Review Article **Open Access**

The effects and practical applications of polyphenols on the human gut microbiome

Danik Martirosyan, Sydney Whited, Adway Kulkarni

[1]Functional Food Institute, 4659 Texas Street, San Diego 92116, CA, USA; [2]Boston University, Boston, MA, 02215, USA; [3]The University of Texas at Austin, 2515 Speedway, Austin, TX 78712, USA

Corresponding author: Danik Martirosyan, PhD, Functional Food Institute, 4659 Texas Street, San Diego 92116, CA, USA

Please cite this article as: Martirosyan D., Whited S., Kulkarni A. The Effects and Practical Applications of Polyphenols on the Human Gut Microbiome. 2025; 2(11): 221-235. DOI: https://doi.org/10.31989/AFBC.v2i11.1839

Submission Date: November 11.19.25; **Acceptance date:** November 27th, 2025; **Publication Date:** November 28th, 2025

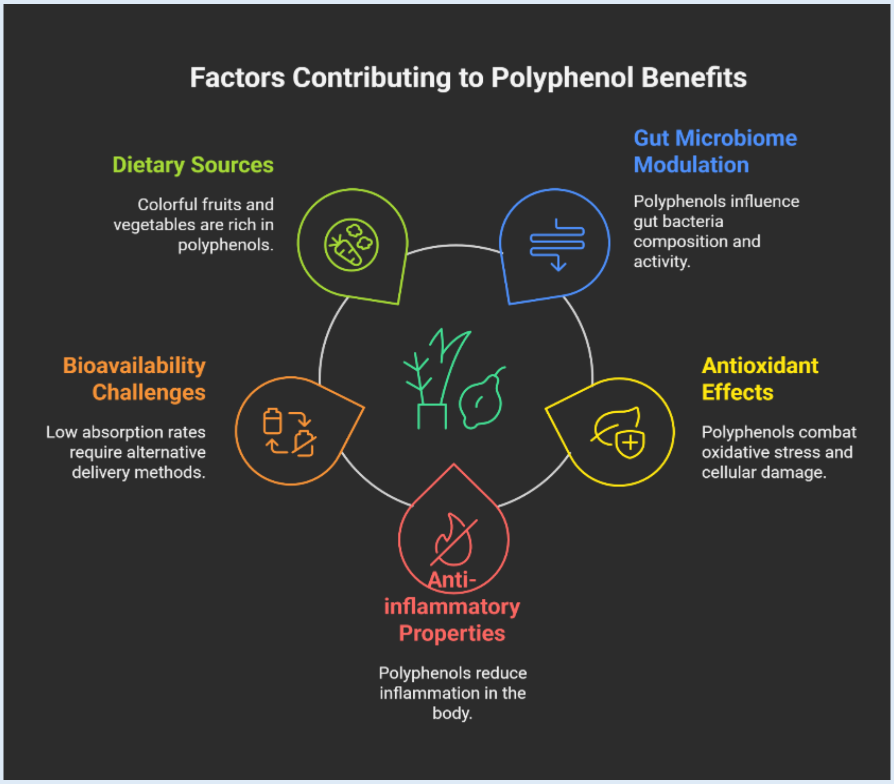
ABSTRACT

Polyphenols, dietary compounds, play a key role in the human gut microbiome. These bioactive compounds are commonly found in fruits, vegetables, coffee, wine, and chocolate, all of which promote gut health. These compounds demonstrate potent antioxidant and anti-inflammatory effects by interacting with the gut microbiome and modulating microbial composition. Foods rich in polyphenols are often colorful, with the highest levels within the skins of produce. Because they reduce oxidative stress, regulate cellular signaling, and protect mitochondria, they have been associated with the prevention of neurodegenerative diseases and cardiovascular disorders. This is due to their ability to cross the blood-brain barrier and improve overall metabolic functioning within the human body. However, their bioavailability is often low due to limited absorption, prompting further research that has led to the discovery of alternative delivery methods. Recent studies have shown that greater habitual polyphenol intake may support a balanced gut microbiome by inhibiting pro-inflammatory bacteria. Diets rich in fresh and minimally processed foods provide greater polyphenol intake than ultra-processed food diets, which are associated with lower overall intake. These findings highlight the therapeutic potential of polyphenols, which may improve overall human health by altering the gut microbiome.

Novelty

This comprehensive review uniquely synthesizes current understanding of dietary polyphenols' multifaceted roles, emphasizing their critical interaction with the human gut microbiome and their ability to cross the blood-brain barrier for systemic health benefits. Specifically, this review moves beyond general associations to detail the mechanistic role of the flavonoid subclass. We emphasize the precise pathway: 1) flavonoid intake, 2) its specific modulation of gut microbial communities, and 3) the resulting downstream health consequences. It particularly highlights emerging alternative delivery methods to overcome inherent low bioavailability and contrasts polyphenol intake from fresh versus ultra-processed foods, providing a nuanced perspective on dietary patterns. Furthermore, it uniquely explores novel applications of polyphenols beyond direct health benefits, including their potential as natural preservatives in food and cosmetics, and as agents for developing hypoallergenic products.

Keywords: Polyphenols, Human Gut Microbiome, bioactive compounds, Functional Foods,



Graphical Abstract: The Effects and Practical Applications of Polyphenols on the Human Gut Microbiome

INTRODUCTION

Diet is a major contributor to the composition of the human gut microbiome [1]. Polyphenols, found in foods such as fruits, vegetables, coffee, wine, and chocolate, are known to promote gut microbiota balance [2]. Specific polyphenols, such as tannins, bolster antioxidant defense in the body and promote overall health [2]. These products' therapeutic potential has increased their popularity among consumers, driven by recent studies associating them with the gut microbiome [3]. Polyphenols have been shown to possess antioxidant, anti-inflammatory, antidiabetic, and anticancer properties through their metabolism by the gut microbiota [3]. The diverse bacterial ecosystems in the human gut affect overall metabolism and the bioavailability of vital nutrients [3]. Since these compounds can modulate the composition and activity of the gut microbiota, these products are beneficial beyond basic nutrition [3]. The symbiotic interaction between the gut microbiome and polyphenol consumption may lead to significant implications for human health and chronic diseases [3].

Foods such as apples, berries, dark chocolate, broccoli, oats, olive oil, wine, and coffee all contain high amounts of polyphenols [4,5]. Herbs and spices such as turmeric and cumin are also known for their polyphenol content [4]. Although this list is not comprehensive, professionals suggest that colorful fruits and vegetables often contain high levels of polyphenols [4]. Simply, the darker the color of the fruit, the greater the polyphenol content [4]. It is important to note that the skins of fruits and vegetables contain most of the polyphenol content [4].

Polyphenols naturally occur in plants and include over 8,000 types, including flavonoids such as quercetin and resveratrol [5]. Berries are low in calories and high in polyphenols, and elderberries contain 870 mg per ½ cup serving [5]. Spices are also known to contain vast amounts of vitamins and minerals, with cloves providing 542 mg of polyphenols per oz [5]. Nuts contain many essential fats, protein, and fiber while adding 347 mg of polyphenols per three nuts [5]. Resveratrol has also been linked to decreased liver function enzymes and lipid peroxidation, leading to reduced pro-inflammatory cytokines [6,7].

Properties of Polyphenols: First and foremost, polyphenols are essential to plants, as they protect them from excess sunlight and disease [8]. Therefore, as beneficial as polyphenols are to the human body, they are vital to the health of the plant itself [8].

Polyphenols are responsible for the flavors and odors of foods [4]. These factors are affected by environmental conditions such as air temperature, water and soil conditions, and the age of the plant [4]. The properties of these bioactive compounds are directly related to the health of the plant itself [4]. Polyphenols directly alleviate issues associated with excess oxidative stress, which is implicated in the pathogenesis of various diseases [9]. These compounds are effective due to their antioxidant mechanism, which involves regulating cellular signaling pathways, metal chelation, and mitochondrial protection [9,10]. Furthermore, polyphenols can modulate enzyme activity, thereby contributing to their anti-inflammatory effects [9].

It is also important to note their effects on the immune system [11]. Polyphenols can promote healthy bacterial growth in the gut, limiting the growth of harmful bacteria [11,12]. Not only does this promote effective digestion, but it also supports longevity and immune health [11].

Types of Polyphenols: Polyphenols can be classified into four categories [8]. Polyphenols can be classified as flavonoids, phenolic acids, stilbenes, and lignans [8]. While many polyphenols are beneficial, this review places a special emphasis on the flavonoid subclass. Specifically, strengthening the mechanistic link between dietary flavonoid intake, the modulation of gut microbiota composition it induces, and the human health outcomes that result from this interaction.

The classification of each polyphenol is determined by its chemical structure, ring count, and molecules attached to its ring(s) [8]. However, the functions of each polyphenol are similar in their ability to maintain overall health and improve immune function [8,13]. Table 1 summarizes these categories by listing the respective compounds, common dietary sources, and the main biological activities associated with each class. This offers a clear comparison of how different polyphenols contribute to similar health-protective effects through diverse chemical structures and food sources. Flavonoids make up 60% of polyphenol content, including compounds such as quercetin, kaempferol, catechins, and anthocyanins, which are found in foods including apples, onions, and dark chocolate [14]. Phenolic acids make up 30% of polyphenols and are found in coffee and cereal [14]. Lignans and stilbenes make up the remainder of polyphenols and are found in items such as spices and berries [14].

Table 1: Example Compounds, Food Sources, and Health Benefits

Polyphenol Categories	Example Compounds	Primary Food Sources	Health-Related Properties	References
Flavonoids	Quercetin, Rutin, Macluraxanthone, Genistein, Scopoletin, Daidzein, Taxifolin, Naringenin, Abyssininones, Eriodictyol, Fisetin, Theaflavin, Peonidin, Diosmetin, Tricin, Biochanin, Hesperidin, Epicatechin, Myricetin, Kaempferol, Luteolin, Apigenin	Green tea, grape seeds, red pepper, apples, citrus fruits, berries, peaches, grapes, strawberries, blueberries.	Flavonoids have anti-oxidative, anti-inflammatory, anti-mutagenic and anti-carcinogenic properties. They are also able to regulate key cellular enzyme functions.	[69]
Phenolic Acids	Sinapic, p-coumaric, ferulic, chlorogenic, caffeic and cinnamic acids are amongst the C3–C6 acids. P-hydroxybenzoic, gallic, ellagic, vanillic, genistic, syringic, salicylic and protocatechuic acids are included in C1–C6	Fruits, Wholegrains, Nuts, Coffee, Beer, Vegetables.	Findings from observational studies have shown that phenolic acids have led to an inverse association with hypertension, type-2 diabetes, metabolic syndrome, and non-alcoholic fatty liver disease. The inclusion of phenolic acids has been shown to lower the incidence of chronic degenerative diseases such as Alzheimer’s disease, cancer, diabetes, and cardiovascular disease.	[70-74]
Stilbenes	Resveratrol, Pterostilbene, Piceatannol, Polydatin, Viniferin, Astringin, Pinosylvin.	Grapes, berries, peanuts, rhubarb, mulberry, pine, conifer bark, red wine	Stilbenes have shown to be antioxidant, anti-inflammatory, antihyperglycemic, and cardioprotective. They have also been shown to prevent cancer and neurodegenerative diseases.	[75-76]
Lignans	Secoisolariciresinol, Matairesinol, Pinoresinol, Lariciresinol, Medioresinol, Syringaresinol, Sesamin, Sesamolin, Arctigenin, 7-Hydroxymatairesinol, 7-Hydroxysecoisolariciresinol, Conidendrin.	Flaxseed, sesame seeds, whole grains (rye, barley, oats, wheat), legumes, nuts, berries, vegetables, fruits, coffee, tea	The health benefits of lignans include lowered risk of heart disease, reduced menopausal symptoms, and decreased osteoporosis and breast cancer. It can also increase anti-cancer, anti-estrogenic, and antioxident activity.	[77]

Neurodegenerative diseases are often due, in part, to oxidative stress and excessive levels of inflammation [9]. This is harmful to the body through its poor effects on mitochondrial function, cellular damage, and DNA repair [9]. With this, diets high in polyphenols and antioxidants have been shown to prevent the onset of neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, and dementia [9,15,16,17,18]. A beneficial mechanism of action of polyphenols includes their ability to maintain healthy aging processes [9,19-20].

Polyphenols have vast benefits for brain health [9]. They improve brain function by directly affecting cells and processes in the central nervous system [9]. For instance, they can overcome the blood-brain barrier and reduce overall oxidative stress [9].

Polyphenols may also help prevent atherosclerosis, a vascular disorder that underlies many cardiovascular diseases [21,22,23]. A significant risk factor for this disease is the type and quality of the food one consumes, suggesting that polyphenols are promising therapeutic agents in this regard [21,24]. Recent studies have shown the promising potential of plant-derived polyphenol compounds for the management of diabetes [25,22,26]. Medicinal plants that can modulate key pathways in the body, such as insulin resistance and inflammation, may play significant roles in metabolic health [25,27]. Despite the lack of clinical data, observational studies have identified promising therapeutic options for managing metabolic diseases [25]. The same has been observed in chronic kidney disease [28].

Sleep has also proven to be affected by one's polyphenol intake [29,30]. Studies have shown that polyphenols dictate sleep architecture and habitual patterns, which could play a role in disease pathogenesis [29].

Some studies show promising results against the onset and symptoms of depression with high polyphenol intake, yet others remain inconclusive [31]. Further studies involving diverse populations are necessary to confirm this finding.

Increasing Polyphenol Levels: The polyphenol content in plants is strongly influenced by soil, climate, fertilization strategies, and overall plant health [32]. For example, bio-organic fertilizers have proven to increase polyphenol content in teas through the increase in soil composition of leucine aminopeptidase, β-glucosidase, and β-N-acetylglucosamine enzymes and soil acid phosphatase, β-cellobiosidase, and β-xylanase [32].

However, it is essential to note that the bioavailability of polyphenols differs by compound, as it is determined by solubility, degree of polymerization, conjugation, or chemical structure [9]. This is due to their inability to penetrate the blood-brain barrier, which is also dependent on brain metabolism and localization [9]. The bioavailability of polyphenols, when consumed orally, is often low [9]. This has effects such as selective permeability across the blood-brain barrier, gastrointestinal transformations, poor absorption, rapid hepatic and colonic metabolism, and elimination before proper absorption [9]. Therefore, most polyphenols have inadequate bioavailability in humans, creating a platform for the emergence of new consumption and production strategies that improve human health by increasing bioavailability [9]. Recent studies have shown that polyphenol encapsulation may be a beneficial method of administration that reduces the risk of neurodegenerative diseases. Yet, more research is needed for conclusive results [9,33].

Improving the Gut Microbiome: Recent studies have examined the relationship between habitual polyphenol consumption and the gut microbiota in healthy human adult samples [34]. A 2024 study measured the effects of differing levels of dietary polyphenol consumption [34]. This study used biomarkers for daily polyphenol consumption (mg/day) including metabolites such as Lactobacillus, Bacteroides, Enterococcus, Eubacterium ventriosum group, Ruminococcus torques group, and Sutterella [34]. The study's results suggested that greater habitual polyphenol intake may support optimal intestinal environments that inhibit the growth and development of pro-inflammatory bacteria in human samples [34].

Flavonoids, making up about 60% of polyphenols, are particularly influential [14]. For instance, flavonoids such as quercetin have been shown to boost Bacteroidetes, lower Firmicutes, and inhibit pathogens [78]. Similarly, flavonoids such as fisetin promote the growth of Akkermansia and help reduce colitis-related dysbiosis. These two flavonoids support a diverse and anti-inflammatory microbiome [80]. These results demonstrate how flavonoids can enhance barrier integrity and foster anti-inflammatory changes in the microbiota [81].

Another study found that higher consumption of fresh or minimally processed foods is associated with greater polyphenol intake [35]. A diet high in ultra-processed foods was found to lower polyphenol intake [35]. Fresh foods were found to contain the largest amounts of polyphenols [35]. Therefore, this study recommends daily consumption of these products, while excessive intake of ultra-processed foods is discouraged due to their low levels of beneficial bioactive compounds [35].

The gut microbiome is directly associated with diet and health outcomes, likely due to its role in metabolite production [36].

Diets such as the Mediterranean diet, which include many polyphenol-containing foods, have been linked to macro- and micronutrient intake that affects one's risk of disease [37]. Nutrition plays a particularly key role in young adulthood and middle age due to its importance for cognitive health in old age. Cardio metabolic risk factors, such as obesity, hypertension, smoking, and physical activity that develop in middle-aged years, display that preventive approaches are necessary for individuals in their 40s and 50s [37]. These years are vital for preventing dementia [37].

It is also important to note that the oral microbiome significantly affects the gut microbiome [38]. Polyphenols have been shown to positively impact the oral microbiome, which plays a key role in oral and chronic diseases [38]. Such compounds may alleviate symptoms associated with poor gut and oral microbiome health [38].

Implications for Health: A key implication for increased research regarding polyphenols lies in their potential for increased bioavailability [11]. Since the gut microbiota has been found to be heavily influenced by polyphenols, the potential for increased bioavailability through alternative administration methods is a promising strategy to prevent neurodegenerative diseases [11,39-40]. These compounds are vital for their effect on gut microbiota composition and functioning [41-43]. Polyphenols such as chlorogenic acid, curcumin, green tea catechins, naringenin, quercetin, resveratrol, and sulforaphane can be explained [41]. Therefore, regulating gut microbiota composition may help alleviate non-alcoholic fatty liver disease by reducing inflammation, liver fat accumulation, and liver enzymes [41,44]. Table 2 summarizes these polyphenol subclasses, listing representative compounds, common dosages, and their documented effects on gut microbial composition and intestinal function. This comparison highlights how structurally different polyphenols influence similar microbiome-related pathways involved in inflammation, barrier integrity, and metabolic health. It also sheds light on dietary needs, as these compounds can support specific health issues.

Table 2. Polyphenol Compounds, Dosages, and Documented Effects on the Human Gut Microbiome

Polyphenol Categories	Compounds	Dosage	Human Gut Microbiome Effect	References
Flavonoids	Quercetin	100–500 mg/day	Quercetin has been shown to increase bacteroidetes, decrease firmicutes, suppress pathogens, induce anti-inflammatory processes, and promote beneficial bacteria	[78]
	Naringenin	150-900 mg/day	Increases Bacteroides, reduces Staphylococcus; enhances motility, anti-inflammatory, beneficial taxa promoted	[79]
	Fisetin	8 mg/kg	Research studies have shown that fisetin increases Akkermansia, reduces colitis-related dysbiosis; shifts toward anti-inflammatory profile.	[80]
	Kaempferol	25–100 mg/kg/day	Improves barrier integrity, reduces inflammation, supports anti-inflammatory microbial shifts	[81]
	Luteolin	25 mg/kg	Lut supplementation mitigated gut microbiota dysbiosis in a UC murine model, increasing the abundance of Muribaculaceae, Rikenella, and Prevotellaceae while decreasing Escherichia_Shigella and Bacteroides levels	[82]
Phenolic Acids	Ferulic acid	400 mg/kg	Ferulic acid in decreased the crypt depth in jejunum (P = 0.01) and caecum (P = 0.04), and increased the ratio of villus height to crypt depth in jejunum (P = 0.02). Ferulic acid increased the populations of genera Faecalibacterium, Paludicola, RF39, and Faecalicoccus in the cecum (P < 0.05), whereas decreased the populations of Anaerofilum and UCG-002. Essentially, it was able to improve the growth performance, antioxidative and immunological capabilities, intestinal morphology, and modulated the gut microbial construction of Linwu ducks at the growing stage.	[83]
	Caffeic acid	251mg/kg	This is a mice model with DSS-induced colitis. Caffeic acid may alleviate colitis by activating Nrf-2 antioxidant pathways, reducing inflammatory cytokines, strengthening tight-junction barrier proteins, and reshaping alleviating toward beneficial taxa such as Akkermansia and Dubosielladecreasing strong potential relevance for improving human gut health.	[84]
	Sinapic acid	50 µM	These experiments were performed on Caco-2 human intestinal cell models and mouse colitis models. Sinapic acid strengthens the intestinal barrier, suppresses early inflammatory signaling, and supports anti-inflammatory microbiome shifts.	[85]
	Chlorogenic acid	150 mg/kg administered daily by gavage	These experiments were performed on a mouse model. Chlorogenic acid improved intestinal barrier integrity, reduced intestinal mucosal permeability and LPS-associated endotoxemia, and significantly changed the gut microbiota by increasing SCFA-producing bacteria (Dubosiella, Romboutsia, Mucispirillum, Faecalibaculum) and Akkermansia.	[86]
Stilbenes	Resveratrol	10 mg/kg/day via oral gavage	This study used Diabetic nephropathy model using male db/db mice. Resveratrol restores gut barrier integrity, reduces intestinal permeability and inflammation, and reverses dysbiosis by increasing beneficial genera such as Bacteroides, Alistipes, Rikenella, Odoribacter, Parabacteroides, and Alloprevotella.	[87]

	Pterostilbene	15 mg/kg body weight per day	This model used Obese Zucker (fa/fa) rats. Pterostilbene reshaped gut microbiota by reducing Firmicutes, increasing Verrucomicrobia, and markedly enriching the mucin-degrading taxa *Akkermansia muciniphila* and *Odoribacter splanchnicus*, producing a healthier microbial profile associated with improved metabolic outcomes.	[88]
Lignans	Secoisolariciresinol	120 mg/kg/day	In this study, 6–8 weeks old, male, C57BL/6J mice were fed high-fat diet to induce chronic colon inflammation. After secoisolariciresinol course, it was shown that restores gut microbial diversity, increases SCFA-producing genera such as Roseburia and Allobaculum, reduces inflammation-associated taxa including Lachnospiraceae, and elevates total SCFA levels, thereby improving gut barrier integrity and reducing colon inflammation.	[89]
	Pinoresinol	5 or 10 mg/kg/day	This study was performed with ovariectomized mice, and showed pinoresinol increased Akkermansia, Parabacteroides, and Alistipes, decreased Ruminococcus, restored SCFAs (acetate, isobutyrate, isovalerate, valerate), and improved colonic tight-junction proteins while lowering colonic TNF-α, IL-1β, IL-6, and LPS.	[90]

As a 2023 study conveyed, dietary guidance is necessary for Americans to follow healthy eating patterns that promote disease prevention strategies [45]. For example, increasing dietary awareness and nutritional education for cancer patients may improve chemotherapy-related symptoms, and previous studies have shown the therapeutic effects of polyphenols in modulating cell signaling, which can prevent and slow the growth of cancer cells [46,47,48,49,40].

However, due to the lack of bioavailability of plant-derived polyphenols, the poor lipophilicity and instability of water-soluble polyphenols must be addressed [50]. This is also due to the inability of current studies to address causality [51]. Studies that can address the mechanism of action of polyphenols in the body have not been conducted due to significant challenges [51]. Research regarding the effect of polyphenols on autophagy must be conducted to support supplementation recommendations for this product [52].

Polyphenols, which have also been used as natural preservatives due to their antioxidant properties, may increase the shelf-life and durability of other food components [53]. When used in the production of perishable goods, the antioxidant and free-radical-scavenging properties of these bioactive compounds could be used in many applications across the medical, food, and cosmetic industries [53]. Cosmetics containing natural ingredients and preservatives have gained global popularity, making products containing polyphenols widely acceptable [54]. The chemical structure of phenolic compounds confers preservative effects and high antioxidant activity, interfering with oxidative mechanisms that degrade the product over time [54]. Furthermore, the effect of polyphenols against hair and skin diseases encourages their use in cosmetic products [55].

Furthermore, polyphenols could be used to produce hypoallergenic products and foods by altering the allergenic properties of proteins [56]. Such findings may lead to groundbreaking research that affects large populations. Implications in this area may benefit overall population health by reducing allergic reactions. This may be advantageous for hospitals, reducing healthcare costs and patient volume due to such complications.

However, as studies have shown the harmful interaction between polyphenols and some medications, extensive research regarding their interaction with the body must be evaluated [57]. For example, polyphenols can block iron uptake, inhibit the production of digestive enzymes, alter intestinal microbiota, and interact with drugs that affect hormonal balance [57-59]. Yet, the toxicities of many health hazards have been mitigated by polyphenols, highlighting the need for increased research in this area [60].

Connection to Functional Food Science: The intricate relationship between dietary polyphenols and the human gut microbiome directly underpins the principles of functional food science. This field is dedicated to understanding how food components, beyond basic nutrition, confer specific health benefits, contributing to disease prevention and management [61]. Polyphenols act as prebiotics that promote beneficial bacteria, modulate microbial composition, and facilitate the production of health-promoting metabolites in the gut [62,63].

These insights are foundational to the development of functional foods. Understanding how polyphenols reduce oxidative stress, modulate cellular signaling, and support mitochondrial function enables the formulation of foods fortified with extracts or enhanced through agricultural practices [64]. The goal is to deliver these compounds effectively to improve gut health, systemic antioxidant defenses, and reduce risks for neurodegenerative, cardiovascular, and metabolic diseases [65].

However, translating science into functional foods presents challenges and opportunities—core to the field. Research prioritizes improving bioavailability via formulations such as nanocarriers, which are essential for efficacy [66]. Equally crucial is clinical validation of health claims through rigorous trials, as well as ensuring taste and convenience for consumers [67]. By addressing bioavailability, efficacy, and consumer acceptability, functional food science bridges research and real-world dietary solutions [68].

Scientific Innovation: This work contributes significantly to scientific innovation by integrating diverse findings on polyphenol mechanisms, from their modulation of gut microbiota composition and activity to their impact on cellular signaling, mitochondrial protection, and enzyme modulation, all of which help reduce oxidative stress and inflammation. It underscores the scientific imperative to develop advanced delivery strategies, such as encapsulation, to overcome bioavailability limitations and thereby unlock polyphenols' full therapeutic potential for neurodegenerative, cardiovascular, and metabolic diseases. The review also highlights innovative applications in food preservation and hypoallergenic product development, showcasing broader scientific utility beyond direct human consumption.

Practical Implications: The practical implications of this review are far-reaching for public health and various industries. It provides strong, evidence-based support for dietary patterns rich in fresh, minimally processed, polyphenol-rich foods as a natural, cost-effective strategy for preventing and managing chronic diseases by optimizing gut health. For the food industry, it suggests avenues for developing novel functional foods with enhanced health benefits through targeted polyphenol incorporation and improved delivery methods. Moreover, the review highlights practical applications in cosmetic and medical industries through polyphenols' preservative, skin/hair health, and hypoallergenic properties, potentially reducing healthcare costs and improving overall population health.

Future Direction: Future research on polyphenols should primarily focus on overcoming their inherent low bioavailability by further exploring and validating alternative delivery methods, such as encapsulation, to ensure their maximal therapeutic potential in vivo. Establishing clear cause-and-effect mechanisms through rigorous human clinical trials, rather than relying predominantly on animal models, is crucial to substantiate health claims for specific polyphenol compounds and dosages, particularly for conditions such as neurodegenerative diseases, cardiovascular disorders, metabolic diseases, and depression. Further investigation into the interaction of polyphenols with the gut and oral microbiomes is also warranted to fully understand their modulatory roles and subsequent health benefits, including their impact on autophagy. Additionally, increased research is needed to comprehensively evaluate potential harmful interactions between polyphenols and existing medications. Beyond direct health implications, exploring the broader applications of polyphenols as natural preservatives in the food and cosmetic industries, and their potential in developing hypoallergenic products, represents promising avenues for future development and utilization.

Limitations of Current Research: Despite advances in understanding the role of polyphenols in the human gut microbiome, several limitations within current research constrain the strength and generalizability of existing conclusions. First and foremost, a large majority of research is derived from animal models, in vitro studies, or short-term human studies, which limits the ability to establish clear relationships between dietary polyphenols and human health. Mouse models—including DSS-induced colitis, high-fat diet (HFD) models, diabetic db/db mice, and ovariectomized models—provide valuable insights, but do not fully replicate the complex human metabolism, microbiome diversity, or long-term dietary patterns. As a result, the translational accuracy of these findings remains uncertain.

Conclusion: Polyphenols are widely recognized as bioactive compounds found in colorful fruits, vegetables, herbs, and minimally processed foods. Their ability to modulate gut microbiota, reduce oxidative stress, and cross the blood-brain barrier makes them promising agents for the prevention and management of chronic diseases, including neurodegenerative, cardiovascular, and metabolic disorders. Despite their poor natural bioavailability, emerging delivery strategies such as encapsulation may provide a new potential for administration. This could allow these products to be utilized in the body more readily. As research continues to uncover the wide-ranging health benefits of polyphenols, encouraging individuals to follow diets rich in these compounds may be an effective, natural way to enhance gut and overall health.

Abbreviations: BBB (Blood–Brain Barrier), SCFAs (Short-Chain Fatty Acids), UC (Ulcerative Colitis), LPS (Lipopolysaccharide), DSS (Dextran Sodium Sulfate), NF-κB (Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells), MAPK (Mitogen-Activated Protein Kinase), HFD (High-Fat Diet), TNF-α (Tumor Necrosis Factor-Alpha), IL-1β (Interleukin-1 Beta), IL-6 (Interleukin-6), TAK1 (Transforming Growth Factor-β-Activated Kinase 1), c-Kit (Tyrosine-Protein Kinase Kit / Stem Cell Factor Receptor), SCF (Stem Cell Factor), db/db (Leptin Receptor–Deficient Diabetic Mouse Model), mRNA (Messenger Ribonucleic Acid), NOVA (Food Classification System Categorizing Foods by Degree of Processing).

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: All authors contributed to the preparation of this review.

Acknowledgments: This review article did not receive any external funding.

REFERENCES:

1. Culp EJ, Nelson NT, Verdegaal AA, Goodman AL. Microbial transformation of dietary xenobiotics shapes gut microbiome composition. Cell. 2024;187(22):6327-6345.e20. DOI: https://doi.org/10.1016/j.cell.2024.08.038
2. El-Saadany MT, Yang T, Saad AM, et al. Polyphenols: Chemistry, bioavailability, bioactivity, nutritional aspects and human health benefits: A review. Int J Biol Macromol. 2024;277(Pt3):134223. DOI: https://doi.org/10.1016/j.ijbiomac.2024.134223
3. Cano R, Bermúdez V, Galban N, et al. Dietary polyphenols and gut microbiota cross-talk: Molecular and therapeutic perspectives for cardiometabolic disease: A narrative review. Int J Mol Sci. 2024;25(16):9118. DOI: https://doi.org/10.3390/ijms25169118
4. What Do Polyphenols Do for You? Cleveland Clinic. Published August 16, 2023. [https://health.clevelandclinic.org/polyphenols]. Retrieved on November 15th, 2025
5. Petre A. What are polyphenols? Types, benefits, and food sources. Healthline. October 23, 2023. Accessed June 28, 2025. [https://www.healthline.com/nutrition/polyphenols]. Retrieved on November 15th, 2025
6. Niu C, Zhang J, Okolo PI 3rd. Unlocking the therapeutic potential of natural polyphenols in esophageal cancer. Curr Treat Options Oncol. 2025;26(4):278-290. DOI: https://doi.org/10.1007/s11864-025-01308-6
7. Rahmani AH, Alharbi HOA, Khan AA, Babiker AY, Rizvi MMA. Therapeutic potential of resveratrol, a polyphenol in the prevention of liver injury induced by diethylnitrosamine (DEN) through the regulation of inflammation and oxidative stress. Funct Foods Health Dis. 2024;14(12):898-920. DOI: https://doi.org/10.31989/ffhd.v14i12.1502
8. Li Q, Van de Wiele T. Gut microbiota as a driver of the interindividual variability of cardiometabolic effects from tea polyphenols. Crit Rev Food Sci Nutr. 2023;63(11):1500-1526. DOI: https://doi.org/10.1080/10408398.2021.1965536
9. Janigashvili G, Chkhikvishvili I, Ratian L, et al. Effects and medical application of plant-origin polyphenols: A narrative review. Bioactive Compd Health Dis. 2024;7(8):375-385. DOI: https://doi.org/10.31989/bchd.v7i8.1414
10. Grabska-Kobyłecka I, Szpakowski P, Król A, et al. Polyphenols and their impact on the prevention of neurodegenerative diseases and development. Nutrients. 2023;15(15):3454. DOI: https://doi.org/10.3390/nu15153454
11. Gahtani RM, Shoaib S, Hani U, et al. Combating Parkinson's disease with plant-derived polyphenols: Targeting oxidative stress and neuroinflammation. Neurochem Int. 2024;178:105798. DOI: https://doi.org/10.1016/j.neuint.2024.105798
12. Cheng H, Zhang D, Wu J, et al. Interactions between gut microbiota and polyphenols: A mechanistic and metabolomic review. Phytomedicine. 2023;119:154979. DOI: https://doi.org/10.1016/j.phymed.2023.154979
13. Vicente-Zurdo D, Gómez-Mejía E, Rosales-Conrado N, León-González ME. A comprehensive analytical review of polyphenols: Evaluating neuroprotection in Alzheimer's disease. Int J Mol Sci. 2024;25(11):5906. DOI: https://doi.org/10.3390/ijms25115906
14. Williamson G. Bioavailability of food polyphenols: Current state of knowledge. Annu Rev Food Sci Technol. 2025;16(1):315-332. DOI: https://doi.org/10.1146/annurev-food-060721-023817
15. Quesada-Vázquez S, Eseberri I, Les F, et al. Polyphenols and metabolism: From present knowledge to future challenges. J Physiol Biochem. 2024;80(3):603-625. DOI: https://doi.org/10.1007/s13105-024-01046-7
16. Gamage E, Orr R, Travica N, et al. Polyphenols as novel interventions for depression: Exploring the efficacy, mechanisms of action, and implications for future research. Neurosci Biobehav Rev. 2023;151:105225. DOI: https://doi.org/10.1016/j.neubiorev.2023.105225
17. Ali Redha A, Kodikara C, Cozzolino D. Does encapsulation improve the bioavailability of polyphenols in humans? A concise review based on in vivo human studies. Nutrients. 2024;16(21):3625. DOI: https://doi.org/10.3390/nu16213625
18. Ziółkiewicz A, Kasprzak-Drozd K, Rusinek R, et al. The influence of polyphenols on atherosclerosis development. Int J Mol Sci. 2023;24(8):7146. DOI: https://doi.org/10.3390/ijms24087146
19. Okechukwu Paul-Chima U, Chinyere Nkemjika A, Melvin Nnaemeka U, Onohuean H. Harnessing plant metabolic pathways for innovative diabetes management: Unlocking the therapeutic potential of medicinal plants. Plant Signal Behav. 2025;20(1):2486076. DOI: https://doi.org/10.1080/15592324.2025.2486076
20. Li C, Chen X, Zha W, et al. Impact of gut microbiota in chronic kidney disease: Natural polyphenols as beneficial regulators. Ren Fail. 2025;47(1):2506810. DOI: https://doi.org/10.1080/0886022X.2025.2506810

21. Pérez-Jiménez J, Agnant K, Lamuela-Raventós RM, St-Onge MP. Dietary polyphenols and sleep modulation: Current evidence and perspectives. Sleep Med Rev. 2023;72:101844. DOI: https://doi.org/10.1016/j.smrv.2023.101844
22. Liu W, Cui S, Wu L, et al. Effects of bio-organic fertilizer on soil fertility, yield, and quality of tea. J Soil Sci Plant Nutr. 2023;23:5109–5121. DOI: https://doi.org/10.1007/s42729-023-01195-6
23. Vita AA, Roberts KM, Gundersen A, et al. Relationships between habitual polyphenol consumption and gut microbiota in the INCLD Health Cohort. Nutrients. 2024;16(6):773. DOI: https://doi.org/10.3390/nu1606773
24. Coletro HN, Bressan J, Diniz AP, et al. Habitual polyphenol intake of foods according to NOVA classification: Implications of ultra-processed foods intake (CUME study). Int J Food Sci Nutr. 2023;74(3):338–349. DOI: https://doi.org/10.1080/09637486.2023.2190058
25. Perler BK, Friedman ES, Wu GD. The role of the gut microbiota in the relationship between diet and human health. Annu Rev Physiol. 2023;85:449-468. DOI: https://doi.org/10.1146/annurev-physiol-031522-092054
26. Puri S, Shaheen M, Grover B. Nutrition and cognitive health: A life course approach. Front Public Health. 2023;11:1023907. DOI: https://doi.org/10.3389/fpubh.2023.1023907
27. Guo Y, Li Z, Chen F, Chai Y. Polyphenols in oral health: Homeostasis maintenance, disease prevention, and therapeutic applications. Nutrients. 2023;15(20):4384. DOI: https://doi.org/10.3390/nu15204384
28. Mohammad Hassani K, Vahedi Fard M, Mottaghi Moghaddam Shahri A, Khorasanchi Z. Polyphenols improve non-alcoholic fatty liver disease via gut microbiota: A comprehensive review. Food Sci Nutr. 2024;12(8):5341-5356. DOI: https://doi.org/10.1002/fsn3.4178
29. Gardner CD, Vadiveloo MK, Petersen KS, et al. Popular dietary patterns: Alignment with American Heart Association 2021 dietary guidance. Circulation. 2023;147(22):1715-1730. DOI: https://doi.org/10.1161/CIR.0000000000001146
30. Fumarola S, Cianfriglia L, Cecati M, et al. Polyphenol intake in elderly patients: A novel approach to counteract colorectal cancer risk? Int J Mol Sci. 2025;26(6):2497. DOI: https://doi.org/10.3390/ijms26062497
31. Wang S, Li Y, Ma C, et al. Enzymatic molecular modification of water-soluble poWang S, Li Y, Ma C, et al. Enzymatic molecular modification of water-soluble polyphenols: Synthesis, structure, bioactivity and application. Crit Rev Food Sci Nutr. 2023;63(33):12637-12651. DOI: https://doi.org/10.1080/10408398.2022.2105301
32. Hao W, Gan H, Wang L, et al. Polyphenols in edible herbal medicine: Targeting gut-brain interactions in depression-associated neuroinflammation. Crit Rev Food Sci Nutr. 2023;63(33):12207-12223. DOI: https://doi.org/10.1080/10408398.2022.2099808
33. Rathee P, Sehrawat R, Rathee P, et al. Polyphenols: Natural preservatives with promising applications in food, cosmetics and pharma industries. Materials (Basel). 2023;16(13):4793. DOI: https://doi.org/10.3390/ma16134793
34. de Lima Cherubim DJ, Buzanello Martins CV, Oliveira Fariña L, da Silva de Lucca RA. Polyphenols as natural antioxidants in cosmetics applications. J Cosmet Dermatol. 2020;19(1):33-37. DOI: https://doi.org/10.1111/jocd.13093
35. Sun M, Deng Y, Cao X, et al. Effects of natural polyphenols on skin and hair health: A review. Molecules. 2022;27(22):7832. DOI: https://doi.org/10.3390/molecules27227832
36. Chandrasekaran V, Hediyal TA, Anand N, et al. Polyphenols, autophagy and neurodegenerative diseases: A review. Biomolecules. 2023;13(8):1196. DOI: https://doi.org/10.3390/biom13081196
37. Roszkowski S. Application of polyphenols and flavonoids in oncological therapy. Molecules. 2023;28(10):4080. DOI: https://doi.org/10.3390/molecules28104080
38. Suzuki T, Ohishi T, Tanabe H, Miyoshi N, Nakamura Y. Anti-inflammatory effects of dietary polyphenols through inhibitory activity against metalloproteinases. Molecules. 2023;28(14):5426. DOI: https://doi.org/10.3390/molecules28145426
39. Mamun AA, Shao C, Geng P, Wang S, Xiao J. Polyphenols targeting NF-κB pathway in neurological disorders: What we know so far? Int J Biol Sci. 2024;20(4):1332-1355. DOI: https://doi.org/10.7150/ijbs.90982
40. Emran TB, Eva TA, Zehravi M, et al. Polyphenols as therapeutics in respiratory diseases: Moving from preclinical evidence to potential clinical applications. Int J Biol Sci. 2024;20(8):3236-3256. DOI: https://doi.org/10.7150/ijbs.93875
41. Duda-Chodak A, Tarko T. Possible Side Effects of Polyphenols and Their Interactions Duda-Chodak A, Tarko T. Possible side effects of polyphenols and their interactions with medicines. Molecules. 2023;28(6):2536. DOI: https://doi.org/10.3390/molecules28062536
42. Pi X, Sun Y, Cheng J, Fu G, Guo M. A review on polyphenols and their potential application to reduce food allergenicity.

Crit Rev Food Sci Nutr. 2023;63(29):10014-10031. DOI: https://doi.org/10.1080/10408398.2022.2078273

43. Raina J, Firdous A, Singh G, Kumar R, Kaur C. Role of polyphenols in the management of diabetic complications. Phytomedicine. 2024;122:155155. DOI: https://doi.org/10.1016/j.phymed.2023.155155
44. Chen Y, Qie X, Quan W, et al. Omnifarious fruit polyphenols: An omnipotent strategy to prevent and intervene diabetes and related complications? Crit Rev Food Sci Nutr. 2023;63(20):4288-4324. DOI: https://doi.org/10.1080/10408398.2021.2000932
45. Niu C, Zhang J, Okolo PI 3rd, Daglilar E. Plant polyphenols in gastric cancer: Nature's healing touch. Semin Oncol. 2025;52(2):152333. DOI: https://doi.org/10.1053/j.seminoncol.2025.01.002
46. Zhang W, Dong X, Huang R. Antiparkinsonian effects of polyphenols: A narrative review with a focus on the modulation of the gut-brain axis. Pharmacol Res. 2023;193:106787. DOI: https://doi.org/10.1016/j.phrs.2023.106787
47. Lin X, Liu W, Hu X, Liu Z, Wang F, Wang J. The role of polyphenols in modulating mitophagy: Implications for therapeutic interventions. Pharmacol Res. 2024;207:107324. DOI: https://doi.org/10.1016/j.phrs.2024.107324
48. Masiala A, Vingadassalon A, Aurore G. Polyphenols in edible plant leaves: An overview of their occurrence and health properties. Food Funct. 2024;15(13):6847-6882. DOI: https://doi.org/10.1039/d4fo00509k
49. Stankovic S, Mutavdzin Krneta S, Djuric D, Milosevic V, Milenkovic D. Plant polyphenols as heart's best friends: From health properties, to cellular effects, to molecular mechanisms of action. Int J Mol Sci. 2025;26(3):915. DOI: https://doi.org/10.3390/ijms26030915
50. Gade A, Kumar MS. Gut microbial metabolites of dietary polyphenols and their potential role in human health and diseases. J Physiol Biochem. 2023;79(4):695-718. DOI: https://doi.org/10.1007/s13105-023-00981-1
51. Hibi M. Potential of polyphenols for improving sleep: Preliminary results from review of human clinical trials and mechanistic insights. Nutrients. 2023;15(5):1257. DOI: https://doi.org/10.3390/nu15051257
52. Shil A, Banerjee A, Roy J, et al. The potential antibacterial effects of tea polyphenols. Drug Metab Pers Ther. 2024;39(3):103-114. DOI: https://doi.org/10.1515/dmpt-2024-0058
53. Islam F, Roy S, Zehravi M, et al. Polyphenols targeting MAP kinase signaling pathway in neurological diseases: Understanding molecular mechanisms and therapeutic targets. Mol Neurobiol. 2024;61(5):2686-2706. DOI: https://doi.org/10.1007/s12035-023-03706-z
54. Pereira QC, Dos Santos TW, Fortunato IM, Ribeiro ML. The molecular mechanism of polyphenols in the regulation of ageing hallmarks. Int J Mol Sci. 2023;24(6):5508. DOI: https://doi.org/10.3390/ijms24065508
55. Gupta N, Singh S, Chauhan D, Srivastava R, Singh VK. Exploring the anticancer potentials of polyphenols: A comprehensive review of patents in the last five years. Recent Pat Anticancer Drug Discov. 2023;18(1):3-10. DOI: https://doi.org/10.2174/1574892817666220512220036
56. Ramos-Lopez O. Personalizing dietary polyphenols for health maintenance and disease management: A nutrigenetic approach. Curr Nutr Rep. 2025;14(1):29. DOI: https://doi.org/10.1007/s13668-025-00620-9
57. Li H, Liang J, Han M, Gao Z. Polyphenols synergistic drugs to ameliorate non-alcoholic fatty liver disease via signal pathway and gut microbiota: A review. J Adv Res. 2025;68:43-62. DOI: https://doi.org/10.1016/j.jare.2024.03.004
58. Perera DN, Palliyaguruge CL, Eapasinghe DD, et al. Factors affecting iron absorption and the role of fortification in enhancing iron levels. Nutr Bull. 2023;48(4):442-457. DOI: https://doi.org/10.1111/nbu.12643
59. Mennen LI, Walker R, Bennetau-Pelissero C, Scalbert A. Risks and safety of polyphenol consumption. Am J Clin Nutr. 2005;81(1):326S–329S. DOI: https://doi.org/10.1093/ajcn/81.1.326s
60. Zhou Y, Jin W, Wu Q, Zhou Q. Acrolein: Formation, health hazards and its controlling by dietary polyphenols. Crit Rev Food Sci Nutr. 2024;64(26):9604-9617. DOI: https://doi.org/10.1080/10408398.2023.2214625
61. Bhattarai S, Janaswamy S. The nexus of gut microbiota, diet and health. Funct Food Sci. 2022;2(2):47–63. DOI: https://doi.org/10.31989/ffs.v2i2.885
62. Tamizifar B, Rezaei S, Ghaedi E, Alavinejad P, Namjooyan F. The effects of probiotics in ulcerative colitis patients: a review of randomized controlled trials. Funct Foods Health Dis. 2023;13(11):605–615. DOI: https://doi.org/10.31989/ffhd.v13i11.1098
63. Yousefi MH, Rahiminejad M. Insights into a traditional Iranian food, “Kashk” as a promising candidate for functional food: a literature review. Funct Food Sci. 2025;5(6):223–237. DOI: https://doi.org/10.31989/ffs.v5i6.1650

64. Singh P, Kasaudhan J, Tripathi M, Gupta MK, Mondal S. Technological approaches for commercial production of functional food through fish farming: Opportunities and challenges. Funct Food Sci. 2025;5(2):46–56. DOI: https://doi.org/10.31989/ffs.v5i2.1551
65. Martirosyan DM, Stratton S. Advancing functional food regulation. Bioact Comp Health Dis. 2023;6(7):166–171. DOI: https://doi.org/10.31989/bchd.v6i7.1178
66. Baghdasaryan A, Martirosyan D. Economic implications of functional foods. Funct Food Sci. 2024;4(6):216–227. DOI: https://doi.org/10.31989/ffs.v4i6.1379
67. Chan W, Xu Y, Qin H, Zhang L, Li J, Zhang Y, et al. Advancements in delivery systems for dietary polyphenols in enhancing radioprotection effects. npj Sci Food. 2025;9:51. DOI: https://doi.org/10.1038/s41538-025-00419-6
68. Zuo WF, Pang Q, Liu KX, Huang XF, Li XQ, Yang SJ, et al. Gut microbiota: a multifunctional target regulated by foods. J Adv Res. 2023. DOI: https://doi.org/10.1016/j.jare.2023.05.011
69. Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. J Nutr Sci. 2016 Dec 29;5:e47. DOI: https://doi.org/10.1017/jns.2016.41
70. Saibabu V, Fatima Z, Khan LA, Hameed S. Therapeutic Potential of Dietary Phenolic Acids. Adv Pharmacol Sci. 2015;2015:1–10. DOI: https://doi.org/10.1155/2015/823539
71. Oluwole O, Fernando WB, Lumanlan J, Ademuyiwa O, Jayasena V. Role of phenolic acid, tannins, stilbenes, lignans and flavonoids in human health – a review. Int J Food Sci Technol. 2022 Oct 18;57(10):6326–35. DOI: https://doi.org/10.1111/ijfs.15936
72. Neveu V, Perez-Jimenez J, Vos F, Crespy V, du Chaffaut L, Mennen L, et al. Phenol-Explorer: an online comprehensive database on polyphenol contents in foods. Database. 2010 Jul 30;2010(0):bap024–bap024. DOI: https://doi.org/10.1093/database/bap024
73. Godos J, Caraci F, Micek A, Castellano S, D'Amico E, Paladino N, et al. Dietary Phenolic Acids and Their Major Food Sources Are Associated with Cognitive Status in Older Italian Adults. Antioxidants. 2021 Apr 29;10(5):700. DOI: https://doi.org/10.3390/antiox10050700
74. Bento-Silva A, Koistinen VM, Mena P, Bronze MR, Hanhineva K, Sahlstrøm S, et al. Factors affecting intake, metabolism and health benefits of phenolic acids: do we understand individual variability? Eur J Nutr. 2020 Jun 21;59(4):1275–93. DOI: https://doi.org/10.1007/s00394-019-01987-6
75. Al-Khayri JM, Mascarenhas R, Harish HM, Gowda Y, Lakshmaiah VV, Nagella P, et al. Stilbenes, a Versatile Class of Natural Metabolites for Inflammation—An Overview. Molecules. 2023 Apr 28;28(9):3786. DOI: https://doi.org/10.3390/molecules28093786
76. Duta-Bratu CG, Nitulescu GM, Mihai DP, Olaru OT. Resveratrol and Other Natural Oligomeric Stilbenoid Compounds and Their Therapeutic Applications. Plants. 2023 Aug 14;12(16):2935. DOI: https://doi.org/10.3390/plants12162935
77. Rodríguez-García C, Sánchez-Quesada C, Toledo E, Delgado-Rodríguez M, Gaforio JJ. Naturally Lignan-Rich Foods: A Dietary Tool for Health Promotion? Molecules. 2019 Mar 6;24(5):917. DOI: https://doi.org/10.3390/molecules24050917
78. Baky MH, Elshahed M, Wessjohann L, Farag MA. Interactions between dietary flavonoids and the gut microbiome: a comprehensive review. British Journal of Nutrition. 2022 Aug 28;128(4):577–91. DOI: https://doi.org/10.1017/S0007114521003627
79. Wu L, Niu Y, Ren B, Wang S, Song Y, Wang X, et al. Naringenin Promotes Gastrointestinal Motility in Mice by Impacting the SCF/c-Kit Pathway and Gut Microbiota. Foods. 2024 Aug 12;13(16):2520. DOI: https://doi.org/10.3390/foods13162520
80. Ashiqueali SA, Chaudhari D, Zhu X, Noureddine S, Siddiqi S, Garcia DN, et al. Fisetin modulates the gut microbiota alongside biomarkers of senescence and inflammation in a DSS-induced murine model of colitis. Geroscience. 2024 Jan 8;46(3):3085–103. DOI: https://doi.org/10.1007/s11357-024-01060-z
81. Chen J, Zhong H, Huang Z, Chen X, You J, Zou T. A Critical Review of Kaempferol in Intestinal Health and Diseases. Antioxidants. 2023 Aug 20;12(8):1642. DOI: https://doi.org/10.3390/antiox12081642
82. Yang S, Duan H, Yan Z, Xue C, Niu T, Cheng W, et al. Luteolin Alleviates Ulcerative Colitis in Mice by Modulating Gut Microbiota and Plasma Metabolism. Nutrients. 2025 Jan 7;17(2):203. DOI: https://doi.org/10.3390/nu17020203
83. Liu Y, Lin Q, Huang X, Jiang G, Li C, Zhang X, et al. Effects of Dietary Ferulic Acid on the Intestinal Microbiota and the Associated Changes on the Growth Performance, Serum Cytokine Profile, and Intestinal Morphology in Ducks. Front Microbiol. 2021 Jul 13;12. DOI: https://doi.org/10.3389/fmicb.2021.698213
84. Wan F, Zhong R, Wang M, Zhou Y, Chen Y, Yi B, et al. Caffeic Acid Supplement Alleviates Colonic Inflammation and

Oxidative Stress Potentially Through Improved Gut Microbiota Community in Mice. Front Microbiol. 2021 Nov 16;12. DOI: https://doi.org/10.3389/fmicb.2021.784211

85. Jang S, Kim S, So BR, Kim Y, Kim CK, Lee JJ, et al. Sinapic acid alleviates inflammatory bowel disease (IBD) through localization of tight junction proteins by direct binding to TAK1 and improves intestinal microbiota. Front Pharmacol. 2023 Aug 15;14. DOI: https://doi.org/10.3389/fphar.2023.1217111
86. Ye X, Liu Y, Hu J, Gao Y, Ma Y, Wen D. Chlorogenic Acid-Induced Gut Microbiota Improves Metabolic Endotoxemia. Front Endocrinol (Lausanne). 2021 Dec 16;12. DOI: https://doi.org/10.3389/fendo.2021.762691
87. Cai TT, Ye XL, Li RR, Chen H, Wang YY, Yong HJ, et al. Resveratrol Modulates the Gut Microbiota and Inflammation to Protect Against Diabetic Nephropathy in Mice. Front Pharmacol. 2020 Aug 19;11. DOI: https://doi.org/10.3389/fphar.2020.01249
88. Etxeberria U, Hijona E, Aguirre L, Milagro FI, Bujanda L, Rimando AM, et al. Pterostilbene-induced changes in gut microbiota composition in relation to obesity. Mol Nutr Food Res. 2017 Jan 3;61(1). DOI: https://doi.org/10.1002/mnfr.201500906
89. Zhang L, Lan Y, Wang Y, Yang Y, Han W, Li J, et al. Secoisolariciresinol diglucoside ameliorates high fat diet-induced colon inflammation and regulates gut microbiota in mice. Food Funct. 2022;13(5):3009–22. DOI: https://doi.org/10.1039/D1FO04037E
90. Li N, Pei H, Luo M, Deng L, Zhang X, Ma C, et al. Pinoresinol diglucoside alleviates ovariectomy-induced osteoporosis by modulating the “Microbiota–gut–bone” axis. Biochem Biophys Res Commun. 2025 Nov;790:152867. DOI: https://doi.org/10.1016/j.bbrc.2025.152867