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SHORT REVIEW

The Nexus between Polyphenols and Gut Microbiota and Their Interplay in Human Health: A Brief Review

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Abstract

Polyphenols are a broad class of naturally occurring substances in plants and have drawn extensive attention as they may possess promising health-promoting benefits. Recently, gut microbiota and polyphenol interactions have been directly linked to the well-being of humans. The classification, sources, and interactions of polyphenols with the gut microbiota are presented in this review, highlighting their key health benefits in humans. Polyphenols undergo complex transformations within the gastrointestinal tract and interact with the gut microbiota, a varied collection of bacteria living in the digestive system. The interactions substantially influence the composition, functioning, metabolic activity, and gut microbiota diversity. Research indicates that polyphenols may possess prebiotic-like properties, favouring *Lactobacilli* and *Bifidobacteria* growth, among other beneficial bacteria. The fermentation of polyphenols is aided by these bacteria, which produce bioactive metabolites that may improve human health and well-being in various ways. Moreover, the alteration of gut microbiology caused by polyphenols has been linked to improvements in several health outcomes, including enhanced metabolic health, fortified immunological function, and a decreased susceptibility to chronic conditions like heart disease and certain forms of cancer. In summary, the intriguing relationship between polyphenols and gut microbiota has significant health implications for humans. Understanding these relationships can open the door to tailored dietary treatments and the development of functional foods to support a balanced gut microbiota and general well-being.

Keywords: Dietary Intake, Functional Food, Gut Microbes, Human Health, Polyphenols, Phytochemicals

1. Introduction

Polyphenols are naturally occurring organic compounds that consist of several units of phenols. Plant-derived secondary metabolites are crucial in several applications, including therapeutic and industrial fields[1-3]. Polyphenols, predominantly derived from plants, represent one of the most extensively researched phytochemical classes. Several of these naturally occurring phytochemicals throughout the entire kingdom of plants make their way into the human diet through various fruits, vegetables, legumes, dry fruits, cereals, herbs and spices, beverages, and other food items[4-6]. Whole plant foods contain over 8000 polyphenolic compounds, encompassing phenolic acids, flavonoids, lignans and stilbenes[4].

Polyphenols are structurally complex, and the fundamental monomer is the phenolic ring. These compounds are categorized into phenolic alcohols and phenolic acids[7]. Plant tissues contain a variety of polyphenols, which exist in different structural forms. These polyphenols are often present as glycosides or complex polymerized molecules with high molecular weights. These may include tannins or combined with various organic acids[7]. Polyphenols, characterized by their large molecular weight of nearly 800 Daltons,

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can transversely cell membranes, allowing them to reach intracellular spaces where they function as phytochemicals or pigments[8].

The healthcare sector is becoming increasingly interested in polyphenols. Numerous research has showcased the health-promoting properties of polyphenols, highlighting their pivotal function in regulating metabolism, addressing chronic disorders, managing weight, and controlling cell proliferation. As many polyphenolic compounds are identified, their comprehensive understanding of long-term and short-term health effects is still incomplete. Evidence from epidemiological tests, human trials, and animal studies suggests that several polyphenols have anti-inflammatory and antioxidant properties. These qualities might have preventive and/or therapeutic implications in various non-communicable disorders, like obesity, cardiovascular diseases, neurodegenerative and cancer[9-14].

2. Polyphenols Classification

Polyphenols are categorized into various groups, encompassing phenolic acids (such as hydroxycinnamic and hydroxybenzoic acids), flavonoids (including flavonols, flavones, isoflavones, anthocyanins, and flavanones), stilbenes (like piceatannol and resveratrol), lignans (such as pinoresinol, sesamol, enterodiol, and sinol), and others including tannins (non-hydrolyzable, and condensed tannins), xanthones, lignins, anthraquinones and chromones[1,8,15]. Figure 1 represents the classification of polyphenols.

2.1 Phenolic Acids

Nearly one-third of the total known polyphenols are represented by phenolic acids. The classification of phenolic acids is represented in Figure 2. The two subcategories of phenolic acids are hydroxycinnamic acids and hydroxybenzoic acid (Figure 3). In nature, phenolic acids are usually found in glycosylated or ester derivative forms rather than in their free form[16]. Hydroxybenzoic acids are benzoic acid ($C_7H_6O_2$) derivatives. The subcategory of hydroxybenzoic acids includes notable examples such as ellagic acid, benzoic acid, gallic acid, protocatechuic acid, salicylic acid and vanillic acid[1,17].

The hydroxybenzoic acids found in olive products have various advantages: anti-inflammatory, cardioprotective actions, and antioxidant[1,8,18,19]. Derived from cinnamic acid, hydroxycinnamic acid is a member of the aromatic acid class (C6–C3)[20]. Common hydroxycinnamic acid examples include caffeic acid, cinnamic acid, coumaric acid, sinapinic acid, and ferulic acid[8]. Cinnamic acid serves as a fundamental structural and biological component constituting cell organelles.

2.2 Stilbenes

Stilbenes are chemical compounds with a condensed structure consisting of a core ethylene component and a single phenyl group (Figure 4). The phenyl group is one of the terminal groups of carbon double bonds[21].

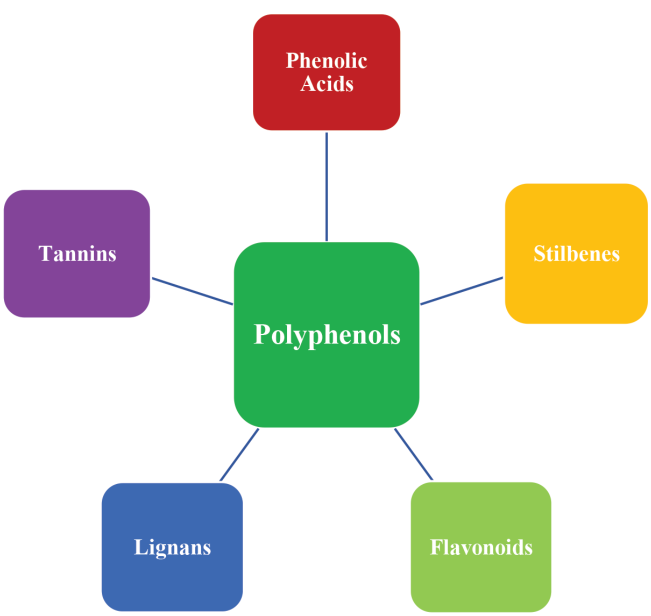


Figure 1. Classification of polyphenols.

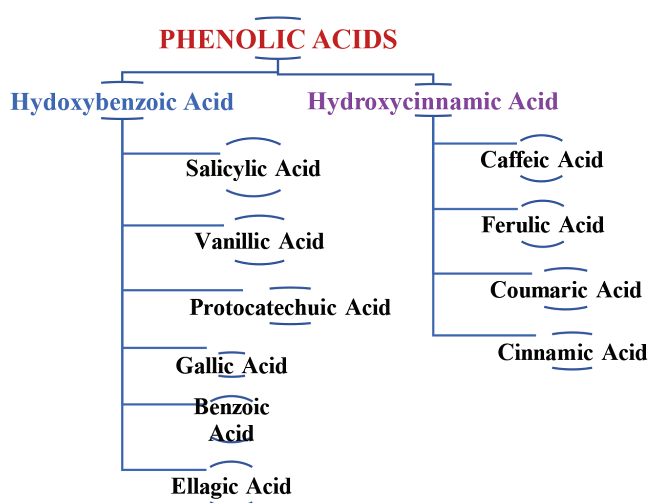


Figure 2. Classification of phenolic acids.

Stilbenes, which are phenolics of low molecular weight, are induced (phytoalexins) in response to both abiotic and biotic stressors[22]. Common sources of stilbenes include peanut (Fabaceae), sorghum (Poaceae), pine (Pinaceae) and grape (Vitaceae)[23]. Resveratrol, one of the extensively studied and renowned stilbenes, is linked to a broad spectrum of pharmacological attributes and is recognized for its numerous health-promoting effects[24-26].

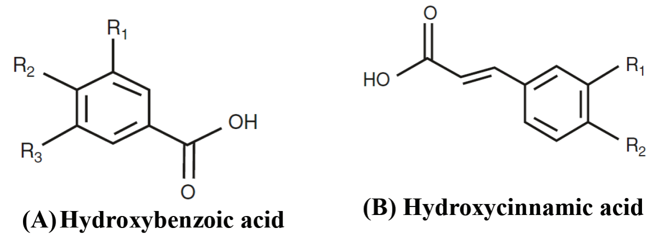


Figure 3. Subclasses of phenolic acids.

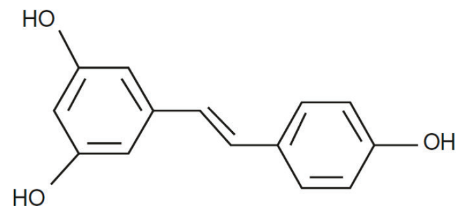


Figure 4. Stilbene.

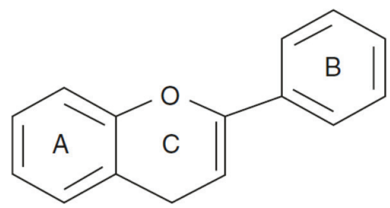


Figure 5. Flavan nucleus.

2.3 Flavanoids

Plants synthesize flavonoids, which have a benzo-γ-pyrone structure, from phenylalanine, tyrosine, and malonate via the phenylpropanoid route[27,28]. The basic building block of flavonoids is the flavan nucleus, which consists of 15 carbon atoms organized into three rings known as A, B, and C. Variations in oxidation and substitution levels of these rings (A, B, C) give rise to different subclasses of flavonoid (Figure 5). Flavonoids are present in nature as glycosides, aglycones, and methylated derivatives[28]. Flavonoids are divided into six subclasses: anthocyanidins, flavones, flavonols, flavan-3-ols, isoflavones, and flavanones[8,15] as presented in Table 1. The examples of the different subclasses of flavonoids are given in Table 1. Flavonoids are predominantly found in foods such as onions, berries, grapes, apples, tea and cocoa, showcasing numerous health benefits.

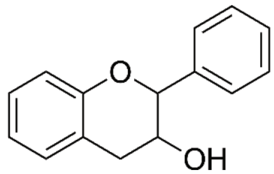
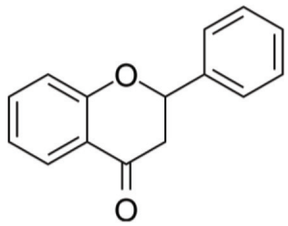
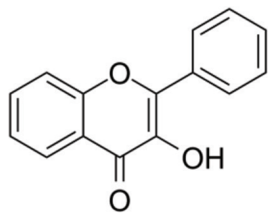
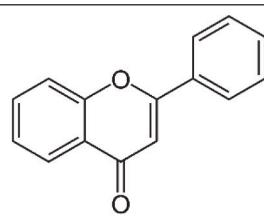
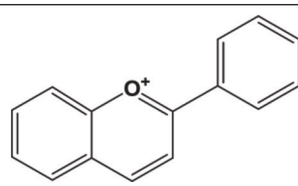
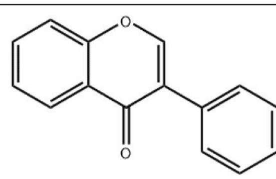
2.4 Lignans

Lignans are dimeric compounds formed by the condensation of two phenylpropanoid C6-C3 units at the β and β' carbon atoms, and they possess the ability to form additional linkages through lactone, ether, or carbon bonds. Their chemical composition resembles that of 1,4-diarylbutan[30], and these compounds are synthesized through the shikimic acid biosynthesis pathway[31]. Lignans can be classified into two chief subclasses: neolignans and classical lignans. Phenylpropane dimers with a β-β' bond are known as classical lignans, and there are six primary subtypes of classical lignans, namely—dibenzylbutyrolactones, aryl tetralin/aryl naphthalenes, dibenzocyclooctadienes, dibenzyl butanes, 2,6-diarylfurofurans and substituted tetrahydrofurans[32-34]. Neolignans exhibit a more diverse range of structures compared to classical lignans. There are fifteen subtypes of neolignans, each selected by nature as well as the linkage position between the phenylpropane units[31,32,35]. The commonest subtypes of neolignans include alkyl aryl ethers, 8-10-bicyclo[3.2.1]octanes, 8-30-bicyclo[3.2.1] octanes, 1,4-benzodioxanes, benzofurans, biphenyls, biphenyl ethers and cyclobutanes. Lignans are secondary metabolites found in vascular plants, exhibiting extensive occurrence throughout the flora. These chemicals possess a diverse range of physiological properties that improve human health[36].

2.5 Tannins

Tannins are widespread natural phenolic compounds abundantly present in the plant kingdom. They are categorized primarily into condensed and hydrolysable types. Polyflavonoid tannins belong to the condensed class, these being less commonly hydrolysable. While ellagitannins and gallotannins fall into the hydrolysable category[37]. Condensed tannins contain flavonoids (flavan 3-ol or flavan 3, 4-diol) with no sugar core. In contrast, hydrolysable tannins compose gallic and ellagic acids with a sugar core, primarily glucose[38,39].

Table 1. The subclasses of flavonoids, structure and examples

Flavonoid Subclass	Structure	Examples	References
Flavanol		Gallocatechin Catechin Epicatechin	4,8,15,29
Flavanone		Hesperetin Naringenin	
Flavonol		Quercetin Kaempferol	
Flavone		Chrysin Apigenin Baicalein	
Anthocyanidin		Delphinidin Peonidin Cyanidin Pelargonidin	
Isoflavone		Daidzein Glycitein	

Hydrolyzable tannins are less frequently found in nature than condensed tannins among the many forms of tannins[40,41]. As a result, condensed tannins account for more than 90% of all commercial tannins and command a dominant market share worldwide[42,43].

3. Major Dietary Sources of Polyphenols

Polyphenols are bioactive compounds majorly found in various fruits, vegetables, herbs, seeds, and beverages namely wine, beer, tea, coffee, chocolate and fruit juice. Dry legumes and grains possess minor amounts of polyphenols[44]. Generally, these chemicals safeguard against plant pathogens and environmental factors. These compounds contribute to the sensory attributes of foods by providing flavours, colours, and astringency. The major dietary sources of polyphenols are represented in Table 2. Currently, polyphenols are receiving immense scientific attention as they possess a wide range of health benefits for humans.

Table 2. Major dietary sources of polyphenols

Class	Sub-class	Dietary Sources	References
Phenolic Acid	Hydroxybenzoic acid	Salicylic acid: Orange, boysenberry, blueberry, raisins, apricot, dates, tomato, cucumber, black tea, and cinnamon bark.	45
		Vanillic acid: Whole grains, beers, wines, green tea, berries, citrus – grape juice, herbs – rosemary, oregano, common thyme, common sage, almonds, and olive – black and green.	46,47
		Protocatechuic acid: Cinnamon bark, bitter melon, buckwheat, whole grain, chicory, gooseberry, raspberry, sorghum, and star anise	45,48,49
		Gallic acid: Blueberries, strawberries, blackberries, tea, grapes, walnuts, mangoes, cashew nuts, plums, wine, and hazelnuts	50,51
		Benzoic acid: Strawberries, salvia, mustard seeds, thyme, cinnamon, cloves, cayenne pepper, and nutmeg	52,53
		Ellagic acid: Raspberries, strawberries, blackberries, and walnuts	45
	Hydroxycinnamic acid	Caffeic acid: Artichokes, apples, coffee, basil, cauliflowers, cabbage, kale, pears, oregano, radishes, turnips, and thyme	54
		Ferulic acid: Whole grains, carrots, oranges, apples, coffee, asparagus, pineapples, and peas	
		Coumaric acid: Cherries, apricots, tonka beans, cinnamon, and strawberries	
		Cinnamic acid: Citrus fruits, cinnamon, tea, grape, spinach, cocoa, and brassicas vegetables and celery	55,56
Flavonoids	Flavanol	Apple, peaches, plum, cherry, apricot, cocoa, pecan nuts, tea, red wine	57,58
	Anthocyanidin	Blueberries, elderberry, grapes, eggplant, tomato, purple cabbage, red wine	
	Flavanone	Lemon, orange, grapefruit, limes, citrus, orange juice, grapefruit juice	
	Flavonol	Asparagus, broccoli, kale, onion, leeks, berries, olive oil, green tea	
	Isoflavone	Tofu, pueraria, legumes, chickpea, soy	
	Flavone	Celery, parsley, wheat sprout, chamomile, pimiento, carrot, sweet pepper, grain mixtures, vegetable oil	
	Chalcone	Mulberry, apple, citrus, soybean, ginger	
Stilbenes	Resveratrol	Red wine, grapes, white wine, blueberries, peanuts, bilberries	59
Lignans	Classical Lignans	Flaxseed, sesame, wheat bran, ground barley	60
	Neolignans	Seeds (flaxseeds), whole grains	61
Tannins	Condensed	Green and red grapes (and their wine as well as juice), apples, pears, cranberries, lentils, red kidney beans, chickpeas, black-eyed peas, cocoa, nuts, chocolate, coffee, and tea.	62
	Hydrolysable	Guavas, grapes, muscadine grapes, mangoes, pomegranates, peaches, strawberries, gooseberries, blackcurrants, bird cherries, blackberries, raspberries, plums, pistachios, chestnuts, apricots, walnuts, hazelnuts, cashew nuts, pimento, persimmons, cloves, and tea.	63

4. Polyphenols' Impact on Gut Microbiota

The human gastrointestinal system contains a vast and varied population of many bacteria, comprising billions of cells[64]. This gut microbiota functions like an organ, actively contributing to the breakdown and utilization of dietary constituents. It significantly impacts human well-being by generating both advantageous and detrimental metabolites, safeguarding against pathogens, regulating the immune system, and providing defence against various illnesses[65,66]. The relevance of gut microbiota in maintaining the host health's physiological balance and affecting the onset of various ailments is well understood. These include neurological diseases, obesity, diabetes, and inflammatory bowel disorder[67].

Multiple factors influence the human gut microbiota: genetics, age, stress, medications, and diet, particularly reflecting long-term dietary habits[68]. Polyphenols, crucial in host health, interact with host physiology and metabolism, playing roles in immune stimulation, oxidative stress regulation, and protection against pathogenic infections[69]. Ample evidence suggests that dietary polyphenols directly influence the gut microbiome, fostering the growth of beneficial microbial species while suppressing harmful ones[67]. Dietary polyphenols have been observed to engage with human and animal gut microbiota, specifically interacting with *Bifidobacteria* and *Lactobacilli*. This interaction has shown a notable increase in butyrate production, contributing to the reduction of colitis and serving as a preventive measure against colitis-associated colorectal cancer. Simultaneously, it leads to a decrease in the presence of harmful microbial species[70]. Polyphenols exhibit a dual effect in the gut by selectively impeding the development of harmful microbes. For instance, flavonoids found in red wine demonstrated a mild inhibitory effect on *Clostridium*, while anthocyanins, ellagic acid in raspberry juice, and grape polyphenols displayed inhibitory actions against *Ruminococcus* and *Clostridium histolyticum*, respectively[71-73]. Conversely, polyphenols promote the proliferation of beneficial gut bacteria. Grape polyphenols, gingerol in ginger, sorghum polyphenols, and tannin in pomegranate were observed to stimulate the growth of *Bifidobacterium*[74-76]. Tannin also contributes to the development of *Lactobacillus*, while grape polyphenols and gingerol support the proliferation of *Enterococci*. *Roseburia*, *Prevotella*, and Lactic acid bacteria are abundant when fructooligosaccharides and sorghum polyphenols are present[73,75,76].

Studies conducted in living organisms have highlighted the effectiveness of polyphenol supplementation in modifying the gut microbiota of animal models. These interventions have demonstrated an augmentation in beneficial microbial populations and a concurrent reduction in harmful microbes. For instance, Orso's research involved administering a diet rich in tannin extracted from chestnut shells to a zebrafish model of intestinal inflammation. This diet notably facilitated the growth of advantageous bacteria, specifically Enterobacteriaceae and *Pseudomonas*[77]. Moreover, specific polyphenols exhibit selective inhibition against pathogenic bacteria. Research on polyphenols derived from *Smilax china* L. rhizome showcased a decreased relative abundance of *Desulfovibrionaceae*, *Lachnospiraceae*, and *Streptococcaceae*[78]. Additionally, grape pomace polyphenols were observed to reduce potentially harmful bacteria in humans, including *Escherichia coli, Proteus, Salmonella*, *Shigella*, and *Yersinia*[79]. The combined administration of quercetin and resveratrol has demonstrated significant inhibition of specific microbial groups—*Desulfovibrionaceae*, *Acidaminococcaceae*, *Coriobacteriaceae*, *Bilophila*, and *Lachnospiraceae*—potentially linked to diet-induced obesity[80]. In another study, blueberry polyphenols administered to ovariectomized rats led to an increase in *Bacteroides dorei* and *Lachnoclostridium* and a decrease in Rikenellaceae and *Eubacterium*[81]. Additionally, the importance of polyphenol supplementation is highlighted by consistent results from animal experiments conducted both in vivo and in vitro, particularly flavonoids and anthocyanins, in increasing the quantity of gut-protective microorganisms in humans, such as *Lactobacillus* and *Bifidobacterium*[82,83].

The prebiotic properties of polyphenols promote the growth of good bacteria, which restricts the availability of nutrients for pathogenic bacteria and functions as a powerful antibacterial agent against them[84]. Research focusing on the benefits of flavonoids from *Theobroma cacao*, present in cocoa-based foods and drinks, shows that these flavonoids ameliorate insulin resistance, change how glucose is metabolized, enhance endothelial tissue function, and lower oxidative stress[85]. Certain substances found in dark chocolate, such as epicatechin and catechin, have been shown to decrease the activity of α-glucosidase, which hinders the intestinal absorption of glucose[85,86].

In a recent investigation utilizing a mouse model of ulcerative colitis to explore the impact of gallic acid, it was observed that it positively mitigated dysbiosis within the gut microbiota. The intake of gallic acid reduced certain detrimental bacteria, such as *Firmicutes* and *Proteobacteria*, while enhancing the presence of the Lactobacillaceae and Prevotellaceae families[87-89]. Gallic acid can reduce environmental stress in beagle puppies, which are thought to be a great model for researching the human microbiota because of their similarity to humans. This reduction in stress levels aids in the restoration of intestinal health by increasing *Lactiplantibacillus* and *Faecalibaculum* and decreasing *Shigella*, *Clostridium*, and *Escherichia*. It is crucial to emphasize that environmental stress is responsible for the imbalance of gut microbiota, increased inflammatory reactions, and disruptions in the integrity of the intestinal barrier[90,91]. Furthermore, women in good health, the gut flora was positively affected by certain polyphenols in orange juice, particularly hesperidin and naringin. These polyphenols had a beneficial effect on the microbiota's composition and metabolic activity in addition to raising important blood biochemical markers like insulin sensitivity, low-density lipoprotein cholesterol, and glucose levels. This was demonstrated by higher production of Short-Chain Fatty Acids (SCFA) and increased *Lactiplantibacillus* and *Bifidobacterium* spp. populations. These results imply that eating oranges helps improve the gut microbiota and the related metabolites it[92].

Polyphenols possess strong antibacterial effects that hinder the proliferation of harmful bacterial species, preventing gut biofilms. Several polyphenols possess antibacterial properties that target harmful bacteria, such as *Salmonella* and *Helicobacter pylori*. These include quercetin, hydroxytyrosol, resveratrol, and phenolic acids. For example, resveratrol can reduce the *E. coli* population and lessen the effects of heat stress in broilers[93]. Quercetin has demonstrated effectiveness against *Salmonella enteritidis* and can impact the expression of genes linked to inflammation[94]. Their antimicrobial activity is mediated by direct suppression of bacterial species, reduction of pathogenic bacteria's ability to adhere, or interruption of ionic fluxes at the cell membrane[95].

Furthermore, polyphenols function as a source of nutrients that promote the growth of populations of specific bacteria, including *Lactobacilli* and *Bifidobacteria*, by acting as prebiotic-like agents[96,97]. Consuming different polyphenols is associated with changes in the composition of gut bacteria, namely boosting the growth of *Bacteroides*, which have more enzymes for breaking down glycans. Supplementing broiler diets with ellagic acid during heat stress has demonstrated noteworthy impacts on the gut microbiota, intestinal barrier function, and antioxidant system. Including ellagic acid in the diet increased Nrf2/HO-1 mRNA levels in the ileum. In addition, it decreased the quantities of specific bacterial species (e.g. *Actinomyces*, *Ruminococcus torques*, *Rothia*, *Neisseria*, and *Lautropia*) in the cecum in a manner that depended on the dosage. Dietary ellagic acid supplementation seemed to improve the body's ability to produce antioxidants, strengthen the intestinal barrier, and reduce heat-related injuries—possibly by controlling the gut microbiota[91]. Additional research is necessary to examine ellagic acid's impact on chickens' gut microbiome under heat-stress conditions.

The role of gut bacteria in atherosclerosis is increasingly attracting attention. The gut microbiota and faecal metabolites are significantly impacted by ferulic acid. Notably, there has been a significant drop in the occurrence of *Firmicutes*, Erysipelotrichaceae, and *Ileibacterium*. These bacteria have been shown to have a favourable relationship with blood lipid levels in animals with atherosclerosis. Ferulic acid has been shown to reduce atherosclerotic damage, which may be partially explained by its influence on gut microbiota and lipid metabolism via the AMPKα/SREBP1/ACC1 pathway[98]. Vanillin has also demonstrated a strong ability to alleviate abnormalities of the gut microbiota linked to obesity, which show up as a reduction in alpha- and beta-diversity. Vanillin increased the variety of *Verrucomicrobiota* and *Bacteroidetes* phyla while decreasing the prevalence of the *Firmicutes* phylum. Notably, vanillin inhibited the growth of bacteria that produce lipopolysaccharide (LPS) from the genus *Bilophila* and H_2S-producing bacteria from the genus *Desulfovibrio*. However, it is unclear exactly how vanillin is related to enhanced gut microbiota in the fight against obesity[99].

Berries have gained more attention recently because they contain phytochemicals that may benefit human health. Berries are abundant in polyphenols, including anthocyanins, flavonols, and flavonols, hydrolyzable and condensed tannins, phenolic acids, stilbenes, and lignans. Berries contain polyphenols that hold promise as bioactive compounds for addressing cancer and associated metabolic disorders by influencing the composition of the gut microbiota[100-102].

Recent studies have explored the potential of tea polyphenols in regulating circadian rhythms and improving sleep, mood and immunity through interactions with gut microbiota. Tea polyphenols can modulate the composition and function of intestinal microbiota, which in turn influences host circadian rhythms and metabolic processes[103-105].

Apple polyphenol extract intervention improved depression-like behaviours in mice fed a high-sucrose diet by reducing stress hormones, increasing an anti-inflammatory cytokine, inhibiting inflammatory pathways, improving gut barrier function, and modulating the gut microbiome. Apple polyphenol extract has potential as a dietary intervention for ameliorating depression-like disorders induced by a sugary diet[106].

Gut microbiota dysbiosis is involved in developing and progressing polycystic ovary syndrome, leading to increased inflammation and metabolic dysfunction. Polyphenols, including anthocyanin, catechins, and resveratrol, can regulate gut microbes and alleviate chronic inflammation in women with polycystic ovary syndrome, providing a potential novel therapeutic strategy. Targeting gut microbiota dysbiosis and reducing chronic inflammation using polyphenols may assist in the development of new treatments for polycystic ovary syndrome[107].

Oat phenolic compounds can alleviate a range of metabolic syndromes in mice fed a high-fat diet, including weight gain, glucose intolerance, elevated lipid levels, oxidative stress, and adipocyte hypertrophy. Oat phenolic compounds can improve the imbalance in gut microbiota caused by a high-fat diet, increasing the abundance of *Bacteroidetes*, reducing the diversity of *Firmicutes*, and modulating the levels of specific gut bacteria[108].

5. Unveiling the Complexity: Polyphenols, Gut Microbiota, and Personalized Health

Among the nearly eight thousand different polyphenols that have been identified, every polyphenol possesses a structure and features that are unique to itself. Studying the specific influence of these diverse compounds on the gut microbiota is challenging. It is possible that a sizeable amount of the polyphenols that are consumed will not be absorbed in the small intestine, and as a result, they will arrive in the colon without being digested. This factor contributes to the complexity of the situation. The potential health benefits they could provide could be jeopardized by this circumstance. The way in which the polyphenols are processed by the bacteria in the gut varies from person to person, and the composition of an individual's gut microbiota determines the metabolic products that are produced.

Polyphenols can affect the variety and composition of the microbiota in the gut. They can either stimulate the growth of those bacteria that are good to the gut, or they can exhibit antibacterial qualities that lower the overall diversity and stability of the microbiota. Due to the distinct microflora in their intestinal tracts, polyphenol consumption can elicit a wide range of responses from individuals. As gut microbiota may be diverse in each individual, personalised strategies may be necessary to maximize the health advantages of polyphenols. Low dosages of polyphenols may have the ability to induce prebiotic effects, but high amounts may have antimicrobial effects that disrupt the equilibrium of the gut microbiota. The influence of polyphenols on intestinal microflora appears to be dose-dependent.

Studies conducted over a short period might not fully capture the comprehensive composition and functionality of the intestinal microbiota, it is of the utmost importance to investigate the temporal effects of polyphenols on the gut microflora. To acquire a thorough understanding of the impacts of polyphenol consumption over the long term, it is necessary to do additional research into the potential temporal dynamics. An investigation into the concept of personalized nutrition based on an individual's gut microbial profile is essential. In this context, identifying the most beneficial polyphenols for individuals with specific gut microbiota compositions is appropriate.

Gut microbiota has emerged as a major component of personalized medicine, and numerous approaches have been developed to modify the gut microbiota composition for therapeutic purposes. These approaches include pre- and probiotic interventions, microbiota transplantation or the inoculation with synthetic gut microbiota[109]. The host's gut microbiota can improve drug efficacy, and inappropriate or unwanted gut bacteria can inactivate a drug. Gut microbiota can impact the safety and efficacy of drugs by enzymatic modification of drug structure, alteration of drug availability, and changes in bioactivity or toxicity[109]. While our understanding of the gut microbiota's effect on drug efficacy is still early, recent studies have underscored its pivotal role. The gut microbiota significantly influences the transformation of pharmaceuticals, affecting their bioactivity, toxicity, and its lifetime within the body. Elucidating the connection of gut microbiota diversity and complexity to drug efficacy can pave the way for precision medicine, aid in toxicology risk assessments, and enhance drug research and development in both pre-clinical and clinical studies[110].

It is important to gain mechanistic insight into how gut microbiota influences diseases and individual responses towards dietary or pharmaceutical management. Modifying these microbial landscapes and their functions can contribute to the development and progression of a wide range of human diseases, such as metabolic disorders, neurological conditions, and cancer. Furthermore, these modifications can influence the effectiveness of various interventions in treating these diseases, including diets, exercise, and medications. Exploring the role of gut microbiota in diseases and drug responses is a pathway towards advancing precision and personalized medicine[111].

To gain a deeper understanding of the intricate interactions between polyphenols and the gut microbiota on a molecular level, it is necessary to use technological advances such as high-throughput sequencing and metabolomics. The complex relationship that exists between polyphenols, gut microbiota, and the health of humans is something that should be investigated further by scientists and medical practitioners. This may pave the way for future developments in tailored nutrition and preventative healthcare treatment methods.

6. Conclusion

Polyphenols and gut microbiota have a dynamic mutual influence, which greatly affects the health benefits of polyphenols in human beings. A better understanding of the dynamic interactions between the polyphenols and the gut microbiota will open new possibilities for preventing illness, enhancing health, and customizing interventions. Finally, to conclude, finding out more about these links could offer the possibility of personalized dietary therapies, as well as functional foods that help to maintain a healthy gut microbiome and, therefore, health.

7. References

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