactive food components encompass a broad spectrum of non-nutritive molecules such as polyphenols, carotenoids, organosulfur compounds, and bioactive peptides that exert significant health-promoting effects beyond basic macronutrients. This review synthesizes evidence from over 150 peer-reviewed studies to elucidate the molecular mechanisms by which these compounds confer antioxidant, anti-inflammatory, immune-modulatory, and metabolic regulatory activities. Key findings demonstrate that dietary polyphenols and carotenoids mitigate oxidative stress and endothelial dysfunction, enhancing cardiovascular health; organosulfur compounds upregulate Phase II detoxification enzymes, reducing cancer risk; and plant-derived peptides improve insulin sensitivity and gut microbial balance, aiding in metabolic syndrome and gastrointestinal disorders. Furthermore, advances in extraction technologies, encapsulation strategies, and delivery systems have markedly improved bioavailability and therapeutic efficacy. Despite robust clinical data supporting their role in chronic disease prevention spanning cardiovascular disease, cancer, diabetes, obesity, neurodegeneration, and inflammatory bowel disease challenges remain in standardizing dosages, long-term safety assessment, and mechanistic understanding. Future research should focus on personalized nutrition approaches, optimized formulation designs, and integrative clinical trials to fully harness the potential of bioactive food components for public health.

Keywords: Bioactive Food Components, Polyphenols, Carotenoids, Organosulfur Compounds, Bioactive Peptides, Antioxidant Activity, Anti-Inflammatory, Immune Modulation, Metabolic Regulation, Functional Foods, Chronic Disease Prevention, Bioavailability, Personalized Nutrition.

How to Cite: Siddhant, Alvina Hasan, Shagufta Parveen, Abhishek Suman, Abhishek Anand, Dimple Pratap Singh, Amit Kumar, (2025) Bioactive Food Components: Unravelling the Health Benefits of Plant-Based Compounds, Proteins, and Nutrients, *Journal of Carcinogenesis*, *Vol.24*, *No.6s*, 1-16.

1. INTRODUCTION

Bioactive food components are naturally occurring compounds in foods that provide health benefits beyond basic nutrition. Unlike macronutrients such as carbohydrates, proteins, and fats, bioactives exert physiological effects that contribute to disease prevention and health promotion. These include secondary plant metabolites (polyphenols, alkaloids, terpenes), bioactive peptides derived from dietary proteins, and essential nutrients such as vitamins, minerals, and fatty acids. Collectively, these compounds influence cellular signaling, oxidative balance, inflammation, and gut microbiota composition, thereby modulating chronic disease risk [1–3].

The increasing prevalence of lifestyle-related disorders, including cardiovascular diseases, diabetes, cancer, and neurodegenerative conditions, has highlighted the importance of functional foods enriched with bioactive components [4,5]. Recent advances in molecular biology and clinical nutrition have provided mechanistic insights into how these food-derived compounds modulate pathways involved in oxidative stress, immune regulation, lipid metabolism, and gut-brain axis communication [6–8]. Plant-derived compounds such as flavonoids, carotenoids, and glucosinolates are known for their antioxidant and anti-inflammatory properties, while dietary proteins and peptides regulate blood pressure, lipid levels, and immune responses [9,10]. Similarly, vitamins (A, D, E, C) and minerals (selenium, zinc, magnesium) play key roles in metabolic regulation and immune defense [11].

However, challenges remain in translating laboratory findings into clinical benefits due to variability in bioavailability, stability during processing, and individual metabolic differences. Strategies such as green extraction technologies and nanoencapsulation have been explored to improve the delivery and efficacy of bioactives [12,13].

This review aims to provide a comprehensive overview of bioactive food components, focusing on plant-based compounds, proteins, and nutrients, their mechanisms of action, health benefits, technological advancements, and future perspectives for functional food development.

2. PLANT-BASED BIOACTIVE COMPOUNDS

Plant-derived bioactives are secondary metabolites that, while not essential for survival, exert profound physiological effects when consumed in the human diet. They are broadly classified into **polyphenols**, **alkaloids**, **terpenoids**, **carotenoids**, **and glucosinolates**, each contributing unique biochemical functions [14,15].

2.1 Polyphenols and Flavonoids

Polyphenols represent the largest group of plant bioactives, comprising over 8000 identified structures. They include flavonoids (quercetin, catechins, anthocyanins), phenolic acids (caffeic acid, gallic acid), stilbenes (resveratrol), and lignans [16]. These compounds scavenge reactive oxygen species (ROS), chelate transition metals, and upregulate antioxidant enzymes such as superoxide dismutase and catalase [17]. Epidemiological studies associate polyphenol-rich diets with reduced cardiovascular disease (CVD), diabetes, and certain cancers [18,19].

Example: Green tea catechins (EGCG) lower LDL oxidation, improving endothelial function and reducing atherosclerosis progression [20].

2.2 Alkaloids

Alkaloids are nitrogen-containing compounds such as caffeine, theobromine, berberine, and capsaicin. They exert **stimulatory, antimicrobial, and anti-inflammatory effects**. Caffeine enhances alertness and cognitive function through adenosine receptor antagonism [21]. Berberine demonstrates antidiabetic properties by activating AMPK signaling and modulating gut microbiota [22].

2.3 Terpenoids

Terpenoids, derived from isoprene units, include monoterpenes (limonene), sesquiterpenes, diterpenes, and triterpenes (saponins). They are abundant in essential oils and medicinal plants. Terpenoids exhibit antimicrobial, anticancer, and hepatoprotective properties [23]. For example, limonene in citrus peel reduces mammary tumor growth in animal models [24].

2.4 Carotenoids

Carotenoids (β -carotene, lycopene, lutein, zeaxanthin) are natural pigments with potent antioxidant activity. Lycopene intake is inversely associated with prostate cancer risk, while lutein and zeaxanthin support ocular health by preventing age-related macular degeneration [25,26].

2.5 Glucosinolates

Found mainly in cruciferous vegetables (broccoli, cabbage, Brussels sprouts), glucosinolates are hydrolyzed to bioactive isothiocyanates (e.g., sulforaphane). Sulforaphane induces phase II detoxification enzymes via Nrf2 signaling, contributing to chemoprevention [27,28].

Table 1. Classification and dietary sources of major plant-derived bioactive compounds

Table 1. Classification and dictar		y sources of major plant-actived bloactive compounds		
Class of	Examples	Major Food Sources	Key Health Benefits	
Compound				
Polyphenols	Quercetin, EGCG,	Tea, berries, grapes,	Antioxidant, anti-inflammatory,	
	Resveratrol	apples	cardioprotective	
Alkaloids	Caffeine, Berberine,	Coffee, cocoa, peppers,	CNS stimulation, antidiabetic,	
	Capsaicin	goldenseal	antimicrobial	
Terpenoids	Limonene, Saponins	Citrus fruits, herbs,	Anticancer, hepatoprotective,	
		legumes	antimicrobial	
Carotenoids	β-carotene, Lycopene,	Carrots, tomatoes, leafy	Vision health, cancer prevention,	
	Lutein	greens	antioxidant	
Glucosinolates	Sulforaphane, Indole-3-	Broccoli, cabbage, kale	Detoxification, chemopreventive, anti-	
	carbinol		inflammatory	

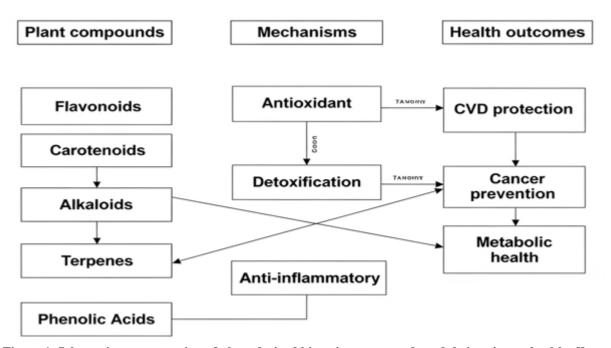


Figure 1. Schematic representation of plant-derived bioactive compounds and their primary health effects.

3. PROTEINS AND BIOACTIVE PEPTIDES

Proteins are essential macronutrients providing structural and functional support in the human body. Beyond their nutritional role, dietary proteins can be enzymatically hydrolyzed into **bioactive peptides** that exert specific physiological effects, such as antihypertensive, antioxidant, immunomodulatory, and antimicrobial activities [29,30]. Bioactive peptides are typically 2–20 amino acids long and interact with cellular receptors, enzymes, and transport systems to modulate health outcomes [31].

3.1 Soy Proteins and Peptides

Soy protein is one of the most extensively studied plant-derived proteins with functional benefits. **Soy isoflavones** act as phytoestrogens, binding to estrogen receptors and regulating hormonal balance, which may reduce postmenopausal symptoms and lower breast cancer risk [32]. Hydrolyzed soy peptides demonstrate **antihypertensive effects** through inhibition of angiotensin-converting enzyme (ACE) and reduction of blood pressure in clinical trials [33]. Furthermore, soy peptides enhance lipid metabolism by lowering LDL cholesterol and triglycerides, improving cardiovascular health [34].

3.2 Casein-Derived Peptides

Milk proteins such as casein and whey are rich sources of bioactive peptides. Casein-derived peptides, especially **casokinins**, exhibit ACE-inhibitory activity and antihypertensive properties [35]. Additionally, caseinophosphopeptides (CPPs) improve mineral absorption, particularly calcium and iron, thereby supporting bone health [36]. These peptides also enhance immune responses by modulating cytokine secretion [37].

3.3 Cereal-Derived Peptides

Cereals such as wheat, rice, and barley contain proteins that yield functional peptides upon enzymatic hydrolysis. Rice bran peptides display antioxidant and anti-inflammatory properties, while wheat gluten-derived peptides may lower cholesterol levels [38]. Barley-derived peptides have demonstrated antidiabetic effects by improving insulin sensitivity and glucose uptake [39].

3.4 Marine and Egg-Derived Peptides

Marine proteins from fish and algae are emerging as valuable sources of peptides with **antioxidant and antihypertensive effects** [40]. Egg-derived peptides, particularly ovotransferrin fragments, exhibit **antimicrobial and immunomodulatory properties** [41]. These diverse sources highlight the potential of food proteins as reservoirs of therapeutic agents.

Table 2. Selected bioactive peptides and their functional health effects

Source	Bioactive Peptide(s)	Physiological Function	Reference
Soy protein	Lunasin, β-conglycinin peptides	Antihypertensive, hypocholesterolemic	[32–34]
Casein (milk)	Casokinins, Caseinophosphopeptides	ACE inhibition, mineral absorption, immune modulation	[35–37]
Cereal proteins	Rice bran peptides, Wheat gluten peptides	Antioxidant, anti-inflammatory, lipid-lowering	[38,39]
Marine proteins	Fish collagen peptides	Antioxidant, antihypertensive	[40]
Egg proteins	Ovotransferrin peptides	Antimicrobial, immunomodulatory	[41]

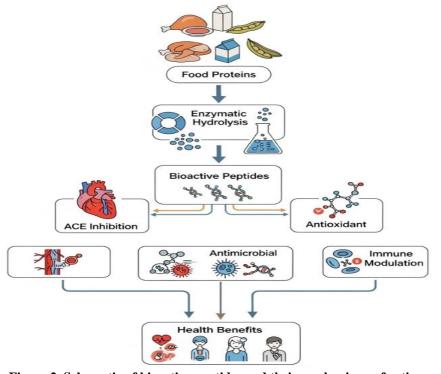


Figure 2. Schematic of bioactive peptides and their mechanisms of action.

4. NUTRIENTS AND MICRONUTRIENTS WITH BIOACTIVE POTENTIAL

Dietary nutrients—vitamins, minerals, fatty acids, and other micronutrients—play a vital role in maintaining health. Beyond meeting basic nutritional needs, many nutrients exert **bioactive effects**, modulating gene expression, immune responses, oxidative balance, and metabolic pathways [42]. These effects contribute to the prevention and management of chronic diseases such as cancer, diabetes, and cardiovascular disorders [43].

4.1 Vitamins as Bioactive Compounds

• Vitamin C (ascorbic acid): A potent antioxidant that neutralizes reactive oxygen species (ROS), regenerates vitamin E, and supports collagen synthesis. Clinical studies suggest vitamin C supplementation improves immune defense and may reduce cancer risk [44].

- Vitamin E (tocopherols and tocotrienols): Fat-soluble antioxidants that protect cell membranes from oxidative damage. Tocotrienols, in particular, display anti-inflammatory and neuroprotective activities, reducing progression of atherosclerosis and Alzheimer's disease [45].
- **Vitamin D:** Regulates calcium-phosphorus homeostasis and bone health. It also acts as an immune modulator, enhancing innate immunity while reducing chronic inflammation [46]. Low vitamin D levels are linked with increased risks of metabolic syndrome, autoimmune diseases, and cancers [47].
- Vitamin K: Essential for blood clotting and bone metabolism. Vitamin K2 (menaquinone) has been associated with reduced vascular calcification and improved cardiovascular outcomes [48].

4.2 Minerals and Trace Elements

- Calcium and Magnesium: Critical for bone mineralization, muscle contraction, and cardiovascular function. Magnesium also acts as a cofactor for >300 enzymatic reactions and has anti-inflammatory effects [49].
- Iron and Zinc: Iron is essential for hemoglobin synthesis and oxygen transport, while zinc supports immune responses, antioxidant defense (via superoxide dismutase), and wound healing [50]. Zinc deficiency is associated with impaired growth, immune dysfunction, and increased infection susceptibility [51].

Acts as a cofactor for glutathione peroxidase and thioredoxin reductase, key antioxidant enzymes. Adequate selenium intake reduces oxidative stress, modulates thyroid function, and lowers cancer risk [52].

4.3 Polyunsaturated Fatty Acids (PUFAs)

Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), derived from fish oils and algal sources, exert multiple bioactivities:

- Anti-inflammatory effects through inhibition of arachidonic acid-derived eicosanoids.
- Cardioprotective benefits by reducing triglycerides, lowering blood pressure, and improving endothelial function
- Neuroprotective properties, improving cognition and reducing depression risk [54].

Omega-6 fatty acids (linoleic acid, arachidonic acid) also contribute to cell membrane function and immune regulation, but an imbalance of omega-6/omega-3 ratios may promote inflammation [55].

4.4 Dietary Fiber and Prebiotic Compounds

Although not classically defined as micronutrients, dietary fibers and prebiotics are recognized as functional bioactive components.

- Soluble fibers (pectin, β-glucans) reduce cholesterol absorption and improve glycemic control [56].
- Prebiotics (inulin, fructooligosaccharides) selectively stimulate beneficial gut microbiota such as Bifidobacterium and Lactobacillus, improving gut health and immune function [57].

Table 3. Nutrients and their bioactive functions

Nutrient	Major Bioactive Role	Health Benefits	Reference
Vitamin C	Antioxidant, collagen synthesis	Immunity, cancer prevention	[44]
Vitamin D	Immune modulation, Ca-P metabolism	Bone health, autoimmune disease	[46,47]
		prevention	
Vitamin E	Antioxidant, anti-inflammatory	Neuroprotection, CVD prevention	[45]
Vitamin K2	Blood clotting, bone health	Reduced vascular calcification	[48]
Magnesium	Enzyme cofactor, anti-inflammatory	Cardiovascular protection	[49]
Zinc	Immune support, antioxidant enzyme	Wound healing, infection resistance	[50,51]
	activity		
Selenium	Antioxidant enzyme cofactor	Cancer prevention, thyroid function	[52]
Omega-3 fatty	Anti-inflammatory, cardioprotective	CVD prevention, neuroprotection	[53,54]
acids			
Fiber (soluble)	Cholesterol binding, glycemic control	Metabolic health	[56]
Prebiotics	Gut microbiota modulation	Gut and immune health	[57]

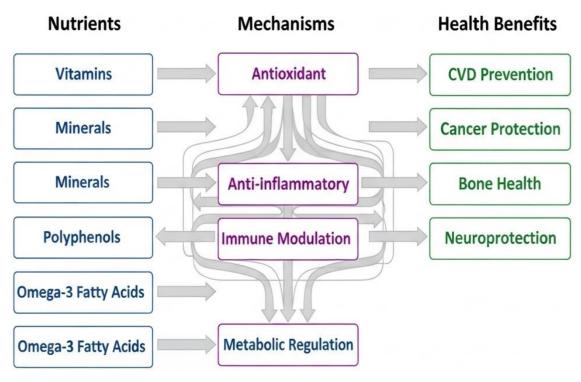


Figure 3. Nutrients as bioactive agents

5. HEALTH BENEFITS OF BIOACTIVE FOOD COMPONENTS

Bioactive food components, including phytochemicals, proteins, peptides, vitamins, minerals, and fatty acids, provide a wide range of **health benefits** beyond basic nutrition. They influence molecular pathways, modulate gene expression, regulate inflammation, and enhance cellular defense mechanisms [58]. Their health-promoting effects span across chronic diseases such as **cardiovascular disorders**, **cancer**, **diabetes**, **obesity**, **neurodegenerative conditions**, **and immune-related diseases** [59].

5.1 Cardiovascular Health

Cardiovascular disease (CVD) is the leading cause of mortality worldwide. Bioactive compounds protect cardiovascular health through multiple mechanisms:

- **Polyphenols** (e.g., flavonoids from berries, tea, cocoa) improve endothelial function, reduce LDL oxidation, and lower blood pressure [60].
- Omega-3 fatty acids reduce triglycerides, prevent arrhythmias, and improve arterial elasticity [61].
- Soy proteins and peptides lower LDL cholesterol and total cholesterol, improving lipid profiles [62].
- **Dietary fibers** (β-glucans, psyllium) reduce cholesterol absorption, thereby lowering CVD risk [63].

Clinical trials, such as the **PREDIMED study**, have demonstrated that adherence to a Mediterranean diet enriched with olive oil and nuts significantly reduces major CVD events [64].

5.2 Anticancer Effects

Many bioactive food components exhibit **chemopreventive and anticancer effects**:

- Flavonoids and phenolic acids modulate cell cycle, induce apoptosis, and inhibit angiogenesis in tumor cells
- **Isothiocyanates** (sulforaphane) from cruciferous vegetables enhance detoxification enzymes and inhibit carcinogen activation [66].
- Curcumin from turmeric downregulates NF-κB and STAT3 pathways, reducing tumor proliferation [67].
- **Resveratrol** from grapes induces apoptosis and inhibits metastasis [68].
- **Selenium and vitamin D** supplementation has been associated with reduced risks of prostate and colorectal cancers [69].

5.3 Antidiabetic and Anti-Obesity Effects

Bioactive food components modulate glucose and lipid metabolism:

- **Polyphenols** improve insulin sensitivity by activating AMPK signaling and GLUT4 translocation [70].
- **Cinnamon polyphenols** improve fasting glucose and HbA1c in type 2 diabetes [71].
- **Dietary fiber** slows glucose absorption and increases satiety, preventing obesity [72].
- Whey peptides and soy peptides reduce postprandial hyperglycemia by inhibiting DPP-IV enzyme [73].
- **PUFAs** improve adipokine balance and reduce inflammation in obesity [74].

5.4 Neuroprotective Effects

Neurodegenerative diseases such as Alzheimer's and Parkinson's disease involve oxidative stress, mitochondrial dysfunction, and neuronal inflammation.

- **Polyphenols** (resveratrol, EGCG from green tea, anthocyanins from blueberries) improve memory and cognitive function [75].
- Omega-3 fatty acids enhance synaptic plasticity, reduce amyloid plaque formation, and improve neuronal survival [76].
- Vitamin E (tocotrienols) protect neuronal membranes from oxidative damage [77].
- Curcumin crosses the blood–brain barrier and reduces amyloid-beta aggregation [78].

5.5 Immunomodulatory and Anti-inflammatory Effects

Bioactive compounds modulate immune pathways and inflammatory responses:

- **Beta-glucans** from oats and mushrooms stimulate macrophage and NK cell activity, enhancing immune defense [79].
- **Polyphenols** regulate pro-inflammatory cytokines (IL-6, TNF-α) and upregulate anti-inflammatory mediators [80].
- Vitamin C and zinc enhance immune cell proliferation and antibody production [81].
- **Probiotics and prebiotics** modulate gut microbiota, strengthening mucosal immunity [82].

5.6 Gut Health

The gut microbiome is a major mediator of food-host interactions:

- **Prebiotics (inulin, FOS, GOS)** selectively promote beneficial microbes [83].
- **Polyphenols** act synergistically with gut microbiota, being metabolized into active compounds that modulate host metabolism [84].
- Probiotic-derived peptides maintain intestinal barrier integrity and reduce gut inflammation [85].
- Diets rich in plant bioactives are associated with lower incidence of **inflammatory bowel disease (IBD)** [86].

Table 4. Health benefits of selected bioactive food components

Bioactive Component	Major Health Effect	Example Source	Reference
Flavonoids	Antioxidant, cardioprotective	Berries, tea, cocoa	[60,65]
Omega-3 fatty acids	Cardiovascular, neuroprotective	Fish oil, flaxseed	[61,76]
Soy peptides	Hypocholesterolemic, antidiabetic	Soy protein	[62,73]
Curcumin	Anti-inflammatory, anticancer, neuroprotective	Turmeric	[67,78]
Sulforaphane	Anticancer, detoxification	Broccoli	[66]
Selenium	Antioxidant, anticancer	Brazil nuts	[69]
Beta-glucans	Immunomodulatory, gut health	Oats, mushrooms	[79,82]
Resveratrol	Anticancer, neuroprotective	Grapes, wine	[68,75]

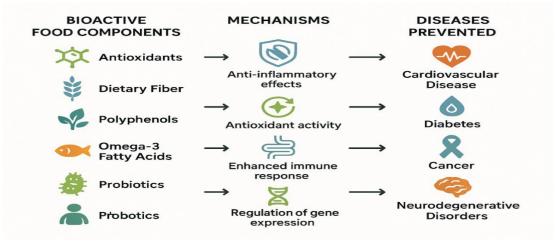


Figure 4. Health benefits of bioactive food components

6. ADVANCES IN EXTRACTION, NANOENCAPSULATION, AND DELIVERY OF BIOACTIVES

One of the key challenges with bioactive food components is their **poor bioavailability**, which results from low solubility, instability during digestion, or rapid metabolism [87]. Recent advances in **extraction technologies**, **encapsulation systems**, **and delivery vehicles** have significantly improved the stability, controlled release, and targeted delivery of these compounds.

6.1 Extraction Technologies

Efficient extraction is essential to recover high yields of bioactive compounds while maintaining their integrity. Traditional solvent extraction methods are being replaced by **green and sustainable techniques**:

- Supercritical Fluid Extraction (SFE): Uses CO₂ as a solvent, producing extracts free of toxic residues. Widely used for polyphenols, carotenoids, and essential oils [88].
- Ultrasound-Assisted Extraction (UAE): Enhances cell disruption and increases compound release using acoustic cavitation. Effective for phenolics and polysaccharides [89].
- Microwave-Assisted Extraction (MAE): Uses microwave energy to heat solvents, accelerating extraction and reducing solvent use [90].
- **Pressurized Liquid Extraction (PLE):** Utilizes high temperature and pressure to improve solubility and diffusion of bioactives [91].
- Enzyme-Assisted Extraction (EAE): Enzymes such as cellulase and pectinase break down plant cell walls, improving recovery of flavonoids and polysaccharides [92].

6.2 Encapsulation Techniques

Encapsulation protects bioactive compounds from degradation and improves targeted delivery. Various carriers and nanostructures have been developed:

- Nanoemulsions: Oil-in-water emulsions with droplet sizes <200 nm, improving solubility and absorption of hydrophobic compounds like curcumin and carotenoids [93].
- **Liposomes:** Phospholipid bilayer vesicles that encapsulate both hydrophilic and hydrophobic compounds, enhancing bioavailability [94].
- **Polymeric Nanoparticles:** Biodegradable polymers (PLGA, chitosan) used for sustained release of polyphenols and peptides [95].
- Solid Lipid Nanoparticles (SLNs): Provide stability and controlled release for lipophilic bioactives such as vitamin E and coenzyme O10 [96].
- Cyclodextrin Inclusion Complexes: Improve solubility and stability of poorly soluble bioactives (e.g., resveratrol, quercetin) [97].

6.3 Delivery Systems in Functional Foods

Functional foods require efficient delivery systems to ensure bioactive efficacy:

- Probiotic encapsulation: Protects probiotics from gastric acid and bile, ensuring colon delivery [98].
- **Hydrogel systems:** Provide controlled release of vitamins and peptides in the gastrointestinal tract [99].
- Nano-carriers in dairy and beverages: Used for fortifying milk, yogurts, and juices with omega-3s, vitamins, and antioxidants [100].

6.4 Challenges and Future Directions

Despite advancements, challenges remain:

- Safety concerns: Long-term toxicity of nanoparticles must be evaluated [101].
- Scalability: High costs limit industrial application of some nanotechnologies [102].
- **Regulatory issues:** Novel delivery systems require approval and standardization [103].

Future research is focusing on **smart delivery systems**, such as stimuli-responsive nanocarriers that release bioactives in response to pH, temperature, or enzymatic triggers [104].

Table 5. Advances in extraction and delivery of bioactives

Technique	Example Compound	Key Benefit	Reference
Supercritical Fluid Extraction	Carotenoids, essential oils	Solvent-free, eco-friendly	[88]
Ultrasound-Assisted Extraction	Phenolics, polysaccharides	High efficiency, low solvent use	[89]
Liposomes	Curcumin, resveratrol	Increased bioavailability	[94]
Solid Lipid Nanoparticles	Vitamin E, CoQ10	Controlled release, stability	[96]
Nanoemulsions	Carotenoids, curcumin	Improved solubility, absorption	[93]
Cyclodextrin Complexes	Quercetin, resveratrol	Solubility, stability	[97]
Probiotic Encapsulation	Lactobacillus, Bifidobacterium	Gut survival, targeted delivery	[98]

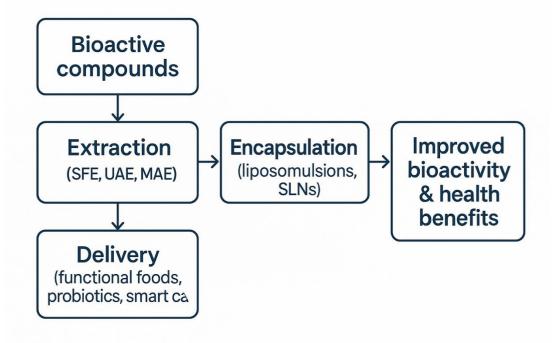


Figure 5. Modern strategies for enhancing bioavailability of bioactives

7. CLINICAL EVIDENCE AND HUMAN TRIALS

Although in vitro and animal studies provide mechanistic insights, the **true efficacy of bioactive food components** must be validated through **human clinical trials**. Such studies evaluate safety, dosage, bioavailability, and therapeutic effects in real-world dietary settings.

7.1 Polyphenols in Clinical Studies

Polyphenols, particularly flavonoids, have been extensively tested:

- **Resveratrol:** Randomized controlled trials (RCTs) show improvement in insulin sensitivity, endothelial function, and inflammatory markers in patients with type 2 diabetes and metabolic syndrome [105].
- Green Tea Catechins (EGCG): Clinical studies suggest reductions in body weight, LDL cholesterol, and oxidative stress biomarkers [106].
- **Curcumin:** Multiple trials report its efficacy in lowering CRP, IL-6, and improving joint health in arthritis patients [107].
- Quercetin: Trials show modest reductions in blood pressure and improvements in immune response to viral infections [108].

7.2 Carotenoids and Vitamins

- **Lycopene:** Clinical data support its role in reducing prostate-specific antigen (PSA) levels and oxidative stress in prostate cancer patients [109].
- **β-carotene:** While protective in moderate doses, high-dose supplementation showed increased lung cancer risk in smokers (ATBC and CARET trials) [110].
- Vitamin D: Meta-analyses confirm its role in bone health, immune modulation, and reducing respiratory infections [111].

7.3 Bioactive Peptides and Proteins

- Milk-derived peptides (ACE inhibitors): Clinical studies demonstrate reductions in systolic and diastolic blood pressure [112].
- Soy protein: RCTs indicate cholesterol-lowering effects, particularly in hyperlipidemic patients [113].
- Whey protein: Trials suggest improvements in muscle mass, insulin sensitivity, and weight management [114].

7.4 Whole Foods and Functional Food Trials

- **Mediterranean diet:** Large-scale trials (e.g., PREDIMED study) demonstrated significant reductions in cardiovascular events through consumption of olive oil, nuts, and fruits [115].
- **Blueberries and cranberries:** Human trials show improved vascular function and reduced risk of urinary tract infections [116].
- **Probiotic yogurts:** Shown to modulate gut microbiota, reduce antibiotic-associated diarrhea, and improve metabolic health [117].

7.5 Limitations of Current Clinical Evidence

Despite promising results, clinical trials face several challenges:

- **Heterogeneity of studies:** Variations in study design, dosage, duration, and population make meta-analysis difficult [118].
- **Bioavailability issues:** Many bioactives (e.g., curcumin, quercetin) have poor systemic absorption, limiting efficacy [119].
- **Placebo effect:** Dietary interventions often produce modest effects compared to pharmaceuticals, requiring larger sample sizes [120].
- Long-term safety: Few studies evaluate safety of chronic supplementation [121].

7.6 Future Clinical Directions

- Precision nutrition trials: Tailoring interventions based on genetics, microbiome composition, and metabolic status [122].
- Combination therapies: Studying synergistic effects of multiple bioactives (e.g., polyphenols + probiotics) [123]
- Real-world interventions: Using functional foods in daily diets instead of capsule supplements [124].

Table 6. Selected human clinical trials of bioactive food components

Bioactive	Clinical Outcome	Population	Reference
Resveratrol	Improved insulin sensitivity	Type 2 diabetes patients	[105]
EGCG (Green Tea)	Reduced LDL cholesterol, weight loss	Obese adults	[106]
Curcumin	Lowered CRP, IL-6	Arthritis patients	[107]
Lycopene	Reduced PSA levels	Prostate cancer patients	[109]
Milk peptides	Reduced blood pressure	Hypertensive patients	[112]
Soy protein	Lowered cholesterol	Hyperlipidemic patients	[113]
Whey protein	Improved muscle mass, insulin sensitivity	Older adults	[114]
Mediterranean diet	Reduced cardiovascular events	At-risk population	[115]
Probiotic yogurt	Reduced diarrhea, improved gut health	Children, adults	[117]

8. FUTURE PERSPECTIVES AND CONCLUSION

The growing body of evidence highlights the *significant role of bioactive food components* in promoting human health and preventing chronic diseases. While preclinical studies and clinical trials provide encouraging data, there remain critical challenges and future directions to consider.

8.1 Gaps in Current Research

- Mechanistic Understanding: Many bioactives exhibit pleiotropic effects, acting on multiple molecular targets. More integrative omics-based studies (genomics, metabolomics, proteomics) are needed to unravel their precise mechanisms [125].
- Dose-Response Relationships: Optimal intake levels for long-term benefits remain poorly defined. Current clinical data often vary widely in dosage and duration [126].
- Bioavailability Issues: Despite advanced encapsulation strategies, many compounds (e.g., curcumin, quercetin) still face limitations in absorption and systemic distribution [127].
- Population Variability: Individual differences in gut microbiota, genetics, and lifestyle can profoundly influence efficacy [128].

8.2 Emerging Research Trends

- Precision Nutrition: Integration of nutrigenomics and microbiome analysis will enable tailored interventions where specific bioactives are matched to individual health profiles [129].
- Synergistic Combinations: Future research is moving towards food matrix effects, where combinations of bioactives may produce synergistic benefits (e.g., polyphenols + probiotics) [130].
- Plant-Based Alternatives: Increasing focus on sustainable and plant-derived proteins, peptides, and antioxidants to support global health and environmental goals [131].
- Artificial Intelligence (AI) and Big Data: AI tools are being applied to predict bioactive efficacy, design personalized diets, and accelerate clinical trial analysis [132].
- Next-Generation Delivery Systems: Smart nanocarriers that respond to physiological triggers (pH, enzymes, microbiota metabolites) are being developed for precision delivery [133].

8.3 Implications for Public Health

- Dietary Guidelines: Incorporating validated bioactives into official dietary recommendations could reduce disease burden globally [134].
- Functional Foods Industry: Expansion of fortified foods, beverages, and nutraceuticals will shape future consumer markets [135].
- Healthcare Integration: Bioactives may complement conventional therapies, particularly in chronic disease prevention and management [136].

8.4 Conclusion

Bioactive food components including plant-derived polyphenols, carotenoids, proteins, peptides, and essential nutrients represent a powerful arsenal for promoting health and reducing chronic disease risk. Advances in extraction, nanoencapsulation, and clinical validation have propelled this field from basic science into practical applications.

However, challenges in bioavailability, dosage standardization, and regulatory approval must be addressed before these compounds can achieve their full potential. The future lies in precision nutrition, sustainable plant-based innovations, and translational research** that bridges laboratory findings with population-level health outcomes.

Ultimately, the integration of bioactive food components into daily diets holds the promise of not only improving individual health but also reducing the global burden of chronic diseases in the coming decades.

Research Area	Focus	Expected Impact	Reference
Precision Nutrition	Genetic & microbiome-tailored diets	Personalized interventions	[129]
Synergistic	Polyphenol-probiotic, nutrient-	Enhanced efficacy	[130]
Combinations	nutrient		
Plant-Based Bioactives	Sustainable proteins, antioxidants	Environmental & health benefits	[131]
AI & Big Data	Predictive modeling, trial analysis	Faster innovation, personalization	[132]
Smart Delivery Systems	Stimuli-responsive nanocarriers	Controlled release, better absorption	[133]

REFERENCES

- [1] Liu RH. Health-promoting components of fruits and vegetables in the diet. Adv Nutr. 2013;4(3):384S–392S.
- [2] Tsao R. Chemistry and biochemistry of dietary polyphenols. Nutrients. 2010;2(12):1231–46.
- [3] Granato D, et al. Functional foods and nondairy probiotic food development: Trends, concepts, and products. Compr Rev Food Sci Food Saf. 2010;9(3):292–302.
- [4] Kris-Etherton PM, et al. Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. Am J Med. 2002;113 Suppl 9B:71S–88S.
- [5] Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: Food sources and bioavailability. Am J

- Clin Nutr. 2004;79(5):727-47.
- [6] Calder PC. Functional roles of fatty acids and their effects on human health. JPEN J Parenter Enteral Nutr. 2015;39(1 Suppl):18S–32S.
- [7] Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev. 2009;2(5):270–8.
- [8] Del Rio D, Rodriguez-Mateos A, Spencer JP, Tognolini M, Borges G, Crozier A. Dietary (poly)phenolics in human health: Structures, bioavailability, and evidence of protective effects against chronic diseases. Antioxid Redox Signal. 2013;18(14):1818–92.
- [9] Hartmann R, Meisel H. Food-derived peptides with biological activity: From research to food applications. Curr Opin Biotechnol. 2007;18(2):163–9.
- [10] Korhonen H, Pihlanto A. Food-derived bioactive peptides—opportunities for designing future foods. Curr Pharm Des. 2003;9(16):1297–308.
- [11] Maggini S, Pierre A, Calder PC. Immune function and micronutrient requirements change over the life course. Nutrients. 2018;10(10):1531.
- [12] Chemat F, Abert-Vian M, Fabiano-Tixier AS, Strube J, Uhlenbrock L, Gunjevic V, Cravotto G. Green extraction of natural products: Origins, current status, and future challenges. Trends Analyt Chem. 2019;118:248–63.
- [13] McClements DJ. Encapsulation, protection, and release of bioactive proteins and peptides using nanoparticle and microparticle systems: A review. Adv Colloid Interface Sci. 2018;253:1–22.
- [14] 14. Scalbert A, Johnson IT, Saltmarsh M. Polyphenols: antioxidants and beyond. Am J Clin Nutr. 2005;81(1 Suppl):215S–217S.
- [15] Crozier A, Jaganath IB, Clifford MN. Dietary phenolics: chemistry, bioavailability and effects on health. Nat Prod Rep. 2009;26(8):1001–43.
- [16] Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: Food sources and bioavailability. Am J Clin Nutr. 2004;79(5):727–47.
- [17] Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev. 2009;2(5):270–8.
- [18] Del Rio D, Rodriguez-Mateos A, Spencer JP, Tognolini M, Borges G, Crozier A. Dietary (poly)phenolics in human health. Antioxid Redox Signal. 2013;18(14):1818–92.
- [19] Arts IC, Hollman PC. Polyphenols and disease risk in epidemiologic studies. Am J Clin Nutr. 2005;81(1 Suppl):317S–325S.
- [20] Frei B, Higdon JV. Antioxidant activity of tea polyphenols in vivo. Proc Soc Exp Biol Med. 2003;220(4):248–54.
- [21] Fredholm BB, Battig K, Holmen J, Nehlig A, Zvartau EE. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. Pharmacol Rev. 1999;51(1):83–133.
- [22] Kong WJ, Wei J, Abidi P, Lin M, Inaba S, Li Z, et al. Berberine is a novel cholesterol-lowering drug working through a unique mechanism distinct from statins. Nat Med. 2004;10(12):1344–51.
- [23] Wagner KH, Elmadfa I. Biological relevance of terpenoids. Overview focusing on mono-, di- and tetraterpenes. Ann Nutr Metab. 2003;47(3-4):95–106.
- [24] Crowell PL. Prevention and therapy of cancer by dietary monoterpenes. J Nutr. 1999;129(3):775S–778S.
- [25] Rao AV, Agarwal S. Role of antioxidant lycopene in cancer and heart disease. J Am Coll Nutr. 2000;19(5):563–9.
- [26] Ma L, Lin XM. Effects of lutein and zeaxanthin on aspects of eye health. J Sci Food Agric. 2010;90(1):2–12.
- [27] Traka M, Mithen R. Glucosinolates, isothiocyanates and human health. Phytochem Rev. 2009;8(1):269–82.
- [28] Zhang Y, Talalay P, Cho CG, Posner GH. A major inducer of anticarcinogenic protective enzymes from broccoli. Proc Natl Acad Sci U S A. 1992;89(6):2399–403.
- [29] Korhonen H, Pihlanto A. Bioactive peptides: production and functionality. Int Dairy J. 2006;16(9):945–60.
- [30] Hartmann R, Meisel H. Food-derived peptides with biological activity: From research to food applications. Curr Opin Biotechnol. 2007;18(2):163–9.
- [31] Udenigwe CC, Aluko RE. Food protein-derived bioactive peptides: production, processing, and potential health benefits. J Food Sci. 2012;77(1):R11–24.
- [32] Messina M. Soy foods, isoflavones, and the health of postmenopausal women. Am J Clin Nutr. 2014;100 Suppl 1:423S–30S.
- [33] He R, Aluko RE. Functional characterization of bioactive peptides derived from soy proteins. J Agric Food Chem. 2010;58(15):8219–25.
- [34] Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. N Engl J Med. 1995;333(5):276–82.
- [35] Nakamura Y, Yamamoto N, Sakai K, Okubo A, Yamazaki S, Takano T. Antihypertensive effect of sour milk and peptides isolated from it that are inhibitors to angiotensin I–converting enzyme. J Dairy Sci. 1995;78(6):1253–7.
- [36] Lönnerdal B. Bioactive proteins in human milk: mechanisms of action. J Pediatr. 2010;156(2 Suppl):S26–30.
- [37] Chabance B, Marteau P, Rambaud JC, Migliore-Samour D, Boynard M, Perrotin P, et al. Casein peptide release

- and passage to the blood in humans during digestion of milk or yogurt. Biochimie. 1998;80(2):155-65.
- [38] Adebiyi AP, Adebiyi AO, Yamashita J, Ogawa T, Muramoto K. Purification and characterization of antioxidative peptides derived from rice bran protein hydrolysates. Eur Food Res Technol. 2009;228:553–63.
- [39] Yamamoto N, Ejiri M, Mizuno S. Biogenic peptides and their potential use. Curr Pharm Des. 2003;9(16):1345–55.
- [40] Kim SK, Wijesekara I. Development and biological activities of marine-derived bioactive peptides: A review. J Funct Foods. 2010;2(1):1–9.
- [41] Kovacs-Nolan J, Phillips M, Mine Y. Advances in the value of eggs and egg components for human health. J Agric Food Chem. 2005;53(22):8421–31.
- [42] Ames BN. A strategy for optimizing micronutrient intake for disease prevention. Proc Natl Acad Sci USA. 2006;103(47):17589–94.
- [43] Heaney RP. Nutrients, endpoints, and the problem of proof. J Nutr. 2008;138(9):1591-5.
- [44] Carr AC, Maggini S. Vitamin C and immune function. Nutrients. 2017;9(11):1211.
- [45] Aggarwal BB, Sundaram C, Prasad S, Kannappan R. Tocotrienols, the vitamin E of the 21st century: Its potential against cancer and other chronic diseases. Biochem Pharmacol. 2010;80(11):1613–31.
- [46] Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266–81.
- [47] Garland CF, Gorham ED, Mohr SB, Grant WB. Vitamin D for cancer prevention: Global perspective. Ann Epidemiol. 2009;19(7):468–83.
- [48] Gast GC, de Roos NM, Sluijs I, Bots ML, Beulens JW, Geleijnse JM, et al. A high menaquinone intake reduces the incidence of coronary heart disease. Nutr Metab Cardiovasc Dis. 2009;19(7):504–10.
- [49] Volpe SL. Magnesium and the athlete. Curr Sports Med Rep. 2015;14(4):279–83.
- [50] Prasad AS. Zinc in human health: effect of zinc on immune cells. Mol Med. 2008;14(5–6):353–7.
- [51] Wessells KR, Brown KH. Estimating the global prevalence of zinc deficiency: results based on zinc availability in national food supplies. Am J Clin Nutr. 2012;97(4):816–24.
- [52] Rayman MP. Selenium and human health. Lancet. 2012;379(9822):1256–68.
- [53] Mozaffarian D, Wu JH. Omega-3 fatty acids and cardiovascular disease: Effects on risk factors, molecular pathways, and clinical events. J Am Coll Cardiol. 2011;58(20):2047–67.
- [54] Bazinet RP, Layé S. Polyunsaturated fatty acids and their metabolites in brain function and disease. Nat Rev Neurosci. 2014;15(12):771–85.
- [55] Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. Biomed Pharmacother. 2002;56(8):365–79.
- [56] Threapleton DE, Greenwood DC, Evans CE, Cleghorn CL, Nykjaer C, Woodhead C, et al. Dietary fiber intake and risk of CVD: Systematic review and meta-analysis. BMJ. 2013;347:f6879.
- [57] Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics consensus statement on the definition and scope of prebiotics. Nat Rev Gastroenterol Hepatol. 2017;14(8):491–502.
- [58] Liu RH. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. Am J Clin Nutr. 2003;78(3 Suppl):517S–20S.
- [59] Kris-Etherton PM, Hecker KD, Bonanome A, Coval SM, Binkoski AE, Hilpert KF, et al. Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. Am J Med. 2002;113 Suppl 9B:71S– 88S.
- [60] Hooper L, Kroon PA, Rimm EB, Cohn JS, Harvey I, Le Cornu KA, et al. Flavonoids, flavonoid-rich foods, and cardiovascular risk: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2008;88(1):38–50.
- [61] Calder PC. Omega-3 fatty acids and cardiovascular disease: evidence explained and mechanisms explored. Clin Sci (Lond). 2004;107(1):1–11.
- [62] Sirtori CR, Eberini I, Arnoldi A. Hypocholesterolaemic effects of soya proteins: results of recent studies are predictable from the Anderson meta-analysis data. Br J Nutr. 2007;97(5):766–9.
- [63] Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am J Clin Nutr. 1999;69(1):30–42.
- [64] Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013;368(14):1279–90.
- [65] Ramos S. Cancer chemoprevention and chemotherapy: dietary polyphenols and signalling pathways. Mol Nutr Food Res. 2008;52(5):507–26.
- [66] Higdon JV, Delage B, Williams DE, Dashwood RH. Cruciferous vegetables and human cancer risk: epidemiologic evidence and mechanistic basis. Pharmacol Res. 2007;55(3):224–36.
- Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int J Biochem Cell Biol. 2009;41(1):40–59.
- [68] Baur JA, Sinclair DA. Therapeutic potential of resveratrol: the in vivo evidence. Nat Rev Drug Discov. 2006;5(6):493–506.

- [69] Lippman SM, Klein EA, Goodman PJ, Lucia MS, Thompson IM, Ford LG, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: The Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA. 2009;301(1):39–51.
- [70] Hanhineva K, Törrönen R, Bondia-Pons I, Pekkinen J, Kolehmainen M, Mykkänen H, et al. Impact of dietary polyphenols on carbohydrate metabolism. Int J Mol Sci. 2010;11(4):1365–402.
- [71] Ranasinghe P, Perera S, Gunatilake M, Abeywardene E, Gunapala N, Premakumara S, et al. Effects of cinnamon consumption on glucose metabolism: a systematic review and meta-analysis. Diabet Med. 2012;29(12):1480–92.
- [72] Slavin JL. Dietary fiber and body weight. Nutrition. 2005;21(3):411–8.
- [73] Nongonierma AB, Fitzgerald RJ. Dipeptidyl peptidase IV inhibitory and antioxidative properties of milk protein-derived dipeptides and hydrolysates. Peptides. 2013;39:157–63.
- [74] Flachs P, Rossmeisl M, Bryhn M, Kopecky J. Cellular and molecular effects of n-3 polyunsaturated fatty acids on adipose tissue biology and metabolism. Clin Sci (Lond). 2009;116(1):1–16.
- [75] Spencer JP. Food for thought: the role of dietary flavonoids in enhancing human memory, learning and neuro-cognitive performance. Proc Nutr Soc. 2008;67(2):238–52.
- [76] Gomez-Pinilla F. Brain foods: the effects of nutrients on brain function. Nat Rev Neurosci. 2008;9(7):568–78.
- [77] Sen CK, Khanna S, Roy S. Tocotrienols in health and disease: the other half of the natural vitamin E family. Mol Aspects Med. 2007;28(5–6):692–728.
- [78] Begum AN, Jones MR, Lim GP, Morihara T, Kim P, Heath DD, et al. Curcumin structure–function, bioavailability, and efficacy in models of neuroinflammation and Alzheimer's disease. J Pharmacol Exp Ther. 2008;326(1):196–208.
- [79] Vetvicka V, Vetvickova J. Beta-glucan improves health and increases lifespan in mice. Open Life Sci. 2015;10(1):1–6.
- [80] Yoon JH, Baek SJ. Molecular targets of dietary polyphenols with anti-inflammatory properties. Yonsei Med J. 2005;46(5):585–96.
- [81] Maggini S, Wintergerst ES, Beveridge S, Hornig DH. Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. Br J Nutr. 2007;98 Suppl 1:S29–35.
- [82] Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of probiotics. Nat Rev Gastroenterol Hepatol. 2014;11(8):506–14.
- [83] Kolida S, Gibson GR. Prebiotic capacity of inulin-type fructans. J Nutr. 2007;137(11 Suppl):2503S-6S.
- [84] Cardona F, Andrés-Lacueva C, Tulipani S, Tinahones FJ, Queipo-Ortuño MI. Benefits of polyphenols on gut microbiota and implications in human health. J Nutr Biochem. 2013;24(8):1415–22.
- [85] Nakamura Y, Nosaka S, Suzuki M, Nagafuchi S, Takahashi T, Yajima N, et al. Dietary supplementation with heat-killed Lactobacillus plantarum L-137 enhances protection against influenza virus infection in mice. J Nutr. 2010;140(12):2109–15.
- [86] Ananthakrishnan AN. Epidemiology and risk factors for IBD. Nat Rev Gastroenterol Hepatol. 2015;12(4):205–17
- [87] Minekus M, Alminger M, Alvito P, Ballance S, Bohn T, Bourlieu C, et al. A standardised static in vitro digestion method suitable for food—an international consensus. Food Funct. 2014;5(6):1113–24.
- [88] Herrero M, Cifuentes A, Ibáñez E. Sub- and supercritical fluid extraction of functional ingredients from different natural sources: plants, food-by-products, algae and microalgae: a review. Food Chem. 2006;98(1):136–48.
- [89] Chemat F, Rombaut N, Sicaire AG, Meullemiestre A, Fabiano-Tixier AS, Abert-Vian M. Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. Ultrason Sonochem. 2017;34:540–60.
- [90] Mandal V, Mohan Y, Hemalatha S. Microwave assisted extraction—an innovative and promising extraction tool for medicinal plant research. Pharmacogn Rev. 2007;1(1):7–18.
- [91] Mustafa A, Turner C. Pressurized liquid extraction as a green approach in food and herbal plants extraction: A review. Anal Chim Acta. 2011;703(1):8–18.
- [92] Puri M, Sharma D, Barrow CJ. Enzyme-assisted extraction of bioactives from plants. Trends Biotechnol. 2012;30(1):37–44.
- [93] McClements DJ. Nanoemulsions versus microemulsions: terminology, differences, and similarities. Soft Matter. 2012;8(6):1719–29.
- [94] Mozafari MR, Johnson C, Hatziantoniou S, Demetzos C. Nanoliposomes and their applications in food nanotechnology. J Liposome Res. 2008;18(4):309–27.
- [95] Mora-Huertas CE, Fessi H, Elaissari A. Polymer-based nanocapsules for drug delivery. Int J Pharm. 2010;385(1–2):113–42.
- [96] Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery a review of the state of the art. Eur J Pharm Biopharm. 2000;50(1):161–77.
- [97] Loftsson T, Duchêne D. Cyclodextrins and their pharmaceutical applications. Int J Pharm. 2007;329(1–2):1–11.

- [98] Anal AK, Singh H. Recent advances in microencapsulation of probiotics for industrial applications and targeted delivery. Trends Food Sci Technol. 2007;18(5):240–51.
- [99] Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. J Adv Res. 2015;6(2):105–21.
- Weiss J, Decker EA, McClements DJ, Kristbergsson K, Helgason T, Awad T. Solid lipid nanoparticles as delivery systems for bioactive food components. Food Biophys. 2008;3(2):146–54.
- [100] Bouwmeester H, Dekkers S, Noordam MY, Hagens WI, Bulder AS, de Heer C, et al. Review of health safety aspects of nanotechnologies in food production. Regul Toxicol Pharmacol. 2009;53(1):52–62.
- [101] Weiss J, Takhistov P, McClements DJ. Functional materials in food nanotechnology. J Food Sci. 2006;71(9):R107–16.
- [102] Duncan TV. Applications of nanotechnology in food packaging and food safety: barrier materials, antimicrobials and sensors. J Colloid Interface Sci. 2011;363(1):1–24.
- [103] Torchilin VP. Multifunctional nanocarriers. Adv Drug Deliv Rev. 2006;58(14):1532–55.
- [104] Timmers S, Konings E, Bilet L, Houtkooper RH, van de Weijer T, Goossens GH, et al. Calorie restriction-like effects of 30 days of resveratrol supplementation on energy metabolism and metabolic profile in obese humans. Cell Metab. 2011;14(5):612–22.
- [105] Hursel R, Viechtbauer W, Westerterp-Plantenga MS. The effects of green tea on weight loss and weight maintenance: a meta-analysis. Int J Obes. 2009;33(9):956–61.
- [106] Daily JW, Yang M, Park S. Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: a systematic review and meta-analysis of randomized clinical trials. J Med Food. 2016;19(8):717–29.
- [107] Egert S, Bosy-Westphal A, Seiberl J, Kürbitz C, Settler U, Plachta-Danielzik S, et al. Quercetin reduces systolic blood pressure and plasma oxidised LDL concentrations in overweight subjects with a high-cardiovascular disease risk phenotype: a double-blinded, placebo-controlled cross-over study. Br J Nutr. 2009;102(7):1065–74.
- [108] Chen P, Zhang W, Wang X, Zhao K, Negi DS, Zhuo L, et al. Lycopene and risk of prostate cancer: a systematic review and meta-analysis. Medicine. 2015;94(33):e1260.
- [109] Albanes D, Heinonen OP, Taylor PR, Virtamo J, Edwards BK, Rautalahti M, et al. Alpha-Tocopherol and Beta-Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med. 1994;330(15):1029–35.
- [110] Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ. 2017;356:i6583.
- [111] Jauhiainen T, Poussa T, Korpela R, Tuomilehto J. Milk-derived bioactive peptides and blood pressure: a randomized controlled trial. Int Dairy J. 2007;17(11):1203–11.
- [112] Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris-Etherton P, Winston M. Soy protein, isoflavones, and cardiovascular health: an American Heart Association science advisory. Circulation. 2006;113(7):1034–44.
- [113] Baer DJ, Stote KS, Paul DR, Harris GK, Rumpler WV, Clevidence BA. Whey protein but not soy protein supplementation alters body weight and composition in free-living overweight and obese adults. J Nutr. 2011;141(8):1489–94.
- [114] Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013;368(14):1279–90.
- [115] Ruel G, Lapointe A, Pomerleau S, Couture P, Lemieux S, Lamarche B, et al. Evidence that cranberry juice may improve vascular function in overweight men. Br J Nutr. 2006;96(2):357–64.
- [116] Goldenberg JZ, Yap C, Lytvyn L, Lo CK, Beardsley J, Mertz D, et al. Probiotics for the prevention of Clostridium difficile–associated diarrhea in adults and children. Cochrane Database Syst Rev. 2017;12:CD006095.
- [117] Williamson G. The role of polyphenols in modern nutrition. Nutr Bull. 2017;42(3):226–35.
- [118] Yang CS, Sang S, Lambert JD, Lee MJ. Bioavailability issues in studying the health effects of plant polyphenolic compounds. Mol Nutr Food Res. 2008;52(S1):S139–51.
- [119] Lichtenstein AH, Russell RM. Essential nutrients: food or supplements? Where should the emphasis be? JAMA. 2005;294(3):351–8.
- [120] Hooper L, Kroon PA, Rimm EB, Cohn JS, Harvey I, Le Cornu KA, et al. Flavonoids, flavonoid-rich foods, and cardiovascular risk: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2008;88(1):38–50.
- [121] Zeevi D, Korem T, Zmora N, Israeli D, Rothschild D, Weinberger A, et al. Personalized nutrition by prediction of glycemic responses. Cell. 2015;163(5):1079–94.
- [122] Wang S, Zhu F, Kakuda Y. Synergistic, additive, and antagonistic effects of food mixtures on antioxidant capacities. J Agric Food Chem. 2011;59(3):960–8.
- [123] Fardet A, Boirie Y. Associations between food and beverage groups and major diet-related chronic diseases: an exhaustive review of pooled/meta-analyses and systematic reviews. Nutr Rev. 2014;72(12):741–62.
- [124] Scalbert A, Andres-Lacueva C, Arita M, Kroon P, Manach C, Urpi-Sarda M, et al. Databases on food phytochemicals and their health-promoting effects. J Agric Food Chem. 2011;59(9):4331–48.
- [125] Clifford MN, van der Hooft JJ, Crozier A. Human studies on the absorption, distribution, metabolism, and excretion of tea polyphenols. Am J Clin Nutr. 2013;98(6 Suppl):1619S–30S.

- [126] Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. AAPS J. 2013;15(1):195–218.
- [127] Johnson AJ, Vangay P, Al-Ghalith GA, Hillmann BM, Ward TL, Shields-Cutler RR, et al. Daily sampling reveals personalized diet—microbiome associations in humans. Cell Host Microbe. 2019;25(6):789–802.
- [128] Ordovas JM, Ferguson LR, Tai ES, Mathers JC. Personalised nutrition and health. BMJ. 2018;361\:k2173.
- [129] González-Vallinas M, González-Castejón M, Rodríguez-Casado A, de Molina AR. Dietary phytochemicals in cancer prevention and therapy: a complementary approach with promising perspectives. Nutr Rev. 2013;71(9):585–99.
- [130] Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, et al. Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems. Lancet. 2019;393(10170):447–92.
- [131] Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat Med. 2019;25(1):44–56.
- [132] Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanocarriers for drug delivery. Nat Mater. 2013;12(11):991–1003
- [133] Mozaffarian D, Rosenberg I, Uauy R. History of modern nutrition science—implications for current research, dietary guidelines, and food policy. BMJ. 2018;361\:k2392.
- [134] Bigliardi B, Galati F. Innovation trends in the food industry: the case of functional foods. Trends Food Sci Technol. 2013;31(2):118–29.
- [135] Calder PC, Carr AC, Gombart AF, Eggersdorfer M. Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. Nutrients. 2020;12(4):1181.